2\textsuperscript{nd} International Nastaran Cancer Symposium 2016

28-29 September 2016
Mashhad, Iran

President of the Congress:
Mostafa Mehrabi Bahar

Co-President of the Congress:
Maryam M. Matin
Heads of Scientific Committee:
Mohammad Reza Abbaszadegan  Abolghasem Allahyari

Heads of Organizing Committee:
Hamid Reza Bidkori  Hojjat Naderi-Meshkin
Members of Scientific Committee:

International Members of Scientific Committee

<table>
<thead>
<tr>
<th>Sr No.</th>
<th>Name</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Dr. Majid Ebrahim-Warkiani</td>
<td>University of New South Wales, Sydney, Australia</td>
</tr>
<tr>
<td>2</td>
<td>Dr. Fujii Yoshiharu</td>
<td>Tokyo University of Agriculture and Technology, Tokyo, Japan</td>
</tr>
<tr>
<td>3</td>
<td>Dr. Hamidreza Sharifi</td>
<td>Karolinska Institute, Stockholm, Sweden</td>
</tr>
<tr>
<td>4</td>
<td>Dr. Ulf Schmitz</td>
<td>University of Sydney, Sydney, Australia</td>
</tr>
<tr>
<td>5</td>
<td>Dr. Shailendra Gupta</td>
<td>University of Rostock, Rostock, Germany</td>
</tr>
<tr>
<td>6</td>
<td>Dr. Saeideh Nakhaei-Rad</td>
<td>University of Dosseldorf, Dosseldorf, Germany</td>
</tr>
<tr>
<td>7</td>
<td>Dr. Lida Radfar</td>
<td>University of Oklahoma, USA</td>
</tr>
<tr>
<td>8</td>
<td>Dr. Ehsan Sarafraz-Yazdi</td>
<td>Downstate Medical Center, State University of New York, United States</td>
</tr>
<tr>
<td>9</td>
<td>Dr. Muhammad Usman Rashid</td>
<td>SKCH &amp; RC, Lahore, Pakistan</td>
</tr>
</tbody>
</table>

National Members of Scientific Committee

<table>
<thead>
<tr>
<th>Sr No.</th>
<th>Name</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Dr. Mohammad Reza Abbazadegan</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>2</td>
<td>Dr. Abbas Abdollahi</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>3</td>
<td>Dr. Hamid Abdollahi</td>
<td>Iran University of Medical Sciences, Tehran, Iran</td>
</tr>
<tr>
<td>4</td>
<td>Dr. Khalil Abnous</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>5</td>
<td>Dr. Amir Afkhami Goli</td>
<td>Ferdowsi University of Mashhad, Mashhad, Iran</td>
</tr>
<tr>
<td>6</td>
<td>Dr. Parvaneh Afsharian</td>
<td>Royan Institute, Tehran, Iran</td>
</tr>
<tr>
<td>7</td>
<td>Dr. Sima Afsharnezhad</td>
<td>Islamic Azad University, Mashhad Branch, Mashhad, Iran</td>
</tr>
<tr>
<td></td>
<td>Name</td>
<td>Institution</td>
</tr>
<tr>
<td>---</td>
<td>-------------------------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>8</td>
<td>Dr. Naghmeh Ahmadian kia</td>
<td>Shahroud University of Medical Sciences, shahrood, Iran</td>
</tr>
<tr>
<td>9</td>
<td>Dr. Mohammad Esmaeil Akbari</td>
<td>Shahid Beheshti University of Medical Sciences (SBUMS), Tehran, Iran</td>
</tr>
<tr>
<td>10</td>
<td>Dr. Seyed Amir Aledavood</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>11</td>
<td>Dr. Mohsen Aliakbarian</td>
<td>Mashhad University of medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>12</td>
<td>Dr. Abolghasem Allahyari</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>13</td>
<td>Dr. Majid Anushiravani</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>14</td>
<td>Dr. Mahmoud Arab Najafi</td>
<td>College of science University of Tehran, Tehran, Iran</td>
</tr>
<tr>
<td>15</td>
<td>Dr. Mehdi Asadi</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>16</td>
<td>Dr. Armin Attaranzade</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>17</td>
<td>Dr. Mohsen Azimi Nejad</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>18</td>
<td>Dr. Hoda Azizi</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>19</td>
<td>Dr. Abdullah Bahrami</td>
<td>Mashhad University of Medical Sciences, Iran</td>
</tr>
<tr>
<td>20</td>
<td>Dr. Ahmad Reza Bahrami</td>
<td>Ferdowsi University of Mashhad, Mashhad, Iran</td>
</tr>
<tr>
<td>21</td>
<td>Dr. Hamid Reza Bahrami</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>22</td>
<td>Dr. Abdullah Banihashem</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>23</td>
<td>Dr. Fatemeh Behnam-Rassouli</td>
<td>Ferdowsi University of Mashhad, Mashhad, Iran</td>
</tr>
<tr>
<td>24</td>
<td>Dr. Javad Behravan</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>25</td>
<td>Dr. Hamid Reza Bidkhori</td>
<td>Academic Center for Education, Culture and Research - Mashhad Branch, Mashhad, Iran</td>
</tr>
<tr>
<td>26</td>
<td>Dr. Sohrab Boozarpour</td>
<td>Gonbad e Kavous University, Gonbad Kavous, Iran</td>
</tr>
<tr>
<td>27</td>
<td>Dr. Mahtab Dastpak</td>
<td>University of Bojnourd, Bojnourd, Iran</td>
</tr>
<tr>
<td>28</td>
<td>Dr. Hesam Dehghani</td>
<td>Ferdowsi University of Mashhad, Mashhad, Iran</td>
</tr>
<tr>
<td>No.</td>
<td>Name</td>
<td>Institution</td>
</tr>
<tr>
<td>-----</td>
<td>-----------------------</td>
<td>-------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>29</td>
<td>Dr. Mahdieh Dayani</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>30</td>
<td>Dr. Marzieh Ebrahimi</td>
<td>Royan Institute, Tehran, Iran</td>
</tr>
<tr>
<td>31</td>
<td>Dr. Leila Etemad</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>32</td>
<td>Dr. Ali Farazmand</td>
<td>University of Tehran, Tehran, Iran</td>
</tr>
<tr>
<td>33</td>
<td>Dr. Farhad Faridhosseini</td>
<td>Shahid Beheshty University of Medical Sciences, Tehran, Iran</td>
</tr>
<tr>
<td>34</td>
<td>Dr. Reza Farid Hosseini</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>35</td>
<td>Dr. Shirin Farivar</td>
<td>Shahid Beheshty University, Tehran, Iran</td>
</tr>
<tr>
<td>36</td>
<td>Dr. Moein Farshchian</td>
<td>Ferdowsi University of Mashhad, Mashhad, Iran</td>
</tr>
<tr>
<td>37</td>
<td>Dr. Asieh Sadat Fattahi Masoom</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>38</td>
<td>Dr. Bibi Sedigheh Fazly Bazzaz</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>39</td>
<td>Dr. Mohammad Naser Forghani</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>40</td>
<td>Dr. Mohammad Mahdi Forghanifard</td>
<td>Islamic Azad University, Damghan Branch, Damghan, Iran</td>
</tr>
<tr>
<td>41</td>
<td>Dr. Kamran Ghaedi</td>
<td>University of Isfahan, Isfahan, Iran</td>
</tr>
<tr>
<td>42</td>
<td>Dr. Seyed Hamidollah Ghaffari</td>
<td>Tehran University of Medical Sciences, Tehran, Iran</td>
</tr>
<tr>
<td>43</td>
<td>Dr. Kamran Ghaffarzadehgan</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>44</td>
<td>Dr. Ali Ghasemi</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>45</td>
<td>Dr. Mohammad Reza Ghavamnasiri</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>46</td>
<td>Dr. Majid Ghayour-Mobarhan</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>47</td>
<td>Dr. Mehran Gholamin</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>48</td>
<td>Dr. Farzad Goli</td>
<td>Danesh-e Tandorosti Institute, Isfahan, Iran AND Energy Medicine University, California, USA</td>
</tr>
<tr>
<td>49</td>
<td>Dr. Farhang Haddad</td>
<td>Ferdowsi University of Mashhad, Mashhad, Iran</td>
</tr>
<tr>
<td>50</td>
<td>Dr. Aliakbar Haddad-Mashadrizeh</td>
<td>Ferdowsi University of Mashhad, Mashhad, Iran</td>
</tr>
<tr>
<td>51</td>
<td>Dr. Farzin Hadizadeh</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>52</td>
<td>Dr. Shahpar Haghigfat</td>
<td>Breast Cancer Research Center (BCRC), ACECR, Tehran, Iran</td>
</tr>
<tr>
<td>53</td>
<td>Dr. Mohammad Hasanazadeh Nazarabadi</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>54</td>
<td>Dr. Maryam Hashemi</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>55</td>
<td>Dr. Alireza Heravi Moussavi</td>
<td>Ferdowsi University of Mashhad, Mashhad, Iran</td>
</tr>
<tr>
<td>56</td>
<td>Dr. Fatemeh Homael Shandiz</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>57</td>
<td>Dr. Masoud Homayouni-Tabrizi</td>
<td>Islamic Azad University, Mashhad Branch, Mashhad, Iran</td>
</tr>
<tr>
<td>58</td>
<td>Dr. Hossein Hosseinzadeh</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>59</td>
<td>Dr. Mehrdad Iranshahi</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>60</td>
<td>Dr. Mahmoud Reza Jaafari</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>61</td>
<td>Dr. Razieh Jalal</td>
<td>Ferdowsi University of Mashhad, Mashhad, Iran</td>
</tr>
<tr>
<td>62</td>
<td>Dr. Abdullah Jamshidi</td>
<td>Ferdowsi University of Mashhad, Mashhad, Iran</td>
</tr>
<tr>
<td>63</td>
<td>Dr. Mokhtar Jalali-Javaran</td>
<td>Tarbiat Modares University, Tehran, Iran</td>
</tr>
<tr>
<td>64</td>
<td>Dr. Fatemeh Kalalinia</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>65</td>
<td>Dr. Mohammad Amin Kerachian</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>66</td>
<td>Dr. Mohammad Reza Khakzad</td>
<td>Islamic Azad University, Mashhad Branch, Mashhad, Iran</td>
</tr>
<tr>
<td>67</td>
<td>Dr. Saeed Khanzadi</td>
<td>Ferdowsi University of Mashhad, Mashhad, Iran</td>
</tr>
<tr>
<td>68</td>
<td>Dr. Abdolali Kharazmi</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>69</td>
<td>Dr. Roya Lari</td>
<td>Ferdowsi University of Mashhad, Mashhad, Iran</td>
</tr>
<tr>
<td>70</td>
<td>Dr. Mohammad Mehdi Kooshyar</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>No.</td>
<td>Name</td>
<td>Institution</td>
</tr>
<tr>
<td>-----</td>
<td>--------------------------</td>
<td>------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>71</td>
<td>Dr. Robab Latifnejad Roudsari</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>72</td>
<td>Dr. Mahmoud Mahmoudi</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>73</td>
<td>Dr. Keivan Majidzadeh Ardebili</td>
<td>Breast Cancer Research Center, Tehran, Iran</td>
</tr>
<tr>
<td>74</td>
<td>Dr. Maryam M. Matin</td>
<td>Ferdowsi University of Mashhad, Mashhad, Iran</td>
</tr>
<tr>
<td>75</td>
<td>Dr. Mostafa Mehrabi Bahar</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>76</td>
<td>Dr. Bahram Memar</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>77</td>
<td>Dr. Zarrin Minuchehr</td>
<td>National Institute of Genetic Engineering and Biotechnology, Tehran, Iran</td>
</tr>
<tr>
<td>78</td>
<td>Dr. Mohammad Mohsenzadeh</td>
<td>Ferdowsi University of Mashhad, Mashhad, Iran</td>
</tr>
<tr>
<td>79</td>
<td>Dr. Majid Mojarrad</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>80</td>
<td>Dr. Mohamad Javad Mokhtari</td>
<td>Islamic Azad University, Zarghan Branch, Zarghan, Iran</td>
</tr>
<tr>
<td>81</td>
<td>Dr. Ali Mokhtariifar</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>82</td>
<td>Dr. Majid Momeni-Moghaddam</td>
<td>Department of Biology, Hakim Sabzevari University , Sabzevar, Iran</td>
</tr>
<tr>
<td>83</td>
<td>Dr. Nasrin Motamed</td>
<td>University of Tehran, Tehran, Iran</td>
</tr>
<tr>
<td>84</td>
<td>Dr. Mansoureh Mottaghi</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>85</td>
<td>Dr. Seyyed Javad Mowl</td>
<td>Tarbiat Modarres University, Tehran, Iran</td>
</tr>
<tr>
<td>86</td>
<td>Dr. Hojjat Naderi-Meshkin</td>
<td>Academic Center for Education, Culture and Research -Mashhad Branch, Mashhad, Iran</td>
</tr>
<tr>
<td>87</td>
<td>Dr. Siavash Naseri Moghadam</td>
<td>Tehran University of Medical Sciences, Tehran, Iran</td>
</tr>
<tr>
<td>88</td>
<td>Dr. Mohammad Reza Nasiri</td>
<td>Ferdowsi University of Mashhad, Mashhad, Iran</td>
</tr>
<tr>
<td>89</td>
<td>Dr. Zeinab Neshati</td>
<td>Ferdowsi University of Mashhad, Mashhad, Iran</td>
</tr>
<tr>
<td>90</td>
<td>Dr. Gholam Hossein Noferesti</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>91</td>
<td>Dr. Ali Reza Pasdar</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td></td>
<td>Name</td>
<td>Institution</td>
</tr>
<tr>
<td>---</td>
<td>--------------------------------</td>
<td>--------------------------------------------------------------------</td>
</tr>
<tr>
<td>92</td>
<td>Dr. Houshang Rafatpanah</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>93</td>
<td>Dr. Seyed Abdol Rahim Rezaee</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>94</td>
<td>Dr. Hassan Rakhshandeh</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>95</td>
<td>Dr. Mohammad Ramezani</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>96</td>
<td>Dr. Reza Raoofian</td>
<td>Islamic Azad University, Mashhad Branch, Mashhad, Iran</td>
</tr>
<tr>
<td>97</td>
<td>Dr. Mohammad Reza Saberi</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>98</td>
<td>Dr. Ali Akbar Sabouri</td>
<td>University of Tehran, Tehran, Iran</td>
</tr>
<tr>
<td>99</td>
<td>Dr. Ariane Sadr-Nabavi</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>100</td>
<td>Dr. Mohammad Safarian</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>101</td>
<td>Dr. Peyman Salehi</td>
<td>Shahid Beheshti University, Tehran, Iran</td>
</tr>
<tr>
<td>102</td>
<td>Dr. Roham Salek</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>103</td>
<td>Dr. Mojtaba Sankian</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>104</td>
<td>Dr Ameneh Sazgarnia</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
<tr>
<td>105</td>
<td>Dr. Mahdi Seilanian Toosi</td>
<td>Mashhad University of Medical Sciences, Mashhad, Iran</td>
</tr>
</tbody>
</table>
Organizing Committee

Heads of Organizing Committee:
- Hamid Reza Bidkhori
- Hojjat Naderi-Meshkin

Secretary: Arezou Zahedi-Zohrabad

Congress Coordinator: Muhammad Irfan-maqsood

Web and IT Affairs: Saman Mohamadi

ePublication Affairs: Monireh Bahrami

Editing and Proofreading Affairs: Mohsen Reza

Scientific Program and Workshops Coordinator: Narjes Khalilipour

Graphics & Design: Mahdi Mirahmadi

International Relation Coordinator: Raheleh Amirkhah

Academic Advertisements Affairs: Masumeh Farshchi

Non-Academic Advertisements Affairs: Omid Nejati

Exhibition and Sponsorship: Elham Eskandari and Abbas Gholipour

Reception and Welcome Affairs: Hedyeh Rahimian, Matineh Barati and Samaneh Sharifi

Hall Management: Amin Afkhami

Poster Management: Sonia Iranpour

Reception Incharge: Mohammad Reza Khojasteh

Cultural Program Management: Mahdieh Sargolzai

Press Coordinator: Ebrahim Morovati

And also gratefully acknowledging the generous help & support of:

Hadi Darvishi          Mahdi Jahan Shargh
Ali Nik Farjam         Rasoul Mardan Nik
Asieh Heirani-Tabasi   Dr. Ali Berenj
Organizers:

- Nastaran Center for Cancer Prevention, Mashhad, Iran
- Ferdowsi University of Mashhad, Mashhad, Iran
- Mashhad University of Medical Sciences, Mashhad, Iran
- ACECR-Khorasan Razavi, Mashhad, Iran
Co-Organized & Co-Sponsored by:
پیام رئیس سمپوزیوم

سرطان دومین عامل مرگ و میر در جامعه است که سالانه موجب مرگ میلیون‌ها انسان در جهان می‌شود. مطالعات نشان داده که چنانچه سرطان در مراحل اولیه شناسایی شود، قابل پیشگیری و درمان خواهد بود.

سمپوزیوم بین المللی سرطان نسترن توسط موسسه پیشگیری نسترن (NCCP) با هدف گردهم آوری پژوهشگران برتر داخلی و خارجی، که دارای تخصص در زمینه تشخیص و پیشگیری از سرطان می‌باشند، برای دو ماه بار برگزار می‌شود.

از تمام دوستان علاقه‌مند به مبحث سرطان و افرادی که قصد انجام تحقیقات در زمینه تشخیص زودهنگام و پیشگیری سرطان را دارند، دعوت به شرکت در این سمپوزیوم می‌گردد. پیشایش ورود شما را به شهر مقدس مشهد و سمپوزیوم بین المللی سرطان نسترن گرامی می‌داریم.

دکتر مصطفی مهراپی بهار

رئیس دومین سمپوزیوم بین المللی سرطان نسترن

پیام رئیس مرکز پیشگیری سرطان نسترن

دومین سمپوزیوم بین المللی سرطان نسترن 1395، ادامه مسیر مباحث نوین در زمینه پیشگیری، تشخیص زودهنگام و درمان هدف‌مند سرطان است که دراسال گذشته در مرکز پیشگیری از سرطان نسترن آغاز شد.

مفيد بردن و بالابردن بار علمی این سمپوزیوم برای شما عزیزان هدف هر ساله ما در این سمپوزیوم است.

مهندس تحقیق میاراحمی

رئیس مرکز پیشگیری سرطان نسترن
Oral Presentations
Cancer Awareness And Prevention

1. Maryam M. Matin (Department of Biology, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran; Cell and Molecular Biotechnology Research Group, Institute of Biotechnology, Ferdowsi University of Mashhad, Mashhad, Iran; Stem Cell and Regenerative Medicine Research Group, Iranian Academic Center for Education, Culture, and Research (ACECR), Khorasan Razavi Branch, Mashhad, Iran)

Abstract

Cancer includes more than hundred diseases which arise from unlimited replication of mutated cells with the potential to invade to other parts of the body. Current research in this field is mainly focusing on carcinogenesis, early detection and improving therapeutic methods with little attention on cancer prevention. According to American Cancer Society, the lifetime probability of developing cancer in males is 1 in 2 and it is 1 in 3 for females, which are quite alarming. However, about one third of cancers can be prevented. Changing life style and taking a few simple steps like maintaining body weight, regular exercises, eating more vegetables and avoiding salt and sugar, not smoking and avoiding excessive exposure to sun can be very useful in cancer prevention. Breast and stomach cancers have the highest incidence in Iranian women and men, respectively. Unfortunately, we are facing a rise in the incidence of some cancers in Iran, which necessitates more work on cancer prevention and early diagnosis to reduce the burden of this monstrous disease.

Corresponding Author: Maryam M. Matin (Department of Biology, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran; Cell and Molecular Biotechnology Research Group, Institute of Biotechnology, Ferdowsi University of Mashhad, Mashhad, Iran; Stem Cell and Regenerative Medicine Research Group, Iranian Academic Center for Education, Culture, and Research (ACECR), Khorasan Razavi Branch, Mashhad, Iran)
Advanced Microfluidic Systems For Cancer Research

1. Majid Ebrahimi Warkiani (University Of New South Wales (UNSW), Sydney, Australia)

Abstract

Cancer has emerged as one of the most severe non-communicable diseases in the past decades. More recently, with improved understanding in cancer biology as well as advancement made in microtechnology and rapid prototyping, microfluidics is increasingly being explored and even validated for use in the detection, diagnosis and treatment of cancer. With inherent advantages such as small sample volume, high sensitivity and fast processing time, microfluidics is well-positioned to serve as a promising platform for applications in oncology. In this seminar, I will describe our recent efforts in development of novel microfluidic tools for enrichment of cancer cells from blood. I will discuss how simple micro-engineered tools (i.e., fabricated using conventional micromilling, 3D printing and MEMS techniques) can be combined with fluid mechanics concepts in order to develop functional devices for both basic and applied research in cancer. I will also give details of our recent works for study of cancer heterogeneity at single-cell level using advanced microfluidic systems.

Corresponding Author: Majid Ebrahimi Warkiani (University of New South Wales (UNSW), Sydney, Australia)
Abstract

The third leading cause of death worldwide is cancer and is projected that by 2030, there will be about 26 million new cancer cases and 17 million cancer deaths per year. The global distribution of cancer continues to change, especially in economically developing countries that include many countries in the Middle East and North Africa regions. Low- and middle-income countries are projected to account for about 60% of all cancers worldwide by 2050. The projected increase will be driven mainly by growth and aging populations in the Middle East populations. Unfortunately, practically no preventive care culture exists in many of the Middle Eastern countries facing the projected increased rate of cancer in the coming decades. Another major problem in the Middle Eastern countries is high prevalence of cancer-promoting behavior such as smoking and a sedentary lifestyle. It is highly recommended that cancer prevention programs which include practical national policies, mass screening, early detection, education programs, access to effective treatments should start soon in many of the Middle East countries facing projected increased cancer incidence in their populations.

Corresponding Author: Ali M. Ardekani (National Institute of Genetic Engineering and Biotechnology, Tehran, Iran)
Meat, Fish, And Esophageal Cancer Risk: A Systematic Review And Dose-Response Meta-Analysis

Abstract

The associations between some of risk factors with esophageal squamous cell carcinoma (ESCC), and esophageal adenocarcinoma (EAC) are well defined while the role of diet (including meat intake) remains controversial. We searched major bibliographic databases for published studies (1990-2011) on the association between consumption of total meat, red meat, processed meat, poultry, and fish and risk of esophageal cancer (EC). Random-effects models were used to pool study results. Subgroup analyses were conducted by histological subtypes, study design and nationality. Four cohorts and 31 case-control studies were identified. The overall pooled relative risk (RR) of EC and the confidence intervals (CIs) for the groups with the highest versus the lowest levels of intake were as follows: 0.99 (95% CI: 0.85–1.15) for total meat; 1.40 (95%CI: 1.09–1.81) for red meat; 1.41 (95%CI: 1.13–1.76) for processed meat; 0.87 (95%CI: 0.60–1.24) for poultry; and 0.80 (95%CI: 0.64–1.00) for fish. People with the highest levels of red meat intake had a significantly increased risk of ESCC. Processed meat intake was associated with increased risk of EAC. These results suggest that low levels of red and processed meat consumption and higher levels of fish intake might reduce EC risk.

Corresponding Author: Maryam Salehi (Department of Community Medicine, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran; Research Center for Patient Safety, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran)
Cohort Designs In Cancer Research

1. Nayyereh Aminisani (Department Of Statistics And Epidemiology, Faculty Of Health Sciences, Tabriz University Of Medical Sciences, Iran)

Abstract

Cancer has a complex etiology; an interaction of environmental, lifestyle and genetic factors is required to cause cancer. In the last decades, using cohort design; one of the fundamental study designs in Epidemiology, researchers were able to provide key insights into environmental, lifestyle, and genetic determinants of this disease and its outcomes. A cohort study begins with a group of individuals who are identified to have a certain exposure and then the group is followed prospectively over time in order to obtain the information on occurrence of the disease of interest. Therefore, cohort studies are considered as a fundamental study design in cancer epidemiology because they allow the calculation of the basic epidemiologic measures of association; incidence and mortality rates, with different types of exposure. Cancer epidemiology cohorts (CECs) are categorized into 1) longitudinal observational studies of healthy individuals, which are followed up until disease occurrence and 2) cancer survivor cohorts which provide information on cancer prognosis and survivorship. The former provides key evidence for the development of risk prediction models, prevention strategies, and guidelines and the latter provides evidence for the efficacy of many treatment and health policy interventions. More recently, in-depth analyses of gene-environment interactions and also patient cohorts come to interest to better examine determinants of clinical, genomic, and lifestyle factors of cancer development as well as cancer prognosis and survival. Although cohort studies have advantages in cancer epidemiology, there are some limitations such as loss to follow up due to a decade or more follow-up period, a need for ample fund and strong project management as well as larger sample sizes. This design is also not suitable for rare cancers.

Corresponding Author: Nayyereh Aminisani (Department of Statistics and Epidemiology, Faculty of Health Sciences, Tabriz University of Medical Sciences, Iran)
Screening Of Allelopathy And Allelochemicals From Plants In Order To Reduce Cancer Risk.

1. Yoshiharu FUJII (Tokyo University Of Agriculture And Technology, Japan)

Abstract

Allelopathy is a phenomenon whereby a plant influences their neighboring plants, insects, microorganism, and animals by natural chemicals called allelochemicals. We have developed specific bioassays for allelopathy, namely: “Plant Box Method”; “Sandwich Method”; and “Dish-pack Method”. Using these methods, we have evaluated more than 4,000 plant species in the world. Our major targets are 1) to isolate innovative bioactive natural chemicals from allelochemicals, including novel medicinal chemicals, and 2) to use allelopathic ground cover plants in agriculture and environment. I will briefly summarize the results of screening of 4,000 plants in the world including 1,500 medicinal plants. Ground cover plants with allelopathic activity could be a natural resource for weed control, supplemental food, medicinal use, or creation of landscape with flowers, leaves or fragrant perfume. Allelopathic cover plants are realized as natural and environmentally friendly way of managing weeds without herbicides. Useful allelopathic plants and their respective allelochemicals include: 1) velvetbean (Mucuna pruriens), L-DOPA; 2) hairy vetch (Vicia villosa), cyanamide; and 3) buckwheat (Fagopyrum esculentum), rutin. These crops are useful resources for food and other practical purposes. Potential allelopathic plants with potent allelochemicals are: 4) Centipedegrass (Eremochloa ophiuroides), tryptophan and other compounds; 5) Ouren (Coptis japonica), berberine; 6) dwarf mondo grass (Ophiopogon japonicus), salicylic acid; 7) hyacinth orchid (Bletilla striata), militarine; 8) red spider lily (Lycoris radiate), lycorine; and 9) Thunberg spiraea (Spiraea thunbergii), cis-cinnamic acid and BCG. I will also explain practical and potential use of these plants for environmentally friendly way of agriculture to produce safe foods and reduce the risk for cancer.

Corresponding Author: Yoshiharu FUJII (Tokyo University of Agriculture and Technology, Japan)
Types Of Cancer Prevention And Cohort Studies In South West Of Iran

1. Abdolhassan Talaiezadeh (Head Of Cancer Research Center, Ahvaz Jundishapur University Of Medical Sciences, Ahvaz, Iran)

Abstract

There is an old American saying (by Benjamin Franklin) «an ounce of prevention is worth a pound of cure» that is true in our contemporary community about cancer. If we could detect risk factors of cancer as possible as, so we can prevent malignancies by eliminating them. Therefore, it is much more cost effective than paying a billion dollars for diagnosis, treatment and rehabilitation of these patients. Prevention may be primary, so that by eliminating cancer- causing agents the cancer incidence in our community will be decreased. For example, vaccination against hepatitis B could significantly reduce liver cancer in Africa, or vaccination against HPV virus recently can reduce the incidence of cervical cancer in women sooner or later in the West. In a study constructed in our center, more than 68% of Khuzestan population harbor the HP bacteria in their stomachs that is the most common cause of gastric cancer. So that gastric cancer that is the most common cancer in Iran may be reduced in our country by helicobacter pylori (HP) eradication in early ages. Another type of prevention is secondary prevention so that by detection of pre-cancerous conditions and their treatment, we can decrease incidence of cancer in the future. For example, treatment of mucosal metaplasia or dysplasia of the stomach can prevent the development of gastric cancer, or by polypectomy in colorectal adenomatous polyps, can reduce colorectal cancer in the future, or total proctocolectomy in diseases such as FAP and ulcerative colitis can prevent colorectal cancer. Another type of prevention is tertiary, so that by actions reduce second primary carcinoma in cancer patients. For example, hysterectomy and bilateral salpingo-oophrectomy (TH-BSO) in a patient with colorectal cancer in underlying Lynch syndrome (HNPPC) whom are menopause or are child complete can eliminate the chance of malignancy in these organs that is higher than the general population. Chemoprevention is a subtype of secondary prevention, so that we can reduce the chance of malignancies by using of some drugs or supplements like tamoxifen or raloxifen can reduce 50-60% breast cancer in women who are at risk. Celecoxib in patients with colorectal polyps can reduce the risk of colorectal cancer by decreasing polyps, or supplements such as 13-cis-retinoic acid ( a certain metabolite of vitamin A) can be used as secondary prevention in patients with head and neck precancerous lesions like leukoplakia or vitamin D can reduce the risk of breast cancer in women. The best way to find the cause and effect in cancer is cohort studies. For this purpose, a cohort study was constructed in Hoveyzeh city located in the South West of Iran, these people are similar in terms of ethnicity and cultural habits and behavior. Deputy Custodian of this project is Vice-Chancellor for development of research and technology of Ahvaz Jundishapur University of Medical Sciences. In this study we included 10000 persons of this town that has special geographic and warm weather condition with petroleum and environmental pollutants which is specific for the south west of Iran. In addition to regional dust, there are intermittent micro and macro dusts that are specifically for the south west of Iran. However, these people are similar in cultural and habitual condition. In addition to the demographic questions, family and drug history, diet and exercise habits will be included, as well. Blood, urine, nail and hair specimens will be
taken, too. We will use these databases for comparing other cohort groups in a different geographic region as North East in Iran without such weather and pollutant condition. When we synchronize these data with incidence of cancer after two to three decades as registered in our center, we may find suspicious causal relationships. In addition, we hope to use these specimens for genetic studies to find common regional mutations as APC or MMR in colorectal cancers that are very common in young people in this region (FAP families are relatively common in Khuzestan Province). Of course, we know that the cause of cancer is multifactorial, but causal effects of some factors such as smoking and alcohol in the lung, esophagus, liver and pancreatic cancers have been discovered in such studies. In the same way, the best way for finding a suitable and effective treatment is a randomized control trial (RCT) study that in medicine it is named as the clinical trial. In the registration unit of our cancer research center, we witnessed an increasing trend of common cancers in our region (curves will be included in the presentation). We hope to find new specific cause effects using these cohort studies. So, we could find effective ways for prevention. However, the effective therapy for cancer patients is starting it in the first stages of the disease. In addition to effectiveness, this way may be easier, lower cost and longer survival. Of course, this requires cancer screening programs for common types of cancer and this cannot be realized unless the results of cohort studies; for example, esophageal cancer screening program in the Gonbad city in the North East of Iran, where was based on cohort studies in this area.

**Corresponding Author:** Abdolhassan Talaiezadeh (Head of Cancer Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran)
Role Of NOTCH Pathway In Targeted Therapy Against The Esophageal Cancer Stem Cells

Abstract

Esophageal cancer is the 6th leading cancer related deaths in the world. It is divided into two subtypes histologically: Esophageal squamous cell and Adeno carcinoma. Squamous type involves more than 90% of Asian cases. It has been shown that the survival in ESCC cases is 10% lower than that in the patients with adeno carcinoma. Cancer stem cells (CSCs) are the main reason of tumor relapse in ESCC patients. These cells have stem cell characteristics and are resistant toward the common chemo radio therapeutic treatments. Regarding the importance of NOTCH pathway in preservation of CSCs, it can be possible to target such cells via the NOTCH pathway. In the present study we isolated the CD44+ ESCC CSCs and designed a targeted therapy against them via the targeting MAML1 as the main transcription factor of NOTCH signaling pathway. Isolation of CSCs was performed using the magnetic cell sorting (MACS) based on CD44 cell surface marker. The isolated CD44+-CSCs were characterized using the molecular technics in the levels of protein and mRNA expression (Real time PCR, IHC, ICC, and WB). Moreover, the isolated cells were characterized in-vivo by NUDE mice injection. Role of MAML1 and NOTCH pathway was assessed in biology of isolated CSC-CD44+ via the MAML1 ectopic expression and silencing by the cellular and molecular technics such as real time PCR, scratch assay, MTT assay, and cell cycle analysis. Finally, drug resistance assay also perform to assess the role of NOTCH pathway in 5FU resistance of CSCs-CD44+. The present study has shown that, the CSC-CD44+ has ability to form sphere in specific medium and form tumor in NUDE mice. MAML1 silencing resulted in a significant decrease in cell migration (p=0.019) and MAML1 ectopic expression resulted in a significant increase in migration of CSCs-CD44+ (p=0.012). Moreover, MAML1 silencing and ectopic expression caused a significant increase and decrease in 5FU resistance, respectively (p<0.05). MAML1 silencing resulted in a significant increase in numbers of G1 cells (p=0.008) and its ectopic expression significantly increased numbers of CSC-CD44+ in S phase (p=0.037). Moreover, we showed that the ABCG2 has the main role in resistance of CD44+ cancer stem cells against the 5FU. Regarding the present study the NOTCH pathway has an important role in preservation of CSC-CD44+ and their drug resistance. Therefore, NOTCH pathway can be used as an efficient targeted therapy in elimination of CSC-CD44+ in ESCC patients with the lowest side effects.

Corresponding Author: Mohammad Reza Abbaszadegan (Division of Human Genetics, Immunology Research Center, Avicenna Research Institute, Mashhad University of Medical Sciences, Mashhad, Iran.)
CDK-FBX028-MYC Axis: A Potential Molecular Drug Target

1. Hamidreza Sharifi (Karolinska Institute, Stockholm, Sweden)

Abstract

SCF (Skp1/Cul1/F-box) ubiquitin ligases act as master regulators of cellular homeostasis by targeting key proteins for ubiquitylation. We identified a hitherto uncharacterized F-box protein, FBXO28 that controls MYC-dependent transcription by non-proteolytic ubiquitylation. SCFFBXO28 activity and stability are regulated during the cell cycle by CDK1/2-mediated phosphorylation of FBXO28, which is required for its efficient ubiquitylation of MYC and downstream enhancement of the MYC pathway. Depletion of FBXO28 or overexpression of an F-box mutant unable to support MYC ubiquitylation results in an impairment of MYC-driven transcription, transformation and tumourigenesis. Finally, in human breast cancer, high FBXO28 expression and phosphorylation are strong and independent predictors of poor outcome. In conclusion, our data suggest that SCFFBXO28 plays an important role in transmitting CDK activity to MYC function during the cell cycle, emphasizing the CDK-FBXO28-MYC axis as a potential molecular drug target in MYC-driven cancers, including breast cancer.

Corresponding Author: Hamidreza Sharifi (Karolinska Institute, Stockholm, Sweden)
Hereditary Cancers, Potentials For Cancer Prevention

1. Keyvan Majidzade (Breast Cancer Research Center, ACECR, Tehran, Iran)

Abstract

According to different estimates around 5 to 15% of all cancers are hereditary. The estimated heritable fraction of human cancers for most of the cancers is more than 25%. This fraction for Prostate, Colon and Breast Cancers are 42%, 35% and 27% respectively. Considering the high prevalence of breast and colon cancer, their relevant hereditary syndrome; hereditary breast-ovarian cancer syndrome (HBOC) and hereditary non-polyposis colon cancer (HNPCC, Lynch syndrome) are among the most identified predisposition syndromes. Scientific information of cancer susceptibility syndromes is remarkably extending and more genes and syndromes are being discovered, The mechanism underlying these syndromes are more explained and development of commercial genetic based diagnostic methods have extensively benefited clinical protocols. Notably hereditary factor is among the most important preventable cancer factors and the magnitude of possible reduction of this factor is around 50%. Therefore Genetic counseling and further genetic testing should be considered as the crucial and key elements for prevention and treatment of cancer.

Corresponding Author: Keyvan Majidzade (Breast Cancer Research Center, ACECR, Tehran, Iran)
Personalized Medicine And Cancer Diagnosis And Medication Using Next Generation Sequencing Technologies: Prospects, Challenges And Hopes

1. Seyed Alireza Salami (University Of Tehran, Tehran, Iran)

Abstract

The rapid emergence and development of new high-throughput sequencing technologies not only led to precise diagnosis and medication but also have substantially reduced both the cost and the time required to deal with cancer. Technologies called Next (Next) Generation Sequencing now a day had a great impact on what we known as personalized medicine and precise medicine. There are many challenges to deal with cancer during routine diagnosis procedures which is summarized to, no effect with the chemotheraphy or radiotherapy, no target drugs to choose, drug resistance, recurrence or metastasis, and no targeted drugs or no potent effect with the targeted drugs after detecting the mutation of EGFR, KRAS, ALK, BRCA1,2 etc. However, the development of cancer genome along with emergence of NGS-based and profiling methods and subsequently improvement in our knowledge of cancer, led to the ability of comprehensive analysis of hundreds of tumor related genes via genetic testing, which could improve the average survival time up to 50%, accompanying with targeting therapy. On the other hand, huge amount of cancer related data and different powerful bioinformatics analysis pipelines and ability to capture ctDNA from blood circulation system, helped us to be in a better position to deal with cancer and to advance personalize therapy based on the genetics of the tumor and the patient. However, there are still a few major challenges once we talk about “Cancer” itself. Cancer is somehow, quantitative change to qualitative change of gene mutations which can be induced by environmental degradation, stress, infection, radiation, diet and aging. It has been proved that the efficacy of cancer treatment is correlated with the unique nature of genetic mutations of patients. Running towards cancer treatment, targeted therapy and targeted drugs have become the hot spot recently. In this regard, a comprehensive targeted genetic testing and analysis about the relationship between the mutations and drugs before treatment, choose the best targeted drugs according to individual patient differences and monitor the acquired drug resistance mutations could be a proper way toward individualizing cancer therapy, not only for the diagnosis in early stage but also as a lost hope.

Corresponding Author: Seyed Alireza Salami (University of Tehran, Tehran, Iran)
Bacteria-Directed Enzyme Prodrug Therapy, A Novel And Reliable Prospective Method For Targeted Cancer Therapy

1. Amin Afkhami (Department Of Biology, Faculty Of Science, Ferdowsi University Of Mashhad, Mashhad, Iran)

2. Maryam M. Matin (Department Of Biology, Faculty Of Science, Ferdowsi University Of Mashhad, Mashhad, Iran; Cell And Molecular Biotechnology Research Group, Institute Of Biotechnology, Ferdowsi University Of Mashhad, Mashhad, Iran; Stem Cell And Regenerative Medicine Research Group, Iranian Academic Center For Education, Culture And Research (ACECR), Khorasan Razavi Branch, Mashhad, Iran)

Abstract

Despite the large number of various anti-cancer drugs on the market, cancer remains one of the most deadly diseases worldwide with the number of cases steadily increasing. Among the most promising, more recent developments are directed enzyme prodrug therapies. All directed enzyme prodrug therapies operate with the same basic concept: a nontoxic prodrug is converted into a toxic drug inside of cells which were transformed with a gene construct (GDEPT) or bacteria (BDEPT) encoding the enzyme needed for the prodrug/drug conversion or antibody (ADEPT) as antibody-prodrug/drug converting enzyme fusion proteins. Recently, several genera of bacteria have been shown to specifically accumulate and replicate within tumors, including Clostridium, Salmonella, Bifidobacterium, Listeria and E. coli. These bacteria can cause cancer cell death by competing for nutrients and/or by secreting toxic bacterial products. In BDEPT method, that has even been used in pilot trials for refractory cancer patients, some of these bacteria are utilized as specific gene delivery vehicles for selective enzyme activation of prodrugs at the tumor microenvironment to increase treatment specificity. Recently, Salmonella expressing carboxypeptidase G2, Escherichia coli expressing β-glucuronidase (βG), Salmonella expressing herpes simplex virus thymidine kinase, Salmonella expressing E. coli cytosine deaminase (CD) and Listeria expressing purine nucleoside phosphorylase (PNP) have been shown to generate potent and selective antitumor activity by converting systemically administered prodrugs to active anticancer agents in various types of tumors, while minimizing exposure of normal tissues to active drugs. Bacteria-directed enzyme prodrug therapy (BDEPT) is a promising therapeutic approach for treatment of some solid tumors. Optimization and improvement of the selected prospective model type of BDEPT would help to improve the development of bacterial-mediated cancer treatment and drug delivery systems and their successful applications in future clinical trials.

Corresponding Author: Maryam M. Matin (Department of Biology, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran; Cell and Molecular Biotechnology Research Group, Institute of Biotechnology, Ferdowsi University of Mashhad, Mashhad, Iran; Stem Cell and Regenerative Medicine Research Group, Iranian Academic Center for Education, Culture and Research (ACECR), Khorasan Razavi Branch, Mashhad, Iran)
Abstract

Obesity defines as excess adipose tissue and results from getting more calories than are burned by normal activities. Diabetes, cardiovascular disease, obstructive sleep apnea, and asthma are some major diseases that are associated with the obesity. Recently, obesity-cancer relationship has been studied carefully and shown that obesity is associated with increased risk of several cancer types such as colorectal, esophageal, kidney, pancreatic, thyroid, endometrial, gallbladder, breast, leukemia, and rectal. Discerning molecular and cellular mechanism of the obesity-cancer could be a persuasive way to recognizing the exact regeneration of the cancer cells and understand how they grow in order to control them. Mathematical modeling of the obesity-cancer connection is an effective technique for this analyzing. In this study, a mathematical model of cancer tumor growth with the immune system response and the effect of the obesity on the cancerous organs is investigated. The Interactions between tumor cells, healthy cells, immune cells, and adipose cells are considered, and different control schemes are examined to control the growth of cancer cells in the presence of obesity. Controlling the contribution of the fat to the tumor growth is the main target and result of the controller. It was shown that by using a robust controller, the connection between the fat and cancer cells has reached the least level and is promising for future usage to bring back hope to the people that are engaged with obesity. All of the simulations and controller designing were performed in MATLAB-SIMULINK environment.

Corresponding Author: Masoud Goharimanesh (Mechanical Engineering Department, Ferdowsi University of Mashhad, Mashhad, Iran)
The Role Of Intron Retention In Cancer

1. Ulf Schmitz (University Of Sydney, Sydney, Australia)

Abstract

Intron retention (IR) occurs when the splicing machinery fails to excise introns from primary transcripts. We have shown that IR is a widespread mechanism of post-transcriptional gene regulation and can induce diverse downstream effects. We also found evidence that IR affects functionally related genes in granulocytes throughout evolution. Retained introns have similar characteristics and there is a strong anti-correlation between the number of intron-retaining genes and the number of protein-coding genes in a genome. IR was recently described as mechanism of tumor-suppressor inactivation, which suggests a significant contribution to cancer emergence and progression. An analysis of TCGA RNA-seq data revealed that acute myeloid leukaemia has the highest number of intron retaining transcripts among 16 cancers analyzed. Compelling evidence indicates that there is increased perturbation in the way genes function in leukaemia due to IR-induced regulation. Currently, we utilize a computational approach to analyze vast amounts of biomedical data that will enhance our understanding of IR. Our preliminary results suggest that IR is an independent mechanism of post-transcriptional gene regulation that supplements or even cooperates with other forms gene regulation and relates to causes for the emergence and progression of different cancers including leukaemia.

Corresponding Author: Ulf Schmitz (University of Sydney, Sydney, Australia)
Tumor Type-Specific Regulatory Core And Key Molecular Signatures Underlying E2F1-Mediated Epithelial To Mesenchymal Transition

Abstract

Tumor metastasis continues to be the most significant problem in the field of cancer. The increasingly high rates of lethal outcome associated with tumor metastasis rely on the acquisition of invasiveness and generation of chemo-resistance. Large number of clinical studies hints at the transcription factor E2F1 that switches duties from tumor suppressor to promotor during invasiveness and metastasis, however the underlying mechanisms are largely unknown. To understand how E2F1 interacts and regulate different molecules and how it mediates cancer related processes, we derived a detailed regulatory and functionally modularized E2F1 interaction map from literatures and our own data. From the interaction map, we identified a large set of regulatory motifs formed by feedback and feedforward loops which induce non-intuitive behavior. We further identified the tumor-type and process specific most important motifs using a novel methodology for motif ranking. From top ranked motifs, we identified a regulatory core that controls the transition from non-invasive to invasive phenotype. Based on the regulatory core, we derived a logic-based model that accounts for the role of E2F1 in epithelial to mesenchymal transition in bladder and breast cancer models. Our simulation indicate that an invasive tumor phenotype in bladder cancer is mainly driven by E2F1 and FGFR1, while in case of breast cancer it is driven by E2F1 together with EGFR. These signatures were further validated using invasive/ non-invasive bladder and breast cancer cell lines and also in the patient data. Further, we have identified novel pro-metastatic cofactors that interact with E2F1 and play a crucial role in switching E2F1 duties during disease progression. Recently, using our computational methods, we screened FDA approved drug library for the identification of potential therapeutic candidates that can inhibit E2F1-cofactor interactions in order to develop novel anti-metastatic therapy. The therapeutic candidates were successfully validated by our experimental partners both in in vitro and in vivo settings. Overall, our study contributes towards a deeper understanding of the highly interconnected E2F1 signaling network for the development of tumor preventative measures and anti-metastatic therapies.

Corresponding Author: Shailendra Gupta (University of Rostock, Rostock, Germany)
Embryonic Stem Cell-Expressed RAS, A Novel Member Of The RAS Family, Modulates Maintenance Of Liver Stem Cells And Survival Of Cancer Cells

1. Saeideh Nakhaei-Rad (Institute Of Biochemistry And Molecular Biology II, Medical Faculty Of The Heinrich-Heine University, Düsseldorf, Germany)
2. Inga Rebecca Heinen (Institute Of Biochemistry And Molecular Biology II, Medical Faculty Of The Heinrich-Heine University, Düsseldorf, Germany)
3. Hossein Nakhaeizadeh (Institute Of Biochemistry And Molecular Biology II, Medical Faculty Of The Heinrich-Heine University, Düsseldorf, Germany)
4. Mohammad R. Ahmadian (Institute Of Biochemistry And Molecular Biology II, Medical Faculty Of The Heinrich-Heine University, Düsseldorf, Germany)

Abstract

RAS proteins are central components of intracellular signaling pathways. Somatic mutations have been identified in 1/3 of human tumors, for example 90%, 50%, 30% and 25% of pancreatic, colorectal, lung and melanoma carcinoma, respectively. Oncogenic activation of three closely related members of RAS family (HRAS, KRAS and NRAS) is mainly due to somatic point mutations in codon 12, 13 and 61. These mutations render RAS protein in its active form that contributes to cell proliferation and anti-apoptosis. However, they are also important for embryo development. Germline mutations of RAS family members and their signaling components causes a cluster of genetic disorders collectively called RASopathies. A novel member of this family, embryonic stem cell-expressed RAS (ERAS), has deviation at codon 12 (HRAS numbering) resulting in a constitutive active protein. ERAS is not regulated at the protein level by GTPase activating proteins (GAPs) but rather at the transcriptional levels through the DNA methylation. Unlike classical RAS isoforms (HRAS, NRAS and KRAS), ERAS harbors an extended N-terminus that is important for protein-protein interaction and probably subcellular localization. In addition, we detected ERAS is differentially expressed in different human cancer cell lines as well as normal cells of the body, including the hepatic stellate cells. ERAS has a distinct amino acid sequence within its effector binding site that modules its cellular functions, especially by activating the PI3K-AKT-mTOR and HIPPO-MST1/2-YAP axes.

Corresponding Author: Saeideh Nakhaei-Rad (Institute Of Biochemistry and Molecular Biology II, Medical Faculty of the Heinrich-Heine University, Düsseldorf, Germany)
Correlation Analysis Between H.Pylori And Expression Changes Of MAML1 And TWIST1 In Gastric Cancer Patients

1. Amir Abbas Hamidi (Human Genetic Division, Immunology Research Center, Bu-Ali Research Institute, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Mohammad Reza Abbaszadegan (Human Genetic Division, Immunology Research Center, Bu-Ali Research Institute, Mashhad University Of Medical Sciences, Mashhad, Iran)
3. Mehran Gholamin (Human Genetic Division, Immunology Research Center, Bu-Ali Research Institute, Mashhad University Of Medical Sciences, Mashhad, Iran)
4. Bahram Memar (Dept. Of Radiation Oncology, Cancer Research Center, Faculty Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran, Islamic Republic Of)
5. Ali Jangjoo (Department Of Surgery, Surgical Oncology Research Center, Imam Reza Hospital, Faculty Of Medicine, Mashhad University Of Medical Sciences, Iran)

Abstract

Gastric cancer is one of the most important causes of death by cancer around the world... It has been shown that the Helicobacter Pylori is one of the main factors in gastric cancer. Helicobacter Pylori alters some of the signaling pathways such as wnt/B-catenin, PI3K/AKT, Hedgehog, and JAK/STAT3 which are involved in tumor progression and EMT through CagA toxin. In present study a probable correlation between H.Pylori and TWIST1 and MAML1 expression was assessed for the first time in gastric cancer patients. Levels of TWIST1 and MAML1 expression were studied in 73 gastric cancer patients using the quantitative realtime PCR method. All the samples were also checked for detection of Helicobacter Pylori by PCR method. Statistical analysis was performed by spss22 software. 48 percentage and 15 percentage of patients showed TWIST1 overexpression and under expression, respectively. Also 46.6 percentage and 16.4 percentage of patients showed MAML1 overexpression and under expression, respectively. for both genes TWIST1 and MAML1 was observed 35 and 34 cases overexpression ,respectively . Thirty four out of 73 cases were Helicobacter Pylori positive. There was a significant correlation between expression of MAML1 and TWIST1 ( p-value < 0.001). Moreover, there were significant correlations between MAML1 gene expression and tumor grade ( p-value= 0.006) and lymph node involvement ( p-value < 0.001 ). There was not any significant correlation between the clinicopathological features of patients and TWIST1 expression. also there were not any significant correlation between H.Pylori infection and expression changes of TWIST1 and MAML1 genes. There was a significant correlation between MAML1 gene expression and gastric cancer progression and metastasis. Whereas, H.Pylori have no effect on the expression levels of two studied genes.

Corresponding Author: Mohammad Reza Abbaszadegan (Human Genetic Division, Immunology Research Center, Bu-Ali Research Institute, Mashhad University Of Medical Sciences, Mashhad, Iran)
Synthesis Of Novel Naphthoquinone Derivatives As Heat Shock Protein 90 Inhibitors And Anti-Breast Cancer Agents

1. Razieh Ghodsi (Biotechnology Research Center, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Sima Golmakaniyon (Biotechnology Research Center, Mashhad University Of Medical Sciences, Mashhad, Iran;Department Of Medicinal Chemistry, School Of Pharmacy, Mashhad University Of Medical Sciences, Mashhad, Iran)
3. Vahid Reza Askari (Department Of Pharmacology, School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
4. Ali Ghasemi (Department Of Pediatric Oncology-Hematology, School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Naphthoquinone based natural products are known to possess anti-cancer activity. On the other hand, the discovery of Hsp90 as the target of anticancer activity of geldanamycin devoted much attention in the inhibition of Hsp90 as a tactic for the treatment of cancer. This interest has led to huge efforts to develop clinically practical small molecule Hsp90 inhibitors possessing quinone moiety, in this study we designed, synthesized and characterized different classes of naphthoquinone derivatives as Hsp90 inhibitors and anticancer agents. For synthesis of desired compounds, initially, 2-hydroxy-1,4-naphthoquinone, aldehyde, amine (in equivalent mole ratio) and InCl3 (20% mole) was refluxed in appropriate solvent for distinct time and the final product was purified by chromatography methods. Then the structures of synthesized compounds were determined by IR, 1H-NMR, 13C-NMR and Mass spectra and finally their anticancer activities were examined against two human cell lines including MCF-7 and PC-3 by MTT test. The effects of two potent anti-breast cancer compounds on Her2 protein expression levels were evaluated in MCF-7 cancer cells employing western blot analysis. Molecular docking studies of potent cytotoxic agents into the binding site of HSP90 demonstrated possible mode of interaction between these compounds and HSP90. In summary, we synthesized and characterized novel naphthoquinone derivatives which can be classified in four different classes including bis naphthoquinone, 2-arylaminonaphthoquinone, benzoxantene-6,11-dione and benzoacridine-5,6-dione derivatives. We have studied the in vitro anti cancer activity of these compounds against MCF-7 and PC3 cell lines by MTT test. The in vitro results revealed that five compounds by the IC50 range of 5.4-47.99 μM are the most anti breast cancer structures. Her2 degradation assay and molecular modeling studies suggested that the 8,9,10-trimethoxybenzo[c]acridine-5,6(7H,12H)-dione scaffold affords fortunate interactions with the binding site of HSP90.

Corresponding Author: Razieh Ghodsi (Biotechnology Research Center, Mashhad University of Medical Sciences, Mashhad, Iran)
Matrix Metalloproteinase-1 Potential Biomarker for Detection and Prognostic Assessment of Patients with ESCCs

1. Sara Shekari (Division of Human Genetics, Immunology Research Center, Avicenna Research Institute, Mashhad University of Medical Sciences, Mashhad, Iran)
2. Reihaneh Alasadat Mahmoudian (Division of Human Genetics, Immunology Research Center, Avicenna Research Institute, Mashhad University of Medical Sciences, Mashhad, Iran)
3. Seyed Amir Aledavood (Department of Radiotherapy and Oncology, Mashhad University of Medical Sciences, Mashhad, Iran)
4. Mohammad Reza Abbaszadegan (Division of Human Genetics, Immunology Research Center, Avicenna Research Institute, Mashhad University of Medical Sciences, Mashhad, Iran)
5. Mehran Gholamin (Immunology Research Center, BuAli Research Institute, Mashhad University of Medical Sciences, Mashhad, Iran)

Abstract

Matrix metalloproteinase 1 (MMP-1) is a zinc-dependent endopeptidase that belongs to superfamily of MMPs. MMP1 gene expression was increased in esophageal cancer and associated with increasing tumor invasion and decreased survival rate. The expression of MMP-1 is increased in tumor tissue, which leads to elevate the levels of circulating enzyme in serum. Accordingly, MMP-1 can introduce as a marker for early detection of esophageal squamous cell carcinoma (ESCC). Our aim in this study was to evaluate the blood marker MMP-1 and its role in the diagnosis and prediction of disease progression and patient survival time of ESCC patients.

The MMP-1 serum levels was evaluated by enzyme-linked immunosorbent assay (ELISA) on 66 ESCC patients prior of any treatment (Endo-SCC-In-sito- 6-, Endo-SCC-Invasive-28-, Esophagectomy included-32 -patients) and 54 healthy controls. MMP-1 serum levels were compared to clinicopathological data of patients through statistical analyses.

The serum level of MMP-1 in patients showed no significantly higher in compared with the control group. No significant correlations were observed between MMP-1 levels and tumor differentiation grade, progression stage, depth of tumor invasion, involvement of lymph nodes, survival time, and location. Previous studies demonstrated increased levels of MMP-1 in gastrointestinal tract cancers, whereas our results did not show a statistically significant correlations. Many factors are involved in this result, including differences between the patients in our country compared with the rest of the world.

Corresponding Author: Mehran Gholamin (Immunology Research Center, BuAli Research Institute, Mashhad University of Medical Sciences, Mashhad, Iran)
Tumor Liquid Biopsy Of CETC – State Of The Art And New Developments

1. Ulrich Pachmann (Maintrac Laboratories And SIMFO Research Ltd, Bayreuth Germany)
2. Katharina Pachmann (Maintrac Laboratories And SIMFO Research Ltd, Bayreuth Germany)

Abstract

100 years of clinical knowledge, metastases are derived from tumor cells shed into the blood 1998 laser scanning microfluorimetry with cell relocation after e.g. secondary staining 2001 first generation tumor cell enrichment, admixture of blood cells and questionable quantitativity, prognostic factor only in metastatic disease 2006 first quantitative determination, distinction between live and dead cells, course of cells dynamics during therapy and over years during maintenance therapy, chemosensitivity 2011 different and partly debatable ways of purification, detection of mutations in single tumor cells, tumor stem cell surrogates 2014 first functional tumor stem cell test, single tumor cell analysis, determination of the AR-V7 splice variant and of immunologically relevant PD-L1 expression 2016 first fully automated quantitation including secondary stainings and chemosensitivity Direct quantitative cell counting yields control in adjuvant therapy, control in neo-adjuvant therapy and control in endocrine treatment (Gynecological / prostate cancers) Additional therapeutically relevant information comes from HER2/neu FISH via receptor blockade, from selective cell killing by cytotoxic agents (movie) as well as from detection of mutations enabling precision therapies (BRAF, KRAS, EGFR-Variants), from Immunological disarmament of the tumor by PD-1 Ligand blockade and from making use of the residual chemosensitivity of the Spheroids of tumor stem cells. No bigger support can be expected because “more specifically personalized” means less cash. The only interventional clinical study was designed not to have success. Despite of evidence of chances for saving money and time and quality of life for the patient there was no cost effectiveness study yet. Therefore attempts to attain official acknowledgement as standard tool failed hitherto, especially in clinically unclear situations (in Germany so called Nikolaus-sentence), and - in well-defined clinical situations without guideline recommendation. By using the circulating epithelial Tumor cells tumor diagnostics will become less laborious and tumor therapy will become more effective and more efficient. The live tumor cell is the measure of success and therefore is the gold standard.

Corresponding Author: Ulrich Pachmann (Maintrac Laboratories and SIMFO Research Ltd, Bayreuth Germany)
Diagnosis And Prevention Of Oral Cancer

Abstract

Oral cancer is the largest group of the head and neck cancer category. Worldwide incidence is exceeding 640,000 cases annually. It is estimated that in year 2016, 48,000 people in the US will be newly diagnosed with oral cancer. There are two distinct pathways by which most people come to oral cancer. One is through the use of tobacco and alcohol, a long term historic problem and cause, and the other is through exposure to the HPV virus. Other factors such as age, genetic susceptibility have an important role in developing oral cancer. If oral cancer is detected in early stage, prognosis will be significantly better than those detected in later stages. Therefore, we emphasize on prevention and early detection of oral cancer. In this presentation oral cancer epidemiology, pathology, risk factors, and prevention will be discussed.

Corresponding Author: Lida Radfar (Oklahoma University, USA)
Hereditary And Familial Colon Cancer

1. Mohammad Reza Farzanehfar (Mashhad University Of Medical Science, Mashhad, Iran)

Abstract

Between 2% to 5% of all colon cancers arise in the setting of well defined inherited syndromes, including Lynch syndrome, familial adenomatous polyposis, MUTYH-associated polyposis, and certain hamartomatous polyposis conditions. Each is associated with a high risk of colon cancer. In addition to the syndromes, up to one-third of colon cancers exhibit increased familial risk, likely related to inheritance. A number of less penetrant, but possibly more frequent susceptibility genes have been identified for this level of inheritance. Clarification of predisposing genes allows for accurate risk assessment and more precise screening approaches.

Corresponding Author: Mohammad Reza Farzanehfar (Mashhad University of Medical Science, Mashhad, Iran)
Minimally Invasive Surgery For Colorectal Cancer: Status And Technical Specifications.

1. Alireza Tavassoli (Mashad University Of Medical Sciences, Mashhad, Iran)

Abstract

In recent years, with the rapid progression of imaging equipment of laparoscope. New technology and ideas are constantly emerging. minimally invasive surgery is rapidly developing for management of patients with Colorectal cancer. And it has already been recommended by NCCN guideline. Laparoscopic colectomy (LC) became the standard of care for treating colon cancer in many centers. However, laparoscopic rectal cancer surgery still needs to wait for survival and recurrence rates of long-term follow-up data for verification. The feasibility, safety, and oncologic equivalence have been proven, and clinical usefulnesses have also been demonstrated over open approaches. Adaptations in laparoscopic technique were developed to increase use of minimally invasive surgery to further optimize patient outcomes. From these needs, single incision laparoscopic surgery (SILS), hand assisted laparoscopic surgery (HALS), and robotic assisted laparoscopic surgery (RALS) were applied to colorectal surgery. Each platform has unique costs and benefits, and similar outcomes when likened to each other in comparative studies. The goal of this paper is to review the history, technical specifications, current status, and evolution of the major minimally invasive techniques for colorectal cancer surgery.

Corresponding Author: Alireza Tavassoli (Mashad University of Medical Sciences, Mashhad, Iran)
Abstract

What are targeted cancer therapies? Targeted cancer therapies are drugs or other substances that block the growth and spread of cancer by interfering with specific molecules ("molecular targets") that are involved in the growth, progression, and spread of cancer. Breast cancer is a heterogeneous group of diseases that are clinically subdivided as hormone receptor-positive, HER2+, and triple-negative breast cancer, to guide therapeutic interventions. Agents that target estrogen receptor (ER) and HER2 are among the most successful cancer therapeutics. About 2 out of 3 breast cancers are hormone receptor-positive (ER-positive or PR-positive). For women with these cancers, treatment with hormone therapy is often helpful. Certain targeted therapy drugs can make hormone therapy even more effective, although these targeted drugs can also add to the side effects. A number of hormonal therapeutic agents have been approved for the treatment of ER+ disease, including tamoxifen, aromatase inhibitors (AIs), and fulvestrant. For about 1 in 5 women with breast cancer, the cancer cells have too much of a growth-promoting protein known as HER2/neu (or just HER2) on their surface. These cancers, known as HER2-positive breast cancers, tend to grow and spread more aggressively, but a number of drugs have been developed that target this protein. For HER2+ breast cancer, a growing number of HER2-targeted agents have become available, including trastuzumab, lapatinib, pertuzumab, and Ado-trastuzumab emtansine (Kadcyla, also known as TDM-1). However, these agents are ineffective for triple-negative breast cancers (TNBC). In addition, de novo or acquired resistance to these agents is common, despite the presence of ER and HER2. Novel therapeutic targets are being developed as treatment strategies for TNBC and resistant ER and HER2+ diseases.

Corresponding Author: Zahra Mozaheb (Mashhad University of Medical Science, Mashhad, Iran)
Intraoperative Radiotherapy For Breast Cancer: Yes Or Not?

1. Fatemeh Homaei Shandiz (Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Radiation therapy (RT) is an essential part of breast cancer treatment for local control. In recent years, a new approach has been gaining around in the treatment of breast cancer: "The less treatment is better" then radical surgical methods are being replaced by less-invasive, breast-conserving surgery (BCS). Such a trend is now also appearing in radiotherapy. Oncologists are moving away from a largely standardized treatment plan to risk-adapted individualized therapy like IORT which takes better account of the individual risk factors of the patients and provides significantly more treatment comfort. There are many questions that are discussed in this lecture.

Corresponding Author: Fatemeh Homaei Shandiz (Mashhad University of Medical Sciences, Mashhad, Iran)
Advances In The Treatment Of Epithelial Ovarian Cancer

1. Ali Shahriari-Ahmadi (Hazrat-E-Rasoul Hospital, Iran University For Medical Sciences, Iran)

Abstract

Epithelial ovarian cancer is a significant cause of morbidity and the commonest cause of death from gynecologic cancer. For most patients presenting with stage III-IV disease, first-line treatment consists of debulking surgery and chemotherapy with a platinum-taxane doublet, most commonly carboplatin and paclitaxel. Despite frequent complete responses to first-line treatment, relapse occurs in up to 85% of patients with stage III-IV disease, with a median time to relapse of 18 months. Approximately a third of these relapses occur within 6 months of first-line treatment, and the disease is then considered primary platinum resistant or refractory. Single-agent treatment with a nonplatinum drug is the preferred treatment option in this setting; commonly used drugs are pegylated liposomal doxorubicin (PLD), topotecan, and, more recently, weekly paclitaxel. However, outcomes are poor, with response rates ranging from 6% to 12% for PLD and topotecan, and 27% to 35% for weekly paclitaxel. Median progression-free survival (PFS) and overall survival (OS) typically range from 3 to 6 months and from 10 to 13 months, respectively, with some improvement in the latter in more recent studies, particularly those incorporating weekly paclitaxel. However, platinum resistance is generally not absolute. Response rates of 29% to 39% have been reported in small studies of platinum-based regimens such as cisplatin-etoposide, cisplatin-gemcitabine, or oxaliplatin-5-fluorouracil in platinum-resistant patients, suggesting that combination cisplatin or oxaliplatin containing chemotherapy can overcome “platinum resistance” in some patients. Consequently, efforts are being made to try new platinum-based combinations both in the platinum sensitive and the “platinum-resistant” setting. Few studies demonstrated a response rate of 41% for recurrent ovarian cancer, relapsing within 12 months of prior platinum treatment, using the 3-drug combination of epirubicin, cisplatin, and continuous infusional 5-fluorouracil. Because the delivery of infusional 5-fluorouracil requires an indwelling central venous catheter, the same group investigated the combination of epirubicin, carboplatin, and the oral fluoropyrimidine capecitabine (ECarboX) in patients with disease relapsing 6 months or more after prior platinum treatment. Eleven (61%) of 18 patients demonstrated either complete or partial radiologic response, implying considerable activity of this combination. However, hematologic toxicity was significant, necessitating frequent dose reductions and interruptions. These encouraging reports of preliminary activity have led to the frequent use of a modified ECarboX regimen in some institutions for fit patients with platinum-refractory or resistant relapse. Specifically, we resubstituted cisplatin for carboplatin to ameliorate haematologic toxicity, leading to a regimen of epirubicin, cisplatin, and capecitabine(ECX).

Corresponding Author: Ali Shahriari-Ahmadi (Hazrat-e-Rasoul Hospital, Iran University for Medical Sciences, Iran)
Intrapitoneal Chemotherapy

1. Omid Rezaie (Zabol Medical University, Zabol, Iran)

Abstract

The most common route of ovarian cancer spread is within the peritoneal cavity. The rationale for administering chemotherapy directly into the peritoneal cavity is supported by preclinical, pharmacokinetic, and pharmacodynamics data. Compared with intravenous (IV) treatment, intraperitoneal (IP) administration permits a several-fold increase in drug concentration to be achieved within the abdominal cavity. In addition, clinical trials have demonstrated a survival advantage to the incorporation of IP treatment in the upfront management of ovarian cancer. Based on available clinical data, intraperitoneal (IP) chemotherapy may be most useful in women with optimally debulked (to ≤1.0 cm) stage III epithelial ovarian cancer (EOC). Some patients with earlier-stage disease may also be candidates. Those patients who have been cytoreduced to no gross residual disease seem to have the greatest benefit from IP chemotherapy and improved overall survival. Furthermore, some experts also utilize IP chemotherapy for women treated with neoadjuvant chemotherapy who undergo an optimal interval cytoreduction.

Corresponding Author: Omid Rezaie (Zabol medical university, Zabol, Iran)
Regulatory Based Target Therapy In Cancer

Abstract

Cancer is the second cause of death after cardiovascular diseases worldwide. It is known as a complex disease caused by the interplay of multiple factors involved in its initiation, growth and progression. The relationship between the cancer and the immune system backs to many years particularly with reference to immune surveillance theory by Bernet in 1957. This conceptual philosophy of cancer paradigm in this theory has been categorized in three steps, including Eradication, Equilibrium and Escape. In the first phase, the tumor in a dynamic system is generating throughout the life but this is the immune system which recognizes the tumor and eradicates it. The second phase discusses a period of consistence interaction between tumor cells and the immune cells, a co-existence period that no signs and symptoms of cancer are detected. The fate of the tumor in this phase is depending on the quality and quantity of the host immune key genes and proteins. In the last phase the chronic pressure of the host immune response on the tumor results in immune selection of a highly replicative and progressive version of tumor cells which this may end-up with tumor cells escape and metastasis. Apart from the chemo-radiation therapy and surgery, advanced cell and gene therapy have provided much hope for the better treatment of cancer. In addition, therapeutical antibodies have been flooded to the market some with high efficacy for the treatment of solid malignancies. The new generation of therapeutic antibodies has been designed in a way to block what we know as the immune check-point inhibitor. The concept of immune checkpoint inhibitor in recent years has generated hopes for the treatment of some uncured cancer cases like some types of lung and melanoma cancers. In this presentation, the concept of regulatory based target therapy in cancer will be discussed. The check point control of the Immune suppression induced by tumor and current immune therapies based on regulatory mechanisms will be reviewed.

Corresponding Author: Abbas Ghaderi (Director Shiraz Institute for Cancer Research, Shiraz University of Medical Sciences, Shiraz, Iran)
Characterizing Immune Landscapes In Human And Murine Non-Small Cell Lung Cancers To Guide Biomarker Discovery

1. Sima Zacharek (Belfer Center For Applied Cancer Science, Department Of Medical Oncology, Lowe Center For Thoracic Oncology, Dana-Farber Cancer Institute; Harvard Medical School, Boston, MA, USA)
2. Patrick Lizzio (Belfer Center For Applied Cancer Science, Department Of Medical Oncology, Lowe Center For Thoracic Oncology, Dana-Farber Cancer Institute; Harvard Medical School, Boston, MA, USA)
3. Elena Ivanova (Belfer Center For Applied Cancer Science, Department Of Medical Oncology, Lowe Center For Thoracic Oncology, Dana-Farber Cancer Institute; Harvard Medical School, Boston, MA, USA)
4. Hongye Liu (Belfer Center For Applied Cancer Science, Department Of Medical Oncology, Lowe Center For Thoracic Oncology, Dana-Farber Cancer Institute; Harvard Medical School, Boston, MA, USA)
5. Samuel Regan (Belfer Center For Applied Cancer Science, Department Of Medical Oncology, Lowe Center For Thoracic Oncology, Dana-Farber Cancer Institute; Harvard Medical School, Boston, MA, USA)
6. Kristin Depeaux (Belfer Center For Applied Cancer Science, Department Of Medical Oncology, Lowe Center For Thoracic Oncology, Dana-Farber Cancer Institute; Harvard Medical School, Boston, MA, USA)
7. Dyane Bailey (Belfer Center For Applied Cancer Science, Department Of Medical Oncology, Lowe Center For Thoracic Oncology, Dana-Farber Cancer Institute; Harvard Medical School, Boston, MA, USA)
8. Martha Gowaski (Belfer Center For Applied Cancer Science, Department Of Medical Oncology, Lowe Center For Thoracic Oncology, Dana-Farber Cancer Institute; Harvard Medical School, Boston, MA, USA)
9. Mari Karaguchi (Belfer Center For Applied Cancer Science, Department Of Medical Oncology, Lowe Center For Thoracic Oncology, Dana-Farber Cancer Institute; Harvard Medical School, Boston, MA, USA)
10. Lynette Sholl (Belfer Center For Applied Cancer Science, Department Of Medical Oncology, Lowe Center For Thoracic Oncology, Dana-Farber Cancer Institute; Harvard Medical School, Boston, MA, USA)
11. Robert Jones (Belfer Center For Applied Cancer Science, Department Of Medical Oncology, Lowe Center For Thoracic Oncology, Dana-Farber Cancer Institute; Harvard Medical School, Boston, MA, USA)
12. Lauren Keogh (Belfer Center For Applied Cancer Science, Department Of Medical Oncology, Lowe Center For Thoracic Oncology, Dana-Farber Cancer Institute; Harvard Medical School, Boston, MA, USA)
13. Sangeetha Palakurthi (Belfer Center For Applied Cancer Science, Department Of Medical Oncology, Lowe Center For Thoracic Oncology, Dana-Farber Cancer Institute; Harvard Medical School, Boston, MA, USA)
14. Jessie English (Belfer Center For Applied Cancer Science, Department Of Medical Oncology, Lowe Center For Thoracic Oncology, Dana-Farber Cancer Institute; Harvard Medical School, Boston, MA, USA)
15. Pasi Jänne (Belfer Center For Applied Cancer Science, Department Of Medical Oncology, Lowe Center For Thoracic Oncology, Dana-Farber Cancer Institute; Harvard Medical School, Boston, MA, USA)
16. Kwok-Kin Wong (Belfer Center For Applied Cancer Science, Department Of Medical Oncology, Lowe Center For Thoracic Oncology, Dana-Farber Cancer Institute; Harvard Medical School, Boston, MA, USA)
17. Mark Bittinger (Belfer Center For Applied Cancer Science, Department Of Medical Oncology, Lowe Center For Thoracic Oncology, Dana-Farber Cancer Institute; Harvard Medical School, Boston, MA, USA)

Abstract

Lung cancers continue to rank among the deadliest malignancies worldwide despite promising new therapeutic advances. Recently approved options for the most common type, Non-Small Cell Lung Cancer (NSCLC) now include the immune checkpoint inhibitors nivolumab and pembrolizumab. While these PD-1 (programmed cell death protein-1)-blocking agents have been shown to extend NSCLC patient survival, currently only a subset of patients benefit from these immunotherapies. Tumor and/or immune cell expression of PD-ligand 1 (PD-L1) may help guide patient selection for anti-PD1 therapies, but does not fully correlate with clinical outcome. Improving our understanding of biomarkers predictive of response and resistance to such immunotherapies could improve patient selection criteria and their clinical response rates. Alterations in oncogenic drivers of NSCLCs can predict response to targeted therapies but whether they can also serve as predictive biomarkers for immunotherapies remains unclear. As the immune composition of the tumor microenvironment has been shown to correlate with response to immunotherapies in other cancer indications (e.g. Tumeh et al., 2014), characterizing the immune landscape across different NSCLC genetic subtypes could clarify whether specific alterations in EGFR, K-Ras, FGFR, or other oncogenes may help to stratify patients likely to respond to immunotherapies, as well as suggest additional biomarkers of response beyond PD-L1. We therefore are profiling the immune landscape across 50+ human NSCLC cases by flow cytometry and are integrating this analysis with clinical and...
histopathologic characteristics, next generation sequencing, mRNA expression, and immunohistochemistry. We are also immuno-profiling several different established autochthonous genetically engineered mouse models (GEMMs) of NSCLC, including those driven by EGFR-, K-Ras-, or FGFR activating mutations. These GEMMs share many features observed in the immune profiles of genetically analogous human lung adenocarcinomas, particularly at the levels of lymphocyte infiltration and T cell exhaustion marker expression. By evaluating the immune landscapes of both human and murine tumors, we are clarifying not only the associations between defined genetic alterations and immune phenotypes, but also the specific GEMMs that most closely recapitulate the complex microenvironmental features of genetically analogous human NSCLC cases. These efforts are facilitating the further advancement of NSCLC GEMMs for improved pre-clinical evaluations of immunotherapies, and the rationale for new combination therapies.

**Corresponding Author:** Sima Zacharek (Belfer Center for Applied Cancer Science, Department of Medical Oncology, Lowe Center for Thoracic Oncology, Dana-Farber Cancer Institute; Harvard Medical School, Boston, MA, USA)
Poster Presentations
Abstract

In this article, γ-Fe2O3 magnetic nanoparticles (maghemite) were prepared by a coprecipitation approach. Oleic acid, a monounsaturated fatty acid were used as the capping and stabilizing agent during the synthesis of the magnetic nanoparticles. The nanoparticles were characterized using powder x-ray diffraction (PXRD) measurement, field emission scanning electron microscopy (FE-SEM), fourier transform infrared spectra (FTIR), and vibrating sample magnetometer (VSM). The crystalline size of γ-Fe2O3 nanoparticles was achieved in the range between 16.2 and 26.8 nm. The FE-SEM demonstrated the regular spheres of γ-Fe2O3 nanoparticles. The obtained maghemite nanoparticles were coated with oleic acid demonstrating by FTIR experiment. The resulted nanoparticles showed superparamagnetic properties (~52 emu/g) even after coating with oleic acid which make them appropriate candidates for theranostic application in future studies.

Corresponding Author: Zahra Meshkat (Women's Health Research Center, Mashhad University of Medical Sciences, Mashhad, Iran)
PMS2 Novel Mutation In Breast Cancer: A Case Report

Abstract

Background: Breast cancer is the second most commonly diagnosed cancer in women. In many cases of familial breast cancer the genetic basis for the disease and the mechanism of inheritance are unclear. Breast cancer from mismatch repair (MMR) gene mutation carriers resembles common breast carcinoma in many respects. The PMS2 gene encodes a protein that plays an important role in repairing DNA. Detection of germline mutation in PMS2 is significantly complicated by the presence of numerous pseudogenes. Methods and Results: We present a woman with familial breast cancer. The pedigree showed the same cases in three generation. Using whole exome sequencing the heterozygous variant c.2350G>A (p.Asp784Asn) on gene PMS2 gene has been found. To validate this novel mutation in probands’ healthy daughter, we used a modified long-range PCR method to evaluate PMS2, thus pseudogene interference has been avoided. Sanger sequencing of PMS2 gene showed no mutation in her daughter. Conclusion: This novel mutation has not been reported before. The clinical outcome of PMS2 germline mutations are poorly understood compared with other MMR gene mutations. The frequency of this mutation in normal population is very low. Bioinformatic analysis of the mutation by PolyPhen2 and SIFT showed that the protein will be damaged. This amino acid change (Asp to Asn) may affect the function of PMS2.

Corresponding Author: Ehsan Ghayoor Karimiani (Department of molecular genetics, Hope Generation Genetic Polyclinic, Mashhad, Iran; Honorary research associate, University of Manchester, UK)
Determining Of Total Data Elements Required In Multi-Disciplinary Breast Cancer Researches

1. Mohsen Goli (Cancer Informatics Department, Breast Cancer Research Center, ACECR, Tehran, Iran.)
2. Alireza Atashi (Cancer Informatics Department, Breast Cancer Research Center, ACECR, Tehran, Iran.)
3. Najme Nazeri (Cancer Informatics Department, Breast Cancer Research Center, ACECR, Tehran, Iran.)
4. Sara Dorri (Cancer Informatics Department, Breast Cancer Research Center, ACECR, Tehran, Iran.)

Abstract

Different disciplines in multiple research centers need to collect a large amount of various data, which commonly spends a lot of cost and time. Principled collection of needed data in each field will increase speed and precision. Having the importance of registries and data quality, in this study, the researchers tried to create a maximum comprehensive dataset for multi-disciplinary breast cancer research field. First, the scientific literature and published studies was systematically reviewed and their related data elements were extracted. The results were presented to specialist’s in different disciplines to have their comments. The next phase was the survey of surveys of experts in a three-step Delphi which had an expert panel in the last step. Finally, a combination of scientific experts and scientific literature review was used. In the first step, 194 data element in 11 specialized breast cancer-related fields formulation were extracted and sent to experts. In the first Delphi step the experts added 37 new data elements, 11 elements were duplicates and not particularly helpful. Finally, the maximum data set was confirmed by members of the Expert Panel with 220 independent data elements in 11 specialized multidisciplinary fields in breast cancer. The results consensused with Delphi method and Expert Panel, was more useful for the breast cancer research center because there were collected for their professionality and usefulness. Using the results of this study will help to increase efficiency in similar breast cancer research centers.

Corresponding Author: Ebrahim Abbasi (Cancer Informatics Department, Breast Cancer Research Center, ACECR, Tehran, Iran.)
Preparation Of Polyoxometalat / Geraphen Nano Catalysts For The Synthesis Of Anticancer Drugs

1. Sina Shakoori (Department Of Chemistry, Neyshabur Branch, Islamic Azad University, Neyshabur, Iran)

Abstract

Geraphen is newest of carbon geraphit family. In 1986 Bohm and co workers called single layer of graphite to geraphen. Attend Functional group in side of graphen give hydrophile property anad cause of good break up in water and organic salutions. Target of this research is synthesis of nano catyliste of polyoxometalat to nano geraphen oxide for use to different drug synthesis like anticancer druge as if in this research we chose Doxorubicin. In this regard for synthesis of geraphene oxide we use to Homer modified. In this way, geraphite powder use to source to first material to generation of geraphen oxide. One of the most usable of hetro poly ions is keggin with different hetro atoms as if have Many advantages as catalyst. In this research keggin polyoxometalat substituted with Cr for [PW11CrO39] nH2O, Synthesized and characterized and their catalytic role in synthesis of Doxorubicin were studied. Doxorubicin with Adriamycin brand is from group of antibiotics/antineoplastic drugs that has wide applications. To verify of synthesis of particles Morphology using scanning electron microscopy. The results of these studies show to us, nano particels of polyoxometalat is Evenly on the graphene film and Maximum speed and best reaction in time 25min and tempreater in 40c cause to the unique structure of nanocomposites polyoxometalat / geraphen, special capacity that can be used as nano-catalysts for the synthesis of new drugs to be used. In summary it can be said that the approach to the use of nano graphene synthesis of new pharmaceutical compounds may be associated with more favorable results from any direction.

Corresponding Author: alireza motavalizadeh kakhki (Department of Chemistry, Neyshabur Branch, Islamic Azad University, Neyshabur, Iran)
Prevalence And Incidence Of Cancer In Patients Admitted To 22 Bahman Hospital Mashhad From 1392 To 1394

1. Omid Nejati (22 Bahman Hospital - Medical And Pathological Laboratory - Islamic Azad University Of Mashhad - Iran)
2. Bahieh Zarif Zakerian (Assistant Professor Of Pathology, Faculty Of Medicine - Islamic Azad University Of Mashhad - Iran)

Abstract

In a recent descriptive study of patients admitted to 22 Bahman hospital, the 1770 of people had undergone surgery for different diagnoses, Their samples were sent to laboratory for pathological evaluation. The 116 cases had cancer (a prevalence of 6.55% in the 1770 cases) Types of diagnosed cancers in order of frequency include ; skin cancer 29 cases (prevalence rate of 25%), bladder cancer 19 cases (prevalence rate of 16.4%), breast cancer 16 cases (prevalence rate of 14%), prostate cancer 11 cases (prevalence rate of 9.5%), gastrointestinal tract cancer (esophagus, sigmoid, gallbladder, stomach, colon, rectum) 9 cases (prevalence rate of 7.7%), kidney cancer (nephroblastoma, renal pelvis carcinoma, Wilm's tumor) 7 cases (prevalence rate of 6%), lymph node cancer 7 cases (prevalence rate of 6%), Uterus cancer 5 cases (prevalence rate of 4.3%), thyroid cancer 5 cases (prevalence rate of 4.3%), lung cancer 5 case( prevalence rate of 4.3%), testis cancer 3 cases (prevalence rate of 2.5 %). In this study of 116 cancer cases were 67 men (58%) and 49 women (42%). The most common organs involved by cancers were skin, bladder, breast and prostate.

Corresponding Author: Alireza rezaei (Assistant Professor of Pathology, faculty of Medicine - Islamic Azad University of Mashhad - Iran)
The Role Of Curcumin In The Treatment Of Breast Cancer

Abstract

Breast cancer is the most common cancer in women worldwide. It has been estimated that the major cause of cancer-related deaths is resulted from failure of cancer chemotherapy. A number of herbal medicinal products were shown to have antitumor effects. Recently, phytochemicals as anticancer agents have been clinically used worldwide. Many studies have shown the effects of Curcumin as a phytochemical-based anticancer and antitumor agent on different cancers including breast cancer. Curcumin is derived from the herbaceous plant, Curcuma longa. This plant is usually found in India, Southeast Asia, China and other tropical Asian countries. Turmeric is a yellow spice derived from the rhizomes of curcuma longa. The yellow color of turmeric is due to Curcuminoids known as fat-soluble, polyphenolic pigments which include Curcumin, Demethoxy Curcumin, and Bisdemethoxy Curcumin. The first major Curcuminoid is Curcumin. The findings of many studies show that Curcumin can positively influence the expression and function of multidrug resistance (MDR) proteins such as multidrug resistance-associated protein (MRP), BCRP, and P-glycoprotein (P-gp). A number of evidence show that Curcumin increases drug sensitivity by inhibiting the expression and function of ATP-binding cassette efflux (ABC) transporters and ATPase activity (26). HER2 is an important oncoprotein which is expressed at very high levels in 15% of breast cancer cases. Curcumin significantly reduces HER2 levels. Besides, development of breast cancer is associated with dysfunction of Wnt pathway of β-catenin. Curcumin has been shown to inhibit the expression of β-catenin protein. Thus, the use of Curcumin as an original composition for designing novel Curcumin analogues as new antitumor drugs is strongly suggested.

Corresponding Author: Maryam Karimi (Department Of Biochemistry, Faculty Of Medicine, Ahvaz Jundishapur University Of Medical Sciences, Ahvaz, IR Iran)
Review The Most Common Diseases And Reasons For Visiting To Section Oncology Hospital Doctor Sheikh Mashhad In He First Quarter Of 95

1. Sara Jahangiri (Department Of Internal Medicine And Surgery, Medical Doctor Sheikh Educational Research Center, Mashhad, Iran.)

Abstract

Although childhood cancers are uncommon; but the second leading cause of death in children under 14 years, and less than 1 percent of all cancers form. The aim of this study was to evaluate various cancers in children. This study was observational - descriptive and cross-sectional was done. In this study epidemiology; types of children's cancer at the Oncology hospital doctor sheikh mashhad referred in the first quarter and treatment; were reviewed. Information extracted from the patient and was questionnaires. The data, using software SPSS16 were analyzed. In this study, 419 children were examined of which 99/72% male and 28/0% were girls. In this study, the most common reason for referral to; patients who were admitted to chemotherapy, patients presenting with fever, patients with ALL, patients diagnosed with thrombocytopenia, patients with neutropenia and patients diagnosed with ITP Formed. In our study of childhood cancer in males more than females And given the high incidence of cancer in children Parents In the field of prevention and screening During pregnancy As well as empower physicians and the public In the context of early detection can be useful.

Corresponding Author: Sara Jahangiri (Department of Internal Medicine and Surgery, Medical Doctor Sheikh Educational Research Center, Mashhad, Iran.)
The Kruppel-like factor (KLFs) family of gene regulatory proteins are transcription factors implicated in the regulation of a wide range of cellular processes, including proliferation, apoptosis, differentiation, inflammation, migration, and tumor formation. Kruppel-like factor 4 (KLF4) is highly expressed in more than 70% of breast cancers and functions as an oncogene. However, an exact mechanism by which KLF4 enhances tumorigenesis of breast cancer remains unknown. Down regulation of KLF4 in colon adenomas, gastric cancer, intestinal adenomas, esophageal cancer, prostate cancer, and lung cancer may contribute to cellular hyperproliferation and malignant transformation, which is consistent with its role in cell cycle arrest and growth inhibition. However, high levels of KLF4 expression are also reported in primary breast ductal carcinoma and oral squamous carcinoma. So our findings have indeed pointed out the importance of the evaluation of conditions which can cause the instability of this protein due to prevent the progression of cancers related to KLF4. To evaluate this process, we used some spectroscopic techniques such as Circular dichroism (CD), Three-Dimesntional (3D) Fluorescence Spectroscopy 2ml of %0.01 KLF4 in KH2PO4 buffer in various amounts of pH and ionic strengths was added and the ranges were measured. The 3D spectra and contour maps of the KLF4 appears some peaks that each one shows some features of the protein structure; The results shows that in all amounts of pH, the ranges of Δλ in both peaks 1 and 2 are the same, indicates that transition of protein chromophors had no modification. The most measure of fluorescence intensity of peak 1 and 2 was related to ethanol-distilled water 50% solution that shows structural changes in protein that causes chromophor transitions to more polar environments and Tyr and Trp residues are involved to solvent. But the most reduction of fluorescence intensity of peaks 1 and 2 was related to ethanol-distilled water 100% that implicates chromophor transitions to more homophobic environments In this study, secondary structural changes of protein in different environments had been studied by CD, which show the dependence of protein to pH, which at pH=7.4 protein maintains it's secondary structure better and from pH=7.4 to the higher and lower pH, secondary structure will experience many changes.

**Corresponding Author:** Negin Alavi (Department of Biology, Faculty of Sciences, Mashhad Branch, Islamic Azad University, Mashhad, Iran)
Application Of Umbilical Cord Blood Stem Cells As A Novel Therapeutic Approach In Cancer

Abstract

Cancer is a group of diseases caused by abnormal growth of body cells. Cancer is known as crab around the world because of they spread to the masses and sometimes migrate to different parts of the body that is called metastasis. One way to treatment of cancerous tumor is cell therapy by using stem cells. Umbilical Cord Blood Stem Cells (UCB-SCs) have been studied widely and proved as effective transplantable cell resources in cellular therapies. UCB-SCs have many advantages over other stem cells, because they are the youngest cells in the body. In addition, availability and high capacity of differentiation are considered as their exclusive and impressive characteristics. For example Leukemia is a cancer that starts from bone marrow and affects blood cells and causes the formation of abnormal white blood cells. In cell therapy for leukemia treatment by using umbilical cord blood, stem cells are replaced the patient's bone marrow. But to prevent transplant rejection and risks, both donor and recipient should be evaluated in terms of antigenic. Application of cord blood stem cells in the laboratory and injection into the bone marrow has been successfully. Also Studies have shown that UCB-SCs secrete a cytokine called IFN-b (UCMS-IFN-b) that inhibits the growth of cancer cells by induction of apoptosis. Apoptosis in cancer cells is a purposeful and useful process to eliminate cancer cells. Several studies concluded that Umbilical Cord Blood Stem Cells (UCB -SCs) are novel resources of stem cells for the treatment of cancer. These stem cells can prevent the growth of cancerous tumors Cell through two important ways: Cell transplantation and replacement and Induction of apoptosis by secreting specific factors.

Corresponding Author: Fahimeh Mobaraki (Anatomical Sciences and Cell Biology, Student Research Committee, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran)
Avicenna’s Views On Cancer And Nutrition

1. Shokouhsadat Hamedi (Department Of Persian Pharmacy, School Of Persian And Complementary Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Masoud Honavar (College Of Food Science & Technology, Tehran Science And Research Branch, Islamic Azad University, Tehran, Iran)

Abstract

Cancer is one of the three main causes of mortality in the word whose prevalence is being increased. The reviewing of Iranian traditional medicine texts specially Cannon determines that preventive rules, which named as six essential rules (Sitteh-e-Zarurieah) are abundantly found, including all identified cancer-related risk factors. One of these rules is nutrition. Avicenna has hypothesized cancer as a disease associated with abnormal black bile humor which is very hard to be diagnosed at early stages. In order to prevention of cancer, Avicenna has proposed that bad black bile should be controlled by adding some additives and spices in foods or eating some vegetables that these days have been proved that they are anticancer herbs. The most additive in Iranian food include: Curcumin in Turmeric have strong antioxidant effect that can help prevent the proliferation of cancer cells. Nigella Sativa is found in many Iranian foods and it has a special place in Iranian traditional medicine. It is strong anti-tumor and anti-oxidant, it increases cellular immune (T cells and B cell and activated macrophages) it also increases activity of NK (natural killer). Garlic: Garlic contains allicin and alial have the inhibitory effects of free radicals and can prevent the occurrence of many types of cancers including lung cancer. Also eating more dark green leafy vegetables such as spinach leaves containing chlorophyll and lutein, have antioxidant properties and the can prevent incidence of cancer, especially liver cancer. Conclusion: As you can see, most of the recommended herbs for traditional medicine that is often added to foods have anti-cancer properties. Although the mechanism of action of these herbs in traditional medicine text are very different from pharmacological effects of these plants, but they can be confirmed traditional food and diet appropriate and benefits.

Corresponding Author: Shokouhsadat Hamedi (Department of Persian Pharmacy, School of Persian and Complementary Medicine, Mashhad University of Medical Sciences, Mashhad, Iran)
Application Of Aptamers In Treatment And Diagnosis Of Leukemia

1. Atefeh Arab (Department Of Pharmaceutical Biotechnology, School Of Pharmacy, Mashhad University Of Medical Sciences, Mashhad, Iran.)
2. Rezvan Yazdian - Robati1 (Department Of Pharmaceutical Biotechnology, School Of Pharmacy, Mashhad University Of Medical Sciences, Mashhad, Iran.)
3. Khalil Abnous (Pharmaceutical Research Center, School Of Pharmacy, Mashhad University Of Medical Sciences, Mashhad, Iran.)
4. Seyed Mohammad Taghdisi (Targeted Drug Delivery Research Center, School Of Pharmacy, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Leukemia is a cancer of blood cells and bone marrow, leading to death in many patients mainly in children. Chemotherapy and bone marrow transplantation are the main approaches for leukemia therapy. However, these therapeutic regimens for leukemia show a rather narrow spectrum as compared with those are available for solid tumors. Over the last several years, aptamers generated by SELEX (Systematic evolution of ligands by exponential enrichment) method, have quickly become a new class of targeting ligands for drug delivery applications and recently have been widely exploited in different biomedical applications, due to several potent properties such as high binding affinity and selectivity, low or no immunogenicity and toxicity, low cost and thermal stability. In this review, we presented in details about aptamers involved in targeting, and treatment of leukemia. Moreover, some analytical approaches such as electrochemical and optical aptasensors were introduced for detection and diagnosis of leukemia. Finally, we discussed about the directions and challenges of aptamer application in this field. In conclusion, in this review article, the advantages and applications of aptamers against leukemia have been reported through descriptions of several research projects. Over the last decades, different aptamers have been selected against leukemia such as sgc8 aptamer which could specifically detect and internalized into ALL cells or AS1411 aptamer, a therapeutic aptamer, which is currently undergoing clinical trials for treating ALL.

Corresponding Author: Seyed Mohammad Taghdisi (Targeted Drug Delivery Research Center, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran)
Epidemiological Analysis In Neuroblastoma Patients In Mashhad From 1387-1394

1. Katayoon Dadkhah (Department Of Biology, Faculty Of Sciences, Gonbad Kavous University, Golestan, Iran)
2. Sakineh Alijanpour (Department Of Animal Biology, School Of Biology, College Of Science, University Of Tehran, Tehran, Iran)
3. Ali Ghasemi (Department Of Pediatric Oncology-Hematology, School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
4. Hossein Sabouri (Department Of Plant Production, College Of Agriculture And Natural Resource University Of Gonbad, Gonbad, Iran)

Abstract

Neuroblastoma (NB) is the third most common malignancy in the pediatric age group, with an incidence of about 650 cases per year in the U.S. and 100 cases per year in the UK following leukemia and brain tumors. Its etiology is not clear, however, the great majority of them are sporadic, and about 1-2% are familial. Neuroblastoma comprises 6-10% of all childhood cancers, and 15% of cancer deaths in children. The annual mortality rate is 10 per million children in the 0- to 4-year-old age group, and 4 per million in the 4- to 9-year old age group. The highest incidence reported in the first year of life, and some cases are congenital. The age range is broad, including older children and adults, but only 10% of cases occur in people older than 5 years of age. This study is the a retrospective, non-randomized analytic research on NB cases referred to Shykh Children Hospital in Mashhad, Khorasan Razavi from 1387-1394 in order to collect regional information about NB cases in North-East of Iran. The information of patients referred to this hospital gathered and analyzed. The age of patients ranged from 1 month to 15 years old with the average of 19 month, and the male/female ratio was 31/24. About 43% of subjects (24/55) were children between 1-18 month and 22%(12/55) are older than 18 month. Parents of 12 patients (21%) were related, and 17 patients (31%) weren't from consanguineous marriages. In 27 patients (49%) tumors were arose from the abdomen and 12 patients (22%) had tumors arisen from adrenal, the rest (29%) were in thorax, neck, brain and spinal cord. History of malignancy in family reported in 15 patients (27%), and 11 patients (20%) didn't know of any malignant case in their family.

Corresponding Author: Hossein Ayatolahi (Cancer Molecular Pathology Research Center, University of Medical Sciences, Mashhad, Iran)
Serial Sphere Formation, A Method For Enrichment Of Gastric Cancer Stem Cells; An Experience On AGS Cell Line

1. Mahdieh Bakhshi (Department Of Molecular Medicine, Faculty Of Advanced Medical Technologies, Golestan University Of Medical Sciences, Gorgan, Iran.)
2. Asadi J (Department Of Molecular Medicine, Faculty Of Advanced Medical Technologies, Golestan University Of Medical Sciences, Gorgan, Iran.)
3. Ebrahimi M (Department Of Stem Cells And Developmental Biology At Haematopoetic And Cancer Stem Cell Research Center, Royan Institute For Stem Cell Biology And Technology, Tehran, Iran)

Abstract

Gastric cancer is one of the most principal causes of cancer-related death worldwide. To overcome therapeutic challenges, new investigations about cancer pathogenesis have been tended to “cancer stem cells” (CSCs) as previously neglected targets. Identification and characterization of CSCs, could help to develop novel therapeutic strategies for gastric cancer. Since the specific CSC makers have not been identified in many malignancies including gastric cancer, functional approaches, including spheroid forming assay, have been taken into consideration. This method relies on functional properties of CSCs, including: self-renewal, proliferation, growing under anchorage independent and poor environmental conditions. Tumor cells from AGS cell line, transferred into the low-attached plates and cultured in low cellular density serum-free medium supplemented by growth factors: EGF, b-FGF and B27 to form spheres. Serial suspension cultures were performed for enrichment of the gastric cancer stem cells by passaging sphere derived cells into the new plates at the same condition each 8 days. After passage 3, cells were removed for characterization by colonogenic assay, drug resistance to cisplatin and docetaxel by MTS assay. Putative stemness markers: CD44, CD24 and CD326 were measured using flow cytometry; and SOX2, OCT4, KLF-4, NANOG and C-MYC expression evaluated by qRT-PCR. sphere cells in comparison with parental cells were more clonogenic (p<0.01), more chemo-resistant to cisplatin and docetaxel (p<0.05). The stemness genes were upregulated (p<0.05) and MFI(mean fluorescent intensity index) of CD44 and EPCAM, was also higher in sphere group. Our results demonstrated that serial sphere formation assay could be a beneficial model for enrichment of the CSCs. This finding supports the concept of “internal hierarchial heterogeneity” of cancers even in some cancer cell lines as well as AGS; however it needs to be confirmed by further techniques such as in vivo tumorigenicity.

Corresponding Author: Asadi J (Department of Molecular Medicine, Faculty of Advanced Medical Technologies, Golestan University of Medical Sciences, Gorgan, Iran.)
Exploiting Live Cell Imaging Techniques For Early Cancer Diagnosis

1. Maryam Sharifmansouri (Cell And Molecular Biology Group, Faculty Of Science, Ferdowsi University Of Mashhad, Iran)

Abstract

Early cancer diagnosis strategies is an urgent need because of high incidence, mortality and cost effectiveness of treatment of cancer. Cancer researchers are increasingly looking for techniques that help to early diagnosis of cancer. Providing the most accurate analysis of tissue, biopsy is the only way to make a definitive cancer diagnosis for most types of cancer. However, Image processing techniques, without the need for invasive procedures such as biopsies or even surgery, are growing as an alternative which allows earlier detection of abnormalities and treatment monitoring. Loss of important spatial-temporal information of cells and a high illumination intensity and long exposure time are limitations associated with conventional imaging of fixed cells and tissues; however, these must be avoided when imaging living cells and consider a compromise between obtaining image quality and maintaining healthy cells. Fluorescently labeled proteins such as fluorescent protein tags and live cell dyes provide a favorable tool for live cells to interrogate virtually any cellular process for instance; dynamic morphology of a cell, track cell movement on a surface, and measure quantities or localization patterns of fluorescently labeled molecules such as proteins and RNAs applied as molecular imaging probes in exosome tracking by streaming digital microscopic images. High-throughput expression techniques genetically can provide distinctive molecular characteristics of malignant cells by comparing expression profiles of malignant and non-tumoral cells. Molecular imaging probes target and highlight these key biomolecules by the selective depiction of cellular properties and their microenvironments characteristic for the malignant state and so, have the potential roles in the different aspect of oncologic practice, including early cancer detection, diagnosis, staging, and personalized treatment, treatment monitoring and follow-up.

Corresponding Author: Maryam Sharifmansouri (Cell and Molecular biology group, Faculty of science, Ferdowsi University of Mashhad, Iran)
The Relationship Between Emotional Intelligence, Spiritual Intelligence And Quality Of Life In Cancer Patients

1. Omolbanin Khaghani (Department Of Psychology, University Of Sistan And Baluchestan, Iran)
2. Mehrdad Mazaheri (Department Of Psychology, Ferdowsi University Of Mashhad; University Of Sistan And Baluchestan, Iran.)
3. Amir Karami (Department Of Psychology, University Of Sistan And Baluchestan, Iran)

Abstract

The main aim of the current study was to investigate the relationship between emotional intelligence, spiritual intelligence and quality of life in cancer patients. A voluntary sample of the 90 women cancer patients were asked to complete the emotional intelligence bar-on, spiritual intelligence king and the quality of life EORTC QLQ questionnaires. Our results indicated a negative significant relation between emotional intelligence and quality of life. Moreover a significant relationship was found for some spiritual intelligence dimensions and quality of life.

Corresponding Author: Mehrdad Mazaheri (Department of psychology, Ferdowsi University of Mashhad; University of Sistan and Baluchestan, Iran.)
Wnt5a: A Key Regulator Of Inflammation

Abstract

Wnt proteins are a family of glycoproteins which upon binding to a member of G-protein coupled receptor, Frizzled (Fz), activates a scaffolding protein Disheveled (Dvl) to elicit their intracellular signaling functions. Wnt signaling is classified to canonical (βcatenin-dependent) and non-canonical (βcatenin-independent) pathways. Wnt5a, a member of Wnt proteins, is consistently up-regulated by endotoxin (LPS) and interferon (INF)-γ via Toll-like receptor (TLR) activation. Through up-regulation of inflammatory cytokines including IL-1β, IL-6, IL-8, IL-1α and activation of inflammatory signaling pathways such as nuclear factor-κB (NF-κB) and JNK, Wnt5a elicits proinflammatory responses in cells. Over the last decades, Wnt5a has been implicated in a variety of inflammatory diseases including atherosclerosis, obesity, sepsis, rheumatoid arthritis, psoriasis, melanoma, and tuberculosis. The elevated levels of Wnt5a in inflammatory diseases support the hypothesis that this protein could be a prognostic marker of inflammation and its suppression either through inhibition of upstream signaling pathways or through Wnt signaling antagonists is an attractive target for therapeutic intervention in inflammatory disorders.

Corresponding Author: Mehran Pashirzad (Department of Medical Biochemistry, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.)
The Effect Of Aerobic Training On Static Balance And Eye-Hand Coordination In Children With Cancer

1. Ezzat Khodashenas (Department Of Pediatrics, Faculty Of Medicine, Mashhad University Of Medical Sciences)

Abstract

Attention, Balance and Coordination (ABC Learning) are importance for learning. Goddard Blythe (2009) stresses the importance of the relationship between these three elements in terms of the child's readiness to learn. If a child cannot maintain good control and coordination over her body, she/he is not well equipped for learning. Once a child has achieved these movement skills to age-appropriate levels, she/he is then perceived to be ready to learn. In children with cancer that physical preparation is damaged because of primary and secondary effects of disease and drug treatments, improvement of these factors is critical. 33 children with cancer (girls= 15 n, boys= 18 n, mean age=10.1, mean weight=31.5) voluntarily were participated in research. Physical activity questionnaire and consent letter were completed by parents. 17 children assigned to aerobic training group and 16 children assigned to control group. Experimental group exercised for 3 months and 3 sessions in week and each session was one hour. Before and after of training protocol, both of groups completed static balance test by BIODEX instrument and eye-hand coordination test with VIENNA. data analysis using spss software and paired-t test showed that static balance and eye-hand coordination of experimental group were improved significantly from beginning to end of protocol (P<..05). however because of treatment problems in control group, they were unable to participate in posttest. So there was not possibility of comparing experimental group with control group. Regular physical activity (Aerobic exercise) can be a good way to prepare children in terms of physical coordination and balance requirements for entry to school and next learning.

Corresponding Author: Ezzat Khodashenas (Department of pediatrics, faculty of medicine, mashhad university of medical sciences)
Early Stage Molecular Markers Of Colorectal Cancer

1. Majidipour Amene (Department Of Veterinary Histology, Veterinary School, Ferdowski University, Mashhad, Iran)

Abstract

Colorectal cancer (CRC) has been most prevalent in developed countries. Both genetics and environmental factor have been consider in CRC. In CRC or Adenoma several forms of genomic instability have been identified, including chromosomal instability (CIN), microsatellite instability (MSI), and Epigenetic gene silencing(DNA methylation). Detection of CRC in early stages can reduce both the incidence and mortality of the disease. Carcinoembryonic antigen (CEA) and carbohydrate antigen (CA) are the two important tumor markers of CRC but they are not early stage indicator and specific markers. So those early stage molecular markers should be considered. There is several kind of marker that can be mentioned as below: RAS family (including HRAS, NRAS and KRAS) that encode membrane protein like GTP- binding protein and Adenomatous polyposis coli (APC) gene as most crucial gatekeeper of colonic epithelial cell proliferation are most important CIN marker that could be applied in early stage of CRC. Bethesda markers(a 5 biomarkers panel that consists of 2 mononucleotide loci (BAT25 and BAT26) and 3 dinucleotide loci (D2S123, D5S346, and D17S250)) based on PCR methods has been developed to assess MSI disorders. Hyper methylation in CpG regions like SEPT9 and MLH1 gene are favorable factor of in CRC patients by epigenetic disorder. Detection of intact unfragments sequences of 1200- 1800 bp long in the stool that are due to diminished rate of apoptosis in CRC beside Faecal occult blood test (FOBT ) as an non invasive and non specific test is common among diagnostic tests. Although DNA-based fecal markers are promising but now are not widely used in clinical settings because of inhibitors such as bilirubin and bile acids. Instead FOBT is more routine and as a challenge in coming years molecular based test will have important position.

Corresponding Author: Mohebalian Hadi (Department of Pathobiology, Veterinary School, Ferdowsi University, Mashhad, Iran)
A Review On Anticancer Activities Of Propolis

1. Vajiheh Jahani (Department Of Pharmacology, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Cancer is an abnormal growth of cells in body that can lead to death. These cells are born due to imbalance in the body and by correcting that, the cancer might be treated. Today Cancer stands as a major public health problem in world, which makes it important to find a way to perfectly cure it, with making sure of the less side effects and best selectivity of the remedy. Our holly book, Quran, maintains a great respect for Bee and its products that names a chapter after it. In this chapter, Quran claims that there is a certain healing effect in bee products, which is the reason of choosing one of these products to study it's anticancer effects in this article. Propolis which is produced by bees from the resin, is collected from trees and shrubs. We have evidences of several uses of it in traditional medicine for treating different diseases. So far, propolis has been in many researchers due to it's antimicrobial, antifungal and antiviral activities. Researches have shown that it can induce apoptosis in several tumor cells. This review summarizes the current knowledge of anticancer activities of propolis, with the hope of finding a promising activity of it in cancer treatment. After studying different articles regarding mechanisms of propolis in it's fight against cancer, I found it's most important pharmacologically active molecules are flavonoids and phenolic acids and their esters. These components lead to propolis anti-inflammatory and immunomodulatory activities. Moreover propolis is able to induce apoptosis pathways in cancer cells, with CAPE and chrysin which are two main agents with antiproliferative effects. Therefore, there is some hope of the possibility of finding a novel targeted therapy for cancer, as it can specifically target tumor cells, so there would be less side effects. By having these sort of information in hand, there might be a new era in cancer treatment in order to save millions of lives.

Corresponding Author: Vajiheh Jahani (Department of Pharmacology, Mashhad University of Medical Sciences, Mashhad, Iran)
Exosome-Encapsulated MicroRNAs As Potential Circulating Biomarkers In Colon Cancer

1. Sara Samadi (Molecular Medicine Group, Department Of Modern Sciences And Technologies School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Soudabeh ShahidSales (Cancer Research Center, School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
3. Reza Nedaeinia (Student Research Committee, Department Of Medical Biotechnology, School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
4. Majid Ghayour-Mobarhan (Molecular Medicine Group, Department Of Modern Sciences And Technologies School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
5. Amir Avan (Molecular Medicine Group, Department Of Modern Sciences And Technologies School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Colorectal cancer (CRC) is third leading cause of cancer related death worldwide. Despite advances in detection of prognostic and diagnostic biomarker, only a very small number of markers have been launched. Recently microRNAs (miRNA) are emerged as a potential markers in different tumor types, including CRC. Exosome-encapsulated microRNAs are being suggested as a new class novel biomarkers as diagnostic and predictive markers in colorectal cancer. These particles are released from many cell types into the extracellular space upon fusion of multivesicular bodies (MVB) with the plasma membrane. MVBs are in fact late endosomes that carry intraluminal endosomal vesicles. They contain a wide variety of information, including proteins, lipids, RNAs, non-transcribed RNAs, miRNAs, which can be circulated in various body fluids (e.g., blood, salvia, ascites, urine). Exosomes can be taken up by neighbouring or distant cells and thereby modulate the function of recipient cells and play a key role in disease progression or facilitate metastasis in cancers. The aim of current review is to give an overview about origin and trafficking of exosomes between cells, techniques to isolate exosomal microRNAs as well as the potential applications of exosome-encapsulated microRNAs as diagnostic markers in clinical settings in colorectal cancer. Therefore, exosomes may consider a house of disease-specific miRNA signature that can control many aspects of human physiological status and are therefore potentially provides a useful information for prognosis of patients than other circulating miRNAs. There is growing body of evidence showing the prognostic and diagnostic value of some exosomal miRNAs in colon cancer (e.g., miR-150, miR-21, miR-192, let-7a, miR-223, and miR-23a). These findings provide a novel insight on novel application of these markers as novel non-invasive biomarkers for early detection and risk assessment patients with colorectal cancer, although further investigations in larger population are required to explore the clinical utility of exosomal miRNAs in CRC patients.

Corresponding Author: Amir Avan (Molecular Medicine Group, Department of Modern Sciences and Technologies School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran)
Does Obesity Effects On Multiple Myeloma?

Abstract

Multiple myeloma (MM) is a cancer resulting from the accumulation of genetic mutations in plasma cells and represents approximately 10% of all hematologic cancers. Along the uncontrolled growth of myeloma cells, MM causes disruption of bone marrow (BM) and cancer-induced bone disease. Adipose tissue is one of the main components of the BM niche, especially in old age and obesity. Adipocytes secrete various adipokines, inflammatory factors and reciprocal signaling between adipocytes and cancer cells which reported to contribute to tumor initiation, growth and metastasis in several types of cancer. Obesity influences myeloma mortality in early adulthood and later in life and women have the highest risk of death from this cancer if they remain heavy throughout adulthood. BMI (body mass index) is routinely used as a measure of adiposity. Adiponectin, a protein that is decreased during obesity and has anti-myeloma properties making it an attractive potential therapeutic in MM. The association between obesity and MM risk may be partly attributed to reduced circulating levels of adiponectin in obese individuals. Low BMI, thrombocytopenia and renal failure were strong predictors for early mortality (EM). Low BMI (<20 kg/m2) was significantly associated with EM, and 27.1% of patients with low BMI died within 12 months of diagnosis. Each 5 kg/m2 increase in BMI is associated with an increase of 10% in cancer-related death. Numerous reports have shown that obesity is positively correlated with leptin expression, and adipocytes, partially through their expression of soluble leptin, contribute to MM pathogenesis. Some studies have reported positive correlation between BMI and adhesion and angiogenesis of MM cells. Moreover, they identified hormonal, lipid, and signaling factor dysregulation in obese adipocytes that can contribute to MM growth and progression. Each 5 kg/m2 increase in BMI is associated with an increase of 10% in cancer-related death. Targeting lipid metabolism of cancer cells and adipocytes in combination with standard anti-myeloma therapies will likely reveal novel therapeutic avenues through which to attack hematological malignancies. Maintaining a healthy body weight throughout life may reduce MM.

Corresponding Author: Saeede Sanchouli (Zahedan University Of Medical Science, Mashhad, Iran)
Nutritional Intervention: Important Aspect Of Treatment In Children With Cancer

1. Bahareh Imani (Department Of Pediatrics, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Hamid Farhangi (Department Of Pediatrics, Mashhad University Of Medical Sciences)

Abstract

Adequate nutrition during cancer plays a significant role in several clinical outcome, such as susceptibility to infections, wound healing, tolerance and response to chemotherapy, biochemical imbalances, quality of life, and cost of care. But, the importance of nutrition in children with malignancies is still an undervalued topic within pediatric oncology. The importance of our work is to reinforce and indicate that malnutrition in children with cancer should not be accepted at any stage of the disease or tolerated as a predictable process. Aim of our paper is the close collaboration, the exchange of knowledge and expertise between pediatric oncologists and a nutritional specialist, as well as the comprehension of the mechanisms during cancer cachexia and malnutrition. We provide a critical review of the current state of research and new knowledge related to nutritional management in childhood cancer. Also we discuss screening methods, including the use of subjective global assessment. Different parts of nutritional assessment include medical history; physical examination; biochemical and hematological data, anthropometric measurements; and food and nutrition history. We review medical tests and procedures to determine nutritional status, including nitrogen balance, delayed cutaneous hypersensitivity, prognostic nutritional index, creatinine height index, maldigestion and malabsorption tests, indirect calorimetry and dual x-ray absorptiometry. The importance of nutrition in children with cancer is an underestimated topic within pediatric oncology. There are new, inexpensive, and noninvasive techniques for the evaluation of the nutritional status providing evidence for the quality of nutritional interventions for children with a high risk of malnutrition and a tendency for body fat accumulation. Nutritional strategies should be considered and integrated as a fundamental feature of pediatric oncology with the same diligence as one does for other supportive care measures to prevent chronic illness and adverse late effects caused by malnutrition in this population. One of the main objectives in this field is the early detection of children with preexisting malnutrition and a high risk of substrate depletion before cancer therapies start employing standardized methodologies. In short, it is essential to establish individualized and patient-centered nutrition therapy for a child with cancer, focusing on proactive, ongoing assessments with early and continuing preventive measures in place.

Corresponding Author: Bahareh Imani (Department of Pediatrics, Mashhad University of medical sciences, Mashhad, Iran)
Gene Expression Detection Of HOXB13:IL17BR In Sentinel Lymph Node Of Primary Breast Cancer Patients Without Macrometastasis

1. Shahrzad Soleimani (Department Of Molecular Genetics, Institute Of Basic Science, Shahrekord Islamic Azad University, Iran)
2. Fateme Zandnya (Department Of Molecular Genetics, Institute Of Basic Science, Shahrekord Islamic Azad University, Iran)
3. Abolfazl Movafaq (Department Of Molecular Genetics, Institute Of Basic Science, Shahid Beheshti University, Tehran, Iran)
4. Neda Mansouri (Department Of Molecular Genetics, Institute Of Basic Science, Shahid Beheshti University, Tehran, Iran)

Abstract

Sentinel lymph node micrometastasis detection improves outcome for breast cancer follow up. The aim of the current study was to identify gene profiles that accurately predicted the outcome of breast cancer patients. The HOXB13:IL17B ratio expression status have been evaluated regarding to tumor's features. 50 tumor samples from breast cancer patients were analyzed for the expression of 3 genes by quantitative real time PCR (Q-PCR) procedure, Master Mix reaction containing SYBER green. Clinically verification for recurrence to distant organs was performed. According to findings, the negative reported lymph nodes for metastasis, had micro metastasis in significant values. There was a significant difference between normal and cancer samples in 3 gene expression marker. A novel gene expression signature predictive of micro metastatic patients was evaluated. In this assessment, relationship between these gene with tumor's features that finding clear role for these genes with tumor's outcome, need to be established.

Corresponding Author: Shahrzad Soleimani (Department of Molecular Genetics, Institute of Basic Science, Shahrekord Islamic Azad University, Iran)
The Prevalence Of HPV16_18 Viruses In The Head And Neck Squamous Cell Carcinoma (HNSCC) In Isfahan City

1. Fateme Zandnya (Department Of Molecular Genetics, Institute Of Basic Science, Shahrekord Islamic Azad University, Iran)
2. Shahrzad Soleimani (Department Of Molecular Genetics, Institute Of Basic Science, Shahrekord Islamic Azad University, Iran)

Abstract

Cell carcinoma of head and neck is a disease that its prevalence is increasing. One of the most important factor for that is the HPV virus so that treat this type of cancer has a better prognosis. The present study aimed to investigate the prevalence of head and neck squamous cell carcinoma associated with the virus in age from 30 to 60 years. In this study, 50 samples from patients had studied during the past two years (1392-95) by HPV virus detection kits with a multiplex PCR method in Isfahan city. After Multiplex PCR on the 50 samples, 4 samples with HPV16, a sample with HPV18 and two samples has identified HPV16 -18 was assessed. Respectively 8% and 2% and 4% of the samples were included. According to the findings of the present the HPV virus has a significant role in head and neck squamous cell carcinoma.

Corresponding Author: Fateme Zandnya (Department of Molecular Genetics, Institute of Basic Science, Shahrekord Islamic Azad University, Iran)
Cancer chemotherapy resistance is one of the most pressing major problem in cancer therapy. Chemoresistance is complicated and multifactorial. numerous factors affect drug sensitivity including: accelerated drug efflux; drug activation and inactivation; alterations in drug target; DNA methylation; processing of drug-induced damage; and evasion of apoptosis. The mechanisms underlying MDR remains far from fully understood. Tumours can be intrinsically resistant to treatment, or resistance may be acquired during treatment. Long non-coding RNAs (lncRNA) and miRNAs are a type of non-coding RNAs (ncRNAs) that recently have emerged as an important class of regulators of gene expression. lncRNAs are a heterogeneous group of non-coding transcripts more than 200nt long. MicroRNAs (miRNAs) are a class of small, nonprotein-encoding RNAs that range in size from 19 to 25 nucleotides (nt). Non coding RNAs was found to be involved in the carcinogenesis, metastasis invasiveness of multiple malignant tumors and chemoresistance through affecting oncogene expression. In this paper, we highlighted new approaches for ascribing lncRNAs and miRNAs expression with Chemoresistance. In order to write this review, we used highly cited articles with keywords such as chemoresistance, Long noncoding RNA, miRNA, gene expression presented in credible databases, Pubmed, Scopus, Google, Medline from 2007 to 2016. Resistance to chemotherapeutical drugs is an important clinical problem. Resistance of cancer cells to cytotoxic drugs may be a result of resistance to apoptosis. Improved understanding of the molecular mechanisms underlying chemo resistance in cancer could be useful for devising targeted therapeutic. miRNAs and lncRNAs have an important role in the development of chemosensitivity or chemoresistance in different cancers. studies indicated a possible link between miRNAs and lncRNAs dysregulation and cancer drug resistance. Furthermore, lncRNAs and miRNAs could be used as biomarkers for Cancer chemotherapy resistance, outcome in cancer and provide a new strategy to treat malignant tumors in the future.

**Corresponding Author:** Zahra Rahmani (BuAli Research Institute, Mashhad University of Medical Sciences, Mashhad, Iran)
Transfer Of Bacterial Plasmid And Ectopic Expression Of MAGE-A4 Gene In ESCC Cell Line (KYSE-30) And Evaluate Tumoral Behavior

1. Maryam Ashkar (Department Of Microbial Biotechnology, Islamic Azad University Of Damghan, Iran)

Abstract

Esophageal cancer is responsible for the death of over ten million people worldwide annually. This is the eighth most common cancer in the world, the sixth cancer leading to death and the third most common gastrointestinal malignancy. There are several treatment methods for cancer; many types of cancers are associated with the reactivation of genes in the germ and fetal layer. One of the most important categories of these genes is Cancer Testis (CT) of genes or CG genes and also one of the most important CTAs is related to the MAGE family. In this study, the behavioral changes of the esophageal cancer cell after receiving MAGE-A4 gene have been investigated regarding the invasion and proliferation. Transferring the plasmid containing Mage-a4 gene to ecoli-top 10 bacteria to proliferate. Isolation of plasmid and double enzyme digestion to confirm the desired piece and then cultivating two cell lines of hek293 and kyse30 to transfer plasmid throughlipofection to the mentioned cell lines. Conducting Mtt and scratch assay tests, rna extraction and then synthesizing cDNA for real time pcr. A 6-unit increase of the expression of mage-a4 gene in both cell lines of kyse-30 and hek293. Mtt test results are as follows, KYSE-30; OD untransfect (3.73) OD transfect (2.78) and HEK-293; OD untransfect (1.159) OD transfect (1.153). The results of the scratch assay test indicated that tumor cell line to which the MAGE-A4 gene was transferred has less invasion. In MTT assay test, the mage-a4 gene transfer to hek-293 cell line caused no change in transfected and Untransfected cell proliferation. But in the tumor cell line (kyse-30) we witnessed a decrease in cell proliferation in cell lines to which MAGE-A4 gene had been transfected. The results of the scratch assay test indicated that the cell invasion rate was reduced in kyse-30 cell line to which the mage-a4 gene was transfected.

Corresponding Author: Maryam Ashkar (Department of Microbial Biotechnology, Islamic Azad University of Damghan, Iran)
Parental Smoking Before Or During Pregnancy And Prevalence Of Brain Tumors In Their Children In Adulthood

1. Parisa Shahinfar (Faculty Of Medicine, Mashhad Islamic Azad University, Mashhad, Iran)
2. Shima Ghari (Faculty Of Medicine, Mashhad Islamic Azad University, Mashhad, Iran)

Abstract

Smoking has been shown to induce tumors in numerous organs and tissues but the association between smoking and brain tumors is not proved completely until now and there are very inconsistent studies about it. The etiology of brain tumors is not understood, in particular it is not known if exogenous chemicals are capable of causing human brain tumors. Whether smoking is shown to be a risk factor, it would determine an important proof of principle that exogenous chemicals are able to cause human brain tumor. Previous studies demonstrated that tobacco contain several carcinogens and also it was showed that neurocarcinogens can cross the placenta and cause different damages. Carcinogenics usually have more effect on fetus than the others, for the reason that central nervous system is excess sensitive in early stage of life. On the other hand nicotine may increase the permeability of the blood brain tumor. There are some hypothesis about number of cancers that presume they begin during the early stage of development therefore we decide to investigate whether parental smoking before or during the pregnancy is a risk factor of brain tumor in their children in adulthood or not. A search for article using PubMed, Google Scholar, and Science Direct with the terms pregnancy, smoking, brain tumor, paternal and maternal smoking, fetus development, carcinogens was performed. The data were collated and analyzed to represent information from the best and current available form of evidence. Our analysis indicate that a majority of the studies believed that overall risk of children blood tumors (CBTs) was not significantly associated with paternal and maternal smoking prior or during the pregnancy. These findings are against of our anticipant and further studies can clear the exact relationship. But a little association between passive and paternal smoking during pregnancy were observed. Most of the studies also determined risk of all kinds of brain tumors separately and astrocytoma in some cases had a correlation with smoking before or during pregnancy.

Corresponding Author: Parisa Shahinfar (Faculty of medicine, Mashhad Islamic Azad University, Mashhad, Iran)
Ginger, An Old Pleasant Spice, A New Potential Drug

1. Somayeh Rahimi Babasheikhali (Faculty Of Science, University Of Isfahan, Isfahan, Iran)
2. Soheila Rahgozar (Faculty Of Science, University Of Isfahan, Isfahan, Iran)

Abstract

Despite the substantial improvements in cancer research and treatment, this disease has still remained a leading cause of death in the world. Considering the limitations of conventional Chemotherapeutic drugs including high toxicities and reduced quality of life among cancer patients, establishment of safe and efficient alternatives with known mechanisms is strongly required. Using the edible phytochemicals is a safe, cheap, acceptable and accessible approach in the prevention, and control of cancer. Ginger (Zingiber officinale Rosc.), an eternal rhizome plant, is one of the widely natural products which can be administered as a spice and medicine for treating nausea, dysentery, flatulence, diarrhea, loss of appetite, infections, cough, and bronchitis since long time ago. The anticancer activity of this plant, that has been reported in several papers, can be attributed to its ability to modulate several signaling molecules like NF-κB, STAT3, MAPK, PI3K, ERK1/2, Akt, TNF-α,COX-2, cyclin D1, cdk, MMP-9, survivin, cIAP-1, XIAP, Bcl-2, caspases, and other cell growth regulatory proteins. The major constituents of fresh and dried ginger are 6-gingerol and in 6-shogoal, receptively, which are categorized as non-volatile substances. Non-volatile compositions are known to be responsible for antioxidative, anti inflammatory, antibacterial and anticancer activities of ginger. Considering the in vitro and in vivo selective cytotoxicity of ginger in different malignancies, such as prostate, skin, leukemia, cervix, breast, and gastrointestinal cancer, and its reduced side effects compared to common chemotherapy drugs, ginger can be introduced as a potential option for cancer treatment. Moreover, the possible inhibitory interaction between ginger and chemotherapy drugs is less announced. Nonetheless more studies are needed to explore the possible influence of ginger in cancer therapeutic strategies.

Corresponding Author: Soheila Rahgozar (Faculty of Science, University of Isfahan, Isfahan, Iran)
Structural And Functional Optimization Of SS1P Based On In-Silico Simulation

Abstract

Immunotoxin (IT) therapy is promising approach for targeted cancer therapy with the minimal side effects. These types of drugs are chimeric proteins with two main parts including death and ligand domains. Accordingly, structural and functional characterization of these types of drugs, based on in-silico simulation, could be providing suitable context for optimization as well as innovation in common immunotoxins. Bearing in mind, structural optimization of SS1P immunotoxin was considered in this study. In this regard, the protein sequence of the SS1P was retrieved from corresponding database such as Google patent. Structural characterization of the immunotoxin was performed via Intrproscan5 and Blast programs. On the other hand, the protein sequence of the mesothelin as specific target of this drug was retrieved from NCBI databank. MODELLER9.15 were used for structural modeling of the sequences. PROTEINATLAS database were used for assessment the expression of the antigen. Furthermore, HADDOCK were used for evaluation the binding affinity. Finally, all statistical analysis were expressed with SPSS 21.0 (SPSS Inc., Chicago, IL, USA). The results of the sequence characterization of the SS1P lead to obvious two main parts in the sequence context including dsfv and PE which are linked to each other with G2S1. Moreover, the structure stability of the protein were confirmed after simulation under 300°K, 100ps of the time for NVT and NPT steps and 20000ps (20ns) for MD step. On the other hand, molecular docking of the mesothelin to the modeled IT as well as optimized IT were confirmed after simulation. Taken together, the results of the present study provide in-silico approaches for optimization as well as innovation in the common sequence context of ITs for novelty in drugs design.

Corresponding Author: ()
An In-Silico Survey On The Structure And Function Of The Corresponding Antigens Of The Esophageal Malignancies In Order To Immunotoxin Development

1. Elham Karimi (Department Of Biology, Science And Research Branch, Islamic Azad University, Khorasan Razavi, Neyshabur, Iran)
2. Aliakbar Haddad-Mashadrizeh (Cell And Molecular Biotechnology Research Group, Institute Of Biotechnology, Ferdowsi University Of Mashhad, Mashhad, Iran)
3. Mohammad Reza Saberi (Department Of Medical Chemistry, School Of Pharmacy, Mashhad University Of Medical Sciences, Mashhad, Iran.)

Abstract

Esophageal cancer that refers to malignancies of the epithelium of the esophagus tissue, is sixth leading cause of death among cancers. This type of cancer is one of the most prevalent cancers in Iran. So that, among 35,000 deaths of cancer in Iran, about 5800 cases of them is due to this type of cancer. Considering, several methods with various efficacy have been developed in the world for prognosis, diagnosis and treatment of this disease. Among therapeutic approaches, immunotoxin development with limited side effects is a desirable way. However, this strategy is demands to characterization of the cell surface specific antigens of esophageal cancer. Bearing in mind, a comprehensive profile of cell surface specific antigens of the esophageal cancer were gathered in this study. Subsequently, the structural and functional characterizations of the antigens were performed, based on in-silico investigation. The results of this study led to the detection of six specific antigens for esophageal cancer with different structural, functional and expression characteristics at the level of transcription and translation, including ADORA3, CLCA2, DSC3, LY6D, HER2, and MUC21. However, among them the MUC21 with the highest level of the expression considered as suitable biomarker for diagnosis as well as immunotoxin development. Accordingly, our investigation led to detection the corresponding ligands of the MUC21 as suitable context for immunotoxin designing which are considered in our group for more analysis.

Corresponding Author: Aliakbar Haddad-Mashadrizeh (Cell and Molecular Biotechnology Research Group, Institute of Biotechnology, Ferdowsi University of Mashhad, Mashhad, Iran)
Assessment Of Changes In Isoforms Of MDM2 Gene, Before And After The Effect Of 5-Fluorouracil In Esophageal Cancer Cell Lines (KYSE-30)

1. Ensiye Khorshidi (Department Of Biology, Damghan Branch, Islamic Azad University, Damghan, Iran)
2. Reihaneh Alsadat Mahmoudian (Division Of Human Genetics, Immunology Research Center, Avicenna Research Institute, Mashhad University Of Medical Sciences, Mashhad, Iran)
3. Kazem Anvary (Cancer Research Center, Omid Hospital, Faculty Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
4. Mohammadreza Abbaszadegan (Medical Genetics Research Center, Medical School, Mashhad University Of Medical Sciences, Mashhad, Iran)
5. Mehran Gholamin (Division Of Human Genetics, Immunology Research Center, Avicenna Research Institute, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Gastrointestinal cancers (GC) are prevalent cancers in the worldwide. Esophageal squamous cell carcinoma (ESCC) is the most human common cancer in the gastrointestinal tract. Genetic factors and oncogenes have a critical role in the development of the disease. A mouse double minute 2 homolog (MDM2) is a significant negative regulator of the p53 tumor suppressor. Mdm2 in overexpressed in the most human malignant tumors. It is noteworthy that, more than 40 different splice variants of MDM2 transcripts have been identified both tumor and normal tissues. The most important three of MDM2 splice variants are Mdm2-A, Mdm2-B, and Mdm2-C. In cancer cells, the Mdm2 protein often contributes to change molecular programs that increase growth-promoting signals and decrease cell death signals. The p53 is introduced as an important growth inhibitory program into noncancerous cells. The anti-cancer peptide PNC-27, containing the MDM2-binding domain of p53, may target MDM2. Our aim of this study was to assess the effects of MDM2 variants on chemotherapy samples. In this study, cell lines KYSE-30, before and after chemotherapy by 5-fluorouracil, was examined for MDM2 mRNA splicing variants by Nested RT-PCR and sequencing techniques. mRNA MDM2 was detected in cell lines KYSE-30. Alternatively MDM2 type 1 spliced variants was indicated in KYSE-30 after chemotherapy by 5-fluorouracil. Moreover, two spliced forms of MDM2 were detected in KYSE-30. Our results indicate that with the use of 5-fluorouracil, can create some new isoforms and disappear some isoform. Overall, our results suggest that chemotherapy with alteration in MDM2 isoforms expression can be assisted in targeted therapy by PNC27.

Corresponding Author: Mehran Gholamin (Division of Human Genetics, Immunology Research Center, Avicenna Research Institute, Mashhad University of Medical Sciences, Mashhad, Iran)
Structural And Functional Optimization Of SS1P Based On In-Silico Simulation

1. Sara Malekzadeh (Department Of Biology, Payam Noor University Of Mashhad, Mashhad, Iran)
2. Aliakbar Haddad-Mashadrizeh (Cell And Molecular Biotechnology Research Group, Institute Of Biotechnology, And Department Of Biology, Faculty Of Science, Ferdowsi University Of Mashhad, Mashhad, Iran)
3. Majid Rajabiyan Noghondar (Department Of Biology, Payam Noor University, Tehran, Iran)

Abstract

Immunotoxin (IT) therapy is promising approach for targeted cancer therapy with the minimal side effects. These types of drugs are chimeric proteins with two main parts including death and ligand domains. Accordingly, structural and functional characterization of these types of drugs, based on in-silico simulation, could be providing suitable context for optimization as well as innovation in common immunotoxins. Bearing in mind, structural optimization of SS1P immunotoxin was considered in this study. In this regard, the protein sequence of the SS1P was retrieved from corresponding database such as Google patent. Structural characterization of the immunotoxin was performed via Intrproscan5 and Blast programs. On the other hand, the protein sequence of the mesothelin as specific target of this drug was retrieved from NCBI databank. MODELLER9.15 were used for structural modeling of the sequences. PROTEINATLAS database were used for assessment the expression of the antigen. Furthermore, HADDOCK were used for evaluation the binding affinity. Finally, all statistical analysis were expressed with SPSS 21.0 (SPSS Inc., Chicago, IL, USA). The results of the sequence characterization of the SS1P lead to obvious two main parts in the sequence context including dsfv and PE which are linked to each other with G2S1. Moreover, the structure stability of the protein were confirmed after simulation under 300°K, 100ps of the time for NVT and NPT steps and 20000ps (20ns) for MD step. On the other hand, molecular docking of the mesothelin to the modeled IT as well as optimized IT were confirmed after simulation. Taken together, the results of the present study provide in-silico approaches for optimization as well as innovation in the common sequence context of its for novelty in drugs design.

Corresponding Author: Aliakbar Haddad-Mashadrizeh (Cell and Molecular Biotechnology Research Group, Institute of Biotechnology, and Department of Biology, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran)
Curcumin Inhibits Cell Growth And Migratory Behaviors Of Human Hepatocellular Carcinoma Cells

1. Faezeh Ghasemi (Department Of Modern Sciences And Technologies, Faculty Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Hasan Fayazbakhsh (Department Of Medical Biochemistry, School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
3. Nahid Kheradmand (Department Of Modern Sciences And Technologies, Faculty Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
4. Seyed Mahdi Hassanian (Department Of Medical Biochemistry, School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
5. Amirhossein Sahebkar (Biotechnology Research Center, Mashhad University Of Medical Sciences, Mashhad, Iran)
6. Amir Avan (Department Of Modern Sciences And Technologies, Faculty Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Hepatocellular carcinoma is the most common type of liver cancer with poor prognosis. There is growing body of data evaluating the antitumor activity of Curcumin in different tumor types. The aim of current study was to explore the effect of curcumin in 2 and 3 dimensional models of Huh 7. Huh 7 were cultured and maintained in DMEM media. MTT assay was employed to evaluate the viability of the cells. The cytotoxicity of curcumin was investigated in 3 dimensional cell culture model (spheroid). Invasion assay was used to assess the invasive behavior of Huh 7 cells before and after treatment with curcumin. The expression levels of some genes involved in apoptosis, migration, as well as the markers of NF-kB pathway, were evaluated by real-time quantitative RT-PCR. Our data showed that curcumin suppressed cell growth via modulation of the NF-kB pathway. We observed tumor shrinkage after 5 days in Huh 7 cells treated with curcumin at IC50 and 5xIC50 values. Curcumin was able to decrease the invasiveness of Huh 7. We demonstrate the antitumor activity of curcumin in a liver cancer cell line, supporting further investigations on the role of this novel anticancer agent in hepatocellular carcinoma.

Corresponding Author: Amir Avan (Department of Modern Sciences and Technologies, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran)
Abstract

Curcumin is a polyphenolic compound derived from Curcumin longa L. There is growing body of data showing the antitumor effect of curcumin in different cancers; however the molecular mechanism underlying of this inhibition in breast cancer is still remained to be elucidated. Here we investigated the antitumor activity of curcumin alone or in combination with paclitaxel in MCF-7 cells in monolayer cell cultures and spheroids models. Moreover, the cytotoxic activity of three different forms of curcumin (phytosomal), phospholipidated curcumin, amorphous curcumin and turmeric oleoresin were evaluated, compared to unformulated curcumin. The antiproliferative activity of 4 different forms of curcumin was assessed in monolayer and spheroid models of MCF-7 cells. The cell cycle modulation and migratory behaviors of the cells were determined by FACS and migration assay before and after treatment with curcumin. Curcumin suppressed cell growth in MCF-7 cells at 110μM IC50 value. The median drug-effect analysis showed a slight-to-moderate synergism with CI values of 0.8. Curcumin was able to reduce the invasiveness of MCF-7, compared to control cells. Moreover, curcumin inhibited the tumor growth in MCF-7 cells, although this inhibition was more pronounced with amorphous/phospholipidated curcumin. Analysis of the sub-G1 region of cell cycle analysis revealed that the treatment with curcumin increased cell death. We demonstrated the antitumor activity of curcumin and its curcumin oleoresin in a breast cancer cell line, supporting further investigations on the therapeutic potential of this novel anticancer agent in in vivo models.

Corresponding Author: Amir Avan (Department of Modern Sciences and Technologies, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran; Cancer Research Center, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran)
**Key Factors In EMT: Critical Process In Breast Cancer Malignancy**

1. Mahya Shariat Razavi (Division Of Genetics, Department Of Biology, Faculty Of Science, University Of Sistan & Baluchestan, Zahedan, Iran)
2. Mohammad Mahdi Forghanifard (Department Of Biology, Damghan Branch, Islamic Azad University, Damghan, Iran)
3. Dor Mohammad Kordi Tamandani (Division Of Genetics, Department Of Biology, Faculty Of Science, University Of Sistan & Baluchestan, Zahedan, Iran)
4. Mohammad Reza Abbazadegan (Division Of Human Genetics, Immunology Research Center, Avicenna Research InstituteMashhad University Of Medical Sciences)

**Abstract**

Epithelial Mesenchymal Transition (EMT) is an event of gaining mesenchymal features by epithelial cells. It has an important role in invasiveness and migration of cancerous cells, besides to tissue development and wound healing. These properties can lead to metastasis and drug resistance which are the main reasons of cancer relapse and death. Although there are advanced therapeutic methods against breast cancer, metastasis of epithelial breast cancer cells complicates the efficiency of treatment causing low survival rate of patients. E-cadherin expression which has key role in cell-cell adhesion decreases during EMT and the cells lose their junctions and can migrate to other sites. Other cell adhesion molecules level such as claudin and occluding decrease in cell membrane. In contrast, expression of mesenchymal genes such as N-cadherin, vimentin and fibronectin increase. A variety of intracellular factors including twist which is a member of basic helix-loop-helix transcription factor, and snail1, snail2 (slug), ZEB1, ZEB2 which can bind to E-box element of cell adhesion genes and regulate EMT. These EMT- related transcription factors are affected by different signaling cascades such as TGF-β, RTKs, Wnt, and notch. All in all, this review article underlines the role of transcription factors and signaling pathways that regulate E-cadherin expression. A comprehensive look at pathway of EMT can help us to choose effective candidate genes for targeted therapy. Moreover, it should be considered that increasing E-cadherin and other cell junction components expression lead to mesenchymal epithelial transition (MET) which is necessary for fixation of migrated tumor cells in distant tissue. Consequently, it is important to choose candidate gene for targeted therapy according to stage of the cancer.

**Corresponding Author:** Mohammad Reza Abbazadegan (Division of Human Genetics, Immunology Research Center, Avicenna Research InstituteMashhad University Of Medical Sciences)
SiRNA Knock-Down Of HIF-1α Resulted In Dramatically Changes In Cell Cycle And Viability Of U87 Cell Line

1. Sara Ehteshamipour (Department Of Genetics, Faculty Of Biological Sciences, Tarbiat Modares University, Tehran, Iran)
2. Sohameh Mohebbi (Department Of Nanobiotechnology, Faculty Of Biological Sciences, Tarbiat Modares University, Tehran, Iran)
3. Smaeil Rahimi (Department Of Genetics, Faculty Of Biological Sciences, Tarbiat Modares University, Tehran, Iran.)
4. Bahram Mohammad Soltani (Department Of Genetics, Faculty Of Biological Sciences, Tarbiat Modares University, Tehran, Iran.)
5. Mehrdad Behmanesh (Department Of Genetics, Faculty Of Biological Sciences, Tarbiat Modares University, Tehran, Iran.)

Abstract

HIF-1 is a transcription factor, composed of HIF-1α and HIF-1β subunits and functions as a master regulator of oxygen homeostasis in all metazoan species. Upon hormonal stimulation or in oxygen-deficient micro-environment, HIF-1α is activated by ROS through a complex signaling network. Some studies showed that overexpression of HIF-1α is a negative prognostic indicator in many human cancers such as breast, cervix, oropharynx, ovary and uterus. Moreover, significant associations between HIF-1α overexpression and patient mortality have been shown in cancers of the brain. Here we aimed that to evaluate the effect of selective gene silencing of HIF-1α with specific short interfering RNA (siRNA) on the cell cycle and viability of U87 cell line as a human primary glioblastoma cell line. U87 cells cultured in DMEM with 10% FBS supplemented with penicillin and streptomycin. Transfer of a specific siRNA against HIF-1α was performed by Lipofectamine® 2000. RT-PCR analysis was performed after 24, 48 and 72 hours posttransfection. Using flow cytometry test and MTT assay, cell cycle and viability of transfected cells were analyzed. Using RT-PCR method, we showed a significant down-regulation of HIF-1α in 48 hours transfected cells in comparison with un-transfected cells. Moreover, we found knock down of HIF-1α significantly affect the cell cycle and survival of U87 cells. Our results highlight the importance of Hif-1a as a candidate target in the field of cancer therapy.

Corresponding Author: Sara ehteshamipour (Department of Genetics, Faculty of Biological Sciences, Tarbiat Modares University, Tehran, Iran)
The Prognostic Significance Of Epithelial Mesenchymal Transition Phenotype In Different Human Cancers

1. Azam Hadi (Cancer Prevention Research Center, Shahroud University Of Medical Sciences, Shahroud, Iran)
2. Naghmeh Ahmadiankia (Cancer Prevention Research Center, Shahroud University Of Medical Sciences, Shahroud, Iran)

Abstract

The epithelial-mesenchymal transition (EMT) roles importantly in cancer progression. It confers more mesenchymal fibroblast-like phenotype and potentially enables and promotes the epithelial cancer cells to detach from the primary tumor location, traverse the basement membrane, and finally leads to metastasis of cancer cells. It has been demonstrated that a series of distinct molecular processes are involved in the EMT, such as the activation of some specific transcription factors like Twist, Slug, ZEB1, ZEB2, Snail1, Snail2, changes in the expression of specific microRNAs and reorganization of some specific proteins like E-cadherin, N-cadherin, vimentin and fibronectin. The purpose of this review was to study the clinical significance and the prognostic impact of EMT phenotype in different human cancers. It has been suggested that the combination of the two markers of E-cadherin and vimentin could be reasonably used to identify the EMT in many cancers. It was revealed that EMT status is an important prognostic factor for pancreatic cancer and associated with portal vein invasion and lymph node metastasis. Additionally, the Immunohistochemical study of breast cancer has shown a significant up-regulation of EMT markers like vimentin, N-cadherin, and cadherin-11. The Immunohistochemical study of gastric cancer has shown a significant decreased in expression of the adhesion molecules of E-cadherin, alpha and beta catenin in diffuse type of gastric cancer compared with intestinal cancer type suggesting that EMT may be involved in determining the gastric cancer type and also resistance to treatment. Evaluation of proteins associated with EMT by using a tissue microarray method in the lung adenocarcinoma has been shown loss of cytokeratin, E-cadherin and acquisition of the expression of TTF-1, β-catenin, vimentin proteins. Gene expression analysis and immunohistochemistry study showed an upregulation of ZEB2 at the invasion front in primary colorectal cancer and liver metastases. Therefore, ZEB2 may be interesting as biomarker and potential target for treatment of colorectal cancer. The current review demonstrated the key role of EMT in carcinogenesis, so that they could be regarded as prognostic factors and targeting these key molecules could be a promising therapeutic alternative.

Corresponding Author: Naghmeh Ahmadiankia (Cancer Prevention Research Center, Shahroud University of Medical Sciences, Shahroud, Iran)
Cancer represents a complex group of heterogeneous diseases. While many cancers share fundamental biological processes (hallmarks of cancer) necessary for their development and progression, cancers also distinguish themselves by their dependence on distinct oncogenic pathways. Over the last decade, targeted therapies have been introduced to the clinic with variable success. Non-coding RNAs represent key regulators of gene expression. Improved knowledge of their biogenesis and function may in turn lead to a better understanding of the heterogeneity of malignancies and eventually be leveraged as diagnostic, prognostic and therapeutic targets. Overwhelming evidence now suggests that small non-coding RNAs such as miRNAs and Long non-coding RNA can be useful tools as biomarkers for molecular diagnostics. miRNAs can serve as biomarkers in a variety of diseases, such as cancer and Long non-coding RNA expression profiles in human cancers have highlighted the potential value of this class of non-coding RNAs as tumor markers in patient diagnosis and prognosis. In this review, we provide a perspective on emerging concepts in the clinical application of miRNA and LncRNA as biomarkers in cancer with an eye on the eventual integration of both miRNA and other non-coding RNA biology into our understanding of cancer pathogenesis and treatment. The selected publications were identified by using up-to-date electronic databases, including PubMed, Medline, EMBASE, Google Scholar. Searching of the published data was in accordance with the systematic reviews guidelines of tumour marker prognostic studies (REMARK), as described previously. The following key words were used for the search: “long non-coding RNA or LncRNA”, “micro RNA”, “cancer or carcinoma or tumour or neoplasia or neoplasm or malignancy or sarcoma”. Noncoding RNAs (ncRNAs) are transcripts that have no apparent protein-coding capacity; however, many ncRNAs have been found to play a major biological role in human physiology. Their deregulation is implicated in many human diseases.

Here, we summarize recent data about the biological characteristics of this non-coding RNA in cancer pathways. We also consider the medical implications, and discuss how this can be used for cancer diagnosis and prognosis, and serve as potential therapeutic targets.
Analysis Of SNP Rs2252070 Of MMP13 Gene In Human Esophageal Squamous Cell Carcinoma In Iranian Population

Abstract

Esophageal cancer is the eight most common cancers and the sixth leading cancer death worldwide. Matrix metalloproteinases (MMPs) include a large group of calcium-dependent zinc containing endopeptidases with the capacity to split peptide bonds in most extracellular matrix proteins. MMP13 as a collagenase, plays a critical role in development of esophageal squamous cell carcinoma (ESCC). Therefore, we tested association SNP rs2252070 of MMP13 in patients with ESCC. DNA was extracted from the blood of 86 healthy individuals and the formalin-fixed paraffin-embedded (FFPE) of tumor tissue and corresponding margin-normal esophageal of 80 patients. The polymorphism rs2252070 was studied by RFLP-PCR and sequencing techniques. Initial results showed that the frequency of G allele was more frequent than A allele in compared with the control group. This findings have shown that MMP13 gene polymorphism could affect the promoter activities. We found that MMP13 rs2252070 G>A genetic polymorphism is significantly associated with ESCC risk in Iranian populations.

Corresponding Author: Mehran Gholamin (Division of Human Genetics, Immunology Research Center, Avicenna Research Institute, University of Medical Sciences, Mashhad, Iran.)
MicroRNAs As A Tumor Suppressor In Glioblastoma Cancer Cells

1. Naser Mobarra (Stem Cell Research Center, Department Of Biochemistry, Golestan University Of Medical Sciences, Gorgan, Iran)
2. Fatemeh Kouhkan (Department Of Molecular Biology And Genetic Engineering, Stem Cell Technology Research Center, Tehran, Iran)
3. Masoud Soleimani (Department Of Hematology, School Of Medicine, Tarbiat Modares University, Tehran, Iran)

Abstract

Glioblastoma and grade IV astrocytoma, is the most aggressive cancer that begins within the brain. Glioblastomas represent 15% of brain tumors. microRNA (miRNA) about 22 nucleotides functions in RNA silencing. MicroRNA-129-1 seems to behave as a tumor suppressor since its decreased expression in glioblastoma multiforme (GBM). Cell lines and patient sample collection: Fifteen fresh GBM tissues (grade IV) and age- sex matched non-cancer postmortem brain tissues were obtained from Sina Hospital (Tehran, Iran), in 2013. As well as, Human glioma cell lines U87, A172, U251 and HEK-293 T cells were purchased. Plasmids, viral vectors construction and luciferase assay: MiR-129-1 coding region was cloned into pLEX. JRed vector and for loss-of-function studies pLenti-miR-Off-129 construct was purchased. For luciferase assays, IGF1, IGF2BP3 and MAPK1 30-UTR, harbouring potential miR-129-1 target sites, were cloned downstream of the luciferase gene in the pSICHECK2 vector. Gene expression analysis: Total RNA was purified from cell lines and reverse transcribed to cDNA, stem-loop RT specific primers (for miR-129-1), Real-time PCR for target mRNAs and miR-129-1 was performed. MiR-129-1 inhibits cell proliferation in GBM cell lines: Three cell lines were transduced with pLEX-miR-129-1, pLenti-miR-Off-129-1, pLEX-Ctrl and pLEX-Scr and evaluated for cell proliferation, cell cycle and apoptosis. Upregulation of miR-129-1 reduced the expression level of IGF1, IGF2BP3, MAPK1 and CDK6 in GBM cell lines. IGF2BP3 and MAPK1 are involved in miR-129-1 dependent Cell cycle arrest: U251 cells were transfected with shIGF2BP3, shMAPK1, shIGF1or shCtrl vectors. IGF2BP3, MAPK1 and CDK6 expression correlate inversely with miR-129-1 expression level in clinical GBM samples. MiR-129-1 is downregulated in GBM cancer tissues compared with adjacent normal brain tissues. Our findings identify miR-129-1 as one of the tumour suppressor microRNAs that can be useful in getting a better understanding of GBM cancer pathogenicity.

Corresponding Author: Naser Mobarra (Stem Cell Research Center, Department of Biochemistry, Golestan University of Medical Sciences, Gorgan, Iran)
Designing And In-Silico Evaluation A Novel Immunotoxin For Renal Malignancies

Abstract

The prevalence of cancer, lead to special attention to the developing new diagnostic and therapeutic approaches. Among all different ways, immunotoxin therapy is known as a promising strategy for targeting cancerous cells. Accordingly, designing, optimization and simulation a new immunotoxin with the ability to targeting renal malignancies have been considered in this study. Whereas, a profile of cell surface specific antigens of renal malignancies was gathered in order to select the target. To fulfill this aim, Proteinatlas database were used for our in-silico expression assays. Likewise, ligands of the selected antigens were detected via STRING program, and then evaluated based on scoring and molecular docking. On the other hand, a comparative analysis on the effective dosage of toxins was accomplished for selection toxin fragments. Moreover, Modeller, GROMACS, MOE, ERRAT, PROCHECK and Verify-3D programs were used for modeling, quality control of the structure as well as structural simulation. Bear in mind, all statistical analysis were expressed with SPSS 21.0 software (SPSS Inc., Chicago, IL, USA). The results of this study demonstrate the high expression of EGFR on the renal malignancies’ cell surface. Whilst, Cetuximab was chosen as the best coordinate ligand of the selected antigen. Furthermore, pseudomonas exotoxin A selected due to the fact of its high efficiency. Finally, the assembling of the selected domains with flexible liker led to design a new immunotoxin, with high stability and functionality after simulation, for targeting renal cancer cells. Nonetheless, the supplementary analysis for confirming the effects of this immunotoxin is ongoing in our group.

Corresponding Author: Aliakbar haddad-mashadrizeh (Cell and molecular biotechnology research group, institute of biotechnology, and Department of Biology, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran)
A Brief Review Of Hyperthermia As An Neoadjuvant Therapy Method Related To Cancer Treatment

Abstract

Hyperthermia refers to elevation tumor temperature from 39 up to 43 degree Celsius. Therapeutic Hyperthermia has been used as an treatment modality for cancer since end of the 19th century after observations William Coley who found that tumor is remission after induction of fever by bacterial toxins. Typically there are three categories for Hyperthermia, including local, regional and whole body. Local Hyperthermia is used to solid, localized and superficial tumors while regional is generally used for deeper diseases, and whole body Hyperthermia typically used for metastatic cancers. Actually the exact mechanism of direct HT-induced cell death is not well understood. Certainly clinical effects of Hyperthermia is more Based on it’s combination with other modalities, and it is more important, it can sensitize tumor cells to other forms of therapy, including RT (Radiation Therapy) and chemotherapy (CT). Molecular effectors of hyperthermia include; Cell membrane Alterations in fluidity/stability, Changes in structure, stability of plasma membrane, membrane potential, cellsurface receptors, transmembranetransport mechanisms, apoptosis, Impairment of ion transport (Ca2+, Na+, Mg+, K+); Impairment of protein synthesis, Induction of HSP synthesis, Generation of reactive oxygen species (ROS), Impairment of RNA/DNA synthesis, inhibition of DNA-repair mechanisms, Modification of gene expression, signal transduction Inhibition of DNA repair enzymes, and Protein synthesis (impaired), misfolding/denaturation/nuclear aggregation. Although the role of HSPs is still under investigation, current evidence has proved that enhanced immunogenicity and HSP expression seen after tumor cells are heated, thermally enhanced immune effector cell activation and function, thermally enhanced vascular perfusion and delivery or trafficking of immune effector cells to tumors. A randomized clinical trial carried out by Jones et al-2005, Has reported CR rates of 23.5% for radiotherapy alone versus 68.2% for Hyperthermia plus Radiotherapy. Conclusion: hyperthermia can be used in combination with other modalities such as radiation therapy or chemotherapy that can have additive effect on the modalities. Actually a large number of studies document clinical effectiveness of hyperthermia in combination with RT or CT in vivo and/or in vitro condition. In spite of many studies which has been published about HT, at now the exact mechanism of it is unclear. Here we will review type of method and description of cellular basic of hyperthermia related to cancer treatment, and summarise the clinical data have been documented effects of hyperthermia in combination with other modalities.
Identify New Polymorphisms Of The CDKN2A Gene In Skin Cancer In Mazandaran

1. Nafise Taheri (Department Of Biology, Islamic Azad University, Damghan Branch, Iran)
2. Ali Akbar Samadani (Cellular And Molecular Biology Research Center, Babol University Of Medical Sciences, Babol, Iran)
3. Lale Vahedi (Bu-Ali Sina Hospital Department Of Pathology, University Of Medical Sciences, Sari, Iran)

Abstract

In general, there are a large number of genes involved in the development of skin cancer with different molecular pathways including CDKN2A. Given the importance of this type of cancer molecular genetics research can be very useful in determining the involved cancer oncogenes and identifying new polymorphisms. The aim of this study is identify new polymorphisms of the CDKN2A gene in skin cancer. In this study 100 of paraffin-embedded skin cancer samples and 50 control samples from people who referred to the hospital for skin irritation are collected. Before extraction, the samples are deparaffinized. Then, the DNA is extracted by tissue DNA extraction mini kit and was evaluated in terms of quality and quantity. The study of polymorphisms of genes CDKN2A was performed using Polymerase Chain Reaction (PCR) and sequencing. According to this research which is conducted on the profiles within the years of 2007 to 2015 in the north of the country, non-melanoma cancer is seen in 100% of the cases in which the ratio of Squamous cell carcinoma (SCC) is more than Basal cell carcinoma (BCC). In order to study intron area polymorphism the samples are sequenced. With respect to all sequences, no polymorphism is observed in rs36168473 in intron (1-2) of gene CDKN2A. Similar studied on the same gene and the same type of cancer with other RSs in different directions has shown a polymorphism with alternating frequency. But given that this rs36168473 is new and selected from gene intron area, no polymorphism is observed in this area.

Corresponding Author: Nafise Taheri (Department of Biology, Islamic Azad University, Damghan Branch, Iran)
Impact Of TWIST1 On OCT-4 Gene Expression In Esophageal Carcinoma Cell Line (KYSE-30)

1. Mohammad Hosein Izadpanah (Department Of Biology, Islamic Azad University, Damghan Branch, Damghan, Iran)
2. Mohammad Reza Abbaszadegan (Division Of Human Genetics, Immunology Research Center Avicenna Research Institute, Mashhad University Of Medical Sciences, MUMS, Mashhad, Iran)
3. Mohammad Mahdi Forghanifard (Department Of Biology, Islamic Azad University, Damghan Branch, Damghan, Iran)

Abstract

Esophageal squamous cell carcinoma (ESCC) is the sixth and ninth most common cancer between men and women worldwide, respectively. TWIST, a member of the bHLH transcription factor family plays a key role in the specification and differentiation of the tissues. It may function as a multifunctional proto-oncogene during tumorigenesis and progression of solid tumors. OCT-4 (also known as POU5F1) is a key regulator of self-renewal in embryonic stem cells. The expression of such genes is probably correlated with tumorigenesis and may have an effect on some aspects of tumor behavior, such as tumor recurrence or resistance to therapies. Our aim in this study was to evaluate the regulatory role of TWIST1 on OCT4 in ESCC cell line KYSE30. mRNA extraction and cDNA synthesis were performed for the ectopic expressed and normal KYSE30 cell lines. The probable role of TWIST1 overexpression in regulation of CSC marker OCT4 was assessed in esophageal squamous cell carcinoma (KYSE-30) using comparative Real-time PCR method. After ectopic expression of TWIST1 in KYSE30 cells, we have observed significant overexpression of TWIST1 nearly 10 fold. This induced expression of TWIST1 caused significant upregulation of OCT4 in KYSE-30 cells. TWIST1 as a mastermind in morphogenesis plays an important role in metastasis and invasion of tumor cells. Furthermore, our results show that TWIST1 overexpression can be correlated with cancer stem cell marker OCT4 as well. TWIST1 may play critical regulatory role in gene expression of CSC marker OCT-4 which is involved in self-renewal process of ESCC. These results suggest new role for TWIST1 in CSC biology.

Corresponding Author: Mohammad Mahdi Forghanifard (Department of Biology, Islamic Azad University, Damghan Branch, Damghan, Iran)
The Effect Of Laughter Therapy On Fatigue In Patient With Cancer Of The Liver

1. Mehrannaghibeiranvand (Department Of Khorram Abad Nursing, Lorestan Medical Sciences, Lorestan, Iran)
2. Shokoufeh Sharaf (Department Of Khorram Abad Nursing, Lorestan Medical Sciences, Lorestan, Iran)

Abstract

Fatigue is one of the serious problems in patients with cancer of the liver. Which reduces the efficiency more patient and underlying problems such as depression is second. The laughter therapy as a treatment alternative medicine is popular. The aim of this study was to determine the effects of laughter therapy on fatigue in patients with cancer of the liver. In this Review study, in the range of 2000 to 2015, Complete search based on any of the keywords Laughter therapy, fatigue, cancer of the liver in a variety of (pubmed, HIB, SID, Irandoc, iranmedex, googlescholare, sciencedirect) and sources and scientific literature and library related The issue of match And studied the paper was written. Studies show The positive effects of laughter therapy On fatigue in patients with cancer of the liver So that after laughter therapy significantly reduced fatigue. Due to the fact that laughter therapy increases the body's oxygen t, Reduce stress, Improve breathing, Muscle and heart function and It is a morale boost, Thereby reduce fatigue patients. The meetings Patients would joke to say And laugh.

Corresponding Author: mehrannaghibeiranvand (Department of khorram Abad nursing, lorestan medical sciences, lorestan, Iran)
Evaluation Of Biological Activity And Specificity Of Mesenchymal Epithelial Transition (MET) Proto-Oncogene In KYSE-30 Cell Line

1. Negin Taghehchian (Department Of Biology, Islamic Azad University, Science And Research Branch, Tehran, Iran)
2. Baratali Mashkani (Department Of Medical Biochemistry, School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
3. Parichehr Yaghmaei (Department Of Biology, Islamic Azad University, Science And Research Branch, Tehran, Iran)
4. Mohammad Reza Abbaszadegan (Division Of Human Genetics, Immunology Research Center, Avicenna Research InstituteMashhad University Of Medical Sciences (MUMS))

Abstract

Esophageal squamous cell carcinoma (ESCC) is the sixth and ninth most common cancer between men and women worldwide, respectively. ESCC is a frequently recurrent deadly cancer for which no efficient targeted drug exists. Uncontrolled cell survival, growth, angiogenesis and metastasis are essential signs of cancer. Genetic and biochemical experiments have demonstrated that hepatocyte growth factor/scatter factor (HGF/SF) and its receptor, the tyrosine kinase MET, have an important role in all of these processes, thus providing a strong rationale for targeting these molecules in cancer. Small Molecules Inhibitors (SMIs) of the kinases are considered as one of the most promising molecular strategies to combat with such aggressive cancers. Heterocyclic compounds composed of a common core structure and different substituents used in this study. KYSE-30 cell line was used for cellular examinations. Cytotoxicity evaluation tests at different concentrations of compounds were performed using Resazurin reagent for this cell line. Graphpad Prism software was used for analysis of the cell survival data and calculation of IC50 values for each compound. Another cellular and molecular experiments such as migration assay and western blot performed to identify the specificity of compounds for MET receptor. Regarding the cytotoxic assessments, the IC50 concentration had a rising trend in D7, 1 and 5, respectively. All of them significantly inhibited the cell growth and proliferation (p<0.05). Moreover, it was observed that all of the compound, had a significant role on cell migration arrest (p<0.05). The western blot also approved that, these drugs have inhibited MET auto phosphorylation. Western blot analysis have shown that the D1, 5 and 7 can be introduced as specific drugs to target the MET receptors. D1 and 7 have shown properly an inhibitory influence on cell growth and migration. Although, 5 was enough specific to target the MET, they require a structural optimization to have a better inhibitory function. In conclusion, regarding the importance of MET inhibition in drug selection, our drugs should be optimized structurally to have more specificity against the MET receptor.

Corresponding Author: Mohammad Reza Abbaszadegan (Division of Human Genetics, Immunology Research Center, Avicenna Research InstituteMashhad University Of Medical Sciences (MUMS))
Clinical Significance Of TEAD4 Expression In Human Esophageal Squamous Cell Carcinoma

1. Yasaman Fahim (Division Of Human Genetics, Immunology Research Center, Avicenna Research Institute, Mashhad University Of Medical Sciences, Mashhad, Iran)

2. Mohammad Reza Abbaszadegan (Division Of Human Genetics, Immunology Research Center, Avicenna Research Institute, Mashhad University Of Medical Sciences, Mashhad, Iran)

3. Mohammad Mahdi Forghanifard (Department Of Biology, Islamic Azad University, Damghan Branch, Damghan, Iran)

Abstract

Esophageal cancer (EC), is one of the lethal malignancies worldwide due to its intensely aggressive nature and poor survival rate of patients. Cell signaling pathways are strongly considered in tumor progression and development. Hippo signaling pathway controls organ size in animals through regulates cell proliferation and apoptosis as well as progression of different malignancies including gastric, breast, lung and colorectal cancers. TEAD4, as the main transcription factor of this pathway binds specifically to the YAP1 oncoprotein and induces transcription of related target genes. Our aim in this study was to examine TEAD4 mRNA expression in esophageal squamous cell carcinoma (ESCC) and evaluate its correlation with different clinicopathological features of the patients. The mRNA expression of TEAD4 was evaluated using Real-time PCR in 50 fresh-frozen tumoral and related margin normal tissues. Data was analyzed using the SPSS 19.9 statistical package. Significant over expression of TEAD4 was observed in 44% of tumor samples. Mean ± SD of gene expression fold change was 1.8412 ± 2.02479. The expression of TEAD4 was directly associated with the stage of tumor cell progression and lymph node metastasis (p≤0.05). Our findings suggest that TEAD4 has markedly different expression pattern in ESCC compared to normal tissues and overexpression of TEAD4 is likely to have important roles in ESCC progression. These findings identify, TEAD4 as a marker of ESCC invasiveness and thus may be useful as a prognostic and therapeutic target for improving survival rate of patients.

Corresponding Author: Mohammad Mahdi Forghanifard (Department of Biology, Islamic Azad University, Damghan Branch, Damghan, Iran)
The Effect Of Music Therapy On Psychological Signs And Pain In Women With Breast Cancer

1. Shokoufeh Sharafi (Department Of Khorram Abad Nursing, Lorestan Medical Sciences, Lorestan, Iran)
2. Mehran Beiranvand (Department Of Khorram Abad Nursing, Lorestan Medical Sciences, Lorestan, Iran)

Abstract

Anxiety and depression, the most common psychological reactions are in women with breast cancer that deal with diagnosis, prognosis and treatment options caused in patient. On the other hand, tolerance of pain in patients impact on the patient's general quality of life. Music caused effective communication in the family and society, feel better, thought deviation and thus reduce stress and pain. The aim of this study was to determine the effects of music therapy on psychological signs in women with cancer of the breast. In this Review study, in the range of 2005 to 2015, complete search based on any of the keywords music therapy, anxiety, depression, pain and breast cancer in a variety of (pubmed.hib, sid, irandoc, iranmedex, googlescholare, sciencedirect) and sources and scientific literature and library related the issue of match and studied the paper was written. Studies show The positive effects of music therapy on anxiety, depression (psychological signs) and pain in patients with cancer of the breast So that after music therapy significantly reduced anxiety, depression and pain. Due to the simplicity and low cost, this method, Can be used as a non-pharmacological methods, non invasive and complement with drug therapy and interventions to promote mental health in these patients.

Corresponding Author: Shokoufeh Sharafi (Department of Khorram Abad Nursing, Lorestan Medical Sciences, Lorestan, Iran)
Design And Production Of Anti Erbb2-Toxin As A Novel Anticancer Candidate Of Breast Cancer

1. Elnaz Yazdani (Department Of Biology, Faculty Of Science, University Of Isfahan, Isfahan, Iran)
2. Mahboobeh Nazari (Monoclonal Antibody Research Center, Avicenna Research Institute, ACECR, Tehran, Iran.)
3. Abolghasem Esmaeili (Department Of Biology, Faculty Of Science, University Of Isfahan, Isfahan, Iran)
4. Arash Minal-Tehrani (Nanobiotechnology Research Center, Avicenna Research Institute, ACECR, Tehran, Iran.)
5. Rahman Emamzadeh (Department Of Biology, Faculty Of Science, University Of Isfahan, Isfahan, Iran)

Abstract

Breast cancer remains the leading cause of cancer death in females. In spite of advanced improvement in clinical medicine, primary and secondary resistance is encountered worldwide. Over expression of human epidermal growth factor 2 receptor occurs in approximately 30% of people with breast cancers. Due to poor patient prognosis, immunotoxins have been suggested and used as an efficient therapeutic agent. Immunotoxins are chimeric proteins contain of a specific cellular targeting domain linked to a cytotoxic factor. In this study, we introduces a novel recombinant immunotoxin-based protein to enhance efficacy of targeting specific cancer cells through conjugating effective toxin to HER2 ligand. In order to produce a recombinant anti Erbb2-toxin consisting of insect toxin with high affinity for HER2/neu receptor, we have used an expression matrix including two expression vectors including pET and Cold Shock expression System, three different E. coli hosts; BL21 (DE3), Rosetta-gami plysS and T7 shuffle B and five solubilization conditions containing 6 different buffers with various organic components in different pH. Our anticancer agent has demonstrated high level of protein expression when produced in Cold Shock expression System (BL21) compared to pET expression system. In addition, the best solubilization buffer contains triton x-100. Anti Erbb2-toxin can be a potential candidate with remarkable proficiency for treating breast cancer patients having high expression levels of Her2 receptor. The generated soluble recombinant immunotoxin is a good candidate for breast cancer therapy.

Corresponding Author: Mahboob Nazari (Monoclonal Antibody Research Center, Avicenna Research Institute, ACECR, Tehran, Iran.)
Evaluation Cytotoxic Effect Of Methanol Extract From Nematocyst Carpet Anemone Against MD-MBA231 Cell Line In Vitro

1. Ziba Moghadasi (Department Of Marine Biology, Faculty Of Marine Sciences And Technologies, Science And Research Branch, Islamic Azad University. Tehran, Iran)

Abstract

Carpet anemone, Stichodactyla haddoni is an ocean dwelling sedentary organism belongs to the family of Stichodactylidae. These family contains specialized cells called nematocysts that produce venom for defense/offence purposes. These compounds is effective in medical applications and prevention of various diseases such as cancer. This study is survey of cytotoxicity of the methanol extract from Persian Gulf sea anemone, S. haddoni on Breast cancer (MD-MBA231) cell line by MTT assay. One sample of S. haddoni were collected from coastal waters of Lark island Persian Gulf the south of Iran in September 2015. The specimen after identification were kept in -20°C. The extraction of methanol from tentacle was performed and to put in store by freeze-drying. Amount of protein content was determined by bicinchoninic acid assay. The cell line was cultured in complete tissue culture medium RPMI+FBS10%+pen/strep. These cells were treatment in presence of different Serial dilution 100 to 0.78 μg of venom extract in duration time 24 hour. The results of Lc50 showed that after passing of 24 hour the death rate was 3.125 μg/ml. Analysis of variance for cytotoxicity of crude venom on MD-MBA231 cell line showed that activity was similar together in almost all doses (P <0.001). Linear regression analysis showed significant correlation between cytotoxicity of crude venom on MD-MBA231 and examined doses (R2 = 0.692). This similarity would be suggested a common dose dependent trend of lethality on cancer cell line. Therefore, further research about these compounds is essential to can provide new biomedical research tools for designing novel anticancer drugs.

Corresponding Author: ziba moghadasi (Department of Marine Biology, Faculty of Marine Sciences and Technologies, Science and Research Branch, Islamic Azad University. Tehran, Iran)
T-Ag Gene Of Polyomavirus JC In Colorectal Cancerous And Non-Cancerous Specimens, The First Report From Iran

1. Samira Izi (Department Of Clinical Biochemistry, School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Masoud Youssefi (Department Of Medical Microbiology And Virology, School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
3. Nema Mohammadian Roshan (Department Of Pathology, Ghaem University Hospital, Mashhad University Of Medical Sciences, Mashhad, Iran)
4. Saeid Amel Jamehdar (Department Of Medical Microbiology And Virology, School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
5. Amir Azimian (Department Of Medical Microbiology, North Khorasan University Of Medical Sciences, Bojnord, Iran)
6. Farnaz Zahedi (Department Of Clinical Biochemistry, School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Colorectal carcinogenesis is regarded as a multistep and multifactorial process. Among the exogenous agents are some infectious agents as important pathogenic elements in human cancer, since almost one fifth of human cancers are associated with infectious agent, including viruses and bacteria. More recently, it has been suggested a possible association between JC virus infection and colorectal cancer. The oncogenic potential of JCV is mediated by a transforming protein, the T-antigen (T-Ag) might contribute to the cancer phenotype and cellular function by several mechanisms. (T-Ag) is a multifunctional protein capable of promoting neoplastic transformation of cells. JCV T-Ag has the ability to bind and inactivate tumor suppressor proteins including p53 and the cell cycle regulator retinoblastoma gene product pRb, leading to their destruction, and allowing replication of cancer cells with damaged chromosomes. The objective of this study was to investigate whether JCV DNA sequences is present in human colorectal cancer tissues and non-cancerous tumor-adjacent tissues in our sociogeographical region. In this study, samples obtained from tumor paraffin embedded tissues and matched normal tissues from 50 CRC patients. Genomic DNA was extracted from the tissue specimens. Real-time PCR method was used to detect the JCV T-Ag sequences. We found that JCV DNA sequences were present in 60% (30/50) of CRC tissues and 38% (19/50) in non-cancerous colorectal mucosa. These data indicate, for the first time, presence of JC virus in colorectal carcinoma samples in Iran. These findings suggest a possible role for involvement of JCV T-Ag in carcinogenesis of colorectal malignancy in Iranian patients. Though, JCV might not necessarily be the main cause of colorectal cancer, but it can contribute to some extent in development of adenocarcinomas at one or several stages of tumor progression.

Corresponding Author: Farnaz Zahedi (Department of Clinical Biochemistry, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran)
How And The Importance Of Prevention And Treatment Of Mucositis And Xerostomia In Treatment Of Head And Neck Cancer

1. Majid Sanatkhani (Faculty Member Of Dentistry, Mashhad University Of Medical Sciences)

Abstract

Oral complications of radiotherapy or chemotherapy treatment in patients with head and neck cancer, has a considerable impact on patients' quality of life. These side effects usually caused by a direct impact on the treatment of oral tissues or indirect effect resulting from treatment due to dry mouth and opportunistic infections. The most common clinical presentation of oral lesions, oral mucositis and dry mouth that nonoperative treatment for head and neck cancers, is. For the prevention and management of this complication, accurate and complete understanding of the mechanism and severity of the damage that causes the complications of diabetes is crucial. Treatment and prevention of dryness, as well as the treatment of oral mucositis in head and neck cancer treatment success will be a great help. The use of salivary stimulants or artificial saliva and oral mucositis treatment and management assistance to local antimicrobial, anti-inflammatory mouthwash has been very useful. Mucositis and xerostomia are common and potentially dangerous complication of head and neck cancers that require special attention and treatment. By oncologists refer their patients before starting treatment, oral diseases specialist to assess and check-mouth plays an important role in the treatment of these patients. Prevention and treatment of oral complications of cancer, cancer is one of the most important responsibilities of doctors and therapists.

Corresponding Author: majid sanatkhani (Faculty Member of Dentistry, Mashhad University of Medical Sciences)
Abstract

Colorectal cancer (CRC) is a heterogeneous disease, and encompasses fundamentally different molecular phenotypes following various pathways of carcinogenesis. Molecular characteristics might predispose tumors to a worse prognosis and identification of those enables identifying patients with high risk of disease recurrence. One of the application of molecular pathology in CRC refers to microsatellite instability (MSI). MSI-H is a hallmark alteration of HNPCC/Lynch syndrome-associated tumors, but is also found in sporadic colon cancers. MSI-H has a significant impact on tumor biology. This is reflected by a more favorable prognosis. MicroRNAs involved in different signaling networks leading to colon cancer metastasis, mainly PTEN/PI3K, EGFR, TGF-beta, and p53 signaling pathways of metastatic colon cancer. The alteration of miRNA profiles has been correlated with the transformation and metastasis of colon cancer. They could directly target genes playing a central role in epithelial-mesenchymal-transition (EMT), a cellular transformation process that allows cancer cells to acquire motility and invasiveness. One of the best known EMT-related miRNAs is the miR-200 family. Tumor specific methylation in circDNA is a potential target for the development of non-invasive, blood-based assays for cancer diagnosis. Following identification as a potential biomarker, SEPT9 gene promoter region was initially identified as being differentially methylated. Other methylation-based plasma biomarkers including the promoters of genes RASSF1A, APC and E-cadherin, and completely novel sequences such as CAHM, a long non-coding RNA gene. Tumor budding is thought to represent the morphological correlate of EMT in colorectal cancers and has been strongly linked to adverse clinicopathological features and poor overall and disease-free patient survival. Colon cancer remains a leading cause of mortality worldwide despite the well-characterized molecular events in the adenoma-to-carcinoma sequence. it is, therefore, apparent that, despite many strides in understanding the development and progression of CRC, a lot remains largely unknown due to the multifactorial process of this disease.
Quantum Dots For Early Detection And Smart Drug Delivery In Cancer Treatment

Abstract

Cancer nanotechnology is an interdisciplinary area of research in science, engineering, and medicine with broad applications for molecular imaging, molecular diagnosis, and targeted therapy. Quantum dots (QDs) are semiconductor inorganic nanomaterials ranging from 1–10 nm. They contain elements found in groups II–IV (eg, CdSe, CdTe, CdS, and ZnSe) or III–V (eg, InP and InAs) of the periodic table. Considerable interest has been shown toward these materials in recent years, especially in view of their potential applications in biology and medicine. They are gaining momentum as imaging molecules with life science and clinical applications. Clinically they can be used for localization of cancer cells due to their nano size and ability to penetrate individual cancer cells and high-resolution imaging derived from their narrow emission bands compared with organic dyes. Owing to their unique properties such as photostability, size- and composition-tunable emission properties (from visible to infrared wavelengths), and their ability to deliver multiple diagnostic or targeting agents, QDs have emerged as a promising nanotechnology for cancer detection. By combination of functional biomolecule-nanoparticle hybrid systems and the optical imaging and biophysics, QDs have been used as optical reporter units of biocatalytic transformations and can probe intracellular processes in vitro. QDs as a novel probe for in vivo analysis and clinic therapy such as cancer research, and in vivo photodynamic therapy (PDT) open an attractive new field with promising perspectives in biomedicine. Their long half-life, high photostability and excellent brightness allow the imaging and monitoring of drug delivery pathways in vivo with sharp resolution and reduced background autofluorescence. These properties make QDs suitable candidates for the use as drug delivery vehicle. The development of QD labeling promotes the research in the nano-drugs in cellular, even at live animal level. The development of fluorescence imaging technology of QDs and the therapy-based multifunctional nano-drugs is expected to apply to diagnosis and treatment of cancers. At the same time, surface modifications with targeting ligands are also commonly used to increase drug-delivery efficiency.

Corresponding Author: samaneh nabavi (Institute of Policy Research and Social Studies, Tehran, Iran)
The Activity And Tissue Distribution Of Thioredoxin Reductase In Basal Cell Carcinoma

1. Seyed Isaac Hashemy (Surgical Oncology Research Centre, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Ahmad Reza Taheri (Department Of Dermatology, Imam Reza Hospital, Faculty Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Basal cell carcinoma (BCC) is the most prevalent dermal tumor in Caucasians. Different mechanisms are proposed to be involved in its pathogenesis such as oxidative stress. Oxidative stress, which is the consequence of the disruption of redox balance in favor of oxidants, is involved in the initiation or progression of many tumors. Thioredoxin reductase (TrxR) is a key enzyme of the thioredoxin (Trx) system, containing Trx and TrxR and NADPH, which is one of the main cellular oxidoreductases with an essential role in cellular health and survival through providing and maintaining redox balance. Therefore, we aimed to study and compare the activity and tissue distribution of TrxR in tumoral tissue and its healthy margin in patients with BCC. After biopsy and taking samples from 20 patients, TrxR activity was measured using a commercial kit and its tissue distribution was assessed immunohistochemically. Both the activity and tissue distribution of TrxR in tumoral tissues were significantly higher compared to their healthy margins. Based on this results, it is concluded that TrxR is involved in pathogenesis of BCC; however, more investigations are required to clarify whether this increase is a consequence of BCC or it is an initiating mechanism.

Corresponding Author: Amir Hossein Jafarian (Department of Pathology, Qaem Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran)
The Effect Of Microgravity On The Cytoskeleton Of Cancerous Cells

1. Fatemeh Salami (1Department Of Physiology, School Of Veterinary Medicine, Ferdowsi University Of Mashhad, Mashhad, Iran.)
2. Fatemeh Yonesi (1Department Of Physiology, School Of Veterinary Medicine, Ferdowsi University Of Mashhad, Mashhad, Iran.)

Abstract

Introduction: Microgravity on space flights effect on the physiology of a cell by affects molecular and cellular functions that are still unclear. In the microgravity environment of space, the apparent weight of a system is reduced compared with its real weight in standard gravity. microgravity or zero gravity alter cancer growth and progression. However, various cancers respond differently to microgravity by changes in cellular processes and functions. As a result of all cell types exposed to microgravity: the alteration of cytoskeletal elements: actin, microfilaments and microtubules occur that can cause changes in cell signaling and migration to cell cycling and apoptosis. Studies illustrate that microgravity effects on cell structure and function, gene expression and signal transduction. Matrix metalloproteinases (MMPs) are a family of extra-cellular zinc-dependent neutral endopeptidases that can degrading various components of the extracellular matrix. Their activity is modulated by tissue inhibitors of metalloproteinases (TIMPs). MMPs and TIMPs play a crucial role in metastasis by the degradation of collagen IV, gelatin, and laminin in the basement membrane, an important step in tumor invasion. TIMP-1 is one of inhibitors of the (MMPs) that prevents apoptosis and grow up the cancer. For example, MMP-9 Considered to be a prognostic marker in stomach cancer. The MMPs acts as mediators of tumor invasion and metastasis by disrupt the tissue barriers. There studies show the role of MMPs in invasion, metastasis and angiogenesis of various cancers. Microgravity has been shown to alter cancer growth However, their responses are different by losing or enhancing cellular functions.

Corresponding Author: amintavassoli (2Department of Biotechnology, School of Veterinary Medicine, Ferdowsi University of Mashhad, Mashhad, Iran)
The Effect Of Microgravity On The Cytoskeleton Of Cancerous Cells

1. Fatemeh Salami (Department Of Physiology, School Of Veterinary Medicine, Ferdowsi University Of Mashhad, Mashhad, Iran.)
2. Fatemeh Yonesi (Department Of Physiology, School Of Veterinary Medicine, Ferdowsi University Of Mashhad, Mashhad, Iran.)
3. Amin Tavassoli (Department Of Biotechnology, School Of Veterinary Medicine, Ferdowsi University Of Mashhad, Mashhad, Iran)

Abstract

Microgravity on space flights effect on the physiology of a cell by affects molecular and cellular functions that are still unclear. In the microgravity environment of space, the apparent weight of a system is reduced compared with its real weight in standard gravity. microgravity or zero gravity alter cancer growth and progression. However, various cancers respond differently to microgravity by changes in cellular processes and functions. As a result of all cell types exposed to microgravity the alteration of cytoskeletal elements: actin, microfilaments and microtubules occur that can cause changes in cell signaling and migration to cell cycling and apoptosis. Studies illustrate that microgravity effects on cell structure and function, gene expression and signal transduction. Matrix metalloproteinases (MMPs) are a family of extra-cellular zinc-dependent neutral endopeptidases that can degrading various components of the extracellular matrix. Their activity is modulated by tissue inhibitors of metalloproteinases (TIMPs). MMPs and TIMPs play a crucial role in metastasis by the degradation of collagen IV, gelatin, and laminin in the basement membrane, an important step in tumor invasion. TIMP-1 is one of inhibitors of the (MMPs) that prevents apoptosis and grow up the cancer. For example, MMP-9 Considered to be a prognostic marker in stomach cancer. The MMPs acts as mediators of tumor invasion and metastasis by disrupt the tissue barriers. There studies show the role of MMPs in invasion, metastasis and angiogenesis of various cancers. Microgravity has been shown to alter cancer growth However, their responses are different by losing or enhancing cellular functions.

Corresponding Author: Amin Tavassoli (Department of Biotechnology, School of Veterinary Medicine, Ferdowsi University of Mashhad, Mashhad, Iran)
Removal Of Cadmium From Aqueous Solutions Using Β-Cyclodextrin Graphene Oxide Adsorbent

1. Elham Einafshar (School Of Chemistry, Damghan University, Damghan, Iran)
2. Azadeh Hashem Nia (Pharmaceutical Research Center, Pharmacy School, Mashhad University Of Medical Sciences, Mashhad, Iran)
3. Ali Haghighi Asl (Faculty Of Chemical, Gas And Petroleum Engineering Department, Semnan University, Semnan, Iran)
4. Mohammad Ramezani (Pharmaceutical Research Center, Pharmacy School, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Nowadays water pollution with heavy metal is one of the main concerns in the pollution management. In the modern world, with the intensive growing industrialization, toxic heavy metals are used extensively and it seems very unlikely that can be avoided. These materials have greatly affected people’s health. One of the most toxic heavy metals is Cadmium which even at very low dosages may cause oxidative DNA damage leading to mutations and cancer initiation. Adsorption is the most common method for trapping heavy metal cautions since it is easily available and benefits from low energy consumption. One of the novel compounds which is highly explored as adsorbent platform is graphene oxide (GO). The surface area of GO contains many polar groups such as hydroxyl, epoxy, carbonyl and carboxyl, making GO a good chemical reactant and superb platform sorbent for organic dyes or heavy metal ions. Besides, on the basis of the previous study, we assumed that grafting β-cyclodextrin (β-CD) onto GO may produce a conjugate with excellent absorption capacity. In this research, first we functionalized graphene oxide with β-cyclodextrin and confirmed the successful synthesis of β-CD-GO by series of analysis such as Fourier transform infrared spectroscopy (FTIR), TEM and thermo gravimetric analysis (TGA), then the modified graphene oxide was used to investigate adsorption of Cd²⁺ ion in aqueous solutions. The effects of various experimental parameters such as initial pH, initial metal ion concentration, adsorbent dosage and contact time on the sorption process were also studied. The absorption data showed the optimum pH for β-CD-GO was considered at PH=11. Kinetics of adsorption, isotherm studies and thermodynamics analysis were studied. The adsorption experimental data is well fitted with the pseudo-second-order model and Freundlich isotherm models. The importance of these results is due to developing an efficient material for the removal of metals and pollutants from water. The results of this work confirmed that β-CD-GO is a powerful and promising candidate for adsorption of heavy metal from wastewater.

Corresponding Author: Mohammad Ramezani (Pharmaceutical Research Center, Pharmacy school, Mashhad University of Medical Sciences, Mashhad, Iran)
An Investigation On The Mesothelin Characteristics For Immunotoxin Development

1. Neda Eskandari-Torbaghan (Islamic Azad University, Neyshabur Branch, Neyshabur, Iran)
2. Aliakbar Haddad-Mashadrizeh (Department Of Biology, Faculty Of Science And Cell And Molecular Biotechnology Research Group, Institute Of Biotechnology, Ferdowsi University Of Mashhad, Mashhad, Iran)

Abstract

Cell surface antigens are critical markers for diagnostic and healing of many diseases such as cancer. In this regard, mesothelin as specific antigen, with low expression on the normal cells and over-expression on the surface of mesothelioma, is suitable candidate for developing approaches of therapeutic and diagnostic of cancer. Bearing in mind, the structural and functional characterization as well as the expressing cells of the antigen was considered in this study for immunotoxin development. Accordingly, the protein sequence of the mesothelin with the accession number ALC62084 were retrieved from NCBI database. PROTEINATLAS were used for assessment the expression of the antigen. On the other hand, corresponding specific ligands of this antigen were detected via STRING program. Structural modeling and quality assessment of the models were carried out by MODELLER and RAMPAGE programs, respectively. Moreover, topology features of the antigen were determined by Mpex program. All data were expressed as mean _standard deviation with SPSS 21.0 (SPSS Inc., Chicago, IL, USA). Topology feature of the antigen showed that the C terminal of the mesothelin is situating on the extracellular with one transmembrane region. Moreover, various expression of the antigen were appeared on the surface of the mesothelial cells. However, the highest expression of this antigen was determined on the surface of ovarian cancer cells. Furthermore, 3D structure of the antigen showed 98% similarity with appropriate in quality. Meanwhile, MUC19, WFDC2, WNT5A, NDUFB5, NDUFB9, MPV17, RALA, LAMTOR3, ZBTB43, RNMTL1, HN1 and MOR Ab-009 propounded as corresponding ligands of the antigen with different affinity. In general, the results of this study provide the context for immunotoxins development with the capacity to targeting mesothelin on the cell surface of the malignancies.

Corresponding Author: Aliakbar Haddad-Mashadrizeh (Department of Biology, Faculty of Science and Cell and Molecular Biotechnology Research Group, Institute of Biotechnology, Ferdowsi University of Mashhad, Mashhad, Iran)
Simulation And Stability Assessment Of Anti-EpCAM Immunotoxin For Multiple Cancer Therapy

1. Seyed-Ali Hosseinian (Department Of Biology, Science And Research Branch, Islamic Azad University, Khorasan Razavi, Neyshabur, Iran)
2. Aliakbar Haddad-Mashadrizeh (Cell And Molecular Biotechnology Research Group, Institute Of Biotechnology, And Department Of Biology, Faculty Of Science, Ferdowsi University Of Mashhad, Mashhad, Iran)
3. Samaneh Dolatabadi (Department Of Biology, Science And Research Branch, Islamic Azad University, Khorasan Razavi, Neyshabur, Iran)

Abstract

Epithelial cell adhesion molecule (EpCAM) is a dominant antigen in human colon carcinoma tissue. Topology features of this antigen is different in normal and malignancies condition, so that in normal cells is predominantly located in intercellular spaces and is sequestered on normal epithelia and, therefore, much less accessible to antibodies than EpCAM in cancer tissue. Accordingly, EpCAM was considered as a suitable candidate for cancer target therapy via immunotoxins (ITs) development. In this regard, several ITs have been developed which could be provided context for ITs optimization. Bearing in mind, we have focused on the stability assessment of an anti-EpCAM-IT (anti-Ep-IT) for designing a novel IT. In this regard, 3D structure of EpCAM and toxin segments of anti-Ep-IT were retrieved from PDB, with the ID numbers 4MZV, 1IKQ, respectively. Discovery Studio3.0 was used for separation of the ligands and water molecules. Alignment of the antibody (Ab) fragment of anti-Ep-IT was performed through BLAST-p, and SWISSMODEL database was used for Ab modeling. Moreover, IT modeling was accomplished through MODELLER9.15. GROMACS5.07, containing gromos96 43a1 force field were used for simulation 300°K, 100ps of the time for NVT and NPT steps and 20000ps(20ns) for MD step. RMSD and RMSF plots were drown by Excel. Finally, ERAAT database was used for quality assessment of the structure. In general, the both modeling results and quality evaluations of them were satisfactory for designing IT. Moreover, RMSD and RMSF plots reveal that IT stability has preserved during the simulation. On the whole, our findings led to designing a new anti-Ep-IT with more stability.

Corresponding Author: Aliakbar Haddad-Mashadrizeh (Cell and molecular biotechnology research group, institute of biotechnology, and Department of Biology, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran)
Oncogene Promoter G-Quadruplexes As Potential Therapeutic Targets Towards Effective New Anticancer Drug Design

1. Saeedeh Ghazaey Zidanloo (Department Of Molecular And Cell Biology, Faculty Of Basic Sciences, University Of Mazandaran, Babolsar, Iran)
2. Abasalt Hosseinzadeh Colagar (Department Of Molecular And Cell Biology, Faculty Of Basic Sciences, University Of Mazandaran, Babolsar, Iran 2 Nano And Biotechnology Research Group, Faculty Of Basic Sciences, University Of Mazandaran, Babolsar, Iran)

Abstract

Besides the B-form canonical duplexes, DNA can fold into different other inter- and intramolecular secondary structures. DNA G-quadruplexes are higher order structures formed in specific G-rich sequences which can assemble into tetrameric structures. G-quadruplexes are over-represented in oncogenes promoter and other regions within the genome with biologically significant role. Attention to the more common therapeutic importance of G-quadruplexes has extended through the past decade and they studied as a new class of novel molecular therapeutic targets in oncology, wherever transcriptional down regulation of oncogenes via stabilization of these structures could be a novel anticancer approach. Recently, researchers have had special interest to find out small molecules that could stabilize these higher order structures, not only by modifying the stability of G-quadruplexes and down regulation of oncogenes expression but also by performing so selectively in the presence of other possible targets such as double-stranded DNA. This interest was triggered by publications displaying the transcriptional repression of the c-MYC, c-KIT, PDGF-A, bcl-2, VEGF, HIF-1α, STAT3, HRAS and WT1 proto-oncogene genes through stabilization of these structures in promoter regions. For the first time we have successfully down-regulated the WT1 oncogene expression in AML leukemia cell line by using this technology in Iran. These findings prepare the foundation for the rational design and improvement of G-quadruplex-stabilizing molecules as new anticancer drugs for targeted cancer therapy which selectively have an antiproliferative and chemosensitizing activity in in vitro and in vivo tumor models, without any noticeable influence on normal cells. In addition the different molecular structures of G-quadruplexes revealed they may be differentially regulated and targeted by different molecules and much studies are being made to improve selection of small molecules with developed G-quadruplex detection and to efficiently affect target gene transcription. In conclusion, the biological significance of promoter G-quadruplexes has strengthened investigation and improvement of G-quadruplex-interactive molecules, as potential anticancer drugs which reveal approximately lower cytotoxicity in normal cells. Some of the G-quadruplex targeting drugs have entered Phase II clinical trials.

Corresponding Author: Abasalt Hosseinzadeh Colagar (Department of Molecular and Cell Biology, Faculty of Basic Sciences, University of Mazandaran, Babolsar, Iran 2 Nano and Biotechnology Research Group, Faculty of Basic Sciences, University of Mazandaran, Babolsar, Iran)
Study Of Tumor Markers In Ovarian Cancer

1. Ala Saber Mohammad (Student Researches Committee Of Faculty Of Nursing And Obstetrics, Mashhad University Of Medical Science, Mashhad, Iran)
2. Zahra Kamali (Student Researches Committee Of Faculty Of Nursing And Obstetrics, Mashhad University Of Medical Science, Mashhad, Iran)

Abstract

Among gynecological malignity, ovarian cancer has the highest mortality. This mortality is mostly due to diagnosis in the advanced stages. For improvement of therapeutic results in ovarian cancer, early diagnosis using specific tumor markers with the diagnostic ability in the early stages is an effective measure. This study aims to analyze the tumor markers in ovarian cancer. Summary of studies indicated that inhibin is increased in patients with ovarian cancer particularly musinosis and granulosa tumors. The mean of copper serum concentration, and ratio of copper to zinc in the patients of malignant group was significantly more than benign group, but no significant difference existed between mean of zinc serum concentration of patients with ovarian cancer and patients suffering from benign lesions. Expression of protein DAL-1 in cancer tissues in comparison to the adjacent normal tissues had been significantly reduced. In addition, reduction of expression of this protein statistically was related to lymph node metastasis, significantly. In the patients with malignant tumors, mean serum level of thrombopoietin, CA125 and HSP70 in ovarian cancer was higher than benign ovarian tumors. Significant difference was observed in the mean concentration of β-hCG between patient and healthy groups, whilst the difference of mean concentration of calcium, phosphor, and alkaline phosphatase activity between patient and healthy group was not significant. Conclusion: Inhibin serum, copper serum and copper to zinc ratio, use of CA125 and inhibin, and HSP70 along with CA125 are assumed as good tumor markers for early diagnosis of ovarian tumors. Reduction of expression of protein DLA-1 may be related to the pathogenesis of ovarian cancer. Thrombopoietin in comparison to CA125 has more sensitivity and virtue for diagnosis of ovarian cancer and its combination with A125 may be a positive prediction indicator for determination of ovarian pathology type. Serum level of β-hCG in patients with ovarian cancer receiving chemotherapy or radiotherapy is higher than healthy persons. In addition, serum level of calcium, phosphor and activity of alkaline phosphatase enzyme in patients with ovarian cancer under treatment has no association with the disease status.

Corresponding Author: Ala Saber Mohammad (Student Researches Committee of Faculty of Nursing and Obstetrics, Mashhad University of Medical Science, Mashhad, Iran)
Relationship Between Nutrition And Physical Activity With Breast Cancer

1. Zahra Kamali (Student Researches Committee Of Faculty Of Nursing And Obstetrics, , Mashhad University Of Medical Science, Mashhad, Iran)
2. Ala Saber Mohammad (Student Researches Committee Of Faculty Of Nursing And Obstetrics, , Mashhad University Of Medical Science, Mashhad, Iran)

Abstract

Breast cancer is one of the most common cancers in women. Whereas the nutrition is one of the effective factors in catching this disease, the present study aims to determine the relationship between nutrition and physical activity and breast cancer. The studies indicated that use of fish, low-fat dairies, vitamin D and calcium reduce the risk of breast cancer in women, whilst use of sausage an bacon, high values of iron and all types of received fat are connected to the increased risk of breast cancer. Shortage of folate was not associated with the risk of breast cancer in the whole women, whilst in women after menopause increased the cancer. Breast cancer in comparison to other cancers has the lowest association with malnutrition. Low physical activity is one of factors of risk of breast cancer in early ages; and high body mass index upon diagnosis and its 5-year changes is assumed as one of breast cancer risk factors within ages below 40. After menopausal ages, for every hour of average physical activity increment per week, the risk of being infected with breast cancer is reduced for 9%. Therefore, whereas lifestyle is adjustable potentially, awareness of the impact of these factors on the risk of catching breast cancer has a considerable importance in prevention of this fatal disease.

Corresponding Author: Zahra Kamali (Student Researches Committee of Faculty of Nursing and Obstetrics, , Mashhad University of Medical Science, Mashhad, Iran)
WNT5A Modulates Integrins Expression Of Human Ovarian Cancer Cells

1. Vajihe Azimian-Zavareh (Department Of Animal Physiology, Developmental Biology Laboratory, School Of Biology, College Of Science, University Of Tehran, Tehran, Iran)
2. Ghamartaj Hossein (Department Of Animal Physiology, Developmental Biology Laboratory, School Of Biology, College Of Science, University Of Tehran, Tehran, Iran.)
3. Marzieh Ebrahimi (Department Of Stem Cells And Developmental Biology At Cell Sciences Research Center, Royan Institute For Stem Cell Biology And Technology, ACECR, Tehran, Iran.)

Abstract

Metastasize of epithelial ovarian cancer (EOC) occurs by forming spheroids in peritoneum cavity accompanied with adherence and disaggregation of cells to mesothelium. Both cell-cell adhesion and cell-ECM interacting molecules play a role in this process and a number of cell adhesion molecules such as integrins have been suggested. WNT5A protein is an important regulator of cancer cell behavior and progression in different types of cancer. Here we sought to determine the modulatory role of Wnt5A on integrin expression by human ovarian cancer cell line SKOV3 in monolayer and spheroid model. Cells were stably transfected with pcDNA3.2/hWNT5A (Wnt5A/SKOV-3) construct or empty vector (mock). Wnt5A, N-cadherin, snail and fibronectin expression levels were assessed by qPCR. Integrins expression was analyzed by using integrin array kit. Effect of ECM components such as collagen type- I and IV, laminin and fibronectin on spheroid formation was assessed by mixing them with Mock and Wnt5A/SKOV-3 cells. Cell's migration was analyzed by using both scratch and transwell assay. Moreover, BOX-5 as a Wnt5A antagonist was used to assess the effect of Wnt5A blockage on integrin expression and migration of Wnt5A/SKOV-3 cells. Wnt5A overexpression decreased compaction of SKOV-3 spheroids relative to mock. Subsequently, levels of mesenchymal markers such as N-cadherin, snail and fibronectin were significantly decreased in Wnt5A/SKOV-3 cells compared to mock. Integrin array analysis showed increased expression levels of α5, αV and β1 integrins and decreased expression levels of α2, α4, αvβ3, β3 and β4 integrins in transfected cells compared to mock. It is noteworthy that the observed changes in integrins expression was similar in both monolayer and spheroid models in Wnt5A/SKOV-3 cells. Whereas α5β1 serves as fibronectin receptor, correspondingly, here, we found increased compaction and adhesion of cells in the presence of fibronectin in transfected cells compared to mock. Wnt5A/SKOV-3 cell migration were increased compared to mock. Interestingly, in the presence of BOX5, we found decreased mRNA levels of ITGA5 and AV integrins as well as reduced levels of Wnt5A/SKOV-3 cell migration compared to mock. Altogether our data suggest that WNT5A may play a promoting role in EOC progression through modulation of integrin expression.

Corresponding Author: Ghamartaj Hossein (Department of Animal Physiology, Developmental Biology Laboratory, School of Biology, College of Science, University of Tehran, Tehran, Iran.)
Effects Of Antioxidants On Matrix Metalloproteinase-2 And 9 In Glioblastoma Multiforme

Abstract

Glioblastoma multiforme (GBM) is a kind of glioma that develops from star-shaped glial cells such as astrocytes and oligodendrocytes. It is the most common and aggressive type of brain cancer with poor prognosis and survival. Matrix metalloproteinases (MMPs) are a big family of proteinases that play a critical role in extracellular matrix (ECM) degradation in a variety of physiological and pathological tissue remodelling processes. Matrix metalloproteinases are secreted as inactive pro-enzymes that are called zymogens. They undergo proteolytic reactions for activation and ECM degradation. Recent studies have reported that tumor invasion in Glioblastoma multiforme has been associated with increased ECM degradation and MMPs activation. In this way, the prevention of MMPs activity is an important agent in GBM prevention. Gelatinases such as MMP-2 and MMP-9 are a group of MMPs. Studies to date suggest that gelatinases have a critical role in glioblastoma multiforme. It has reported that antioxidant can prevent the activation of MMPs. Several researchers have suggested that dietary antioxidants can act as potent inhibitors of matrix metalloproteinases activities. It has been shown that green tea polyphenols especially (3)-epigallocatechin 3-gallate inhibited Matrix metalloproteinase-2 activity in glioblastoma cells. Other antioxidant components such as vitamin A, C, D and E were effective inhibitors of glioma cells in cell culture but studies demonstrated the different results of these vitamins in vivo. Further studies, both in vitro and in vivo are necessary to detect the influence of antioxidant vitamins in GBM prevention or treatment. Not only vitamins but also minerals such as selenium and copper that are involved in antioxidant enzyme (glutathione peroxidase and superoxide dismutase) activity can decrease the GBM possibility. Recent researches demonstrated that selenium induces tumor cell-specific apoptosis and has anti-invasive characteristics. In conclusion, dietary antioxidant nutrients can decrease the possibility of GBM incidence and further researches are needed to confirm our results.

Corresponding Author: Mina Bagheri Varzaneh (Department of Animal Sciences, Isfahan University of Technology, Isfahan, Iran)
Background: Breast cancer is the most common cause of cancer death among women worldwide. miRNAs are the large subgroup of non-coding RNAs with 18-25 nucleotides inhibiting the expression of target genes by means of binding to their 3’UTR. They can also have tumor suppressor or oncogenic role in cell cycle pathways. Recently, relations between breast cancer risks and some SNPs are located in miRNA seeds or 3’UTR of their target, in some populations have been shown. Aberration in signal transduction pathway of Znf350 family in human tumors is a common phenomenon. Znf350 as an oncogene and also tumor suppressor gene is a member of Znf350 family. miRWalk2 database was used to identify the has-miR-150 predicted target genes. In next step, DAVID database were used to investigate the function and the related signaling pathways of obtained has-miR-150 target genes. In silico investigation of SNPs in the 3’UTR of Znf350 gene showed that rs2278414 could alter the binding properties of has- miR-150. Due to binding information of rs2278414 to has-miR-150 based on G, the binding activity of this microRNA (as oncomiR) undergoes respectively; this SNP could act as a good-prognostic factor. It also appeared that predicted target genes of our microRNA are related to the most probably cancer pathways such as “ERBB SIGNALING PATHWAY” and “PATHWAYS IN CANCER”. Bioinformatically rs2278414 could have association with breast cancer, especially with prognosis of patients. Since has-miR-150 binds to rs2278414 within ZNF350 and based on in silico information this microRNA involves in cancer pathways, it is predicted that the regulation of ZNF350 by has-miR-150 influences the development of breast cancer.
Evaluation Of Anti-Proliferative Effects Of Two Hydrazone Derivatives On Breast, Colon And Hepatic Cancer Cells

1. Mehrasa Shademani (Department Of Toxicology & Pharmacology, Faculty Of Pharmacy, Islamic Azad University, Pharmaceutical Sciences Branch, Tehran, Iran (IAUPS))
2. Raheleh Tahmasvand (Department Of Physiology & Pharmacology, Pasteur Institute Of Iran, Tehran, Iran)
3. Zahra Mousavi (Department Of Toxicology & Pharmacology, Faculty Of Pharmacy, Islamic Azad University, Pharmaceutical Sciences Branch, Tehran, Iran (IAUPS))
4. Ali Almasirad (Department Of Medicinal Chemistry, Faculty Of Pharmacy, Islamic Azad University, Pharmaceutical Sciences Branch, Tehran, Iran (IAUPS))
5. Mona Salimi (Department Of Physiology & Pharmacology, Pasteur Institute Of Iran, Tehran, Iran)

Abstract

Cancer is an increasing health issue whose worldwide incidence is about 6 million cases per year and characterized by unregulated cell proliferation. Despite the advancing researches about cancer, there were not efficient strategies for cancer treatment. Therefore, scientists are still trying to find new compounds for treatment of this disease. A number of compounds including hydrazone and ureido derivatives have been increasingly investigated as targets for different pharmacological activities containing analgesic, anti-inflammation and anticancer. To the best of our knowledge, there are no study about anti-proliferative as well as apoptotic effects of compounds A (1-(4-(3-nitrobenzylidene aminocarbamoyl)phenyl)-3-(4-chlorophenyl)urea) and B (1-(4-(3-chlorobenzylidene aminocarbamoyl)phenyl)-3-(4-chlorophenyl)urea). The anti-proliferative activity was measured by MTT assay at 24, 48 and 72 h on MDA-MB-231(human breast adenocarcinoma), HT-29 (human colon adenocarcinoma) and HepG2 (liver hepatocellular carcinoma) cells. Apoptotic experiments were performed using Annexin V/PI (Roche Applied Science, USA) and flow cytometry. Our obtained IC50 values (concentration at which 50% inhibition occurred) indicated that MDA-MB-231 cell revealed the most sensitivity and 72 h was the most effective incubation time for both compounds. In this regard, compound A showed a considerable potency in inhibition of breast cancer cells growth compared with compound B (IC50 = 1.95±1.09 vs 3.48±1.11 µM ) after 72 h treatment. Our flow cytometric results confirmed the cytotoxicity data and exhibited apoptotic effect of both compounds at early and late stages; however, compound A was the most potent one. Conclusion: The results presented here could be used as a starting point for the development of powerful chemotherapeutic agents to treat breast cancer.

Corresponding Author: Mona Salimi (Department Of Physiology & Pharmacology, Pasteur Institute of Iran, Tehran, Iran)
Crosstalk Between EMT And Stemness State In Esophageal Squamous Cell Carcinoma

Abstract

Epithelial-mesenchymal transition (EMT) is crucial for specific morphogenetic movements during embryonic development as well as pathological processes of tumor cell invasion and metastasis. TWIST1, as a highly conserved member of the basic helix-loop-helix (bHLH) transcription factors, plays key roles in EMT for either embryogenesis or tumorigenesis. SOX2 is an important key transcription factor involved in self-renewal and pluripotency characteristics of undifferentiated embryonic stem cells. Our aim in this study was to elucidate probable crosstalk between these factors. Expression pattern of TWIST1 and SOX2 was analyzed in 55 ESCC patients using relative comparative Real-time PCR. In silico analysis of the SOX2 gene was performed. Using a retroviral system, KYSE30 cells were transduced to ectopically express TWIST1, followed by qRT-PCR to elucidate the regulatory role of TWIST1 on SOX2 gene expression. Co-overexpression of TWIST1 and SOX2 was detected in ESCC patients significantly (p<0.05). The TWIST1 transduced KYSE30 cells showed significantly high level of TWIST1 expression compared to control cells. Enforced expression of TWIST1 in KYSE30 dramatically increased SOX2 gene expression. Direct correlation between TWIST1 and SOX2 mRNA levels may introduce novel molecular gene expression pathway connecting EMT process and stemness state of tumor cells during ESCC aggressiveness and tumorigenesis. Consequently, these data extend the spectrum of biological activities of TWIST1 and propose that therapeutic repression of TWIST1 may be an effective strategy to inhibit cancer stem cell characteristics.

Corresponding Author: Mohammad Reza Abbaszadegan (Division of Human Genetics, Immunology Research Center, Avicenna Research Institute, Mashhad University of Medical Sciences, Mashhad, Iran)
Abstract

For evaluating health status of a country and determining priority of risk factors, some epidemiological indicators are needed. One of the most widely used indicators is Years of life lost (YLL) due to premature death. To have an exact estimate of YLL, an accurate death registry data is needed but based on the report of Iranian death registry, about 20% of deaths are registered in misclassified groups. The aim of this study is to estimate the change in years of life lost due to gastric cancer mortality after correcting for misclassification in registering causes of death using Bayesian method. For this study gastric cancer data for years 2006 to 2010 for Iran were extracted from national death statistics. Rate of misclassification in registering causes of deaths due to gastric cancer in cancer without label group, was estimated using Bayesian method for each year. Years of life lost due to gastric cancer is estimated before and after Bayesian correction. Using Bayesian method, misclassification rate for gastric cancer in cancer without label group were estimated to be 5%, 3%, 3%, 7% and 7% respectively for years 2006 to 2010. Estimated Years of life lost due to gastric cancer before correcting misclassification were respectively 111684.93, 114957.31, 112391.93, 112250.53 and 113300.92 person-years for years 2006 to 2010. After correcting misclassification, YLL of gastric cancer increased 1535.19, 921.11, 908.39, 2566.39 and 2507.00 person-years, respectively for years 2006 to 2010. If health policy makers ignore the existence of misclassification in registered causes of death they may underestimate the cause specific burden of disease and consequently programming for cancer control and prevention will done erroneously.

Corresponding Author: Mohammad Amin Pourhoseingholi (Gastroenterology and Liver Diseases Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran)
Association Between Plasma Levels Of Ceruloplasmin And Adiponectin With Medullary Thyroid Carcinoma

1. Fatemeh Razavi (Islamic Azad University, Pharmaceutical Sciences Branch, Tehran, Iran)
2. Mehdi Hedayati (Cellular And Molecular Endocrine Research Center, Research Institute For Endocrine Sciences, Shahid Beheshti University Of Medical Sciences, Tehran, Iran)
3. Shadi Fathi Saffar (Islamic Azad University, Pharmaceutical Sciences Branch, Tehran, Iran)
4. Tahereh Naji (Islamic Azad University, Pharmaceutical Branch, Tehran, Iran)
5. Sara Sheikholeslami (Cellular And Molecular Endocrine Research Center, Research Institute For Endocrine Sciences, Shahid Beheshti University Of Medical Sciences, Tehran, Iran)
6. Laleh Hoghooghi Rad (Cellular And Molecular Endocrine Research Center, Research Institute For Endocrine Sciences, Shahid Beheshti University Of Medical Sciences, Tehran, Iran)
7. Hoda Golab Ghadaksaz (Cellular And Molecular Endocrine Research Center, Research Institute For Endocrine Sciences, Shahid Beheshti University Of Medical Sciences, Tehran, Iran)
8. Marjan Zarif Yeganeh (Cellular And Molecular Endocrine Research Center, Research Institute For Endocrine Sciences, Shahid Beheshti University Of Medical Sciences, Tehran, Iran)

Abstract

Ceruloplasmin and Adiponectin are Adipokines with important biological role. Plasma Ceruloplasmin level increases in some cancers because of its positive effect on angiogenesis. Adiponectin is exclusively secreted from adipose tissue. Large epidemiological studies show that obesity, which is known as one of the most important public hygiene issues, may play a role as a risk factor for thyroid carcinoma. This study aimed in assessing serum levels of Ceruloplasmin and Adiponectin in patients with medullary thyroid Carcinoma; in the hope of finding biomarkers which decrease expenses and time requiring of MTC diagnosis. In this matched case-control study, 45 MTC patients and 45 healthy controls were included. Plasma levels of Ceruloplasmin and Adiponectin were measured by Sandwich ELISA method. Data analyses were performed by SPSS software version 22. There was no significant difference between the mean Ceruloplasmin levels of case and control groups (P>0.05). MTC patients had lower Plasma level of Adiponectin in comparison with control group, it was not statistically significant though. Since Ceruloplasmin and Adiponectin levels in medullary thyroid cancer patients were the same, therefore these two Adipokines cannot be used as the marker of these groups in order to separate them.

Corresponding Author: Mehdi Hedayati (Cellular and Molecular Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran)
Investigating The Cytotoxic And Immunomodulatory Nature Of Zinc Oxide Nanoparticles Synthesized Using Aspergillus Niger Mushroom On MCF7 Cells

Abstract

Nanoparticles have a potential role in a range of fields including medicine, technology, medical, industrial and etc. The use of fungi, plants and other environmentally friendly compounds for the synthesis of nanoparticles is of particular importance due to the elimination of hazardous chemicals in the process. Due to the widespread use of the new nanoparticles with environmentally friendly methods (NPS) such as zinc oxide (ZnO) extensive research has been done in pharmaceutical and health fields. In this study, the cytotoxicity and anti-inflammatory potential of zinc oxide nanoparticles were evaluated against MCF7 cells (Human breast cancer cells). The Mcf7 cells were cultured in vitro to achieve the logarithmic growth phase then seeded and treated with various concentrations of NPs (0, 200, 400, 600, 800, 1000 µg/ml) followed by colorimetric cell survival assay using MTT. Morphological changes in the cells was determined using inverted microscope. The Real Time PCR assay was carried out on the synthesized cDNA to evaluate the expression of genes (IL-1β, IL-10) involved in the immune system. ZnO NPs demonstrated moderate cytotoxic activity against Mcf7 cells with IC50 about 600 µg/ml and exhibited anti-inflammatory effect through dose-dependently suppression of IL-1β and increased IL-10 expression. The expression of IL-1β gene was reduced from 1 in untreated cells to 0.04 in treated cells with 800 µg/ml of ZnO-NPs while the expression of IL-10 showed an increase of 1 to 7.2 at similar concentrations. This study elucidates moderate toxicity effect of nanoparticles as well as excellent its anti-inflammatory potential in MCF7 cells and Provides grounds for the application of nanomaterial's in therapies for a variety of diseases, including cancer, autoimmune and other diseases.

Corresponding Author: Mozhgan Soltani (Department of Biology, Mashhad Branch, Islamic Azad University, Mashhad, Iran)
Foot Track Of LncRNAs In Cancer

1. Mohammad Mahdevar (Department Of Biology, Hakim Sabzevari University, Iran)
2. Madjid Momeni-Moghaddam (Department Of Biology, Faculty Of Sciences, Hakim Sabzevari University, Sabzevar, Iran)

Abstract

Only small portion of transcripts in the whole human genome are coding proteins, while more transcripts are non-coding RANa (ncRANs). A kind of ncRNA, called long non-coding RNA (lncRNA) that are longer than 200 nucleotides, have been recently discovered. LncRNAs involved in various cellular processes so they can involve in diverse diseases. HOX antisense intergenic RNA (HOTAIR), a lncRNA located in the HOXC locus that it is about 2158 nucleotides in size, has been shown to repress HOXD gene expression. Studies about the binding domain of HOTAIR elucidated that a 5′ domain binds to PRC2 while 3′ domain binds to the LSD1/CoREST/REST complex which leading to trimethylation of H3K27 and also H3K4 demethylation respectively. EZH2 Subunit of PRC2 contains a binding domain for HOTAIR. Furthermore, revealed that BRCA1 tumor suppressor protein interacts with the EZH2 and Inhibits the binding of EZH2 to HOTAIR. The EZH2 is phosphorylated during cell cycle by CDK1 and CDK2. This Phosphorylation is essential for binding to HOTAIR. In addition, demonstrated that HOTAIR expression is induced by estradiol. Genome-wide analysis showed that knock down of HOTAIR affects the expression of genes associated with apoptosis, tumor suppression, cell differentiation, and proliferation. Induction of HOTAIR expression in cancer cells cause increase invasion and metastasis. HOTAIR is overexpressed in primary breast tumors and expression level is a powerful predictor of eventual metastasis and death, in return depletion of HOTAIR can inhibit cancer invasiveness. Also, in Hepatocellular carcinoma (HCC) increase expression of HOTAIR that associated with increased risk of recurrence after hepatectomy. Moreover, knock down of HOTAIR in HCC as a result decrease cell proliferation and matrix metalloproteinase-9 levels. Furthermore, HOTAIR can be used as a biomarker for HCC. Studies about HOTAIR expression in Colorectal cancer (CRC) indicates that it is level positive relation between its increasing level and CRC cells amplification and invasiveness. This reviews show that HOTAIR has a key role in the proliferation and metastasis of cancer cells.

Corresponding Author: Madjid Momeni-Moghaddam (Department of Biology, Faculty of Sciences, Hakim Sabzevari University, Sabzevar, Iran)
Cytotoxic Effects Of Extract Origanum Vulgare On Human Colon Cancer Cells

1. Ali Ghorbani Ranjbary (Department Of Biotechnology, School Of Veterinary Medicine, Ferdowsi University Of Mashhad, Mashhad, Iran)

Abstract

Origanum Vulgare contains chemical materials, that has anticonvulsant, antifungal, antioxidant, anti-inflammatory, anti-infection and antidiabetic properties, it stimulates central nervous system, a wellknown herbal medicine in Iran. The aim of the present study was to investigate the chemical composition, antioxidant, cytotoxic and apoptotic effect of Origanum Vulgare extract against human colon cancer (HT29) cells by using real-time polymerase chain reaction and flow-cytometry methods. This experimental study was carried out in Islamic Azad University, Kazerun Branch. At first, the Origanum Vulgare chemical constituents were analyzed by gas chromatography-mass spectrometry (GC-MS) technique. In addition, antioxidant assay and anticancer effect was performed using 1,1-diphenyl-2-picrylhydrazyl (DPPH) and 3-(4,5-dimethylthiazol-2-yl)-2,5 diphenyltetrazolium bromide (MTT) methods, respectively. We extracted total RNA molecules by using RNX solution, after which cDNA was synthesized. Finally, the pro-apoptotic (Bax) and anti-apoptotic (Bcl2) gene expression was performed by real-time polymerase chain reaction and apoptotic effects were analyzed using Flow-cytometry method. The major components of Origanum vulgare were carvacrol, β-fenchyl alcohol, thymol, and γ-terpinene. The antioxidant activity of the extract was IC50= 0.7±0.04 mg/ml. Cytotoxic results revealed that the Origanum vulgare extract have IC50= 23.4 ± 0.52 mg/ml against colon cancer (HT29) cell line and real-time polymerase chain reaction results showed the expression level of Bax and Bcl2 was increased and decreased respectively in colon cancer cell line (4.560 ±0.23 (P< 0.05), 0.51 ±0.29 (P< 0.05)). In addition, the flow-cytometry results indicated the 39.57% apoptosis in colon cancer cell line. According to the results, it seems that Origanum vulgare extract has potential antioxidant and anticancer effects and it suggested that further studies were performed for Origanum vulgare pharmaceutical importance.

Corresponding Author: Ali Ghorbani Ranjbary (Department of Biotechnology, School of Veterinary Medicine, Ferdowsi University of Mashhad, Mashhad, Iran)
A Novel Chitosan Derivative For Breast Cancer Targeting

Abstract

Chitosan is a biopolymer composed of glucosamine and N-acetylglucosamine units which is biocompatible, non-toxic and biodegradable, so it can be a suitable choice for drug/gene delivery and biomedical applications. Moreover, chitosan is modifiable to improve specificity of delivery or targeting system, due to existence of two functional groups on its backbone (OH and NH2). While about 75% of breast cancer cells express the estrogen receptor (ER), blocking ER function can reduced the risk of advance in breast cancer. Raloxifene belongs to Selective estrogen receptor modulators (SERMs), that are a class of compounds that bind competitively with estrogen receptors and depending on the structure and position, act as agonist or antagonist of these receptors. Raloxifene shows antagonist activity in breast and uterus. In this study, raloxifene-chitosan conjugate was synthesized as a potential ER targeting vehicle to breast cancer cells. Conjugation of raloxifene to chitosan was performed by different methods. The conjugates were investigated by means of FTIR, TGA and physical properties assessments. In addition, Cell viability was evaluated using XTT assay. FTIR and TGA results confirmed that the conjugation between chitosan and raloxifene occurred more efficiently when trimethyl chitosan in the presence of triethylamine and excess amount of linker was used. XTT assay on MCF-7 cell line illustrated that more than 80% of cells were viable after 24 hours exposure to selected molecules. These findings confirm that the conjugation of raloxifene-chitosan can occur successfully using special synthesis condition and this novel chitosan derivative can be introduced as a potential drug/gene targeting agent.

Corresponding Author: Zohreh Mohammadi (Nanobiotechnology Research Center, Avicenna Research Institute, ACECR, Tehran, Iran)
Comparison Of Inflammatory Factors In Patients With Oral Lichen Planus And Quamous-Cell Carcinoma (SCC) Of The Oral Cavity

1. Ali Ghorbani Ranjbary (Department Of Biotechnology, School Of Veterinary Medicine, Ferdowsi University Of Mashhad, Mashhad, Iran)

Abstract

Lichen planus (LP) is a relatively common chronic skin-mucous membrane disease that affects the oral mucous. Etiology and pathogenesis of the disease are not well identified. Some evidence suggests that the immune system may play a role in the lichen planus formation and progress. On the other hand it is likely to convert to SCC of the oral cavity. This survey was carried out with the aim of exploring serum levels of CRP, IL1 α, IL6, and TNF α in oral lichen planus and SCC of the oral cavity. In this cross-sectional study, 25 patients with lichen planus and 25 patients with oral SCC were chosen, as well as 25 healthy individuals, as the control group. IL1 α, TNF α, IL6, and CRP were measured in serum and in order to compare the means one-way variance analysis and SPSS version 16 were applied (α = 0.05). According to one-way variance analysis, the mean level of IL6, TNF, and CRP in a group of patients with lichen planus were 37.23 ng/ml, 26.5 pg/ml, and 41.16 ml/dl respectively, in addition to the group of patients with SCC of the oral cavity they were respectively 49.53 ng/ml, 10.64 pg/ml, and 48.35 ml/dl and in the control group they were 39.37, 33.29 ng/ml and 9.7 pg/ml. IL6 and CRP means were higher in the carcinoma group than the other two groups, on the other hand, CRP in oral lichen planus group was significantly higher the normal group, however; the value of IL1 α mean was not significantly different among various groups. According to the results, although IL6 and CRP serum levels increase in patients with SCC of the oral cavity and IL6 and TNF α levels rise in patients with lichen planus, there was no meaningful difference in IL1 α level of the two mentioned groups in comparison to the control group.

Corresponding Author: simin shadanpour (Department of physiology, School of Veterinary Medicine, Ferdowsi University of Mashhad, Mashhad, Iran)
Abstract

Alterations in the structural and functional characteristics of the cells are critical biomarkers of malignancy. Bearing in mind, the accurate characterization of these markers would be providing novel therapeutic and diagnostic solutions for these types of diseases. In this regard, in-silico analyses of the BCAN, a cell surface specific antigen of neural malignancies, were considered in this study. For this aim, protein sequence of this antigen, with accession number AAH27971, were retrieved from protein databank of the NCBI. PROTEIN ATLAS databank were used for in-silico expression assays. Detection the corresponding ligands of the antigen were evaluated by STRING program. Structural modeling and quality assessment of the models were carried out by MODELLER and MOE programs, respectively. Moreover, topology features of the antigen were determined by HMMTOP program. All data were expressed as mean-standard deviation with SPSS 21.0 (SPSS Inc., Chicago, IL, USA). The results of this analysis led to reveal that the BCAN, with 911 amino in the length, has three transmembrane regions. On the other hand, the overexpression of this antigen, in addition to glioma, apparent in the melanoma and lymphoma using CAB025862 and HPA007865 monoclonal antibodies. Furthermore, in addition to the above monoclonal antibodies, the binding affinity of the antigen to the TNR, as new ligand, was appeared. In general, the results of this study led to provide the 3D structure of the BCAN and its topology on the cell membrane. Meanwhile, the overexpression of the BCAN appeared as suitable biomarker for glioma, melanoma and lymphoma. Furthermore, this analysis provides a new corresponding ligand of BCAN, which could be used for immunotoxins development

Corresponding Author: Fatemeh Khademolhossini (Department of Biology, Islamic Azad University, Khorasan Razavi, Science and Research branch, Neyshabur, Iran)
Comparative Proteome Analysis Of Colorectal Cell Carcinoma And Adjacent Normal Tissues

1. Niloufar Saber-Moghadam Ranjbar (School Of Pharmacy, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Rezvan Yazdian-Robati (Department Of Biotechnology, School Of Pharmacy, Mashhad University Of Medical Sciences, Mashhad, Iran)
3. Khalil Abnous (Pharmaceutical Research Center, School Of Pharmacy, Mashhad University Of Medical Sciences, Mashhad, Iran)
4. Mohammad Ramezani (Nanotechnology Research Center, Department Of Biotechnology, School Of Pharmacy, Mashhad Iran)

Abstract

The Colorectal Cancer (CRC) is the third prevalent and invasive cancer in the world. The incidence rate of CRC in Iran is about 6-7.9 cases per 100000 and represents one of the main leading causes of cancer death. Major reason for the low survival and mortality of patients with CRC is late diagnosis. Therefore, the detection of tumor in early stages is necessary for well-timed treatment of CRC. Previous studies demonstrated the molecular etiology of colorectal cancer is related to both genomic expression and protein levels. The main goal of this proteomics study is to find biomarkers related to CRC in order to detect CRC patient in early phase. In this present study, we used patient-based proteomics and Mass spectrometry approach to analyze CRC tissues. The differential protein expression between cancerous and normal colorectal tissues was detected by two-dimensional polyacrylamide gel electrophoresis (2D-PAGE) and matrix-assisted laser desorption/ionization tandem time-of-flight mass spectrometry (MALDI-TOF/TOF-MS) followed by database searching using MASCOT. Using proteomic approach, we reported five differentially expressed proteins may involved in the pathological process of CRC including serum albumin (ALB), Serotransferrin (TF), Actin-gamma enteric smooth muscle (ACTG2), transgelin (TAGLN) and actin-aortic smooth muscle (ACTA2). This selected Biomarkers suggested may be useful in identifying biomarkers involved in CRC. Moreover these finding may have important role in diagnosis and tumorigenesis of cancer.

Corresponding Author: khalil abnous (Pharmaceutical Research Center, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran)
Plasticity Of Th17 Cells Are Regulated By The Cross Talk With Tumor Cells.

1. Alaleh Rezalotfi (Immunology Department, School Of Medicine, Hamadan University Of Medical Sciences, Hamadan, Iran.)
2. Ghasem Solgi (Immunology Department, School Of Medicine, Hamadan University Of Medical Sciences, Hamadan, Iran.)
3. Marzieh Ebrahimi (Department Stem Cells And Developmental Biology, Cell Sciences Research Center, Royan Institute For Stem Cell Biology And Technology, Tehran, Iran.)

Abstract

Different subsets of T cells which are differentiated by Stimulation of antigens and particular cytokine signals, perform distinct functions contrary to their identical origin; TCD4+ precursors. T helper 17 (Th17) cells are characterized by high production of IL-17 and inflammatory cytokines, considered as crucial cells to induce inflammation and also indicated as a clue in pathogenesis of many autoimmune diseases and allergy reactions. The role of Th17 in tumor immunity has been remained controversial. Therefore, in this review we aimed to clarify the role of Th17 in tumor promotion or suppression. Recently some data demonstrated that high percentage of Th17 cells infiltrated to tumor site, more than other tumor infiltrating lymphocytes (TILs). Under normal conditions IL-6 with TGF-β induce Th17 and inhibit Treg differentiation. This proved that IL-6 is a critical factor to create a balance between Th17/Treg differentiation. Moreover, Th17 is able to convert into Th1, Th2 and Treg based on cross talk with tumor microenvironment and to exhibit both anti-tumor and pro-tumor activity. IL-17 production by Th17 cells might lead to angiogenesis and recruitment of myeloid-derived suppressor cells (MDSCs). Furthermore, TGF-β in tumor microenvironment might induce differentiation of Th17 into Treg by induction of ectonucleotidases expression. Although, tumor cells and tumor associated fibroblast cells are able to provide cell-cell contact in addition to secret pro-inflammatory cytokines, which cause to Th17 cells expansion. Th17 cells were shown to inhibit tumor growth by induction of effector cells recruitment in tumor and by activation of tumor-specific T CD8+ cells. As well as, plasticity might add more functions to Th17 cells in tumor immunity. Whether Th17 conversion to Treg cells requires further confirmation, but might cause to immunosuppression features in Th17 cells. On the opposite side, Th17 cells might convert to Th1 cells phenotype and produce IFN-γ and TNF-α in the tumor site which in turn could lead to tumor growth inhibition. Tumor microenvironment with infiltrated cells such as Fibroblast, immune cells and mesenchymal stem cells provide milieu can affect on th17 plasticity. Moreover, Th17 plays dual role in tumor site, promoting or suppressing based on crosstalk with tumor microenvironment.

Corresponding Author: Marzieh Ebrahimi (Department Stem Cells and developmental Biology, Cell Sciences Research Center, Royan Institute for Stem Cell Biology and Technology, Tehran, Iran.)
Breast Cancer Screening Barriers Among Iranian Women: A Systematic Review

1. Koosha, Maryam (Prevention Department, Breast Cancer Research Center, ACECR, Tehran, Iran)
2. Haghighat, Shahpar (Quality Of Life Department, Breast Cancer Research Center, ACECR, Tehran, Iran)
3. Bahrami, Alireza (Prevention Department, Breast Cancer Research Center, ACECR, Tehran, Iran)
4. Khosravi, Nasim (Quality Of Life Department, Breast Cancer Research Center, ACECR, Tehran, Iran)

Abstract

Breast cancer screening and early detection is one of the most crucial strategies in cancer prevention that can lead to early treatment and increasing patient survival. Various factors such as socioeconomic status, lifestyle, health education, social support and attitude and behavior types can affect the screening behavior. This study is part of a systematic review which is assessed breast cancer related articles conducted in Iran from 2005 to 2015. Various databases were searched including PubMed, Scopus, Web of science and SID and IRAN MEDEX as Iranian resources. After three steps fourteen articles met the inclusion criteria. These article were about the barriers in breast cancer screening (BSE, CBE and mammography) and the factors affecting it. The results respectively showed lack of knowledge of breast cancer and failure to identify breast cancer symptoms and screening procedures, lack of social support (emotional support, financial and informational), beliefs and cultural attitudes toward breast cancer, the unavailability of a specialist physician, are the most important barriers. The other factors such as having fear of detection, shame and lack of motivation to perform screening behavior, lack of importance and necessity of screening for breast cancer in the next steps are outlined barriers. Therefore, enhancing health literacy breast cancer on awareness and changing attitudes toward screening behaviors and the need to facilitate social support for screening behaviors as of early detection of cancer and as solutions to resolved these barriers its necessary to be considered.

Corresponding Author: haghighat, shahpar (Quality Of Life Department, Breast Cancer Research Center, ACECR, Tehran, Iran)
Resistance To Photodynamic Therapy For Cancer: Mechanisms, Origins, Challenges And Solutions.

Abstract

Photodynamic therapy (PDT) is clinically approved, and a minimally invasive treatment method that can be apply selectively cytotoxic activity against several types of cancer cells. PDT is composed of three essential components: photosensitizer (PS), oxygen and light. The Anti-tumor effects of PDT are obtained from three related mechanisms, including direct cytotoxic effects on tumor cells, tumor blood vessel damage and induce strong inflammatory reaction that can lead to the development of systemic immunity. During PDT, reactive oxygen species are produced and thus antioxidant defense mechanisms that play an important role to deal with injuries, induced and causes activation of heat shock proteins (HSP). At later stages, includes processes such as repairing of protein's damages, activation of multiple paths to survive, induction of stress response genes and Hypoxia. The Hypoxia leads to increased rates hypoxia-inducible factor 2 alpha (HIF2A), that this factor is mediating factor for the expression of genes such as Oct4, Nanog and C-MYC, Which makes protects the cancer stem cells. Therefore, therapies that are effective at hypoxic conditions in the microenvironment could potentially reduce the development of drug resistance and to prevent tumor recurrence. Lower rates of oxygen consumption by PS, allowing sufficient time for replenishment of tumor's oxygen and prevent the rapid depletion of oxygen. Switching mechanism of free radical production from reaction type 2 to reaction type 1,Which is only slightly dependent on oxygen, that is fascinating strategy to improve the effectiveness of PDT. Understanding the basic mechanisms of resistance to PDT, will help to improve the efficacy of PDT and eventually achieve a new treatment protocol, which will lead to more efficient ways to treatment of patients. In this review, we examined the most important mechanisms of resistance to PDT, and focus on the recent strategies based on nanotechnology and stem cells for overcoming these mechanisms to improve PDT.

Corresponding Author: Ameneh Sazgarnia (Department and Research Centre of Medical Physics, Avicenna Research Institute, Mashhad University of Medical Sciences, Mashhad, Iran.)
Exosome–Based Cell Free Vaccine: An Alternative To DC- Based Cancer Immunotherapy

1. Maryam Ahmadakhoundi (Department Of Developmental Biology, University Of Science And Culture, ACECR, Tehran, Iran, Department Of Stem Cells And Developmental Biology At Cell Science Research Center, Royan Institute For Stem Cell Biology And Technology, ACECR, Tehran, Iran)

2. Mojgan Barati (Department Of Developmental Biology, University Of Science And Culture, ACECR, Tehran, Iran, Department Of Stem Cells And Developmental Biology At Cell Science Research Center, Royan Institute For Stem Cell Biology And Technology, ACECR, Tehran, Iran)

3. Marzieh Ebrahimi (Department Of Stem Cells And Developmental Biology At Cell Science Research Center, Royan Institute For Stem Cell Biology And Technology, ACECR, Tehran, Iran)

4. Seyedeh-Nafiseh Hassani (Department Of Stem Cells And Developmental Biology At Cell Science Research Center, Royan Institute For Stem Cell Biology And Technology, ACECR, Tehran, Iran)

Abstract

In addition to cytokines and growth factors, all cells secrete a large amount of membrane vesicles into the extracellular environment that modulate the function of the other cells. The most prominent of the extracellular vesicles are exosomes. Exosomes are nano vesicles (30–100 nm) derived from the late endosomal membrane structures and play an important role in intercellular communication by transferring cargo molecules including proteins, lipids and genetic materials (such as mRNA, microRNA and other non-coding RNAs). It has been observed that a wide range of cell types secrete exosomes, including macrophages, dendritic cells (DCs), B cells, cytotoxic T lymphocytes (CTLs), platelets, mastocytes, fibroblasts, epithelial cells, and tumor cells. DCs are the most potent antigen presenting cells for activation of tumor specific CTLs which identify and eliminate cancer cells. In case of DC vaccine, mostly, peptides, RNA or whole tumor cell lysate are used as an antigen for pulsing DCs and activated DCs can elicit a specific CTL response against tumor cells. Also recent studies showed that tumor-derived exosomes can be implemented as a new source of tumor antigen for DC stimulation and induction of immune response. It is shown that DC-derived exosomes (Dex) have similar biology to DCs and have the capacity to induce potent immune responses. Moreover, Dex is more stable than DCs because of their lipid composition. As well they are enriched in active peptide-MHC II complexes and are not reliant on chemotactic signaling hence they can access their target organ easily. These characteristics give Dex an advantage over DC cell based cancer immunotherapy. Although Dex is considered as an important candidate for clinical trial but their effect has only been shown on malignant tumors including non-small cell lung carcinoma and metastatic melanoma. In conclusion exosome based cell free vaccine can be used as a new approach in cancer therapy and its effect on other cancers should be more investigated.

Corresponding Author: Seyedeh-Nafiseh Hassani (Department of Stem Cells and Developmental Biology at Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran)
Cytotoxic Effects Of Gold Nanoparticles Coated With Amino Acid Aspartate And Glutamate On PC12 Class Cells

1. Ali Ghorbani Ranjbary (Department Of Biotechnology, School Of Veterinary Medicine, Ferdowsi University Of Mashhad, Mashhad, Iran)

Abstract

Nowadays, the gold nanoparticles in cancer therapy will provide an entirely new technology. The aim of this study was to investigate the toxic effects of gold nanoparticles coated with amino acids of Aspartate and Glutamate on PC12 category cells. In this empirical study after PC12 cell category culture as in vitro these cells are divided into 9 groups and separately for 48 hours exposed to varying concentrations of gold nanoparticles (1, 2 and 4 µM gold nanoparticles, gold nanoparticles coated with amino acids Aspartate and Glutamate). At last, the effect of nanoparticle cytotoxicity using MTT and LDH release from the cells was examined. The phase contrast microscopy was used to evaluate the cellular morphology. At end, the level of ROS in the cells using fluorescent probes 2’, 7’-Dichlorofluorescein diacetate was measured. The average diameter of the gold nanoparticles in the case of uncoated and coated with amino acids Aspartate and Glutamate was calculated at size of 10±0.2, 24±0.4 and 27±0.4 nm, respectively. The most damaging effect of the studied cells by concentration of 5 µM of gold nanoparticle coated with amino acid Aspartate occurred at a rate of 47%, when compared to the group treated with bare gold nanoparticles and gold nanoparticles coated with Glutamate had a statistically significant difference (p≤ 0/05). The results of this study indicate that the majority of cell death of incubated cells with uncoated and coated gold nanoparticles is as apoptosis. The results showed that gold nanoparticle coated induces cell death and also gold nanoparticle coated with amino acid can destroy cancer cells through apoptosis.

Corresponding Author: Ali Ghorbani Ranjbary (Department of Biotechnology, School of Veterinary Medicine, Ferdowsi University of Mashhad, Mashhad, Iran)
Cancer And The Role Of Nutrition In Risk And Prevention

1. Mahdiye Razi (School Of Nursing And Midwifery, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Maryam Sharifniya (School Of Nursing And Midwifery, Mashhad University Of Medical Sciences, Mashhad, Iran)
3. Elham Zafariyan (School Of Nursing And Midwifery, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Between eating behaviors and the risk of cancers are directly related. Nutritional behaviors in life plays an important role in cancer prevention. Various studies show that nutrition is the main environmental factor in the risk of cancer and 30 to 40 percent of cancers, especially cancers of the stomach is affected. Thus, this study aimed to investigate the role of nutrition in in risk and prevention of cancer. Evidence shows that high-fat foods, low in fiber and lack of daily consumption of fruits and vegetables that is a rich source of vitamins and phytochemicals, linked with an increased incidence of various cancers. As the studies show that the risk of gastric cancer with high consumption of fruits, especially citrus and a variety of fresh vegetables in the allium family is reduced. Green tea consumption also reduces the risk of gastric cancer. On the other hand consumption of processed meats, salt and salted foods also associated with an increased risk of stomach cancer. According to the studies and determine the basic role of nutrition in the risk of cancer, Scientists believe that changes in feeding behavior can be a greater incidence of cancers can be prevented. Other studies also suggest it is important that unfortunately the performance or behavior of families regarding the consumption of bad food and nutrients with low nutritional value, instead of nutrient-rich foods are consumed at the family table. Thus, according to the results of research on the effects of nutrition on disease and cancer prevention and on the other hand the increase in cancer in the country and the gap in nutrition education and emphasis on the importance of nutrition in reducing the incidence and prevention of cancer, recommended healthy nutrition education component of health system priorities and agenda, and on the necessity of training was emphasized.

Corresponding Author: Mahdiye Razi (School of Nursing and Midwifery, Mashhad University of Medical Sciences, Mashhad, Iran)
Preparation, Characterization And In Vitro Anticancer Assessment Of Different Formulations Of Koetjapic Acid Isolated From Sandoricum Koetjape

1. Seyyedeh Fatemeh Jafari (EMAN Research And Testing Laboratory, School Of Pharmaceutical Sciences, USM, Penang, Malaysia)
2. Shokouh Shahrokhi (Department Of Medical Genetics, Faculty Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Secondary metabolites can serve as potential anticancer drugs by either either actuating selective cytotoxicity against cancer cells or modulating the tumor advancement procedure. Sandoricum koetjape Merr. is a traditional medicinal plant belonging to the family Meliaceae, which is native to Malaysia, Cambodia and Southern Laos. Koetjapic acid (KA) isolated from the bark of this plant is a bioactive triterpenoid chemically characterized with seco-Arings oleanene group. Previously, we have reported that KA is the active principle of S. koetjape which contributes to the anticarcinogenicity activity of the herb against human colon cancer cell line (HCT 116). We have found that KA blocked the sprouting of microvessels from rat aorta and obstructed major functions such as proliferation, migration and differentiation of endothelial cells by inhibiting the vascular endothelial growth factor expression. On the other hand, we have found that KA significantly actuates the apoptosis cascade in colon cancer cells while inhibiting the metastatic property in breast cancer cells. Target of this study is to enhance solubility of KA using different formulations and to evaluate anticancer their efficiency in human colorectal cancer cells. Therefore, (2-Hydroxypropyl)-β-cyclodextrin inclusion complex and solid dispersions (carboxymethyl cellulose, polyvinylpyrrolidone and sodium lauryl sulphate) of KA were prepared. Furthermore, a salt of KA, potassium koetjapate, was synthesized. Potassium koetjapate demonstrated higher solubility than the other tested formulations with enhanced cytotoxicity against HCT 116 cells. The enhanced efficacy of potassium koetjapate is attributed to apoptotic induction of nuclear condensation and disruption of mitochondrial membrane potential in the cells. The salt formulation of KA performs to modulate the ability of the parent compound by enhancing its solubility while improving its bioefficacy against colon cancer cells which suggest its potential anticancer application.

Corresponding Author: Seyyedeh Fatemeh Jafari (EMAN Research and Testing Laboratory, School of Pharmaceutical Sciences, USM, Penang, Malaysia)
Association Of SOX15 And Epstein-Barr Virus Infection With Clinical Outcome Of Patients With Esophageal Squamous Cell Carcinoma

1. Ali Moradi (Department Of Biology, Islamic Azad University, Damghan Branch, Damghan, Iran)
2. Soodabe ShahidSales (Cancer Research Center, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Esophageal squamous cell carcinoma (ESCC) is among the leading cause of cancer related death worldwide. Several studies have been shown the association of Epstein Barr Virus (EBV) infection with the development of malignancies including B-cell non-Hodgkin lymphoma, Hodgkin disease and Burkett lymphoma, although its potential role in ESCC is still remained to be elucidated. Against this background, sex-determining region Y-box (SOX) 15 is recently been identified as a novel tumor suppressor in pancreatic cancer with a potential role in modulating Wnt/b-catenin signaling. The aim of present study was to investigate the association of EBV and SOX15 expression with pathological information and clinical outcome of 108 ESCC patients. In the current study one hundred and eight patients were recruited. DNA and RNA were extracted. The expression pattern of Sox15 was evaluated by real time RT-PCR, while the present of EBV was evaluated using a diagnostic EBV-PCR detection Kit. Univariate/multivariate analyses were used to assess the correlation of EBV and SOX15 with overall survival and progression free survival. Among the patients, 48% of patients were female, and 52% were male with mean age of 59.2±11.1yr. 5.6%, 21.3%, and 71.3% of patients were T1, T2, T3, respectively, while 32.4% of cases had lymph node metastases. In order to explore whether patient characteristics might influence clinical outcome, we analyzed data on PFS and OS according to patients’ clinicopathological features. Tumor size, node and metastasis status, and stage were associated with shorter OS and PFS. We found the present of EBV in 7 cases, and 42.8% of these subjects had lymph node positive. Moreover, patients with low mRNA expression of SOX15 had statistically significantly shorter survival, compared to the patients with high expression of SOX15. Our findings demonstrated the presence of EBV in a small proportion of ESCC patients, supporting further studies in multi-center setting to determine its association with development and progression of ESCC. Also SOX15 expression was associated with clinical outcome of patients, although functional analyses are needed to explore its role in ESCC.

Corresponding Author: Soodabe ShahidSales (Cancer Research Center, Mashhad University Of Medical Sciences, Mashhad, Iran)
Is Vitamin D Preventive Against Colorectal Cancer?

1. Fateme Rostami (Faculty Of Medicine, Mashhad University Of Medical Science, Mashhad, Iran)

Abstract

Colorectal cancer is known as a major health problem and ranked as the third most common cancer all over the world. Vitamin D plays an important role not only in bone mineralization but also in prevention of cancer. It seems that both Vitamin D and its analogs, have powerful inhibitory effects on development and metastasis of colorectal cancer (CRC). Considering the synergetic effect of vitamin D and calcium, both of them together are recommended in cancer prevention programmes. This study is done by searching electronic database (pubmed until 2016); we reviewed 12 relevant articles for our aim. In this research we evaluated the role of vitamin D in prevention of cancers such as colorectal cancer and the mechanisms by which this happens. It is obtained that there is an association between the intake dose of some nutrients and minerals with lower risk of CRC. Some of the examples are like: fiber, milk, fruits, soy beans, folate, calcium, vitamin D, etc. Also there are some other nutrients that their levels are associated with higher risk of CRC such as: preserved food, high sugar foods, cholesterol, spicy foods, etc. Moderate elevation of 25(OH) vitamin D concentration is linked with observable decrease of CRC incidence. The fact behind this happening is that 1α,25-dihydroxyvitamin D3 (calcitriol) interferes with angiogenesis and acts like an antiproliferative agent in most of our tissues - like colon tissue - that growth of malignant cells is inhibited by that. Some of the mechanisms by which vitamin D directly acts on colon epithelium are: adjusting the cell cycle and differentiation and also apoptosis. Regulating the signaling and synthesis of the cytokine and growth factor are included in these mechanisms as well. Diet is affecting in CRC development. Vitamin D is potentially preventive against cancer incidence and recurrence.

Corresponding Author: Fateme Rostami (Faculty of Medicine, Mashhad University of Medical Science, Mashhad, Iran)
Abstract

Since the caregivers of cancer patients have the main and basic role in caring, support and monitoring of treatment of these patients, providing their mental health is essential for continuing care. Because of the importance of spirituality in recent years in the field of health, this research is done with the purpose of effect of Spiritual Support on caregiver's stress of children aged 8-12 with leukemia. In this clinical trial study participated 60 caregivers of children with leukemia. Intervention group was under 5 sessions based on spiritual intervention on the Richards and Bergin pattern by focusing on the rituals of Islam and includes psycho-spiritual components: prayer, trust and appeal, patience, gratitude and forgiveness, each day will be for 60 minutes. Research tools consisted of demographic data questionnaire, spiritual health questionnaire, DASS questionnaire that completed before and after the intervention. Statistical analyses were conducted with SPSS version 16. Based on the results with Paired t-test to compare before and after the intervention, Stress in intervention group was significantly lower than the control group (p = 0.067). The sessions of spiritual support had been able to reduce the stress of caregivers of children with leukemia. So it is recommended, such interventions be done for caregivers of children with leukemia due to the low cost, safety and effectiveness.
Abstract

Quality of life is closely related to Nursing, Because caring not only reduce mortality and increase survival but also Relationship with parents and helping them can effect on caring function, such as controlling the side effects of disease and changing body image. Because of the importance of spirituality in the field of health, this research is carried out aimed at examining the effect of Spiritual Support of caregiver on social dimension of quality of life of children aged 8-12 with leukemia. In this clinical trial study participated 60 caregivers of children with leukemia. Intervention group was monitored in 5 sessions based on spiritual intervention on the Richards and Bergin pattern by focusing on the rituals of Islam and including psycho-spiritual components: prayer, trust and appeal, patience, gratitude and forgiveness, each day during 60 minutes. Research instruments consisted of demographic data questionnaires, spiritual health questionnaires and teenager quality of life questionnaires being completed before and after the intervention. Statistical analyses were conducted with SPSS version 16. According to findings by Wilcoxon test before the intervention, The difference of social dimension of quality of life between two groups was not significant) P=0.344). After the Intervention, the social dimension of quality of life was significantly lower than the control group) P=0.033). Sessions of spiritual support for caregivers can increase social dimension of quality of life of children with leukemia.

Corresponding Author: Hamidreza Behnam Vashani (Pediatric and Infant Nursing, School of Nursing and Midwifery, Mashhad University of Medical Science, Mashhad, Iran)
Socioeconomic Status And Other Characteristics In Childhood Leukemia

Abstract

Some epidemiological studies have found a relationship between socio-economic status (SES) and some childhood cancers. In the present study an attempt was made to assess socio-economical class in a case-control study. A case-control study conducted on 100 case of acute lymphoblastic leukemia age 1-14 years in Department of Pediatric Oncology of Dr sheikh Hospital in Mashhad - Iran and matched on age and sex to 400 healthy controls. Data was collected by interview using a questionnaire. Data analyzed by chi-square test and Regression analysis. 95% confidence intervals were used to measure the relation between childhood A.L.L and parental education, income status, father's job (Socioeconomic status), number of children, birth score and paternal smoking. There was a significant difference in parental education level (P-value=0.02, P-value=0.01), income status (P-value=0.01), number of children (P-value=0), birth score (P-value=0), father's job (P-value=0.02) and paternal smoking between two groups. Regression analysis showed the risk of childhood A.L.L associated with paternal smoking (P-value=0, OR=12.6, CI 95%, 7.4-21.5) and father's high risk job (P-value=. OR=11.9, CI 95%, 6.2-22.9). Most of case (50%) and control group (35%) located in upper lower and Lower middle class of socioeconomic status respectively. There is a meaningful different between Socioeconomic status in two groups (p=0.01). But risk of childhood A.L.L did not associated with Socioeconomic status. The results suggest that paternal smoking and father's high risk job are related to risk of childhood leukemia. It should be considered for planning support.

Corresponding Author: Haleh Boroumand (Mashhad University of Medical Sciences, Mashhad, Iran)
Effectiveness Of Permanent Implantable Catheter (Polysite) In Children With Cancer

1. Haleh Boroumand (Pediatric Surgery Department, Mashhad University Of Medical Sciences, Iran)
2. Mozhgan Darabian (Mashhad University Of Medical Sciences, Mashhad, Iran)
3. Marjan Joodi (Pediatric Surgery, Mashhad University If Medical Sciences)

Abstract

Implantable central catheters like as Polysite are devices with capability of multiple injections and long term infusion of different material. Due to low infection rate, patients comfort ability, less chance of extravasation and leak of infused material to subcutaneous area, especially chemotherapy drugs, these devices is preferred route of intravenous access compare with conventional external peripheral or central access. In this article we present the quality of nursing care, complications and effectiveness of polysite implantation in 48 children who suffered different type of cancer disease. 48 cases of pediatric with different cancer disease (lymphoma-leukemia-sarcoma and wilms' tumor) were included in this study. In 39 cases polysite were inserted via internal jugular vein (Right in 34 and left side in 14 cases). Patency, duration of polysite usage and complications were recorded by staff nurses. Conventional dressing was removed after 3days of catheter implantation. Cleaning and washing of injection sites performed before and after of each injections. 2 cases (4.1%) have wound infection in injection site and tissue injury that were controlled with start of antibiotics. Catheter disconnection from injection site silicon bobbles in 2 cases. Silicon bobbles displacement in 3(6.2%) cases. Catheter and system blocking in 4 cases (8%). Implantable central catheters like as Polysite are effective and safe way of prolong infusion of different types of material especially chemotherapy drugs in children with low complication rates. Better nursing care is achieved when we use this modality of venous access especially in children with cancer who need prolong therapy course and chemotherapy.

Corresponding Author: Haleh Boroumand (Pediatric surgery Department, Mashhad University of Medical Sciences, Iran)
Epidemiology Of Childhood Cancer In Northeast Iran Between 2006-2014

1. Haleh Boroumand (Department Of Nursing, Dr Sheikh Hospital, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Haydeh Hashemizadeh (Department Of Nursing, Quchan Branch, Islamic Azad University, Quchan, Iran.)
3. Mozhgan Darabian (Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Malignant neoplasms remain the second leading cause of death in children after accidents and Leukemia is the most common malignancies in t. The aim of this study was to assess epidemiology of childhood cancer in Northeast Iran. This descriptive cross- sectional study has been done in Dr Sheikh Hospital in Mashhad University of medical science in Iran on 1764 children younger than 14 years old during 2006-2014 with cancer that has been pathologically confirmed. All information about the age, sex, type of cancers and residence of patients were collected from their medical records. For classification of the lesions the tenth edition of International Classification of Childhood Cancer (ICCC-10) coding system was used. 1764 forms were completed and the data were analyzed by SPSS-21. Required data such as sex, age, pathology of cancer, place of residence were collected and included in a checklist form. Frequency distribution of childhood cancers in less than 14 year old was evaluated and incidence rates were calculated per 1000,000 people a year. 1047 (59.4%) of cases were male and rest of them were female by sex ratio 1.5 to 1. The mean age of patients was 5.8± 4.2 and 30% were in age group 3-6 years. 1186(67%) of cases were from Razavi khorasan province. Results showed that leukemia (56.4%), Lymphomas (10.4%), renal tumor (9%), malignant bone tumor (4.4%) and CNS tumor (4.1%) were the most prevalent malignancies in Northeast Iran. Form leukemia cases (86.9%) were acute lymphatic leukemia (ALL). Over in nine years period, lowest and highest age standardized incidence rate was 114 (year 2006) and 142 (year 2014) cases per every 1000,000 person, respectively. The frequency of malignant diseases is more common in males than in females which are the same as other studies. The frequency and distribution of malignant diseases is the most in children aged 3-6 years that is different from some studies. Leukemia is the most prevalent malignant disease in the pediatrics which followed by lymphoma and renal tumor, that is different from some studies. In most study CNS tumor was the second malignancy, but as the majority of children with CNS tumor admitted in another hospital, it was reported lower the another study.

Corresponding Author: Haleh Boroumand (Department of nursing, Dr Sheikh hospital, Mashhad University of Medical Sciences, Mashhad, Iran.)
Nipple Discharge: A Short Review On Diagnostic And Therapeutic Approaches

1. Ehsan Shahverdi (Blood Transfusion Research Center/High Institute For Research Center & Education In Transfusion Medicine, Immunohematology Department, Tehran, Iran)
2. Seyed Abbas Mirmalek (Department Of Surgery, Islamic Azad University, Tehran Medical Sciences Branch, Tehran, Iran)

Abstract

Nipple discharge is a main concern for most women during their reproductive age; most complaint and visit to doctors are mainly in regard of breast and it can be one of the symptoms for breast cancer. There is a weak relationship between nipple discharge and breast cancer. The main objective of this review was to summarize and update information about nipple discharge. Intraductal papilloma was the most common cause of nipple discharge. Each diagnostic method has its strengths and weaknesses, therefore, no definitive diagnostic method exists to find the cause of the cancer, but ductoscopy is very useful. In addition, excision of the main ducts is currently the treatment of choice.

Corresponding Author: Ehsan Shahverdi (Blood Transfusion Research Center/High Institute for Research Center & Education in Transfusion Medicine, Immunohematology Department, Tehran, Iran)
Central Nervous System Toxoplasmosis In Relapsed Hodgkin’s Lymphoma: A Case Report

1. Ehsan Shahverdi (Blood Transfusion Research Center/High Institute for Research Center & Education in Transfusion Medicine, Immunohematology Department, Tehran, Iran)

2. Hassan Abolghasemi (Department Of Pediatrics, Baqiyatallah University Of Medical Sciences, Tehran, Iran)

Abstract

Patients with immunosuppression have an increased incidence of toxoplasmosis characterized by involvement of the central nervous system. Only a few cases of toxoplasmosis associated with immunosuppressive agents have been reported. Such cases have been reported in immune suppressed patients outside the Iran, but a search of the literature has not revealed any previous reports from this country. We described a 17-year-old male, a known case of Hodgkin's lymphoma with the diagnosis of central nervous system (CNS) toxoplasmosis. As a conclusion, CNS toxoplasmosis should be considered as a differential diagnosis in immunosuppressed patients who present with neurological manifestations.

Corresponding Author: Ehsan Shahverdi (Blood Transfusion Research Center/High Institute for Research Center & Education in Transfusion Medicine, Immunohematology Department, Tehran, Iran)
Evaluation Of The Diagnostic Value Of Sentinel Lymph Node Biopsy In Gastric Adenocarcinoma

1. Aliakbarian Mohsin (Surgical Oncology Research Center, Imam Reza Hospital, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Jangjo Ali (Surgical Oncology Research Center, Imam Reza Hospital, Mashhad University Of Medical Sciences, Mashhad, Iran)
3. Pakdel Akbar (Surgical Oncology Research Center, Imam Reza Hospital, Mashhad University Of Medical Sciences, Mashhad, Iran)
4. Motie Mohamad Reza (Surgical Oncology Research Center, Imam Reza Hospital, Mashhad University Of Medical Sciences, Mashhad, Iran)
5. Taheri Reza (Surgical Oncology Research Center, Imam Reza Hospital, Mashhad University Of Medical Sciences, Mashhad, Iran)
6. Razeghian Masud (Surgical Oncology Research Center, Imam Reza Hospital, Mashhad University Of Medical Sciences, Mashhad, Iran)
7. Memar Bahram (Surgical Oncology Research Center, Imam Reza Hospital, Mashhad University Of Medical Sciences, Mashhad, Iran)
8. Sadeghi Ramin (Nuclear Medicine Research Center, Qaem Hospital, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Currently, lymphadenectomy is recommended in Gastric Cancers but SLNB could prevent unnecessary dissections by diagnosing the involvement or noninvolvement of the lymph nodes if its efficiency is approved. This study was performed to evaluate the diagnostic value of SLNB in patients with Gastric Adenocarcinomas. This descriptive study was performed on 34 patients diagnosed with Gastric Adenocarcinoma admitted in Surgery Ward of Imam Reza Hospital during 2013 to 2016 who had resectable cancer before and during surgery and had no lymphatic involvement. Sentinel Lymph Node (SLN) was detected with Blue dye and sent for pathological study after resection. In 31 out of 34 patients, Sentinel lymph node was detected with blue dye mapping. (Detection Rate= 91%). In 7 patients, SLN involvement was reported negative while other lymph Nodes were involved (False Negative=33%). SLNB has 77% accuracy, 58.8% sensitivity, 100% specificity, positive predictive value 100% and Negative predictive value 66.7% in lymph node involvement of Gastric Adenocarcinoma. Due to its high false negative rate (33%), SLNB with blue dye mapping alone is not enough for diagnosing lymph node involvement in Gastric Adenocarcinoma.

Corresponding Author: Taheri Reza (Surgical Oncology Research Center, Imam Reza Hospital, Mashhad University Of Medical Sciences, Mashhad, Iran)
Biological And Clinicopathological Significance Of Cripto-1 Expression In The Progression Of Human ESCC

1. Reihaneh Alsadat Mahmoudian (Division Of Human Genetics, Immunology Research Center, Avicenna Research Institute, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Mohammad Reza Abbaszadegan (Medical Genetics Research Center, Medical School, Mashhad University Of Medical Sciences, Mashhad, Iran)
3. Mohammad Mahdi Forghanifard (Department Of Biology, Damghan Branch, Islamic Azad University, Damghan, Iran)
4. Meysam Moghbeli (Division Of Human Genetics, Immunology Research Center, Avicenna Research Institute, Mashhad University Of Medical Sciences, Mashhad, Iran)
5. Faezeh Moghbeli (Department Biology, Mashhad Branch, Islamic Azad University, Mashhad, Iran)
6. Mehran Gholamin (Division Of Human Genetics, Immunology Research Center, Avicenna Research Institute, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Human Cristo-1, a member of the EGF-CFC family, is involved in embryonic development, embryonic stem cell maintenance, and tumor progression. It also participates in multiple cell signaling pathways including Wnt, Notch, and TGF-β. Remarkably, it is expressed in cancer stem cell (CSCs) compartments boosting tumor cell migration, invasion, and angiogenesis. Although Cripto-1 is overexpressed in a variety of human malignant tumors, its expression in esophageal squamous cell carcinoma (ESCC) remains unclear. Our aim in this study was to evaluate the possible oncogenic role of Cripto-1 in ESCC progression and elucidate its association with clinicopathological parameters in patients. In this study, Cripto-1 expression in 50 ESCC tissue samples was analyzed and compared to corresponding margin-normal esophageal tissues using quantitative real-time-PCR. Cripto-1 was overexpressed in nearly 40% of ESCC samples compared with normal tissue samples. Significant correlations were observed between Cripto-1 expression and tumor differentiation grade, progression stage, and location (p < 0.05). Our results indicate that overexpression of Cripto-1 is involved in the development of ESCC. Further assessment will be necessary to determine the role of Cripto-1 cross talk in ESCC tumorigenesis.

Corresponding Author: Mehran Gholamin (Division of Human Genetics, Immunology Research Center, Avicenna Research Institute, Mashhad University of Medical Sciences, Mashhad, Iran)
Evaluation Of In Vitro Cytotoxicity Of Curcumin Nanomicelle And Free Curcumin Against A Colorectal Cancer Cell Line

1. Elham Zendehdel (Department of Biochemistry and Biophysics, Faculty of Sciences, Islamic Azad University Mashhad Branch, Mashhad, Iran)
2. Jamshidkhan Chamani (Department of Biochemistry and Biophysics, Faculty of Sciences, Islamic Azad University Mashhad Branch Mashhad, Iran)
3. Fatemeh Gheybi (Department of Medical Nanotechnology, School of Advanced Technologies in Medicine, Tehran University of Medical Sciences, Tehran, Iran)
4. Mahmoud Reza Jafari (Department of Pharmaceutics, Mashhad University of Medical Sciences, Mashhad, Iran)

Abstract

Curcumin, a natural polyphenol derived from the rhizomes of turmeric (Curcuma longa), is a highly lipophilic molecule. Although curcumin showed potent anticancer and cancer preventive effects due to targeting various signaling pathways its clinical usage is limited due to poor bioavailability. Nanomicelle formulations of curcumin have been developed to enhance the bioavailability and the solubility of this lipophilic compound. In this study the cytotoxicity of curcumin nanomicelle against C26 colorectal cancer cell line was evaluated in vitro by MTT assay. Nano-Curcumin is a registered curcumin product (SinaCurcumin®) for use which has been developed in Nanotechnology Research Center of Mashhad University of Medical Sciences, Mashhad, Iran and marketed by Exir Nano Sina Company in Tehran-Iran (IRC:1228225765). colorectal cancer cell line were treated by the drugs and incubated for 48 h. Cytotoxicity was examined by MTT assay. Our results indicated that the IC50 concentration of the micelle form of curcumin showed higher toxicity than that of non-micelle form (25.02 vs 18.90 respectively). The micelle form of curcumin is expected to increase the efficacy of curcumin against C26 colorectal cancer cells.

Corresponding Author: Elham Zendehdel (Department of Biochemistry and Biophysics, Faculty of Sciences, Islamic Azad University Mashhad Branchy, Mashhad, Iran)
Abstract

Definitely, gene therapy is considered as a great and fundamental change and evolution in the treatment of many genetic diseases. In cancer Gene therapy, especially in breast cancer, have had a tremendous and increasing growth and development and has seriously shifted from the theoretical range of works to the practical and clinical field. Some of the methods that are currently used to treat breast cancer, including: Chemotherapy, Radiation Therapy, Surgery, Hormone Therapy, and Laser Therapy; however, these methods have some side effects for the patients. But there are some modern molecular methods, which are used in gene therapy. These methods are including: Oncolytic Viruses, Suicide Gene, Anti-angiogenesis, Tumor Suppressor Genes, Immunotherapy, and Antisense Targeting that are considered to be utilized for the treatment of breast cancer, which is the most common cancer type observed among women. Utilizing suitable viral and non-viral carriers, by selection and design of suitable carriers, the target gene can be selectively introduced into the cells or a specific gene can be made off within the cells; the work which has very effective role in the treatment process. Gene therapy is very useful not only in the field of complete treatment for cancer, but also in the exact and early diagnosis, and moreover in the prognosis of cancer diseases. Gene therapy has made a great evolution to the future of treatment process, and especially of cancer treatment and is an important step towards Personalized Medicine. However, many questions have been remained unanswered in this context.

Corresponding Author: Seyed Mohammad Amin Kormi (Cancer Genetics Research Unit, Reza Radiation Oncology Center, Mashhad, Iran)
PI3K Pathway

Abstract

Phosphatidylinositol-3 kinases, PI3Ks, is a family of lipid kinases that it causes phosphorylate inositol phospholipids to make signal passway, that regulators many essential cellular functions, consist of cell survival, growth, and differentiation in cells. PI3K pathway and cancer: a- Somatic changing: 1- Genetic mutations/loss of function: one of most reform genetic can activate the PI3K/AKT signaling, and the second is inactivation of the PTEN: protein truncations, missense mutations, Transcriptional repression and epigenetic silencing. It can be deleted by two forms which are heterozygous and Homozygous loss. 2- Genetic amplification of PI3K: These mutations cause various human tumors consist of breast, colon, and endometrial cancers and glioblastoma. Mutation in PIKCA genes (encode p110α) is usual mutation, which intensification p110α activation. So PI3K pathway will be hyperactivated. 3- AKT overexpression: overexpression AKT1,2 cause different cancer. AKT1: breast, colorectal, endometrial, and ovarian cancers. AKT2: colorectal cancers and metastases. b- Activate RTK: Mutation in different RTK result different cancer: epithelial growth factor receptor (EGFR) cause lung cancers and human epidermal growth factor receptor 2 (HER2) mutations cause breast cancers. Study of this pathway is important for tumor development and tumor's treatment. Targeted agents are designed for PI3K/Akt signal region. Four important classes are: dual PI3K-mTOR inhibitors, PI3K inhibitors, AKT inhibitors, mTOR catalytic site inhibitors. Base on function and structure there are three classes of PI3Ks grouped (class I,II,III). Most of human cancer in PI3K pathway related to Class I PI3Ks, which is heterodimers consists of an adaptor/regulatory subunit (p85) and a catalytic subunit (p110). Growth factor binds to receptor tyrosine kinases (RTKs) after that phosphorylate it. This process releases inhibitor from the p110. Thereby PI3K localize in the plasma membrane, after that PI3K phosphorylate phosphatidylinositol4,5-bisphosphate (PI[4,5]P2), shift it to PIP3. Further PI3K is stimulated by activated Ras, which binds p110 directly. The p110 can also be activated by G-protein_receptors complex. PTEN is a tumor suppressor phosphatase that dephosphorylates PIP3 to PIP2, it is conversely action PI3K and finish PI3K signal pathway. PIP3 transfer intracellular signaling to cell molecular by binding signaling proteins such as AKT (AGC kinase family). AKT promotes several acts in cells: AKT can inhibit proapoptotic Bcl-2 family that causes cell survival. AKT increase transcription of antiapoptotic and prosurvival genes. AKT Phosphorylate Mdm2 to gender apoptosis and AKT can decrease proteins of cell death-promoting. AKT relieves inhibit of the rheb, so reduce protein.

Corresponding Author: Madjid Momeni-moghadam (Department of Biology, Faculty of Sciences, Hakim Sabzevari University, Sabzevar, Iran)
The Role Of EpCAM In Cancer Progression

1. Fateme Oladi
2. Elnaz Yossefi
3. Madjid Momeni-Moghaddam (Department of Biology, Faculty of Sciences, Hakim Sabzevari University, Sabzevar, Iran)

Abstract

Cancer is one of the important causes of death in the world. The main cause of death in cancer is invasion and metastasis. Tumor invasion and metastasis is a complex process and continuous and include multiple steps like Set at the cellular level by cell adhesion molecule (CAM), catabolic enzyme protein, growth factor and various factor of angiogenesis. Ig,CAM, the immunoglobulin super family is a large group of cell surface and soluble protein that are involved in the recognition, binding or adhesion process of cell. One CAM is EpCAM (epidermal cell adhesion molecule) that involvement in tumor progression. EpCAM is glycoprotein with the weight of (40KDa) that known as a marker for cancer. EpCAM effects of not sticking include multiple signaling process and migration, proliferation and differentiation. EpCAM expression is associated with age, tumor site, tumor size, metastasis, lump node. EpCAM expression in esophageal cancer, pancreas, colon, gastric and prostate cancer. Expression of EpCAM is an independent prognostic factor. EpCAM,CD326 is ecological potential inhibition in multiple tumor. That encoded by TACSTD1. Recently EpCAM to become in interested in the study because it is a signal converter and is a potential marker for the onset of cancer cells. EpCAM also known as KSA, ESA, 17-1A, and GAV33-2. Conclusion: EpCAM have biological role in tumor development and progression. As a cell adhesion molecule EpCAM mediated cell adhesion is hemophilic as a result of metastasis prevent. The over expression in colorectal cancer cells inhibiting tumor metastasis and invasion. Retells EpCAM inhibits migration and invasion promote inflammation and the innate immune response. EpCAM is dual role in tumor development and should be planning.

Corresponding Author: Madjid Momeni-Moghaddam (Department of Biology, Faculty of Sciences, Hakim Sabzevari University, Sabzevar, Iran)
Occupational And Environmental Carcinogens And Prevention Of Exposure

1. Seyyedeh Negar Assad (Management And Social Determinants Of Health Research Center, Department Of Occupational Health Engineering, School Of Health, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

There are many known occupational and environmental carcinogens for human being, but the research has followed by related scientists, agencies and institute. Objective was introduction the occupational and environmental carcinogens and prevention of exposure. In the review article the author searched in scientific references, journal and websites specially international agency for research on cancer or IARC and found the important results. There were many text and article about the preventive methods in the workplaces and other environment. Recently the international agency for research on cancer has reported the classifications of carcinogens according to new researches. In group 1: Carcinogenic to humans has 118 hazard factors, in group 2A: probably carcinogenic to humans has 80 factors and agents, in group 2B: possibly carcinogenic has 289 items, in group 3: not classifiable has 502 and in group 4: probably not has 1 agent. Many of them are in the environment and workplaces. Prevention of them is necessary with scientific and preventive works and devices. Examination and screening for persons in exposure should be done. Prevention of exposure to carcinogens is necessary in all environments. Knowledge about the carcinogens is important item in medical sciences education.

Corresponding Author: Seyyedeh Negar Assad (Management and Social Determinants of Health Research Center, Department of Occupational Health Engineering, School of Health, Mashhad University of Medical Sciences, Mashhad, Iran)
Defective Lifestyle: Mechanisms And Prevention Of Cancer

1. Elham Navipour (Department Of Biostatistics & Epidemiology, Faculty Of Health, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Cancer is a chronic disease and non-contagious that wide variety of disease will be included. This disease happening for each person, any age group and in any race and as a health problem is an effective on public health. Cancer was the second and the third leading cause of death in developed countries and the developing countries respectively There is while that about one third of ten million new cases annual on a cancer preventable and one third of causes is treatable with the possibility of early and appropriate diagnosis. Only 5 to 10 percent of cancers are due to genetic and 95 to 90 percent remaining are due to lifestyle such as smoking, diet and nutrition, alcohol, physical activity, obesity, exposure to sun, infections and environmental pollutants. These factors play an important role in the prevention of cancer. Among lifestyle factors, nutrition and related factors play an important role in Incidence of cancer. Defective style if cause of two important phenomenon non activity and increase calorie consumption. The aim of this study is defective lifestyle: Mechanisms and Prevention of Cancer. Healthy lifestyle behaviors are recommended to reduce cancer risk and overall mortality. Healthy lifestyle measures such as regular exercise, avoiding overweight, not smoking and limiting the intake of alcohol can therefore also be recommended as helping to reduce the risk of cancer it is necessary to consider all aspects of the person's lifestyle include: methods, insights and observance the value of educative, cultural, social and economic society. As a result, it is necessary in the field of strategic planning, resource allocation and training of human resources is necessary to be considered finally planning authorities and health care especially, community health nurses, to modify life style, until be prevention from cancer incident greatly.

Corresponding Author: ali taghipour (Department of Biostatistics & Epidemiology, Faculty of health, Mashhad University of Medical Sciences, Mashhad, Iran)
Cytotoxicity And Apoptosis In Breast Cancer Cell Line Exposed To An Extract Of The Scrophularia Umbrosa Dumort

1. Leila Etemad (Pharmaceutical Research Center; Mashhad University Of Medical Sciences; Mashhad, Iran)
2. Mostafa Mansouri (Department Of Pharmacology And Toxicology, Islamic Azad University, Pharmaceutical Science Branch, Tehran, Iran)

Abstract

Breast cancer is the most common cancer in women worldwide, especially in developing countries. Scrophularia Umbrosa Dumort is an Iranian medicinal plant which is used for various disorders in traditional medicine. In this study we investigated the anti-cancer and cytotoxic effects of plant root extracts on human breast cancer and normal cell lines. Six extracts of plant including the methanol, dichloromethan, water, butanol, ethyl acetate, petroleum ether were evaluated. Cytotoxicity effect of the extracts on MCF-7 (breast cancer cell line) and NIH3T3 (normal fibroblast cell) was investigated by MTT assay. In addition apoptotic induction was measured using flow cytometry. The results showed that the water and butanol extracts had no cytotoxic effects but methanol, dichloromethan, ethyl acetate, petroleum ether extracts significantly showed cytotoxic effects in a dose dependent manner on the breast cancer cell line. The ethyl acetate has the lowest IC50 on cancer cell line (400 µg/ml) that differs extremely from the IC50 for NIH cells (1500 µg/ml). Flow cytometric analysis showed apparent increase of apoptotic cells in mentioned extract. Our findings suggest that this plant may contain potential bioactive compound(s), especially ethyl acetate extract, that can be used in the treatment of breast cancer.

Corresponding Author: Leila Etemad (Pharmaceutical Research Center; Mashhad University of Medical Sciences; Mashhad, Iran)
Nutritional Status Of Pediatric Cancer Patients In Iran: A Clinical Audit

1. Leila Khajavi (Department Of Nutrition, Faculty Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Sara Movahed (Department Of Nutrition, Faculty Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
3. Hamidreza Farhangi (Department Of Pediatric Hematology-Oncology, Doctor Sheikh Pediatric Hospital, Mashhad University Of Medical Sciences, Mashhad, Iran)
4. Fatemeh Nejati Salekhani (Department Of Nutrition, Faculty Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

This study assess the nutritional status of outpatient cancer children referred to the hematology and oncology clinic at Doctor Sheikh Hospital, a pediatric teaching hospital in Mashhad, Iran. We performed a clinical audit. Nutritional status was assessed by anthropometric indices. STRONGkids tool was applied for screening risk of malnutrition. A total of 61 pediatric cancer patients were assessed. 77 percent of patients were male (47 patients) and the mean age was 8.4 years (Range: 6 month to 18 years). Acute lymphoblastic leukemia (ALL) (84.7%) and Wilms tumor (26.6%) was the most prevalent cancer among hematologic and solid tumors respectively. Results showed that 26.2% of patients had malnutrition by BMI for age z-score index (underweight), 24.5% by weight for height (WFH) index (wasting) and 21.3% by HFA index (stunting). The prevalence of underweight, wasting and stunting was higher among patients with solid tumors than patients with hematological malignancies. However, results showed that the prevalence of malnutrition was not statistically significant between the two groups. The STRONGkids classified 34.4% of patients as moderate risk, and 65.6% as high risk of malnutrition. Patients with solid tumors were more in high risk group than patients with hematological malignancy (40% vs 32.6%) although it was not statistically significant (p>0.05). Malnutrition was prevalent among pediatric cancer patients in this study. So appropriate nutritional screening and support plans should be implemented for improving the nutritional status of these children.

Corresponding Author: Abdolreza Norouzi5 (Department of Nutrition, Medical school, Mashhad University of Medical Sciences, Iran)
Use Of Myeloid-Derived Suppressor Cells As A Targeted And Promising Delivery System For Tumor Immunotherapy

1. Amin Afkhami (Department Of Biology, Faculty Of Science, Ferdowsi University Of Mashhad, Mashhad, Iran)

2. Maryam M. Matin (Department Of Biology, Faculty Of Science, Ferdowsi University Of Mashhad, Mashhad, Iran; Cell And Molecular Biotechnology Research Group, Institute Of Biotechnology, Ferdowsi University Of Mashhad, Mashhad, Iran; Stem Cell And Regenerative Medicine Research Group, Iranian Academic Center For Education, Culture And Research (ACECR), Khorasan Razavi Branch, Mashhad, Iran)

Abstract

The highly important roles of immune system in cancer development has made immune cells and their related factors as attractive research tools in cancer immunotherapy. One of these cell types includes myeloid-derived suppressor cells (MDSCs), a heterogeneous population of myeloid progenitor cells, i.e., immature granulocytes, macrophages, and dendritic cells (DCs). Two major types of MDSCs are: CD11b+Gr1high (CD11b+Ly6G+Ly6Clow) with a granulocytic phenotype (gMDSC), and CD11b+Gr1low (CD11b+Ly6G-Ly6Chigh) with a monocytic phenotype (mMDSC). In cancer patients, these immature cells, in response to some tumor related cytokines or factors such as GM-CSF or S100, migrate from the bone marrow to primary or metastatic tumors. These tumors block their differentiation to mature cells and instigate them to produce some immunosuppressive cytokines such as IL-6, IL-10, and TGF-β, and some factors such as arginase 1, reactive oxygen species (ROS) and inducible nitric oxide synthetase, that modulate cancer cell killing responses of T cells and natural killer cells in the tumor microenvironment (TME). In tumor-bearing mice, ROS impair DC maturation while sustaining the accumulation of myeloid-derived cells with an immature phenotype, i.e. MDSCs. Due to specifically homing of MDSCs in tumors, in recent studies, MDSCs have been used for specific delivery of curative agents to TME in two approaches: first, as vehicles for delivery of immune cells activator agents, such as bacteria, to tumors; afterwards, this infected tumor cells will become a target for the activated immune cells. In second approach, MDSCs have been used as delivery systems for tumor cytotoxic agents to TME; in case of engineered tumor killing bacteria, injection of bacteria-infected MDSCs into the tail vein of tumor-bearing mice, resulted in selectively delivery of bacteria to metastatic sites, where it could spread from One cell to another without being eliminated by the immune system; however, it was very poorly delivered to normal tissues such as spleen. These observations indicate high capacity of MDSCs to be targeted to various histological types of cancers and highlight the great potential of immune cells that naturally home to the TME for selective delivery of anticancer agents.

Corresponding Author: Maryam M. Matin (Department of Biology, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran; Cell and Molecular Biotechnology Research Group, Institute of Biotechnology, Ferdowsi University of Mashhad, Mashhad, Iran; Stem Cell and Regenerative Medicine Research Group, Iranian Academic Center for Education, Culture and Research (ACECR), Khorasan Razavi Branch, Mashhad, Iran)
Serious Fungal Mycotoxins Carcinogenic Agents

1. Majid Ganjbakhsh (Student Research Committee, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Fatemeh Afsharzadeh (Medical Science Of Mashhad University)

Abstract

Mycotoxins (fungal toxins) are various secondary chemical metabolites that produced by a group of microscopic fungi on human foods, animal husbandry and poultry. This production occurs in favorite heat and humidity and can have devastating effects on human and animal tissues and due to wide Range of diseases like acute or chronic toxicity, carcinogenic effects and even cause death. More than 200 species of fungi cause more than 100 different mycotoxins are known today. One of these mycotoxins is aflatoxin. that due to the effects of carcinogens is the most dangerous and most deadly mycotoxins in fungi that produced by Aspergillus species. Aflatoxin in very small quantities, is toxic and can cause cirrhosis, liver inflammation, liver carcinoma and malignant tumors. In some areas of Asia and Africa has been found a significant relation between absorption of aflatoxin and primary liver cancer. Therefore, it is so important to manage about identify and quantify these deadly toxins and public training and preventive actions about contaminated foods and materials

Corresponding Author: Marzieh eidi (Medical Science Of Mashhad University)
Abstract

HTLV-I is a worldwide distribution retrovirus which north east of Iran especially Mashhad is one of the endemic areas. In spite of the healthy carriers are the majority of HTLV-I-infected individuals but small proportion of infected population developed two progressive diseases: ATL and HAM/TSP. ATLL is a very poor prognosis aggressive T-cell proliferation caused by HTLV-1. BCL-XL belongs to BCL2 family which inhibits apoptosis in cell so over express of this gene may promote the uncontrolled cell proliferation. High TAX, HBZ and proviral load level can be potential HTLV-I markers for pushing cell into malignancy; therefore in this study correlation between them and BLC-XL were evaluated. In this study, 38 HTLV-I positive samples including 20 ATL subjects and 18 asymptomatic were investigated. mRNA were extracted and convert to CDNA from Peripheral blood mononuclear cells (PBMCs) then expression of TAX HBZ and BCL-XL investigated by TaqMan qPCR. DNA was execrated from PBMCs and used for proviral load. The analysis of data showed a significant positive correlation between TAX, HBZ and BCL-XL gene expression ATL and carriers $P= (0.000)$. There is no statically correlation between the proviral load and Bcl-xl entire the population ($P= 0.961$). The present study demonstrated that TAX and HBZ can promote Bcl-xl gene expression which may a causative important role in disrupting cell life cycle then progress the cells into malignant stage of proliferation. Therefore apoptosis may get interrupted by virus onco proteins. In spite of rising HTLV-I proviral load in ATLL patients it seems do not have an direct effect on TAX, HBZ and Bcl-xl gene expression.

Corresponding Author: Mohammad Mehdi Akbarin (Inflammation and inflammatory research centre, Medical School, Mashhad University of Medical Science, Mashhad- Iran)
TAX And HBZ Gene Expression In Association Of HTLV-I Proviral Load Compared Among Adult T Cell Leukemia/Lymphoma (ATLL) And Healthy Carriers

1. Mohammad Mehdi Akbarin (Inflammation And Inflammatory Research Centre, Medical School, Mashhad University Of Medical Science, Mashhad- Iran)
2. Sysed Abdollahim Rezaee (Inflammation And Inflammatory Research Centre, Medical School, Mashhad University Of Medical Science, Mashhad- Iran)
3. Abass Shirdel (Internal Medicine Dept. Medical School, Mashhad University Of Medical Science, Mashhad- Iran)

Abstract

Mashhad is one of the endemic areas for HTLV-I infection. The small proportion of infected subjects developed in two progressive diseases: ATL and HAM/TSP. ATLL caused by the aggressive T-cell proliferation and is associated with a very poor prognosis. Two major oncoproteins TAX and HBZ are the main cause of malignancy which another virological marker such as proviral load could be used full for disease monitoring progression, therefore in this study co expression of TAX, HBZ and proviral load were evaluated. 38 HTLV-I infected individuals including 18 asymptomatic and 20 ATL subjects were investigated. PBMCs mRNA converted to CDNA and extracted DNA used for assessment of TAX and HBZ expression and proviral load then investigated by TaqMan qPCR. Data showed a significant difference of TAX and HBZ expression among study groups (ATL and carriers P= (0.003 and 0.000) respectively, furthermore significant statically difference of proviral load observed entire study population (ATL vs carrier P=0.002). Moreover, the means values in ATLL group were 11431.70± 3774.3, 0.199±0.164, 0.101±0.061 and among healthy carrier were 513.25±119.23, 0.000074±0.00006, 0.000012±0.000005 for proviral load, TAX/β2 and HBZ/β2 respectively. The present study demonstrated that HTLV-I proviral load, TAX, and HBZ were higher in ATL group in comparison with healthy carriers. Therefore, TAX, HBZ and proviral load can be used as prognostic and monitoring marker for the efficiency of therapeutic regime and prognosis of HTLV-I associated malignancy.

Corresponding Author: Mohammad Mehdi Akbarin (Inflammation and inflammatory research centre, Medical School, Mashhad University of Medical Science, Mashhad- Iran)
Design A Model To Build A Computerized Guideline To Detect Breast Cancer

1. Sara Dorri (Cancer Informatics Department, Breast Cancer Research Center, ACECR, Iran)
2. Najme Nazeri (Cancer Informatics Department, Breast Cancer Research Center, ACECR, Iran)
3. Alireza Atashi (Cancer Informatics Department, Breast Cancer Research Center, ACECR, Iran)
4. Mohsen Goli (Cancer Informatics Department, Breast Cancer Research Center, ACECR, Iran)

Abstract

Medical guidelines are an important tool for improving health care quality. Studies have shown implementation oncology guidelines improve clinical outcomes in patients' overall survival and in preventing cancer from returning. But overall adherence to guidelines in format of paper text is very low. One way to change the presentation guideline's content is a variety of computer methods for representation of knowledge. The first step in computerization of paper guidelines is converted the knowledge of them to electronic format. Compliance of paper based guidelines on breast cancer, is close to 51 percent, while we know the computerized guidelines can reduce cost of medical errors and can help doctors make better decisions by providing the right information at the point of decision-making and to provide specific reminders can improve patient care and patient safety. In this study we want design a model to detect breast cancer through computerized guideline. In this study, we design a computerized model of breast cancer IBCRC guideline. In the first step we have several meetings with clinicians (oncologist and Surgeon) to study guideline and identify ambiguity and reach agreement to solve them. In the next step we produce ontology of guideline to design Ontology Based model, completely. After all, evaluation can done by the clinician via real scenarios of patients. In first phase of study, it is time consuming to collect participant and investigate a bout guideline. We collect the opinion of participant, identify ambiguity and bottleneck of guideline. Then we build computerized model and the findings of evaluation was acceptable. Using of computer guidelines could possibly reduce the costs associated with medical errors and increase the quality of care for patients.

Corresponding Author: Sara Dorri (Cancer Informatics Department, Breast Cancer Research Center, ACECR, Iran)
Natural Killer Cells; A Novel Cell Therapy For Osteosarcoma Hopes And Prospects

Abstract

Osteosarcoma which has been described as a malignant tumor, and has believed that arisen from production of malignant osteoid, remained as a debilitating disease. Surgical removal of lesions is the mainstay of therapy which must be followed by chemo radiotherapy. Although outcomes have not changed dramatically recently. Over last decades nk cell therapy has been emerged as a hot topic in the field of osteosarcoma cell therapy. Methods: We performed a systematic search with combining the key words ‘Natural killer cells’, ‘osteosarcoma’, ‘malignancy’, 'Adoptive celltherapy' on PubMed, Medline, Embase, scopus, science direct (Elsevier) and ovid from September 2014. English articles published Nk cells as adovant therapy of osteosarcoma. The result of our search strategy included 14 possibly related articles that, 2 were clinical trial; 4 were in vivo animal model study, 2 were ex vivo human study and 7 were review articles. Ex vivo expanded NK cells has been studied in phase I/II clinical trials as well as experimental studies. A majority of these investigations report that NK cell expansion takes place appropriately up to 691.4+/−170.2 fold with 95.2% viability. Cytotoxicity assays against Various showed acceptable cytolytic activity. With regard to efficacy, most of these observations report the infusion of NK cells to be well tolerated and almost effective in autologous and allogenic haploidentical setting. Although NK cells have demonstrated to target human tumor cells, it is important to optimize and standardized the ex vivo activation and expansion in advance to adoptive immunotherapy. It is also necessary to gather clinical data from controlled trials to assess NK cells usefulness whether in combination therapy strategy or alone.
Study Of The Effects Of Prunus Africana And Lycopene On Prostate Cancer

1. Mahdi Abbasian (Medical Laboratory Science Student Of Qom University Of Medical Sciences - Qom - Iran)
2. Mahmoudreza Hamidi (Medical Student Of Qom University Of Medical Sciences - Qom - Iran)

Abstract

Prostate cancer is one of the most common cancer in men is prostate cancer. Most prostate cancers grow slowly, but some grow relatively fast. Cancer cells may spread from the prostate, particularly the bones and lymph nodes and create difficulties in urination, blood in the urine or pain during urination in the pelvis and lower back. A condition called benign prostatic hyperplasia, can also bring about similar symptoms. The aim of this study is to investigate articles that relate the effects of Lycopene and Prunus Africana on prostate cancer cells. The study was done by searching some Web site such as PubMed and SID and using right keywords. Lycopene is chemical found in some fruits and vegetables and there is high power in inhibiting prostate cancer. Lycopene is a carotenoid in the blood that has antioxidant properties. The results indicate that, Lycopene that is found in abundance in tomatoes inhibitory effect against prostate cancer. Prunus Africana is an evergreen plant native to Africa. There are fatty acids at its extracts that have properties similar to fatty acids Sapalmtv. Studies show that Docosanol can reduce levels of testosterone hormone and Luteinizing hormone. Docosanol a chemical that has been found in Prunus Africana and could reduce the levels of the hormone prolactin. Also strolic section of Prunus Africana acts against the aggregation of testosterone in the prostate. Such studies report that Prunus Africana has significant effects on prostate cancer. Result of this studies show that Lycopene and Prunus Africana with direct effects on prostate cancer cells, can inhibit growth of this cells; such that can reduce the risk of this type of cancer with the effects on prostate cells. Prunus Africana effect on increasing the secretion of prostate and seminal composition can also play an important role in preventing prostate enlargement and cancer have it.

Corresponding Author: Mahdi Abbasian (Medical Labratory Science Student of Qom University of Medical Sciences - Qom - Iran)
association of VEGF -634G>C (Rs2010963) gene polymorphism with breast cancer risk in northwest of Iran

Abstract

Breast cancer is one of the most prevalent cancers between women worldwide, that is considered as main cause of cancer-related death in females. In many investigations and researches that were done in different areas, significant association was observed between VEGF -634G>C polymorphism and breast cancer risk that is due to most important rolls of this gene in angiogenesis and finally regenerating the new vessels in breast cancer cell nourishment. Due to specific importance of this gene in angiogenesis, we investigated this single nucleotide polymorphism in 60 DNA specimen from both patients with breast cancer and normal persons by isolating DNA from peripheral blood by salting out method, and genotypes were determined and assessed by the use of RFLP-PCR (Restriction fragment length polymorphism polymerase chain reaction) technique. The data were analyzed by javastat online statistics software, using Chi-square (v2) with a significance level of 0.05. In this study, CC recessive genotype frequency was higher in case group than the control group (45% and 28.33% respectively) and statistical significant difference was observed (OR=3.206, 95% CI=1.69-6.112, P=0.102). GC genotype frequency in control and case groups was 20 and 30 percent respectively, which was significant in control group (OR=0.483, 95% CI=0.257-0.905, P=0.014). GG dominant genotype frequency was higher in control group than the case group (51.66 and 25 percent respectively) (OR=0.583, 95%CI=0.289-1.173, P=0.0001). G allele frequency in case and control groups was 40 and 61.66 percent respectively (OR=2.413, 95% CI=1.316-4.439, P=0.002). C allele frequency in case and control individuals was 60 and 38.33 percent respectively (OR=0.415 95% CI=0.225-0.760). CC genotype in case group had significant increase, GG genotype in control subjects had significant increase, GG genotype in control subjects had significant increase. C allele in case individuals and G allele in control group had significant increase.

Corresponding Author: Mohammad Ali Hosseinpourefeizi (Radiobiology Laboratory, Natural science department, Tabriz University Tabriz, Iran)
Psychological Characteristics Of Women With Breast Cancer

1. Mahmoudreza Hamidi (Medical Student Of Qom University Of Medical Sciences - Qom - Iran)

Abstract

Today, cancer is one of the main causes of death in the world that is known. Breast cancer is the most common cancer in women. The disease that in addition to the individual, effects the community. What is important to consider the psychological aspects of the disease. Depression is one of the effects of cancer. Depressed people lose better opportunities in the rest of his life for living. Hope force the man to be ready for work, provide flexibility, vitality and life satisfaction can be increased. Patients with malignant disease have a higher depression and their hope is the lower rate of patients whose disease is a benign. This indicates that it is broadly to decrease depression in cancer patients need to promote hope they understand. In another study also showed that the spiritual experiences of women with breast cancer is more than in healthy women. Women who were satisfied with their relationship reported less body image disturbance than did dissatisfied women after 2 weeks. Being married was also associated with less body image disturbance at that time. The protective effect of these relational variables was still observable 1 year later. Changes in body image disturbance over time were explained by the negative impacts of mastectomy and chemotherapy. Also a study is showed that Spirituality and social support breast cancer patients have an impact on growth after injury. With education and interventions that include increasing levels of spirituality and social support, they can improve patients’ post-traumatic growth. We know that some patients after treatment show positive psychological characteristics such as extraversion, sociability, devotion, altruism, resilience, spirituality, optimism and some other The negative characteristics such as anxiety, loneliness, depression, sadness, anger and frustration manifest. It can be said that there are Complex relationship between psychological characteristics and breast cancer. If we improve positive psychological characteristics, spirituality and religious beliefs in women, we can treat patients easily and. love, devotion, and spirituality help us more than other.

Corresponding Author: Mahdi Abbasian (Medical Labratory Science Student of Qom University of Medical Sciences - Qom - Iran)
Serum Chemokine Ligand 5 (CCL5/RANTES) Level Might Be Utilized As A Predictive Marker Of Tumor Behavior And Disease Prognosis In Patients With Gastric Adenocarcinoma

1. Zahra Mahdian Baygi (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad, Iran; 3. Student Research Committee, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Rana Rahimi Kakhki (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad, Iran; 2. Student Research Committee, Faculty Of Medicine, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
3. Zahra Behrooznia (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad, Iran; 2. Student Research Committee, Faculty Of Medicine, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
4. Fatemeh Hosseinzadeh (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad, Iran; 2. Student Research Committee, Faculty Of Medicine, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
5. Hosein Jalali Rad (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad, Iran; 2. Student Research Committee, Faculty Of Medicine, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
6. Maryam Ghandehari (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad, Iran; 2. Student Research Committee, Faculty Of Medicine, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
7. Pouya Ghaderi (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad, Iran; 2. Student Research Committee, Faculty Of Medicine, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
8. Ali Shariat Razavi (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad, Iran; 2. Student Research Committee, Faculty Of Medicine, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
9. Mokhtar Ahmadi (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad, Iran; 2. Student Research Committee, Faculty Of Medicine, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
10. Sepideh Mansouri Majordi (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad, Iran; 2. Student Research Committee, Faculty Of Medicine, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
11. Kamran Ghaffarzadegan (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad, Iran)
12. Seyed Tahereh Mohaddess (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Gastric cancer is the second leading cause of cancer-related deaths worldwide and the most common gastrointestinal cancer in Iran. Chemokine ligand 5 (CCL5/RANTES) is one of the most potent angiogenic factors that plays an important role in tumor growth, invasion, and metastasis. We aimed to assess the serum level of CCL5 in patients with gastric adenocarcinoma and its relation with histological grade and tumor stage, as well as the disease prognosis. Seventy-four patients with gastric adenocarcinoma that had undergone gastrectomy and 96 non-tumoral cases in which gastric cancer was ruled out by gastroscopy and biopsy were enrolled. Demographic and epidemiological characteristics and patient survival data were reviewed. Histological type, grade, and tumor stage (TNM) were determined by a single expert pathologist. Helicobacter pylori infection status and CCL5 serum level were measured by ELISA. Data were analyzed using SPSS software version 16. Patients with gastric adenocarcinoma had significantly higher serum CCL5 level compared with control group (P < .001). Higher serum CCL5 levels were associated with lower histological differentiation (P < .001), higher depth of tumor invasion (P = .022), more frequent lymph nodes involvement (P = .028), and advanced tumor stage (P = .002). The overall survival of patients with CCL5 levels higher than 70.671 pg/ml was significantly lower than those with lower than this cutoff (P = .043). Serum CCL5 levels might be utilized as a predictive marker of tumor behavior and disease prognosis in patients with gastric adenocarcinoma. Further studies to assess tissue expression of CCL5 and its gene polymorphisms are suggested.

Corresponding Author: Alireza Bari (Gastric cancer research group, Mashhad University of Medical Sciences, Mashhad, Iran)
Abstract

To live in the materialistic world, the truth of the human existence must physically take the distinctive feature of this world, movement, to help the realization of his potential. Occasionally, physically living reverse mastering the physical environment and cancer cells become a threat to the human life. Since human seek for the existence truth, this can be the way to stimulate the mind intelligence, performance accuracy, and developed sentimentality. It may seem harsh in common view, but it reflects the unique presence of each component of the cosmos. With a truth-seeking vision, we would realize that cancer cells expose their potentials. From the philosophy perspective, the cancer significance is a strong motivation for life, as the human would understand and apply his physical, mental, and sole abilities. With a quick look at the emergence and growth of cancer in human body parts, this article examines different medical approaches and mental imagery as well as the ability of human sole in cancer treatment and improvement of life quality. From the physical perspective, this is a confrontation between human body normal cells and cancer cells for resources exploitation; contrasting the fact that this is an encountering between the truth existence of human as a multi-dimensional being and various forms of cancer. Regarding the sole as the director of all human actions, the perception of sole ability to dominate the body represents a link between theory and practice to deal with cancer.
Anatomical Distribution And Demographic Data Of Esophageal Cancer From 1997-2013 In Mashhad, Iran

1. Kamran Ghaffarzadegan (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad Iran.)
2. Ali Reza Bari (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad Iran.)
3. Ahmad Gholipour (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad Iran; Student Research Committee, Faculty Of Medicine, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
4. Zahra Behrooznia (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad Iran; Student Research Committee, Faculty Of Medicine, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
5. Rana Rahimi Kakhki (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad Iran; Student Research Committee, Faculty Of Medicine, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
6. Zahra Mahdian Beygi (Student Research Committee, Faculty Of Medicine, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
7. Farnaz Torabian (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad Iran; Student Research Committee, Faculty Of Medicine, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
8. Soode Moghadari (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad Iran; Student Research Committee, Faculty Of Medicine, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
9. Fatemeh Hamidi (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad Iran; Student Research Committee, Faculty Of Medicine, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
10. Nazanin Yoosofli (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad Iran; Student Research Committee, Faculty Of Medicine, Islamic Azad University, Mashhad Branch, Mashhad, Iran)

Abstract

Esophageal cancer is the eighth most common cancer in the world which consists of two main histological types: Squamous cell carcinoma (SCC) and adenocarcinoma (AC). It is characterized by rapid development and fatal prognosis in most cases. The global statistics show that Over 80% of esophageal cancers occur in developing countries. The highest incidence is in the age group 50-70 years. The disease is diagnosed more frequently in males than in females and the incidence rate varies widely from area to another. This study was designed to determine a new data of anatomical distribution and demographic data of this cancer in North East of Iran. Records of patients diagnosed with esophageal cancer from March 1997 to February 2013 in Qaem and Omid hospital of Mashhad were reviewed for demographic data and anatomical location of tumor. Results were analyzed by SPSS version 16. 4616 patients, 2518 (55%) were male and 2098 (45%) were female with a mean age of 65 years. About 85% of patients have squamous cell carcinoma (SCC) and 10% adenocarcinoma and 5% were unspecified. The distribution of esophageal cancer by anatomical location was 5% in upper third, 26% in the middle third and 40% in the lower third of esophagus. SCC occurred in 39% of cases with involvement of upper third of the esophagus whereas adenocarcinoma arose primarily from the lower third. There was not a meaningful different between sex variables and pathology statistically. Our results showed that the most common area of esophageal cancer is lower third of esophagus. SCC was the most frequent type of this cancer. Carefully designed epidemiologic studies are required to increase our understanding of the complexity of esophageal cancer.

Corresponding Author: seyyede tahereh mohaddes (Student Research Committee, faculty of medicine, Islamic Azad University, Mashhad branch, Mashhad, Iran)
Effect Of Oral Copper-Methionine On Matrix Metalloproteinase-2 In The Brain Of Broiler Chickens As An Animal Model For Malignant Ascites

Abstract

This study was aimed to investigate the effect of copper-methionine on matrix metalloproteinase-2 (MMP-2) changes in brain of ascitic broiler chickens under cold stress. Ascites was induced by growing in cold temperature in broiler chickens from 28 to 45 d of age. 480 one-day-old broiler chickens were randomly assigned to six treatments (two temperature (thermoneutral and cold stress) and there levels (0, 100, 200 mg/kg) of copper- methionine with four replication in each treatment. Data were analyzed using the General Linear Model procedure of SAS software. Treatment means were compared by the Least Significant Difference test and P-values less than 0.05 were statistically significant. Ascites (abdominal and pericardial fluid accumulation) were detected at 45 d of age in broiler chickens reared in cold temperature and fed a diet without copper-methionine supplementation. The brains were collected, and immediately stored at -80 °C for gelatin zymography and gelatin reverse zymography techniques. MMP-2 increased in brain of ascitic broilers. The results of zymography demonstrated that cold temperature increased MMP-2 and feeding with copper-methionine was useful in prevention of MMP-2 in cold condition but it was not statistically significant. Feeding different levels of copper- methionine in normal temperature did not change MMP-2 in brain of broiler chickens. Tissue inhibitor matrix metalloproteinase-2 (TIMP-2) was not affected by temperature and different levels of copper- methionine in brain of broiler chickens. Therefore, TIMP-2 showed the same results in different treatments. In conclusion, oral copper-methionine can reduce ascites possibility in cold-stressed broiler chickens.

Corresponding Author: Mina Bagheri Varzaneh (Department of Animal Sciences, Isfahan University of Technology, Isfahan, Iran; Unité de Recherche “Matrice Extracellulaire et Dynamique Cellulaire” (MEDyC), UMR CNRS/URCA NO 7369, Faculté de Médecine de Reims, 51095 Reims Cedex, France)
Phytoconstituents And Anticancer Potential Of Wild Achillea Millefolium L. Native To Khorasan Razavi, Iran

1. Ehsan Karimi (Department Of Biochemistry And Biophysics, Mashhad Branch, Islamic Azad University, Mashhad, Iran)
2. Ehsan Oskouei (Agricultural Biotechnology Research Institute Of Iran (ABRII)-East And North-East Branch, P.O.B. 91735/844, Mashhad, Iran)
3. Afshin Karimi (Quality Department Of Nutricia, Mashhad Milk Powder Industrial, Mashhad, Iran.)
4. Masoud Homayoni-Tabrizi (Department Of Biochemistry And Biophysics, Mashhad Branch, Islamic Azad University, Mashhad, Iran)

Abstract

Medicinal plants are known to have weak or strong therapeutic abilities and contribute in reducing risk of diseases of various biological activities likes inflammatory and cancer. This is attributed to the large amounts of phytoconstituents such as flavonoids, phenolics and saponins found in herbs. These bioactive compounds have received considerable attention due to their therapeutic potential for antimicrobial, anti-inflammatory, anticancer and antioxidant activities. Achillea millefolium L., commonly known as yarrow, belongs to Asteraceae family and it is widely used in Europe as a remedy to treat digestive problems, diabetes, hepato-biliary diseases and amenorrhea, and also consumed for its antitumour, antimicrobial, anti-inflammatory and antioxidant properties. The aim of our study was to evaluate the phytochemical composition and anticancer potential of wide Achillea millefolium L. native to Khorasan Razavi, Iran. Based on the results obtained in this study, the total phenolics of Achillea millefolium was $7.23 \pm 0.13$ mg gallic acid equivalent (GAE)/g dry weight (DW), the total flavonoids was $3.65 \pm 0.04$ mg rutin equivalent/g DW and the total saponin was $72.77 \pm 0.04$ mg diosgenin eq./g DW. Furthermore, the anticancer activity of the extracts was investigated in vitro against human liver cancer cell line (HPG2), human colon carcinoma cell line (HT-29) and normal human hepatocyte (Chang). The obtained result indicated the moderate to appreciable activities against all the tested cell lines. These findings suggest the potential use of Achillea millefolium as a natural medicine and indicated the possible application of this medicinal plant as anticancer agent.

Corresponding Author: Ehsan Karimi (Department of Biochemistry and Biophysics, Mashhad Branch, Islamic Azad University, Mashhad, Iran)
Inorganic PolyP, A Molecule With Opposite Functions

Abstract

Inorganic polyPhosphate (polyP) is a polymer of orthophosphate molecules which are linked by phosphoanhydride bonds. PolyP has been found in prokaryotes and eukaryotes with different chain length. Negatively charged polyP is capable to form complexes with proteins, RNA, Ca2+, Mg2+ and nucleic acids. In mammalian cells, polyP is localized in different organs like brain, liver, heart and regions inside the cell including nuclei, mitochondria and plasma membrane. PolyP metabolism is mediated through polyP kinase and polyphosphatase which catalyze synthesis and degradation of polyP respectively. But in eukaryotes, polyP synthetizing enzyme is not identified yet. Recent studies have been shown that polyP in mammalian cell contributes in proliferation and mineralization of stem cells amplifying nuclear cytokine-mediated proinflammatory signaling and modulating Wnt/β-catenin signaling in primary human umbilical vein endothelial cells. Interestingly, the data presented in a recent study implicated that polyP prevents apoptosis via inducing ERK pathway. Similarly, the results of a recent study showed that polyP has an anti-angiogenic and anti-metastatic effect on pulmonary metastasis by reducing metastatic lung colonies, blocking of bFGF-induced angiogenesis and inhibition of angiogenesis via suppressing the activation of ERK and p38 MAPK. Taken together, these results clearly suggest that polyP is a new key modulator of cell proliferation and apoptosis which could regulate clinical and therapeutic outcomes under (patho)physiological conditions. As a general summary, it can be concluded that polyP could be as an important molecule in diagnosis and treatment of disease including inflammation and cancer. Recent studies provide little information about the importance of polyP and further investigation is needed to understand the exact mechanisms of interactions between polyP and other pathways and role of this molecule in pathogenesis of disease. Further characterization of these mechanisms may provide important clues about the characteristic, application and functions of polyP.

Corresponding Author: Seyed Mahdi Hasanian Mehr (Department of Clinical Biochemistry, Faculty of Medicine, Mashhad University of Medical sciences, Mashhad, Iran.)
Bioactive Phytochemicals, Antioxidant And Anti-Cancer Potential Of Hulls From Pistachio (Pistacia Atlantica Subsp. Mutica) Grown In Khorasan Razavi, Iran

1. Ehsan Oskoueian (Agricultural Biotechnology Research Institute Of Iran (ABRII)-East And North-East Branch, Mashhad, Iran)
2. Ehsan Karimi (Department Of Biochemistry And Biophysics, Mashhad Branch, Islamic Azad University, Mashhad, Iran)
3. Reza Nora (Department Of Agriculture, Payam Noor University (PNU), P.O.B. 19395-3697, Tehran, Iran)
4. Afshin Karimi (Quality Department Of Nutricia, Mashhad Milk Powder Industrial, Mashhad, Iran)
5. Armin Oskoueian (Ferdowsi University Of Mashhad, International Branch, P.O. Box 91779/4888, Mashhad, Iran)

Abstract

Iran has been known as the largest exporter of pistachio in the world and pistachio is one of the principal agriculture plants in Iran. Pistacia atlantica var. Mutica is a member of Anacardiaceae family which distributed in the Western of Asia such as Syria, Iran and Turkey. Pistacia atlantica subsp. Mutica is widely grown in some parts of Khorasan Razavi province. The hulls of pistachio nuts have historically been used in traditional medicine to treat the sore throat, hemorrhages, diarrhea and gastrointestinal upsets. However, not much information is available regarding the possible pharmaceutical applications of hulls from Pistacia atlantica subsp. Mutica as sources of anti-cancer bioactive compound. Therefore, this research was conducted to evaluate the bioactive phytochemical compounds, antioxidant and anti-cancer potential of this inexpensive and readily available agricultural by-product. The results revealed that hulls contained total phenolic content of 146.5±0.12 mg GAE/ g DM and total flavonoid compounds of 82.6±0.28 mg rutin equivalent/ g DM. The hulls extract showed the appreciable antioxidant activity against DPPH free radicals with the IC50 value of 128 μg/ml. In addition, the extract potentially inhibited the proliferation of human colon carcinoma cell lines (HT-29) while relatively induced toxicity in human liver cells (Chang cell line) as well. Overall, these results indicated that the hulls extract from Pistacia atlantica subsp. Mutica could be considered as a promising and natural source of bioactive compounds to develop a value-added product for treatment or retarding the proliferation of colon cancer cells.

Corresponding Author: Ehsan Oskoueian (Agricultural Biotechnology Research Institute of Iran (ABRII)-East and North-East Branch, Mashhad, Iran)
Evaluation Of The Long Non-Coding RNA UCA1 Expression In Breast Tumors

1. Hossein Pour Faizi Mohamad Ali (Department Of Animal Biology, Natural Science Faculty, University Of Tabriz-Iran)
2. Zendedel Mona (Department Of Animal Biology, Natural Science Faculty, University Of Tabriz, Iran)
3. Pouladi Naser (Azarbaijan Shahid Madani University, Azarbaijan, Iran)

Abstract

Breast cancer is the most commonly occurring cancer in women, comprising almost one third of all malignancies in females. Long non-coding RNAs (lncRNAs) have been shown to play an important regulatory roles in cancer biology, and functional lncRNAs can be used for cancer diagnosis and prognosis. One lncRNA that has attracted significant attention is urothelial carcinoma-associated 1 (UCA1), which is significantly up-regulated in most cancers such as bladder cancer, and colorectal cancer, but the role of long non-coding RNA UCA1 in the breast cancer is largely unknown. The present study is aimed to evaluate the expression of lncRNA-UCA1 in breast tumors and matched adjacent normal tissues by using quantitative real-time PCR. A total of 30 breast tumor specimens with stages 1 up to 3 and adjacent nontumorous tissues were collected from female patients undergoing surgery for breast cancer. All specimens were frozen in liquid nitrogen immediately after collection and stored at 80 °C until use. Total RNA were isolated from tissues by using RNX-plus kit, and quantified by absorbance at 260 nm, then RNAs were reverse-transcribed into cDNAs. Real-time PCR was performed using the standard SYBR Green PCR kit protocol. B2m (beta-2-microglobulin) was used as the endogenous control gene. The evaluations done by SPSS software showed that the expression of UCA1 in breast tumor tissues was obviously higher than what observed in adjacent nontumourous tissues. (p<0.05). The current results indicated that expression of UCA1 lncRNA was enhanced in breast tumors.

Corresponding Author: Zendedel Mona (Department of Animal Biology, Natural Science Faculty, University of Tabriz, Iran)
Aptamer-Functionalized Dextran Coated Nano-Graphene Oxide For Targeted Drug Delivery To Breast Cancer Cells

Abstract

Cancer is the second leading cause of death after heart diseases worldwide. Breast cancer is the most prevalent cancer among women which ranks second for cancer death. Development of chemoresistance is the most pressing major dilemma in cancer therapy. Targeted drug delivery to cancer cells could be a promising approach to deliver a higher dose of therapeutics to the specific tumor cells while reducing the associated adverse effects. Aptamers are favorable targeting agents made of single-stranded, synthetic DNA or RNA molecules which specifically recognize and bind tightly to their targets due to their secondary or tertiary structure. Nucleolin is a trans membrane glycoprotein highly expressed in the plasma membrane of tumor cells. It is demonstrated that cell surface nucleolin acted together with protein complexes is associated with tumorgenesis and angiogenesis. To improve the therapeutic efficiency we fabricated a novel functionalized antiparticle composed of graphene oxide-dextran-AS1411 aptamer and used the complex as a delivery platform for curcumin (which is the main component of Curcuma longa and it is found to have wide range of medicinal properties such as anticancer and anti-inflammatory effects) against nucleolin positive breast cancer cells. First of all, graphene oxide was synthesized from graphite powder using the modified hummers method. Then, it was covalently conjugated to amine modified dextran and AS1411 aptamer was covalently attached to the surface of the fabricated platform. Thereafter, curcumin which is an aromatic ring-containing drug was loaded onto the surface of the nanoparticle. Physicochemical characteristics of the newly synthesized nanoparticle was evaluated. Then, release study, cellular viability study and cellular uptake was investigated. The GO-DEX-Apt-CUR could efficiently enter into 4T1 and MCF-7 nucleolin over-expressed cancer cells confirmed by fluorescence microscope and flowcytometry, also it showed significantly higher cytotoxicity compared to non-targeted agents. These types of targeted nanoscale drug delivery vehicles on the basis of DEX coated GO may find potential application in cancer chemotherapy.

Corresponding Author: Mona Alibolandi (Pharmaceutical Research Center, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran)
Global Map Of Genomic And Environment Effects Relationship In Colon Cancer

1. Hamed Abbaszadeh (Quchan University Of Advanced Technology, Quchan, Iran)
2. Mohammad Mahdi Khakshoor (Quchan University Of Advanced Technology, Quchan, Iran)
3. Kazem Pourbadakhshan (Quchan University Of Advanced Technology, Quchan, Iran)
4. Ladan Goshayeshi (Medical University Of Mashhad, Mashhad, Iran)
5. Hesam Dehghani (Ferdowsi University Of Mashhad, Mashhad, Iran)

Abstract

Gastrointestinal cancer is one of the most serious diseases and contributing factors in the death rate in the worlds. In Iran, environmental factors as well as genetic and nucleotide changes are the most important reasons of colon cancer. There is a hypothesis that more than one genetic or environmental factor affected on creating and development of colon cancer. In this article, tried to arrange 17 genetic factors that direct or indirect affected on colon cancer and create global map from dependent and independent gens for finding the relations. This global map can be used for preparation of comprehensive complete models of colon cancer based on the genomic changes. There are types of genes involving in Gastrointestinal system. Dependency of these genes to other ones causes Nucleotide changes and mutations in them, that this is an introduction to the incidence of diseases in the gastrointestinal tract. Using a map of the genes is achieved, it can be fitted before the process of changes of the nose and do this to some extent prevent changes. Of course, it is necessary to consider that the environmental factors along with of gene factors are effective in the incidence of cancer of the gastrointestinal tract.

Corresponding Author: Hamed Abbaszadeh (Quchan University of Advanced Technology, Quchan, Iran)
Matrix Metalloproteinase-2 And Tissue Inhibitor Matrix Metalloproteinase-2 Changes In The Liver Of Broiler Chickens Fed With Copper-Methionine: An Animal Model For Secondary Cancer In The Liver And Ascites Incidence

1. Mina Bagheri Varzaneh (Department Of Animal Sciences, Isfahan University Of Technology, Isfahan, Iran) 2Unité De Recherche “Matrice Extracellulaire Et Dynamique Cellulaire” (MEDyC), UMR CNRS/URCA NO 7369, Faculté De Médecine De Reims, 51095 Reims Cedex, France
2. Hamidreza Rahmani (Department Of Animal Sciences, Isfahan University Of Technology, Isfahan, Iran)
3. Rahman Jahanian (Department Of Animal Sciences, Isfahan University Of Technology, Isfahan, Iran)
4. Amir Hossein Mahdavi (Department Of Animal Sciences, Isfahan University Of Technology, Isfahan, Iran)
5. Corinne Perreau (Unité De Recherche “Matrice Extracellulaire Et Dynamique Cellulaire” (MEDyC), UMR CNRS/URCA NO 7369, Faculté De Médecine De Reims, 51095 Reims Cedex, France)
6. Gwenn Perrot (Unité De Recherche “Matrice Extracellulaire Et Dynamique Cellulaire” (MEDyC), UMR CNRS/URCA NO 7369, Faculté De Médecine De Reims, 51095 Reims Cedex, France)
7. Stéphane Brézillon (Unité De Recherche “Matrice Extracellulaire Et Dynamique Cellulaire” (MEDyC), UMR CNRS/URCA NO 7369, Faculté De Médecine De Reims, 51095 Reims Cedex, France)
8. François-Xavier Maquart (Unité De Recherche “Matrice Extracellulaire Et Dynamique Cellulaire” (MEDyC), UMR CNRS/URCA NO 7369, Faculté De Médecine De Reims, 51092 Reims Cedex, France 3CHU De Reims, Laboratoire Central De Biochimie , 51092 Reims Cedex, France)

Abstract

The aim of this study was to investigate the effects of different levels of oral copper-methionine on ascites incidence, matrix metalloproteinase-2 (MMP-2) and Tissue inhibitor matrix metalloproteinase-2 (TIMP-2) changes in liver of broiler chickens were reared under low temperature conditions. A total of 480 broiler chickens were studied within 6 treatments (two ambient temperature and there levels (0, 100, 200 mg/kg) of copper-methionine) and four replication. Following 4 weeks of rearing at normal ambient temperatures, half of broilers were exposed to low temperature (15-19°C) and half of them were kept in normal temperature (25-28°C) from 28 days to 45 days. Ascites happened at 45 d of age in broiler chickens reared in low temperature without feeding copper-methionine. It was detected according to abdominal and pericardial fluid accumulation. The liver was collected, and immediately stored at -80°C for biological analysis such as gelatin zymography and gelatin reverse zymography for MMP-2 and TIMP-2 detection respectively. MMP-2 increased in liver of ascitic broilers. The results of zymography demonstrated that feeding with copper-methionine significantly decreased pro-MMP-2 in cold condition. TIMP-2 didn’t change in liver of broilers reared in different treatments. Therefore, cold temperature and feeding the different levels of copper-methionine didn’t change TIMP-2. Feeding 100 and 200 mg/kg of copper-methionine showed the same results. In this way, feeding with 100 mg/kg of copper-methionine is preferable. These results suggest that feeding copper-methionine decreased MMP-2 and ascites possibility. Finally, copper-methionine can be useful for prevention of secondary cancer in the liver.

Corresponding Author: Mina Bagheri Varzaneh (Department Of Animal Sciences, Isfahan University Of Technology, Isfahan, Iran) 2Unité de Recherche “Matrice Extracellulaire et Dynamique Cellulaire” (MEDyC), UMR CNRS/URCA NO 7369, Faculté de Médecine de Reims, 51095 Reims cedex, France)
Brain Tumor Association With Mobile Phones

Abstract

Global demand for being connected immediately has resulted in a massive network in which individuals are connected to each other through mobile phones. Distributing signals through non-ionizing Radio frequency Electromagnetic Field (RF-EMFs), the cellular phone seems to have met man's urge for instant connection. Nevertheless, solid evidence based on its inducement to generate any brain tumors (glioma, acoustic Neuroma, and meningioma) created uncertainty regarding operating such devices. On 31st of May 2011, International Agency for Research on Cancer (IARC) categorized RF-EMFs associated with mobile phone radiations as a possible carcinogenic element (group 2B). However, debates and investigations are still undertaken. The aim of this review was to establish an additional study to clarify any possible linkage. Through PubMed search, 30 articles assessing risks of intracranial neoplasm due to microwave absorption by brain have been reviewed and a relative comparison was drawn. 60 percent of resources contributed to the hypothesis of causal association between brain tumors and the rate of mobile phone use with excessive risk for ipsilateral use (same side as the tumor) which is proved by 22 percent of this category. However, 17 percent of them were merely concerned with long-term use of cellular phones (10 years or more). Moreover, 11 percent of these reviews declared stronger susceptibility for children before age 20, due to a larger volume of water in their bodies. Nonetheless, 40 percent of analyses refuted any linkage between intracranial neoplasm and mobile phone emission; among which 25 percent of them still indicate plausible peril for long term use. In conclusion, abstinence from excessive and continual utilization of cellular phones is recommended due to the distinct possibility of a causal association between intracranial neoplasm and the rate of mobile phone use.

Corresponding Author: Ayda Radfar (Faculty of Medicine, Mashhad University of Medical Sciences (MUMS), Mashhad, Iran)
Anticancer Drug Screening Based On Label-Free Cytochrome C Assay By Fluorescent DNA Probe

1. Fatemeh Molaabasi (Department Of Chemistry, Tarbiat Modares University, Tehran, Iran)
2. Mojtaba Shamsipur (Department Of Chemistry, Razi University, Kermanshah, Iran)

Abstract

Anticancer drugs mainly kill tumor cells via inducing intrinsic apoptosis. This process primarily is initiated by release of Cytochrome c (Cyt c) from mitochondrial into the cytosol and thereupon apoptosome formation. Therefore, the release of Cyt c is perceived as a robust signal for detection of early stage apoptosis and evaluation of anti-cancer agents. Cyt c is typically recognized by Western blot and ELISA, which are semi-quantitative, time-consuming and tedious methods. Fluorescent metal nanoclusters (NCs) consisting of a few metal atoms with an ultra-small size ranging from sub-nanometer, have received highly attention in the past few years owing to their great promise as a novel, green fluorescent probe in a wide range of applications. Here, we have designed and fabricated a novel biosensor based on aptamer-stabilized nanoclusters for rapid and inexpensive evaluation of anticancer drugs. Oligonucleotide sequences were chemically synthesized and used for growth of fluorescent DNA/AgNCs. Quantitative analysis of release of Cyt c from mitochondria was performed by addition of drug treated cells to DNA/AgNCs. After for 20 min incubation, the fluorescence intensities were measured by Spectrofluorometer under excitation wavelength of 560 nm. The aptamer-stabilized Ag NCs could be used for qualitative and quantitative determination of label-free Cyt c with the linear range from 0 to 1 µM and a detection limit of 15 nM. In this study, we have developed an aptamer-based fluorescent probe using luminescent metal nanoclusters (NCs) to screen anti-cancer drugs. Aptamer as a short single-stranded DNA with showed high binding affinity and specificity to its target, due to its unique structures. The resulting data suggest that the designed sensing platform can be used for monitoring of Cyt c in the apoptotic cells after the exposure to an anti-cancer drug (e.g. doxorubicin) and also can provide precise information regarding the amounts and kinetics of release under various conditions.

Corresponding Author: Saman Hosseinkhani (Department of Biochemistry, Tarbiat Modares University, Tehran, Iran)
Anticancer Drug Screening Based On Label-Free Cytochrome C Assay By Fluorescent DNA Probe

1. Fatemeh Molaabasi (Department Of Chemistry, Tarbiat Modares University, Tehran, Iran)
2. Mojtaba Shamsipur (Department Of Chemistry, Razi University, Kermanshah, Iran)
3. Saman Hosseinkhani (Department Of Biochemistry, Tarbiat Modares University, Tehran, Iran)

Abstract

Anticancer drugs mainly kill tumor cells via inducing intrinsic apoptosis. This process primarily is initiated by release of Cytochrome c (Cyt c) from mitochondrial into the cytosol and thereupon apoptosisome formation. Therefore, the release of Cyt c is perceived as a robust signal for detection of early stage apoptosis and evaluation of anti-cancer agents. Cyt c is typically recognized by Western blot and ELISA, which are semi-quantitative, time-consuming and tedious methods. Fluorescent metal nanoclusters (NCs), have received highly attention in the past few years owing to their great promise for highly sensitive detections. Here, we have designed and fabricated a novel biosensor based on aptamer-stabilized nanoclusters for rapid and inexpensive evaluation of anticancer drugs. Oligonucleotide sequences were chemically synthesized and used for growth of fluorescent DNA/AgNCs Quantitative analysis of release of Cyt c from mitochondria was performed by addition of drug treated cells to DNA/AgNCs After for 20 min incubation, the fluorescence intensities were measured by Spectrofluorometer under excitation wavelength of 560 nm. The aptamer-stabilized Ag NCs could be used for qualitative and quantitative determination of label-free Cyt c with the linear range from 0 to 1 μM and a detection limit of 15 nM. In this study, we have developed an aptamer-based fluorescent probe screen anti-cancer drugs. The resulting data suggest that the designed sensing platform can be used for monitoring of Cyt c in the apoptotic cells after the exposure to an anti-cancer drug (e.g. doxorubicin).

Corresponding Author: Fatemeh Molaabasi (Department of Chemistry, Tarbiat Modares University, Tehran, Iran)
The Effects Of Educational Interventions On Changing Attitude And Behaviors Leading To Early Diagnosis Of Colorectal Cancer In People Referring To Health Centers In Lenjan City

1. Mehrdad Sadeghi (Lenjan Of Health Department, Isfahan University Of Medical Science)
2. Farzaneh Tahari (Lenjan Of Health Department, Isfahan University Of Medical Science)

Abstract

To achieve success in the colorectal cancer screening programs, promoting attitudes and participation of people about the importance of these programs is required. This study was conducted to evaluate the effect of educational on changing attitudes and behaviors leading to early diagnosis of colorectal cancer. This is semi-experimental study. In this study, 146 eligible people (up to 50 years) who referred to health centers are selected and are divided randomly-cluster into two groups (73 in case group and 73 in control group). Data gathering tool is a questionnaire consisting of 3 sections: demographic, Question related to attitude and health behavior questions associated with screening colorectal cancer. People are invited to perform free tests for Faecal Occult Blood Test (FOBT) to the designated place. Then the training program is conducted for the case group. While holding several group learning sessions and face to face training during 4 month and presented to each of the people an educational pamphlet about colorectal cancer and screening methods. finally attitude and participation to go to a designated laboratory for testing are examined in the two group. In the case group, the attitude of 2.7±3.9 before intervention comes after 10.3±1.8 after the intervention. This is despite the fact that there is no statistically significant difference in the control group before and after intervention. In the state of people's willingness to participate in the screening program, 56 patients (38.35%) were not very interested and their most common cause is absence of signs. Also there is a significant increase between the rates of referrals for FOBT of case group than the control group. Preparation for the implementation of developed training programs based on needs and culture is effective in promotion attitudes and Health behavior related to screening. By focusing on reducing barriers in future training programs, participation of people in screening can be improved. Keywords: colorectal cancer, early diagnosis, educational intervention

Corresponding Author: Farzaneh Tahari (Lenjan of health department, Isfahan University of Medical Science)
The Effects Of Educational Interventions On Changing Attitude And Behaviors Leading To Early Diagnosis Of Colorectal Cancer In People Referring To Health Centers In Lenjan City

1. Mehrdad Sadeghi (Lenjan Of Health Department)

Abstract

To achieve success in the colorectal cancer screening programs, promoting attitudes and participation of people about the importance of these programs is required. This study was conducted to evaluate the effect of educational on changing attitudes and behaviors leading to early diagnosis of colorectal cancer. This is semi-experimental study. In this study, 146 eligible people (up to 50 years) who referred to health centers are selected and are divided randomly-cluster into two groups (73 in case group and 73 in control group). Data gathering tool is a questionnaire consisting of 3 sections: demographic, Question related to attitude and health behavior questions associated with screening colorectal cancer. People are invited to perform free tests for Faecal Occult Blood Test (FOBT) to the designated place. Then the training program is conducted for the case group. While holding several group learning sessions and face to face training during 4 month and presented to each of the people an educational pamphlet about colorectal cancer and screening methods. finally attitude and participation to go to a designated laboratory for testing are examined in the two group. In the case group, the attitude of $2.7\pm 3.9$ before intervention comes after $10.3\pm 1.8$ after the intervention. This is despite the fact that there is no statistically significant difference in the control group before and after intervention. In the state of people's willingness to participate in the screening program, 56 patients (38.35%) were not very interested and their most common cause is absence of signs. Also there is a significant increase between the rates of referrals for FOBT of case group than the control group. Conclusion: Preparation for the implementation of developed training programs based on needs and culture is effective in promotion attitudes and Health behavior related to screening. By focusing on reducing barriers in future training programs, participation of people in screening can be improved. Keywords: colorectal cancer, early diagnosis, educational intervention

Corresponding Author: farzaneh tahari (lenjan of health department)
The CHEK2 1100delC Deletion Mutation Molecular Relevancy In Breast Cancer

1. Mahdi Hosseinzadeh (Biological Research Center, Imam Hossein Comprehensive University, Tehran, Iran)
2. Javid Taghinejad (Department Of Microbiology, Islamic Azad Universit, Malekan Branch, Iran)
3. Leila Abdollahi (Dr. Shahinfar Midwifery Faculty, Islamic Azad University, Mashhad, Iran)

Abstract

Breast cancer is one of the oldest known forms of malignancies affecting women that constitutes a major public health issue globally. There are various factors playing role in the incidence of Cancer including CHEK2 gene a putative tumor suppressor which has a prominent part in response to DNA damage through halting cell cycle progression. The CHEK2 mutation is recurrent in populations of different races or ethnicities and is a risk factor for breast cancer. 1100delC deletion mutation of CHEK2 gene is one of the mutations that is by some mean related to breast cancer. The main purpose of current review is to identify additional CHEK2 mutations potentially contributing to breast cancer susceptibility and particularly the 1100delC deletion mutation. In the present review, we evaluated the role of CHEK2 1100delC as a susceptibility mutation of breast cancer through comprehensive, computer-based searches of PubMed, EMBASE, Google scholar and Web of Science with keywords like breast cancer, gene mutation, Molecular bases, CHEK2 genes and 1100delC. 50 articles were chosen and studied. The significance of CHEK2 1100delC in predisposition to breast cancer was evaluated by assessing its frequency in articles of different countries which emphasizes that is an important breast cancer-predisposing gene in several population. Regarding many parameters in cancer, 1100delC appears to be the only recurrent CHEK2 mutation associated with a potentially significant contribution to breast cancer risk in the general population. Findings highlight the notion that there are research gaps and recommend further research in this area with screening more cases in all countries.

Corresponding Author: Mahdi Hosseinzadeh (Biological Research Center, Imam Hossein Comprehensive University, Tehran, Iran)
The Study Of Knowledge, Health Behaviour And The Obstacles Of Pap Smear In Married Women Living In Cities Of Noshahr And Chalus In 2005 And 2016

1. Maryam Ghamkhar (Department Of Midwifery, Faculty University Of Azad Chaloos)
2. Neda Ghazinezhad (Department of Midwifery, Teacher University Of Azad Chaloos)
3. Mina Nademi (Department of Midwifery, Student University Of Azad Chaloos)

Abstract

Cervical cancer is the second common cancer among women in worldwide after breast cancer. This is a cross-sectional study on 600 married women residing in Chalus and Noshahr, that was conducted at two points in 2005 (300 women) and 2016 (300 women). The data were collected using questionnaires and were compared using SPSS. In both years, the most of respondents aged 20-39 years, married for more than 15 years, and were housewives. The majority of subjects had at least one Pap smear test. Education level in the majority of them in 2005 and 2016 was the high school and college, respectively. According to respondents in both of years similarly, the knowledge and trust of the Pap smear, suitability of the test, and the risk of cervical cancer were moderate. The effective factors to do Pap test were: proselytism, being free the test, death of family, knowledge and cognition of the test, the views of husband and others and guidance of health personals. The majority of the subjects had little information about symptoms of cervical cancer and the most of them have not been trained about Pap test, however, they considered enough to access to expert personals for doing Pap test. According to the majority of respondents pap tests could be an important factor in the identification and prevention of cervical cancer. In 2016, the hope for treatment and diagnosis of cervical cancer symptoms increased, compared to 2005. Given the importance of Pap test for cervical cancer prevention and increased hope for treatment of this cancer, the Pap test need to be taken in consideration in implementing women's health initiatives.

Corresponding Author: Neda Ghazinezhad (Department of Midwifery, Teacher university of Azad chaloos)
The Effects Of Total Extract Of Fennel On Liver Cancer Cells In Vitro

1. Zeinab Mousaee (Islamic Azad University Iran, Tehran Medical Branch)
2. Khadije Nejad Shahrokhhabady (Mashhad Islamic Azad University Iran)
3. Malihe Entezary (Islamic Azad University Iran, Tehran Medical Branch)

Abstract

Human liver cancer is the fifth most common cancer world wide. Hepatocellular carcinoma is the most malignant tumor with poor prognosis. This cancer is resistant to many common treatments. As a result, a liver transplantation is the only treatment accepted that this treatment limited to the early presence detection. We assessed Hydro-alcoholic extract of fennel that included Fenchon, Camphene, Limonen, Estragole and Phellandrene. Our studies show that this extract due to its existing ethanol is apoptotic activity. HepG2 which secrete a variety of important plasma proteins such as anti-trypsin and transferin and ect which is a human liver cell line used due to the absence of viral infection. HepG2 cells were cultured in 96 plate in concentrations of 10, 50, 200, 400, 800, 1000 µg/ml. The test MTT showed that IC50 total extract of fennel on the cells of liver cancer, after 48 and 72 hours respectively, 100 and 200 µg/ml. Total extract of Fennel is a plant material with toxic effects on the cells of the liver cancer. Future studies need to investigate the mechanisms of cytotoxicity and anti-cancer effect of this extract is in vitro and in vivo.

Corresponding Author: Malihe Entezary (Islamic Azad University Iran, Tehran Medical Branch)
The Effect Of Curcumin In Breast Cancer Prevention And Treatment

1. Vajihe Rouki (Neurogenic Inflammation Research Centre, Mashhad University Of Medical Sciences, Mashhad, Iran; Department Of Physiology, School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)

2. Mohammad Hossein Boskabady (Neurogenic Inflammation Research Centre, Mashhad University Of Medical Sciences, Mashhad, Iran; Department Of Physiology, School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)

3. Zahra Gholamnezhad (Neurogenic Inflammation Research Centre, Mashhad University Of Medical Sciences, Mashhad, Iran; Department Of Physiology, School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Breast cancer is among the most common malignant tumors all around the world. For years the medical community is trying to find a way to treat carcinoma. Investigating new anticancer treatments with greater efficacy and fewer side effects is still a significant challenge of the medical society. Curcumin, a hydrophobic polyphenol derived from rhizome of Curcuma longa had been appreciated for many therapeutic effects in traditional medicine, as well as recent investigations. Several studies have shown various activities for it; such as anti-hyperlipidemic and metabolic syndrome, anti-inflammatory, antioxidant, immunomodulatory and neuroprotective properties. In a few clinical trials the anti-cancer effect of curcumin has been seen, especially as a chemoprevention agent in colon and pancreatic cancer, cervical neoplasia and breast metaplasia. The anticancer effects of curcumin may be mediated through the different biological pathway, including anti-proliferation, enhancing apoptosis, cell cycle arrest and antioxidant and anti-angiogenic properties. It had been indicated that curcumin may modulate several molecular target and receptor affinity, including transcription factors (signal transducer and activator of transcription 3, and nuclear factor-κB), receptors (estrogen receptor, interleukin 8, and human epidermal growth factor receptor), kinases (extracellular-signal-regulated kinases, and Janus kinase), cytokines (tumor necrosis factor, interleukin, chemokine (C-X-C motif) ligand -1 and 2), enzymes (Matrix metalloproteinases, and inducible nitric oxide synthase), growth factors (Epidermal growth factor), oncogenes (microRNA, DNA, histone, and mitochondria). In addition, curcumin may act as a chemosensitizer in multi-drug-resistant breast cancer cells and curcumin supplementation with conventional chemotherapeutic agents could increase their efficacy as well as reducing drug toxicity. Conclusion: Many basic in vivo and in vitro studies introduced the chemopreventive and anti-breast cancer effects of curcumin via modulation various biological pathways (cell signaling and gene expression). However, there are few standard clinical trials for evaluating those basic beneficial effects. In addition, clinical trials showed that the systemic bioavailability of oral administration of this safe medicinal agent is relatively low which reduced its potential therapeutic effects. Therefore, the more standard clinical trial with curcuma longa (with determined curcumin content) or curcumin supplementation is needed to suggest the plant as an inexpensive potential biological adjuvant therapy in breast cancer.

Corresponding Author: Zahra Gholamnezhad (Neurogenic Inflammation Research Centre, Mashhad University of Medical Sciences, Mashhad, Iran; Department of Physiology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran)
Expression And Breast Cancer Cell Inhibiting Effect Of Recombinant Camel Lactoferrin Peptides

1. Marjan Azghandi (Department Of Animal Science, Ferdowsi University Of Mashhad, Mashhad, Iran.)
2. Mohammad Hadi Sekhavati (Department Of Animal Science, Ferdowsi University Of Mashhad, Mashhad, Iran.)
3. Mojtaba Tahmoorespur (Department Of Animal Science, Ferdowsi University Of Mashhad, Mashhad, Iran.)
4. Mohammad Ramezani (Pharmaceutical Research Center, School Of Pharmacy, Mashhad University Of Medical Sciences, Mashhad, Iran)
5. Ali Javadmanesh (Department Of Animal Science, Ferdowsi University Of Mashhad, Mashhad, Iran.)
6. Sara Amel Farzad (Pharmaceutical Research Center, School Of Pharmacy, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Lactoferrin is a glycoprotein with broad range of antimicrobial activates. Recent studies indicate that the anti-cancer effect of LF is attributed mostly to its ability to inhibit tumor cell proliferation, enhance apoptosis or necrosis in cancer cells. It is well documented that LF contains several peptides with multiple biological functions. In this study, we expressed a chimeric Camel Lactoferrin peptide (cLF36) in Human Embryonic Kidney cells and tested its cytotoxic activity on a human breast cancer cell line Mcf7. The cLF36 sequence was codon optimized and synthesized. Vector harboring cLF36 sequence was digested, and ligated into the pcDNA3.1+ vector, then transformed into TOP10 bacterium. The recombinant vector transfected into the HEK293 cells, using calcium phosphate method and were selected by G418 antibiotic. The culture medium upon cells was collected for SDS-PAGE analysis. MTT assay was used to examine the cytotoxicity of cLF36 against of Mcf7 cells. Mcf7 cells were treated with medium containing the peptide and the culture medium without the peptide and with DOXORUBICIN served as the negative and positive control respectively. The results of sequencing showed that cLF36 fragment was successfully cloned. Expression of the cLF36 in HEK293 cells was evaluated by SDS-PAGE, suggested that the protein was properly translated and secreted into medium culture. The result of MTT assay, showed significant increase the rate of cell death when the cells treated with the medium containing cLF36 peptide. Treatment with cLF36 decreased viability level of Mcf7 cells to 32%. The main mechanism of anticancer activity of lactoferrin peptides is still unknown, but it has been shown that lactoferrin can target the negatively charged of cancer cells. Our results revealed that cLF36 is cytotoxic for Mcf7 cells, and it has considerable potential for therapeutic use in the treatment of breast cancer.

Corresponding Author: Mohammad Ramezani (Pharmaceutical Research Center, School Of Pharmacy, Mashhad University Of Medical Sciences, Mashhad, Iran)
Human Embryonic Stem Cells- Derived Extracellular Vesicles Suppress Breast Cancer Cell Proliferation, Clonogeneity And Sphere Formation

1. Maryam Ahmadakhoundi (Department Of Developmental Biology, University Of Science And Culture, ACECR, Tehran, Iran. Department Of Stem Cells And Developmental Biology, Royan Institute For Stem Cell Biology And Technology, Tehran, Iran)

2. Soura Mardpour (Department Of Stem Cells And Developmental Biology, Cell Science Research Center, Royan Institute For Stem Cell Biology And Technology, Tehran, Iran)

3. Marzieh Ebrahimi (Department Of Stem Cells And Developmental Biology, Royan Institute For Stem Cell Biology And Technology, Tehran, Iran)

4. Seyedeh-Nafiseh Hassani (Department Of Stem Cells And Developmental Biology, Cell Science Research Center, Royan Institute For Stem Cell Biology And Technology, ACECR)

Abstract

Aggressive cancer cells have similar characteristics to embryonic stem cells (ESCs). Some of these common characteristics are self-renewal, differentiation to multipotent lineage cells, gene expression signature and plasticity, and consequently engaging in a dynamic reciprocity with their microenvironment. However, ESCs have microenvironment which regulates balance of self-renewal and differentiation. In contrast, cancer cells have uncontrolled proliferation potential. Based on the aberrant and deregulated expression of embryonic genes in tumor cells, there is an open question whether these cells can respond to regulatory cues controlling self-renewal pathways which might be sent from microenvironment of ESCs; And as a result whether tumorigenic phenotype of cancer cells can be supressed. Pervious works have reported that the exposure of aggressive cancer cell line to human ESCs (hESCs)-conditioned matrix or medium, induces reprogramming of aggressive cancer cells to normal differentiated phenotype that has less aggressive state and less proliferation potential. This suggests a potential ability of pluripotent stem cell-conditioned medium as a cell-free therapeutic approach. The purification of conditioned medium has since revealed that ESCs release small molecules, including cytokines, chemokines, growth factors and also a large quantity of extracellular vesicles which can exert paracrine effect on cells. The current study has focused on effects of hESCs-derived extracellular vesicles as bioproduct of hESCs-conditioned medium on proliferation, differentiation and aggressive properties of cancer cells. At first, we extracted extracellular vesicles from hESCs and characterized them. In the next step, we exposed the breast cancer cell lines to hESCs-derived exosomes. It is observed that the treatment of exosome on aggressive breast cancer cell line reduced the proliferation, colonogeneity, and sphere formation of breast cancer cells. This findings suggest that microenvironment of human embryonic stem cells has the potential to modulate stemness property of aggressive cancer cells and limit the proliferation of this cells.

Corresponding Author: Marzieh Ebrahimi (Department of Stem Cells and Developmental Biology, Royan Institute for Stem Cell Biology and Technology, Tehran, Iran)
Efficient Non-Viral Gene Delivery System Based On Single-Walled Carbon Nanotubes- Polyethylenimine To Cancer Cells

1. Mahboubeh Ebrahimian (Faculty Of Veterinary Medicine, Ferdowsi University Of Mashhad, Mashhad, Iran)
2. Alireza Haghparast (Division Of Biotechnology & Immunology Section, Faculty Of Veterinary Medicine, Ferdowsi University Of Mashhad, Mashhad, Iran)
3. Mohammad Ramezani (Pharmaceutical Research Center, School Of Pharmacy, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Gene therapy is a part of modern molecular medicine that uses genes to treat or prevent diseases. We propose that combining of genes with polymers will solve the problem of low transfection efficiency, bringing a revolution in molecular medicine and in applications of gene therapy based on nanomaterials in humans. Brand-new carriers were synthesized with functionalized single walled carbon nanotubes (fSWCNTs) with Polyethylenimine 10kDa (PEI 10). Characterization of vectors was carried out. Fourier transform infrared spectroscopy (FTIR) was used to analyze the PEI conjugation to SWCNT. Particle size and zeta potential of the polyplexes were measured. Buffering capacity and condensation assay of the vectors were evaluated. Transfection efficiency and cytotoxicity of nanoparticles in murine neuoblastoma cell lines (Neuro2a cells) were also measured. Presence of the special peak in FTIR confirmed the occurrence of the reaction. The average size of nanoparticles was in the range of 90-127 nm with positive zeta potential charges. SWCNTs functionalized with PEI showed lower cytotoxicity and significant increase transfection efficiency in Neuro2a when compared to unmodified PEI. These modifications of SWCNTs with PEI10 kDa can significantly improve transfection efficiency and reduced cytotoxicity. Due to the high gene expression in cancer cells with low cytotoxicity, this modified carrier could be used for cancer gene therapy in in vivo study.

Corresponding Author: Mohammad Ramezani (Pharmaceutical Research Center, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran)
The Role Of Curcumin In Cancer Treatment: The Call Of Nature

1. Mohammad Ali Emrani (Faculty Of Medicine, Mashhad University Of Medical Sciences (MUMS), Mashhad, Iran)

Abstract

Cancer is one of the leading causes of morbidity and mortality worldwide, with nearly 14 million new cases and 8.2 million cancer related deaths in 2012. Available anti-cancer drugs have severe side effects and are also expensive. So, the more researches for identifying new pharmacological agents, without this disadvantages, are needed. Curcumin, a polyphenolic compound which derived from Turmeric, is one of such agents. Turmeric is a rhizome from the herb Curcuma Longa. Its powder has 77 % Curcumin that has been shown to be pharmacologically safe compound with a very low or no toxicity. We searched the PubMed and Google Scholar databases using the search terms: Curcumin, Cancer and Clinical Trial. 15 studies were identified and reviewed. The articles were published from 2002 up to 2016. Among studies, There was an emphasis on apoptotic, anti-proliferative and anti-angiogenic properties of Curcumin. It can suppress cell growth and tumor formation by inhibiting several cell signaling pathways such as transcription factors (NF-kB and AP-1), enzymes (COX-2, MMPs), cell cycle arrest (cyclin D1), proliferation (EGFR and Akt), survival pathways (bcatenin and adhesion molecules), and TNF. Curcumin up-regulates caspase family proteins and down-regulates anti-apoptotic genes (Bcl-2 and Bcl-XL). Pre-clinical studies in a in a variety of cancer cell lines including breast, cervical, colon, lung, gastric, hepatic, leukemia, melanoma, lymphoma, oral epithelial, ovarian, pancreatic, and prostate have demonstrated that Curcumin has anti-cancer activity in vitro and in pre-clinical animal models. It's important that cancerous cells arrested in mitosis due to Curcumin treatment, acquire double-strand DNA damage. Curcumin also induce apoptosis in cells selectively. Thus using Curcumin as an anti-cancer drug is safe and without side effects. A study showed Curcumin induces cell apoptosis in Non-Small cell lung cancer by increasing the level of intracellular free calcium. NSCLC is responsible for nearly 85% of the total lung cancer cases that isn't sensitive to the majority of conventional cytotoxic treatments, such as chemotherapy and radiotherapy. In another studies, showed that Curcumin can suppress the proliferation of both the androgen-dependent prostate cancer cell line, LNCaP, and the androgen-independent DU145 line. And also in a clinical trial on intravaginal application of curcumin based capsule or vaginal cream at bed time for 4 weeks has shown remarkable (∼80%) clearance of the virus. HPV is a small DNA tumor virus which has been shown to be prevalent in about 90% of cervical cancers and 70% of vaginal cancers. Curcumin, A derivative of turmeric, has great anti-cancer effects, demonstrated by various researches. Although Curcumin-based drugs in near future will play a significant role in healing cancer patients, using turmeric powder as a dietary supplement is an easy way toward cancer treatment and chemoprevention.

Corresponding Author: Mohammad Ali Emrani (Faculty of Medicine, Mashhad University of Medical Sciences (MUMS), Mashhad, Iran)
Brain-derived neurotrophic factor (BDNF) is a member of the neurotrophin family of growth factors, and has a physiologically involvement in the differentiation, proliferation, and survival of neural cells in both central and peripheral nervous systems. It has recently been shown that BDNF plays a critical role in cancer biology. The aim of this systematic review was to determine the extent of BDNF association with different cancers. ISI Web of Knowledge, Science direct, PubMed, Scopus and Google Scholar were searched for related studies using the related keywords as: BDNF, TrkB, cancer, tumor, carcinoma, neoplasms. Relevant and available articles were selected for inclusion in this study. Studies have shown that BDNF and TrkB receptors might be involved in cancer growth, metastasis, resistance to treatment in variety of malignant tissues, including pancreatic ductal carcinoma, prostate cancer, ovarian cancers, lung cancer, hepatocellular carcinoma, non-small cell lung cancer (NSCLC), colorectal cancer (CRC), bladder cancer, large cell neuroendocrine carcinoma (LCNEC), leukemia, gastric carcinoma, Wilm's tumor, bone cancer, brain tumors, neuroblastoma, head and neck squamous cell carcinoma (HNSCC), squamous cell carcinoma (SCC) of the uterine cervix, endometrial cancer, retinoblastoma, chronic myelogenous leukemia, glioma, medulloblastoma, chondrosarcoma, and breast cancer. BDNF may exert influence on different cancers by different mechanisms. Identifying the function of BDNF in various cancers can be useful to detect the disease, response to treatment as well as the identification of new therapeutic drugs. However, in addition to replication of findings in different populations, functional and clinical studies are still required for a better understanding of the involved specific pathways.

Corresponding Author: Amir Tajbakhsh (Mashhad University of Medical Sciences)
Association Of IL-1B+3954 Polymorphism In Chronic Gastritis As Risk Factors Of Gastric Cancer Development

1. Neda Motamedirad (Department Of Medical Genetics, Medical Faculty, Hormozgan University Of Medical Sciences, Bandar-Abbas, Iran)
2. Meysam Rezaeishahmirzadi (Department Of Medical Genetics, Medical Faculty, Hormozgan University Of Medical Sciences, Bandar-Abbas, Iran)
3. Mohammad Shekari (Department Of Medical Genetics, Medical Faculty, Hormozgan University Of Medical Sciences, Bandar-Abbas, Iran)

Abstract

Epidemiological investigations indicated Helicobacter pylori are the major cause of chronic gastritis and intestinal type of gastric cancer. IL-1B gene has been proposed as key factors in determining risk of gastritis and malignant transformation. Purpose of the study: We aimed to determine if IL-1B+3954 polymorphism are associated with the risk of chronic gastritis in Iranian population. 198 individuals who showed the symptoms of chronic gastritis with coexisting infection of H. pylori participated in the case group. Individuals without chronic gastritis were selected as the control group and we also confirmed the presence of anti-H. Pylori serum IgG in 321 control subjects. IL-1B+3954C/T polymorphism was analyzed through PCR-RFLP. Results: IL-1B+3954 TT were associated with a high risk of gastritis [Odds Ratio (OR) = 2.75, 95% Confidence Interval (CI) = (1.50-5.03) (P-value: <0.001). Our results indicate that +3954C>T polymorphism of IL-1B gene increase susceptibility to inflammatory response of gastric mucosa H.pylori-infected patients and plays a significant role in the development of chronic gastritis and the initiation of carcinogenesis.

Corresponding Author: Mohammad Shekari (Department of Medical Genetics, Medical Faculty, Hormozgan University of Medical Sciences, Bandar-Abbas, Iran)
The Use Of Dendritic Cells In Cancer Immunotherapy

1. Kimia Alizadeh (Veterinary Medicine Student, Ferdowsi University Of Mashhad)
2. Kasra Alizadeh (B.A. Student Of Human Biology, The University Of Kansas)

Abstract

Immunity is controlled by a network of professional antigen presenting cells (APCs), the most important of which are known as dendritic cells (DC). Dendritic cells are professional APCs that are designed to activate T cells toward various antigens, such as tumor-associated antigens, due to their potent co-stimulatory activity. They play a crucial role of constantly sampling the microenvironment for ‘danger signals’, which include inflammatory signals and pathogens. The availability of large numbers of DC, generated either from hematopoietic progenitor cells or monocytes, holds great promise in the development of cancer immunotherapy as well as the treatment of autoimmune diseases and suppressing several viruses. Accordingly, appropriately pulsed or transfected DC may be used for vaccination in the field of infectious diseases or tumor immunotherapy to induce antigen-specific T cell responses. Unlike infectious pathogens, tumors do not induce an effective inflammatory response suitable for optimal activation of DCs, and as a result the immune response is weak and ineffective. The primary purpose of vaccinating individuals with cancer is to overcome this flaw by channeling tumor antigens into DCs and providing the conditions for their optimal maturation into potent immunostimulatory APCs. This article will focus specifically on the use of DCs as vaccines for cancer immunotherapy. We will examine DC biology, preclinical and clinical studies and finally efforts to improve current vaccine formulations.

Corresponding Author: Kimia Alizadeh (Veterinary Medicine Student, Ferdowsi University of Mashhad)
Abstract

FAS ligand (FASL) is one of the crucial ligands in programmed cell death. It acts in association with FAS receptor to trigger extrinsic apoptotic pathway. Inactivating of this pathway results in apoptosis failure and may cause tumor formation. Functional polymorphisms in FASL gene is associated with breast cancer risk and Breast cancer is one of the major causes of cancer-related death among women worldwide. The aim of this study was to investigate association of FASL INV2nt-124 A/G (rs5030772) polymorphism and breast cancer risk. A case-control study was done on 80 breast cancer patients and 80 normal women from Iranian-Azeri population. Genomic DNA isolated from blood of case and control individuals by salting out method. Genotyping was performed by tetra-ARMS PCR (amplification refractory mutation system polymerase chain reaction) method. The data were analyzed by Javastat Online Statistics Software, with a significance level of 0.05. In present study, AA dominant genotype frequency was higher in case group than the control group (56.25 and 17.5 percent respectively) and statistical significant difference was observed (OR=6.061, 95%CI=3.023-12.268, P=0.0001). AG genotype frequency in control and case groups was 81.25 and 41.25 percent respectively, which was significant in control group (OR=0.162, 95%CI=0.081-0.322, P=0.0001). GG recessive genotype frequency in control and case groups was 1.25 and 2.5 percent respectively, which significant difference in genotype distribution between two groups was not observed (OR=2.026, 95%CI=0.189-34.282, P=0.574). G allele frequency in control and case group was 41.875 and 23.125 percent respectively (OR=2.395, 95%CI=1.245-4.628, P=0.005). A allele frequency in control and case subjects was 58.125 and 76.875 percent respectively (OR=0.418 95%CI=0.216-0.803). The FASL -124 (rs5030772) AA genotype and A allele seem to be associated with a good prognosis in patients with breast cancer.

Corresponding Author: Mohammad Ali Hosseinpoure feizi (Natural Department of Tabriz University)
Removal Of Cadmium From Aqueous Solutions Using B- Cyclodextrin Graphene Oxide Adsorbent

1. Elham Einafshar (School Of Chemistry, Damghan University, Damghan, Iran; Pharmaceutical Research Center, Pharmacy School, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Azadeh Hashem Nia (Pharmaceutical Research Center, Pharmacy School, Mashhad University Of Medical Sciences, Mashhad, Iran)
3. Mohammad Ramezani (Pharmaceutical Research Center, Pharmacy School, Mashhad University Of Medical Sciences, Mashhad, Iran)
4. Ali Haghghi Asl (Department Of Chemical Engineering, Semnan University, Semnan, Iran)

Abstract

Nowadays water pollution with heavy metal is one of the main concerns in the pollution management. In the modern world, with the intensive growing industrialization, toxic heavy metals are used extensively and it seems very unlikely that can be avoided. These materials have greatly affected people's health. One of the most toxic heavy metals is Cadmium which even at very low dosages may cause oxidative DNA damage leading to mutations and cancer initiation. Adsorption is the most common method for trapping heavy metal cautions since it is easily available and benefits from low energy consumption. One of the novel compounds which is highly explored as adsorbent platform is graphene oxide (GO). The surface area of GO contains many polar groups such as hydroxyl, epoxy, carbonyl and carboxyl, making GO a good chemical reactant and superb platform sorbent for organic dyes or heavy metal ions. Besides, on the basis of the previous study, we assumed that grafting β-cyclodextrin (β-CD) onto GO may produce a conjugate with excellent absorption capacity. In this research, first we functionalized graphene oxide with β-cyclodextrin and confirmed the successful synthesis of β-CD-GO by series of analysis such as Fourier transform infrared spectroscopy (FTIR), TEM and thermo gravimetric analysis (TGA), then the modified graphene oxide was used to investigate adsorption of Cd²⁺ ion in aqueous solutions. The effects of various experimental parameters such as initial pH, initial metal ion concentration, adsorbent dosage and contact time on the sorption process were also study. The absorption data showed the optimum pH for β-CD-GO was considered at PH=11. Kinetics of adsorption, isotherm studies and thermodynamics analysis were studied. The adsorption experimental data is well fitted with the pseudo-second-order model and Freundlich isotherm models. The importance of these results is due to developing an efficient material for the removal of metals and pollutants from water. The results of this work confirmed that β-CD-GO is a powerful and promising candidate for adsorption of heavy metal from wastewater.

Corresponding Author: Mohammad Ramezani (Pharmaceutical Research Center, Pharmacy school, Mashhad University of Medical Sciences, Mashhad, Iran)
The Impact Of Education On Children With Cancer

1. Mohammad Reza Mostafaei (Instructor, School Of Nursing And Midwifery, University Of Medical Sciences, Qazvin, Iran.)

Abstract

Children make up the bulk of the population. One of the most important cause of cancer deaths in the world. They have an important role in improving the quality of life. This study aimed to determine the effect of education on children with cancer Qods Hospital. A quasi-experimental study that was performed as a team before and after the intervention, the number three match training session was held for children with cancer in Qods hospital. Sampling and includes 46 patients were treated. The questionnaire consisted of 50 questions about demographic information and social awareness and mental performance. Questions before and one month after the training was completed by interview. Results using descriptive statistics (t-test and repeated comparisons) and software SPSS / 16 was analyzed. Majority (55/2%) were female. Degree 79/3% of them were high school diploma Minister, as well as the average age of caregivers in the range of 35/28±5/23 years. The disease duration in months 10/75 ± 14/60 with the standard deviation. The results showed that the training does not affect interventions in families of children with malignancies (p=0/80). The researchers argue that their training before the full support of the government and non-governmental organizations need. Distribution of subjects in terms of the overall impact of family interventions for children with cancer (mean 69/74 before and 70/80 after, p=0/80) showed that training whatsoever The frequency distribution of the results of research in terms of the effect of education on emotional factors in families of children with cancer using descriptive statistics (mean 73/29) before and 78/34 after the training, p =0/22) showed that, Effects of education on emotional factors in families of children with cancer do not have, as well as the results of a study on the impact of education on communication factors Families of children with cancer (mean 67/60 68/80 before and after, 68 /80 p =0/68) was ineffective. The results showed that education on families of children with cancer was not statistically positive impact that this may be due to Multiple problems, including the economic problem involved in this study we investigated the family's economic situation. According to the conclusion families to enhance the quality and comfort of living and overcome difficulties, in addition to psychosocial support to economic support from non-governmental organizations need. The result of this study is that, unlike the past, the effects of education on compliance families had children with malignancies And this can be a wake-up call for all education authorities chronic patients That the failure to provide the necessary conditions to get the desired result is not possible, It should be noted that this study was limited in scope and was performed on a small number of families.

Corresponding Author: Mohammad Reza Mostafaei (instructor, School of Nursing and Midwifery, University of Medical Sciences, Qazvin, Iran.)
5p12 And 5q11 Variants And The Risk Of Breast Cancer In Khorasan Population

1. Abolfazl Nosrati Tirkani (Department Of Medical Biochemistry, School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Babak Rabbani (Department Of Biochemistry, Faculty Of Basic Science, Islamic Azad University Damghan Branch, Damghan, Iran)
3. Amir Tajbakhsh (Molecular Medicine Group, Department Of Modern Sciences And Technologies, Mashhad University Of Medical Sciences, Mashhad, Iran)
4. Mahdi Rivandi (Molecular Medicine Group, Department Of Modern Sciences And Technologies, Mashhad University Of Medical Sciences, Mashhad, Iran)
5. Fahimeh Afzal Javan (Molecular Medicine Group, Department Of Modern Sciences And Technologies, Mashhad University Of Medical Sciences, Mashhad, Iran)
6. Alireza Pasdar (Molecular Medicine Group, Department Of Modern Sciences And Technologies, Mashhad University Of Medical Sciences, Mashhad, Iran; Department Of Modern Science And Technologies; School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran; Medical Genetic Research Centre, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Breast cancer affecting 1.4 million people in 2012, is known as the most common cancer among women worldwide. Despite a decreased breast cancer rate in developed societies, there is still a high mortality rate in many developing countries. Different risk factors, including modifiable and non-modifiable, are involved in developing breast cancer in which genetic backgrounds plays a crucial role in increasing the risk of the disease. These genetic variations can be used as a marker for early diagnosis and prognosis. Several studies have shown the association between different SNP (Single Nucleotide Polymorphism) and breast cancer risk in different populations. GWAS studies have shown the association between rs889312 and rs4415084 and breast cancer risk in the Caucasians. As there is no data on the association of these markers with breast cancer in our population, the present study was conducted to investigate the relationship between rs889312 and rs4415084 and breast cancer risk in Khorasan population. This case-control study was performed on 160 female breast cancer patients and 180 women with no evidence of breast cancer in the control group. Genomic DNA was extracted and ARMS_PCR method was conducted for genotyping. The data were analyzed using SPSS statistical software. P<5% was considered to be statistically significant. The results indicated that there was no significant difference in genotype frequencies between patients and control group for rs889312 (P=0.77). No significant difference was also found in allele frequencies between patients and controls. However, regarding the rs4415084, there was a significant difference in genotype frequencies between patient and control groups (P<0.001). Furthermore, a significant difference was observed in allele frequencies between two groups (P<0.001). According to the results, rs4415084 may be associated with the risk of breast cancer in our population.

Corresponding Author: Alireza Pasdar () Molecular Medicine Group, Department of Modern Sciences and Technologies, Mashhad University of Medical Sciences, Mashhad, Iran; Department of Modern Science and Technologies; School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran; Medical Genetic Research Centre, Mashhad University of Medical Sciences, Mashhad, Iran)
Breast cancer is the second cancer-related death, the most common carcinoma among women worldwide, developing about 1.6 million people in 2015 and 230,000 new cases will be added each year. According to histological studies, breast cancer is divided into non-invasive and invasive carcinoma, both of them subdivided in ductal and lobular. Diverse risk factors are involved in breast cancer progression, among them genetic background is known as an unchangeable risk factor and used as a marker for early diagnosis and/or prognosis. Several studies have shown the deregulation of microRNAs and genomic changes in human breast cancer. Also, it has been proven that a number of microRNAs express differently in breast tumor. MicroRNAs (miRNAs) are a class of single-stranded non-coding RNA molecules containing 20-22 nucleotides which have a key role in post-transcriptional gene expression regulation. The miRNAs which are found in organized nucleus containing DNA, generally transcribed by RNA polymerase II and III that characterized by the hairpin structure. The function of miRNAs in human is complicated and largely unknown. The miRNAs are involved in biological activities such as cell cycle regulation and bacterial division, cell development and differentiation and inactivation of human X-chromosome. Deregulation of miRNAs and related enzymes severally described in onset, progression, and diagnosis of diseases and cancers. In different cancers, the miRNAs play the main role in tumor secretion and initiation, tumor cell division and metastasis. In breast cancer, the platform of miRNAs is different with the healthy group and between breast cancer sub-types with clinical implications. A number of miRNAs expression are associated with tumor sub-type and coordinated with stage and severance of the carcinoma. In this regard, this paper will focus on the role of microRNAs in breast cancer prognosis and diagnosis and will review the possible changes in the expression platforms of microRNAs which are clinically correlated with breast cancer. It has been confirmed that miRNAs play a key role in various cancers including breast cancer, by regulation expression of a wide range of genes of a cell. Therefore, a comprehensive perspective of possible changes in the expression platforms of microRNAs and their roles in breast cancer progression will greatly aid in early detection and management of breast cancer.
Clinical Oncolytic Virus-Based Therapy For Hepatocellular Carcinoma

1. Elnaz Fazeli (Department Of Laboratory Sciences, Faculty Of Paramedical Sciences, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Fahimeh Mobaraki (Faculty Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
3. Farnaz Torabian (Islamic Azad University Of Mashhad, Mashhad, Iran)
4. MohammadReza Khohasteh (Faculty Of Medicine, Islamic Azad University Of Mashhad, Mashhad, Iran)

Abstract

Hepatocellular carcinoma (HCC), also called malignant hepatoma, is the most common type of liver cancer. HCC is the third leading cause of cancer deaths worldwide, with over 500,000 people affected. It carries a poor prognosis, because the advanced disease is resistant to both radiotherapy and conventional cytotoxic drugs which have limited therapeutic index and lots of treatment-related side effects. Therefore, new therapeutic strategies are needed to selectively destroy the tumor cells and leave the normal cells undamaged. Viral oncotherapy is a promising treatment that offers unique chance for tumor targeting. Oncolytic viruses (OVs) are designed to replicate in and lyse cancer cells. The premise of OVs lies in their preferential genomic replication, protein expression and productive infection of malignant cells. Different OVs have been tested in preclinical models of HCC, with reasonable evidence of anti-tumor efficacy. Efforts to influence the performance of these agents have concentrated on engineering OV cellular specificity, immune evasion, enhancing anti-tumor potency and improving delivery. The lead agent in HCC clinical trials, JX-594, a recombinant Wyeth strain vaccinia virus, that was genetically modified to inactive the endogenous thymidine kinase gene and to express human GM-CSF and LacZ genes, has demonstrated evidence for important benefit and earned orphan drug status. Thus, JX-594 seems to be transcending the barrier between novel laboratory science and credible clinical therapy. Few other OVs have entered clinical testing, which is an obstacle that must be destroyed if important progress is to be made in this field. This article indicated that viral oncotherapy can be effective on treating hepatocellular carcinoma.

Corresponding Author: Elnaz Fazeli (Department of Laboratory Sciences, Faculty of Paramedical Sciences, Mashhad University of Medical Sciences, Mashhad, Iran)
Role Of Diet In Prevention And Therapy Of Cancer

1. Mahboubeh Ghaemi (Department of Biology, Faculty of Science, University of Isfahan, Isfahan, Iran)

Abstract

There are many substances that will have some benefit for cancer therapy. Most of these substances are found in foods, but their effective doses for therapy are much higher than the normal concentration in the food. Fruits, vegetables and physical activities possibly by influencing levels and availability of female hormones or insulin resistance. Increased levels and availability of circulating estrogens may also explain the relationship between overweight and postmenopausal breast cancer. Several prospective cohort studies have found associations between high intake of lycopene and reduced incidence of prostate cancer. Intravenous ascorbate may be a very beneficial adjuvant therapy for cancer with no negative side effects when administered properly. Also, green tea contains a flavanol, epigallocatechin-3-gallate (EGCG), which can inhibit metalloproteinases, among several possible other mechanisms. Vegetable fiber encourages the growth of beneficial bacteria. Beneficial bacteria can help prevent cancer at various stages of development. These good bacteria can improve mineral absorption, maximizing food utilization. They also can help strengthen the immune system. Curcumin, the major component of the spice turmeric, inhibits the generation of reactive oxygen species (ROS) and the c-Jun NH2-terminal kinase (JNK) pathway. Expanding adipose tissue in obesity could make to the development of cancer via dysregulated secretion of pro-inflammatory cytokines, chemokines and adipokines such as TNF-α, IL-6, leptin, adiponectin, visfatin and PAI-1. Obesity increases breast cancer risk in postmenopausal women by around 50%, probably by increasing serum concentrations of free estradiol. In animal studies that employ a transgenic adenocarcinoma of the mouse prostate (TRAMP), which is a model that mimics progressive forms of human prostatic disease, it is observed that oral infusion of a polyphenolic fraction isolated from green tea (GTP) at a human achievable dose (equivalent to 6 cups of green tea/d) significantly inhibits Pca (Prostate cancer) development and metastasis. Much remains to be learned about the role of nutritional factors in therapy and prevention of cancer. Diets that have adequate vegetables, fruit, whole grains, and low-fat dairy foods and that are low in saturated fat may help to lower overall disease risk. Curcumin, Lycopene, vitamin C, vitamin E, B-carotene, vegetable oil, grape seed extract, green tea are substances which can prevent and also modify growth of cancer cells.

Corresponding Author: Mahboubeh Ghaemi (Department of Biology, Faculty of Science, University of Isfahan, Isfahan, Iran)
MUC1 Protein: A Potential Opportunity For Cancer Treatment And Diagnosis

Abstract

MUC1 protein normally exists on the apical surface of most normal secretory epithelial cells. Abnormally overexpressed in most human carcinoma like 90 % of epithelial ovarian cancer, including platinum-resistant tumours, 77% primary lung cancer, 96.7% invasive lung cancer, 70 % of breast cancer, 90% pancreatic invasive carcinomas, 90% of lymph node metastases and 58% of primary lesions in prostate cancer. It also finds on 60% of captured circulating tumor cells of metastatic breast, lung, pancreatic and colon cancer patients. The difference between normal MUC1 and tumor-associated MUC1 makes it as attractive tumor-associated marker for diagnostic, drug delivery, immunotherapy and therapeutic inhibitors. Tumor associated MUC1(TA-MUC1) differs from MUC1 which it is exist on normal cell in the following characteristics: 1- Underglycosylated, Abnormally glycosylated MUC1 protein allows exposure of immunogenic epitopes of the VNTR region in cancer cells, which has been hidden by the extensively branched sugar chains on normal MUC1. 2-Over- expression and loss of polarization localization 3-Exuding of MUC1 fragments, MUC1 expression is increased in malignancy, and it could be detected in serum of patients with breast cancer, ovarian carcinoma and Pancreatic cancer. High MUC1 serum levels associate with progressive disease. A project was performed by National Cancer Institute to prioritize therapeutic cancer antigens; MUC1 had held the second rank between 75 cancer vaccine antigen candidates.Chemotherapy is a main method for cancer therapy, but its adverse effects make it unsuitable procedure. Targeting chemotherapy could overcome some non-specific side effects. Abnormally MUC1 over-expression in cancer cells makes it a potential tool for targeting drug or gene delivery into the cancerous tissue. Since no cancer diagnosis or treatment base on MUC1 can enter to the pharmaceutical market, design novel drug or diagnosis system may confer a new hope for cancer control.

Corresponding Author: Mohammad Ramezani (Masshad univercity of medical student, pharmacy school)
Abstract

Colorectal cancer is the third most common cancer and the fourth leading cause of death due to cancer. Of all deaths related to cancers, 10% is due to colorectal cancer. The purpose of this article is to study on the 316 colorectal cancer data related to patients of Imam Reza hospital in Mashhad, despite the limited features for collecting data, we utilized a powerful decision tree method for data mining. Data related to 316 patients with colorectal cancer admitted to Imam Reza Hospital, Mashhad, Iran, were extracted and analyzed by RapidMiner software using the data mining method. Variables used include age, gender, location of cancer and family history, Decision tree models were concluded and data patterns were illustrated. The results which obtained from this research indicate that the incidence of cancer in patients admitted in the treatment center has different symptoms in compare with the other studies in the world. For example, the incidence of cancer in the lower than the ages of 30 mostly has not important dependency in the inheritance factor. In addition, most of cancers in terms of the location of cancer was the left cancer (distal) that were taken, according to the studies, the prevalence of left cancer observed in high-risk communities. There is a very high data mining abilities with high limits on the information predicting the disease process and the appropriateness of the data was very sensible. Therefore, due to the very high risk of this cancer in Iran, it is recommended that in addition to collect the basic information of the patient, we should consider other parameters like genetic, geographic data and other important factors to more accurate and effective ability of predicting on the collected information of patients.

Corresponding Author: Mohammad Mahdi Khakshoor (Quchan University of Advanced Technology, Quchan, Iran.)
Halophile and Halotolerant Bacteria As A New Source For Anti-Cancer Stem Cell Metabolites

1. Atefeh Safarpour (Department of Stem Cells and Developmental Biology, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran)

2. Marzieh Ebrahim (Department of Stem Cells and Developmental Biology, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran)

3. Seyed Abolhassan Shahzadeh Fazeli (Microorganisms Bank, Iranian Biological Resource Centre (IBRC), ACECR, Tehran, Iran; Department of Molecular and Cellular Biology, Faculty of Basic Sciences and Advanced Technologies in Biology, University of Science and Culture, ACECR, Tehran, Iran.)

4. Mohammad Ali Amoozegar (Extremophiles Laboratory, Department of Microbiology, Faculty of Biology and Center of Excellence in Phylogeny of Living Organisms, College of Science, University of Tehran, Tehran, Iran)

Abstract

Because of their short life span, microorganisms known as easy producers of natural products. Halophile and halo tolerant microorganisms are extremophiles with ability to live in high salt concentrations. There is some assumption that living in salt concentrations resemble to human blood plasma makes them a good source of novel bioactive compounds or secondary metabolite with fewer side effects. A total of 36 microbial metabolites from saline environment of Iran have been evaluated for their anticancer potential against six human cancer cell lines of breast, lung and prostate cancers and a fibroblast cell line as control. Downstream analysis of two most potent metabolites was done using various assays to test the effect of these metabolites on cancer stem cells including sphere formation assay, colony formation assay, scratch assay, invasion and migration assay. Among these 36 strains, seven metabolites were found to be cytotoxic against one or more cancer cell lines after 48 h with cell line specific activities. The metabolite from two strains has the potent cytotoxic effect on breast cell lines with IC50 of 100 µg/ml and lowered the size and number of sphere and colonies of this cell line. Scratch assay exhibited that this metabolite affects the migration ability of cell lines negatively and invasion and migration assay confirms scratch results. Altogether, the study offers novel findings regarding the anti-cancer and anti-cancer stem cell potential of several halophilic bacterial species inhabiting the saline environment of Iran, which constitute valuable candidates for further isolation and characterization of bioactive molecules.

Corresponding Author: Marzieh Ebrahim (Department of Stem Cells and Developmental Biology, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran)
The Effect Of Stress Management To Reduce Anxiety In Cancer Patients

1. Elham Navipour (Department Of Biostatistics & Epidemiology, Faculty Of Health, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Ali Taghipour (Assistant Professor, Department Of Biostatistics & Epidemiology, Faculty Of Health, Mashhad University Of Medical Sciences, Mashhad, Iran)
3. Ehsan Navipour (Department Of Biostatistics & Clinical Psychology, Faculty Of Medicine, Islamic Azad University Of Sari, Sari, Iran)

Abstract

Cancers are a broad range of diseases that each of them have their etiology, treatment program and prognosis. After cardiovascular disease, cancer is the second cause of death in human societies, in the world Cancer of public opinion is, as a crippling disease and incurable. Psychological stress caused by the cancer, causing anxiety and depression in these patients, failure to treat these reactions are reason, longer stay in the hospital, disorder in medical treatments, reducing the chance of survival in these patients. Anxiety and depression are common psychological responses in cancer patients. Treatment also can be anxiety-provoking for patients. On the other hand, Pain tolerance in cancer patients has the impact on the quality of life of the patient. Stress management, effective strategy to improve the different attitude, social problem solving skills and patients can reduce the anxiety, stress, and turbulence caused by cancer. The aim of this study is effect of stress management to reduce anxiety in patients with cancer. Anxiety and stress have a psychological effect directly on immune system and reduces the body's resistance. Results show that the prevalence of stress and, in general, psychological problems in patients with cancer is 25 to 30 percent. There are relation among depression, stress, and anxiety there, so that cancer patients with anxiety and stress have higher rates of depression and vice versa. Anxiety, response to a threat, and cancer is a threat, so a lot of cancer patients are anxious, this necessary pay attention to psychological interventions based stress reduction, reducing psychological symptoms and improved methods contrast with cancer as a chronic disease.

Corresponding Author: ali taghipour (Assistant professor, Department of Biostatistics & Epidemiology, Faculty of health, Mashhad University of Medical Sciences, Mashhad, Iran)
Survey The Effect Of Spiritual Intervention On Promotion Hope And Mental Health In Cancer Patients

1. Elham Navipour (MSC Student Biostatistics, Department Of Biostatistics & Epidemiology, Faculty Of Health, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Ali Taghipour (Assistant Professor, Department Of Biostatistics & Epidemiology, Faculty Of Health, Mashhad University Of Medical Sciences, Mashhad, Iran)
3. Ehsan Navipour (MSC Student Clinical Psychology, Faculty Of Medicine, Islamic Azad University Of Sari, Sari, Iran)

Abstract

Cancer is cell disease that characterized by unlimited and uncontrolled proliferation of malignant cells that form tumors. Cancer is the second cause of mortality after cardiovascular diseases in the world. It is predicted that the annual number of new cases reach in 2020 from 10 million to 15 million. though, mental health cancer affects but seems to be the biggest issue at this time for the patient, a sense of frustration and despair. Throughout history, various schools of anthropology and psychology and research to provide solutions to human needs have given him. Spiritual studies in psychology in the world is a serious matter and essential Spirituality is an important component that is increasingly attracted the attention of psychologists and mental health professionals. Most people who diagnosis with cancer will experience a period of mental stress, which reduces the quality of life and daily functioning, as a result, due to the psychological burden that this disease is to them the need of spiritual intervention. Spirituality is a strong predictor for hope and mental health, an important source of physical health and improvement disease. In fact, a matter that for intervention in cancer patients is necessary. This study aimed to evaluate the effect of spiritual intervention to promotion hope and mental health in cancer patients. During recent two decades spiritual and religious interventions were employed by a large number of experts and clinical psychology in the treatment of cancer patients. The effectiveness of spiritual intervention has been proven in many studies. As for essential role of spirituality in returning to normal life, for these patients is necessary to pay special attention to this issue. Therefore, it is suggested that in order to comprehensive planning in health care - support and relief in patients with cancer, spirituality and solidarity in psychotherapy as an important issue, to be considered

Corresponding Author: ali taghipour (Assistant professor, Department of Biostatistics & Epidemiology, Faculty of health, Mashhad University of Medical Sciences, Mashhad, Iran)
The Role Of Education On Behaviors Leading To Early Diagnosis Of Cancer

1. Elham Navipour (MSC Student Biostatistics, Department Of Biostatistics & Epidemiology, Faculty Of Health, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Ali Taghipour (Assistant Professor, Department Of Biostatistics & Epidemiology, Faculty Of Health, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Lack of exercise, obesity and increasing use of poor nutrition, air pollution, caused an increased incidence of non-contagious diseases such as cancer. Cancer is known as an important problem in human society. Cancer is the second cause of mortality after cardiovascular disease in the world. Economic and psychological consequences and also disabilities that is followed by cancer, an attempt to make early diagnosis and effective treatment, as a result one of the existing needs in the treatment of different types of cancers is early diagnosis in the early stage. Early diagnosis and successful treatment of cancers are effective. Educational intervention caused to change in knowledge, attitude, and behavior controlling. The present study was aimed at determining the role of education on behavior leading to early diagnosis of cancer in order to increasing screening people at risk of cancer and the postponement of the screening of low - risk, For reducing the financial burden of individuals, health systems and reduce unwanted damages. Because of the lack of intervention programs for health education in Iranian society, is necessary to regular planning programs community oriented that would increase the level of awareness, the cancer society's attitude, methods of prevention and early diagnosis in Iran. As far increasing of cancers in Iran and refer many of people with advanced stage, is necessarily to consideration and addressing this problem via the educational intervention promotion behaviors lead to early diagnosis of cancer that is important to reduce mortality.

Corresponding Author: Ali Taghipour (Assistant professor, Department of Biostatistics & Epidemiology, Faculty of health, Mashhad University of Medical Sciences, Mashhad, Iran)
Pathway Analysis For Pancreatic Cancer Using Path Visio

1. Reza Tohidi (Department Of Agriculture, University Of Torbat-e Jam, Mashhad Iran)
2. Mohammadreza Nasiri (Institute Of Biotechnology, Ferdowsi University Of Mashhad, Mashhad Iran)
3. Zahra Roudbari (Department Of Animal Science, Faculty Of Agriculture, Ferdowsi University Of Mashhad, Mashhad Iran)

Abstract

It has been estimated that 170,000 new cases of pancreatic cancer occur worldwide per year. Approximately 80 – 90% of cases diagnosed happen in advanced stage of disease. The occurrence of diseases has two sides of genetics and environment. Microarray technique make it possible to analyze the expression of a large number of genes, simultaneously. The aim of this study was to use of microarray data for analyzing of biological pathways involved in pancreatic cancer. The microarray data were obtained from ArrayExpress data bank (ebi.ac.uk/arrayexpress; Accession No: E-GEOD-27890). The quality of data was controlled using the facility available in ArrayAnalysis.org website. Gene expression in pancreatic adenocarcinoma and adjacent ductal epithelia from the same patient using laser capture microdissection dissected samples was analyzed. Path Visio 3.2.2 was utilized to perform pathway analysis. From the 20,111 genes that passed the quality control, 19,966 genes could be linked to Ensembl identifiers by Path Visio. Only 6097 of these genes were associated with the human pathways in the Path Visio repository. The number of genes on the pathways that passed the criterion was 1074. Twenty two biological pathways had highest positive $z$ score and were ranked as most regulated. The results show that the biological pathways that are involved in cell apoptosis are highly active in pancreatic cancer. The transforming growth factor (TGF) beta signaling pathway, TGF beta receptor signaling, Oxidative stress and lung fibrosis are included in this pathway. There are many genes that up/down regulated in these biological functions. The results of this study revealed that several pathways interfered in pancreatic cancer. The transcription level of genes were different, so some genes were significantly upregulated and some suppressed. However, apoptosis was a process that was indicated significantly including in pancreatic cancer. It is necessary that the genes involved in apoptosis are investigated in details for their functions and pathways.

Corresponding Author: Reza Tohidi (Department of Agriculture, University of Torbat-e Jam, Mashhad Iran)
Colorectal Cancer And Alcohol Consumption

1. Soheila Seddighi (Department Of Research Committee, Faculty Of Medicine, Mashhad University Of Medical Sciences (MUMS), Mashhad, Iran)

Abstract

CRC is a hereditary nonpolyposis neoplasms that occur much later, in the fourth and fifth decades. This cancer is the third most diagnosed cancer in men and the second in women and in Iran we have 5000 new cases in year. The International Agency for Research on Cancer (IARC) ressulted there is a relationship between alcohol consumption and colorectal cancer (CRC). Studies suggest that high alcohol consumption can cause deficiency of folate then hypermethylation may happened. Other human studies show that alcohol/beer consumption and adenomatous polyps can be related to each other, that alcohol may stimulates the colorectal mucosa. Also there are some evidences that show colorectal cancer cells may metastasis to the liver. Current data were obtained from electronic databases (PubMed and Google Scholar sites; until 2016). In this study, 7 relevant articles were reviewed. In this study we evaluated the effects of alcohol consumption on CRC. Some effects of alcohol include immunodepression, accelerating liver metastasis of colorectal cancer cells through the modification in immune surveillance, increasing proliferation of cells, activation intestinal and liver procarsinogens, inducing inflammatory response, changes in promoter hypermethylation in CRC, and in bile composition because of increasing in nitrosamine levels in tissues. This changes were more in males than in females, and for rectal than for colon cancer and the effect of beer is more stronger than wine or spirit, and in adult who drink for long-term the risk of that can be two- to threefold. Infact alcohol consumption can increase the risk of CRC but the effects of that can be different in various bycolorectal site, geographical region, sex and dose, especially about of light (≤1 drink/day) and moderate (2-3 drinks/day) quantities, the effect of that is not clear. So more study needed to investigate the different dimensions of effects of alcohol consumption. On present evidence, that alcohol, especially beer consumption and in long-term, is a risk factor for CRC for every one.

Corresponding Author: Soheila Seddighi (Department of Research Committee, Faculty of Medicine, Mashhad University of Medical Sciences (MUMS), Mashhad, Iran)
The Etiology Of Breast Cancer, From The Perspective Of Traditional Iranian Medicine

1. Hamide Khorrampajouh (Department Of Persian Medicine, School Of Persian And Complementary Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Soude Teymuri (Department Of Persian Medicine, School Of Persian And Complementary Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
3. Mojdeh Khodabakhsh (Department Of Persian Medicine, School Of Persian And Complementary Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Traditional Iranian medicine dating back more than two thousand years ago, and has many points in causes, treatment and prevention of diseases such as cancer, which is sadly neglected in recent decades. Books that come down to us from the fourth century AD indicate that Iranian medicine sages knew at that time have cancer. Book reached us from the fourth century indicate that Iranian physicians knew many important things about cancer, some theories of famous Iranian physicians about the cause of cancer, proven in recent studies. In this study we examine the causes of breast cancer, from the perspective of Iranian traditional medicine. This study is a review article, based on five sources Traditional Iranian medicine, including Canon of medicine, Al-Havi, The Students Handbook of Medicine, Zakhireye Kharazmshahi, Kamil al-Sinaa al Tibbiya. In general, cancer is more common in women. Breast cancer is the most common, followed by the uterus. Ahvaz and Razi has been clearly determined the relationship between breast cancer and quality and quantity of uterine bleeding. That means that if we have regular and normal range of uterine bleeding, the risk of breast cancer may reduce. Breast cancer is also associated with liver and spleen know. Ahwazi referred to the role of genetics in the transfer of some cancers. Some of cancer’s etiology listed in traditional medicine, such as the role of nutrition in cancer development or the role of genetics has been proven in modern medicine. Other etiologies of further studies in this area, is going to make the blind spots in the prevention and treatment of this disease.

Corresponding Author: Hamide khorrampajouh (Department of Persian Medicine, School of Persian and Complementary Medicine, Mashhad University of Medical Sciences, Mashhad, Iran)
Reducing The Incidence Of Cancer Using Herbal Medicines

1. Mojdeh Khodabakhsh (Department Of Persian Medicine, School Of Persian And Complementary Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)

2. Hamideh Khorrampajouh (Department Of Persian Medicine, School Of Persian And Complementary Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)

3. Zohre Feyzabadi (Department Of Persian Medicine, School Of Persian And Complementary Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Cancer, or Crab, is asymmetric division of cells in the body. Cancer cells of the central division and growth of cells fall apart. The exact cause of this phenomenon is unknown, but genetic factors or issues that are likely to disrupt cell activity are entered in the cell nucleus forms, such as radioactive substances, toxic chemicals or radiation exceeded sunlight. Cancer of the most important non-communicable diseases is a major burden on society imposes. Currently, it causes 12% of deaths worldwide. So the cancer care system as one of the main priorities is the health care system. Anti-cancer effects include dry mouth, nausea, vomiting, fatigue, memory impairment, depression, hearing loss, muscle damage, hair loss, Infertility. This makes it imperative need for applying efficient treatment. Using alternative medicine and herbal remedies may be able to decrease the side effects of chemical drugs, reduce the symptoms. This study is a review article. In this study of medicinal plants in the treatment of cancer, four books of reference of Traditional Iranian medicine, was extracted. Include: Qanun fi al-Teb, Al Havi, Tazkere Davud Antaki, and Tohfat Al momenin. 46 drugs proposed for the treatment of cancer was found. 43 plants and three of them were animals. In the meantime, such as Dorema ammoniacum, Glycyrrhiza glabra, Crab, have been mentioned several times in Traditional Iranian medicine resources. Today, laboratory studies have shown that many of the plants used in Traditional Iranian medicine, such as ginger and licorice has antioxidant and anti-cancer effects in animal studies has been on the cell lines. Given the potential of these plants for use in the treatment of various cancers, laboratory and clinical research is needed.

Corresponding Author: Mojdeh Khodabakhsh (Department of Persian Medicine, School of Persian and Complementary Medicine, Mashhad University of Medical Sciences, Mashhad, Iran)
Abstract

Nowadays, the personalized medicine, the prescription of a particular and selective therapeutic approach best suitable for an individual, has attained a worldwide attention. Current insights obtained from the newly emerged molecular and omics sciences has opened new avenues from personalized medicine approach towards individualization of the cancer therapies. Cancer genomic analysis indicate its heritable and multi-gene basis which lead to genetic alterations and somatic mutations. Personalized medicine in commencing to play a crucial role for cancer diagnosis, prognosis, prediction of risks and treatment with more effectiveness and robustness, with less unwanted effects on the patients and minimum cost of care. Published literature identification through systematic search in pubmed, scopus and google scholar (from 1990 to 2016) sing the search terms “Personalized medicine”, “Cancer therapy”, “Cancer genomics”, “Oncology”, “Omics technologies” and “Systems medicine”. The results of some molecular studies on cancer had revealed a great and serious role of genetic variety for different classes of cancer that appear with a same molecular pathology. Moreover, there is a rising concerns towards genetic diversity occurring in a single tumor and tumor heterogeneity. Exploitation of the cancer genomics approach has shed light on better understanding the cancer pathology and its clinical therapy. Trastuzumab, a monoclonal antibody interfering with HER2/neu receptor has been extensively employed to treat certain types of breast cancer. This therapeutic approach will be successful only in individuals with over expression of the HER2/neu receptor. Moreover, Imatinib, a tyrosine kinase inhibitor has administered for treatment of chronic myeloid leukemia (CML) in patients with a reciprocal translocation between chromosomes 9 and 22. This medicine specifically hampers the Ableson tyrosine kinase (ABL). The mentioned rational cancer drug therapy approaches have been also studied for other types of cancer. Future personalized therapy approaches to effective cancer care could be extended to improve the quality of life of human being, early detection and clinical management of the cancer, and its investigations. Besides it will change the current concepts about cancer therapies and also the molecular mechanisms of cancer through a systems medicine approach.

Corresponding Author: ohammad Hossein Morowvat (Pharmaceutical Sciences Research Center, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran)
Anti-Proliferative And Differentiation Inducing Activities Of Guanosine 5'-Triphosphate On Osteosarcoma Cell Line

1. Azadeh Meshkini (Department Of Chemistry, Faculty Of Science, Ferdowsi University Of Mashhad, Mashhad, Iran.)

Abstract

Among differentiating agents, purine bases and their corresponding nucleosides and nucleotides have been the center of focuses due to their important and diverse effects on many biological processes and also their physiological roles as extracellular signal molecules. Recent studies have proved that among purines, guanosine-base purines inhibit the excessive proliferation of a wide variety of cancer cells and guide them toward the maturation pathways. Based on these facts, anti-proliferative and osteogenic differentiation potential of guanosine 5'-triphosphate (GTP) on human osteosarcoma cell line Saos-2 was evaluated. Cell viability was measured by tetrazolium-based colorimetric assay. Cell cycle was analyzed by propidium iodide staining using flow cytometry. Osteogenic differentiation responses were registered by assessment of alkaline phosphatase activity and the level of extracellular matrix mineralization which is detected and quantified by alizarin red S staining. Single dose treatment with variable concentrations of GTP revealed that GTP inhibits cell growth after 24 h of exposure and continued to increase in a time dependent manner, reaching a maximum value at 72-96 h of treatment. Cell cycle analyses by flow cytometry disclosed that growth inhibition was accompanied with an accumulation of cells in the S-phase of the cell cycle. Moreover, precise assessment showed that GTP has ability to induce osteogenic differentiation which was quantified by monitoring ALP activity and calcium deposition. A significant increase was observed in ALP activity in GTP (400 µM) treated cells as compared with control. Osteogenic differentiation was further confirmed by calcium mineralization under the influence of GTP. These finding may pave the way for further pharmaceutical evaluation of GTP as a suitable differentiating agent for poorly-differentiated osteosarcoma cells.

Corresponding Author: Azadeh Meshkini (Department of Chemistry, Faculty of Science, Ferdowsi University of Mashhad, Mashhad, Iran.)
Pancreatic cancer is the fourth leading cause of cancer deaths among men and women, being responsible for 6% of all cancer-related deaths. Approximately 75% of all pancreatic carcinomas occur within the head or neck of the pancreas, 15-20% occurs in the body of pancreas, and 5-10% occurs in the tail. It is more common in men than women and is predominantly a disease of elderly people. This study was designed to determine a new data of anatomical distribution and demographic data of pancreatic cancer in North East of Iran. Records of patients diagnosed with pancreatic cancer from March 1997 to February 2013 in mashhad Qaem and Omid hospital were reviewed for demographic data and anatomical location of tumor. Statistical analysis was performed using the SPSS software. There was 408 patients with pancreatic cancer (mean age of 60.45±0.63). Participants were 262 men (64.2) and 146 women (35.8) with a mean age of 60.55 ± 0.83 and 60.27±1.04 years, respectively. Location of lesion in 131 patients was in head of pancreas, the most prevalent part. 267 Patients were suffered from lesions in unspecified of pancreas. Tail of pancreas in 4 of cases, Body of pancreas in 6 of cases patient were involved. Pathology shows that the most form of pancreatic cancer was adenocarcinoma (64.8%). Our results showed that the most common area of pancreas involved in cancer located in the head, and there is no statistical significant difference between male and female, and the body of pancreas was involved more than the tail.
Risk Of Testicular Cancer And Treatment Options For Fertility Preservation

Abstract

Testicles are the male sex organs and they are responsible for producing and storing the sperm and releasing the testosterone. One of the most common cancers in patients of reproductive age is testicular germ cell tumors. Testicular cancer is a rare disease that is caused due to uncontrolled growth of spermatogenic cells in the seminiferous tubules. The number of young men with testicular cancer has increased in recent years significantly and so prevention and early detection for treatment is important. Cryopreservation of semen before the cancer treatment starts, is currently the only method to maintain male fertility because chemotherapy and radiation therapy are long-term protocols, and also they have impaired fertility. The amount of damage of these treatments on spermatogenesis depends on combination of drugs and radiation intensity used that may cause infertility in men. After treatment of cancer, many patients need artificial reproductive methods for fertility for example, in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) are successful techniques for treatment. New therapeutic methods such as stem cell therapy has been suggested, which is still in the phase of research and clinical trials. New fertility preservation techniques use testis spermatogonial stem cells before cancer treatment. Several studies concluded that Risk of Testicular Cancer has increased and the need to novel treatment methods to be felt for Infertility Preservation before or after treatment of cancer. Current treatments including chemotherapy and radiation therapy may cause low quality semen and azoospermia after the treatment process because germ cells are being very sensitive to chemicals and irradiation. New therapeutic approaches such as cell therapy has been successful in animal models before cancer treatment. Also, IVF and ICSI can be useful to make fertility after testicular cancer treatment.

Corresponding Author: Fahimeh Mobaraki (Departmen Of Anatomical Sciences And Cell Biology, Student Research Committee, Faculty Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
Analysis Of Cancer Stem Cells (CSCs) In The Prevention And Treatment Of Cancer

1. Ghanbar Mahmoodi Chalbatani (Cancer Institute, Tehran University Of Medical Sciences, Tehran, Iran.)
2. Ellahie Gharaghouzlo (Cancer Institute, Tehran University Of Medical Sciences, Tehran, Iran.)
3. Amir Hossein Muhammad Zadeh Hosseini (Department Of Biology, Damghan Branch, Islamic Azad University, Damghan, Iran.)
4. Ashkan Abbasi Fard (Department Of Biology, Damghan Branch, Islamic Azad University, Damghan, Iran.)

Abstract

According to research, cancer stem cells (CSCs) are rare cells in various cancers, including leukemia and various solid tumors have been identified. Evidence suggests that cancer stem cells with are capable of renewal and differentiation in a variety of cancers. Dysregulation of gene expression and signaling pathways in cancer stem cells compared some with other malignancies attracts a lot of attention. Recently cancer stem cell hypothesis, given the high potential for the discovery and development of this cells, associated with attracting and identify key molecules in controlling their unique properties, has attracted a lot of attention. In recent years, in order to capitalize on new drugs such as: nano-medicine, the possibility of using molecular markers of cancer stem cells to targe this cells or various signaling pathways, many efforts have been. Various new techniques and strategies, to targeting this cells have been identified, Some of them in pre-clinical studies and clinical trials have been evaluated. In this review we discussion new discovery on cancer stem cells, and unique identify and isolate this cells and advances in studies of drug resistance, as well as the innovative therapy systems and different strategies for targeting cancer stem cells. Finally, we discuss the mechanisms by which cancer stem cells may resist medical therapy and contribute to tumor relapse.

Corresponding Author: Amir hossein Muhammad zadeh hosseini (Department of biology, Damghan Branch, Islamic Azad University, Damghan, Iran.)
The Stem Cell Theory Of Cancer As A Novel Therapeutic Strategy

1. Fahimeh Mobaraki (Department Of Anatomical Sciences And Cell Biology, Student Research Committee, Faculty Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Elnaz Fazeli (Department Of Laboratory Sciences, Faculty Of Paramedical Sciences, Mashhad University Of Medical Sciences, Mashhad, Iran)
3. Farnaz Torabian (Student Of Medicine, Faculty Of Medicine, Islamic Azad University Of Mashhad, Mashhad, Iran)
4. MohammadReza Khojasteh (Faculty Of Medicine, Islamic Azad University Of Mashhad, Mashhad, Iran)

Abstract

Cancer is a disease sweeping across the world and there are many questions about how it works. How it starts and how it spreads. Cancer stem cell theory, proposes that specific stem cells similar to normal stem cells are involved in tumor. This theory can explain to a large extent about the process of starting, growing and expanding cancerous mass and about how a normal cell turns into a cancer cell. Understanding the concept of stem cells and their function can have an impact on cancer definitive treatment. If cancer stem cells are responsible for maintaining tumor growth, then eliminating these cells can cure the patient eventually. So even many new anti-cancer therapies are in order to shrink or withdraw cancer mass and eliminate it while cancer stem cells remain in the cancer tissue and can continue to self-renew and tumor grows again. Recent researches have shown that compared to other cell, cancer stem cells are more resistant to chemo and radiotherapy. This could be one cause of tumor relapse after therapy. Some researchers suggest that significant changes in DNA sequences make changes in cellular regulation and any cell in the body can undergo these changes and become a cancerous outlaw. Novel treatment methods have been created in order to remove the cancer stem cells or induce their differentiation that named differentiated treatment. These treatments are based on the idea that undifferentiated stem cells have the ability to divide and reproduce indefinitely so if they become distinct, Their ability to grow and self-renewal will be limited. Finally the ability to remove malignant cells is provided. Several studies concluded that, cancer stem cells arise from normal stem cells and they can also act as a reservoir of cancer cells that may cause a relapse after surgery, radiation or chemotherapy has eliminated all observable signs of a cancer. Cancer stem cells have more resistant to treatment than other cells. So to eliminate cancer cells, cancer stem cells should be induced to differentiate or eliminate them completely.

Corresponding Author: Fahimeh Mobaraki (Department of Anatomical Sciences and Cell Biology, Student Research Committee, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran)
Breast Cancer Cells Imaging By Targeting Gd3+-Based Silica Nanoprobe

1. Bita Mehravi (Radiation Biology Research Center, Iran University Of Medical Sciences, Tehran, Iran)
2. Khadijeh Ashtari (Department Of Medical Nanotechnology, Faculty Of Advanced Technology In Medicine, Iran University Of Medical Sciences, Tehran, IR Iran)
3. Hojatola Nazari (Department Of Medical Nanotechnology, Faculty Of Advanced Technology In Medicine, Iran University Of Medical Sciences, Tehran, IR Iran)
4. Neda Iranpour (Department Of Medical Nanotechnology, Faculty Of Advanced Technology In Medicine, Iran University Of Medical Sciences, Tehran, IR Iran)
5. Mojdeh Mohseni (Department Of Medical Nanotechnology, Faculty Of Advanced Technology In Medicine, Iran University Of Medical Sciences, Tehran, IR Iran)
6. Safura Chahabi (Department Of Medical Nanotechnology, Faculty Of Advanced Technology In Medicine, Iran University Of Medical Sciences, Tehran, IR Iran)
7. Roya Ilka (Department Of Medical Nanotechnology, Faculty Of Advanced Technology In Medicine, Iran University Of Medical Sciences, Tehran, IR Iran)

Abstract

Cancer cells diagnostic in early stage using noninvasive techniques is high global interest. Mesoporous silica nanoparticles functionalized by targeting group were further modified by loading with fluorescent and contrast agent with the aim of specifically targeting cancer cells imaging with reduced side effects. Due to the high abundance of folate receptors in various cancer cells, folic acid was used as the targeting group. The intracellular uptake of this nanoprobe was analyzed quantitatively and qualitatively by inductively coupled plasma atomic emission spectroscopy (ICP-AES), T1 and T2 mapping in vitro in a 3 T MRI scanner, flow cytometry, and fluorescent microscopy in cell lines expressing different levels of folate receptors. The cellular uptake of foliconanoprobe was about 62.01% in cancer cell. 2.6 times more foliconanoprobe were internalized by cancer cells expressing folate receptors as compared to the normal cells expressing low levels of the receptor and. Average cellular uptake of 0.7 ± 0.007 pg Gd3+ per cancer cell without any cell toxicity. The r1 relaxivity of this nanoprobe in the cancer cells was measured to be 12.9 ± 1.6 mM−1s−1 and on a per Gd3+ basis. These results showed that GSN provided a critical guideline in selecting these nanoparticles as an appropriate contrast agent for nanomedicine applications.

Corresponding Author: Bita Mehravi (Radiation Biology Research Center, Iran University of Medical Sciences, Tehran, Iran)
Human T-lymphotropic virus type 1 (HTLV-I) infects about 20 million people worldwide. About 2% to 5% of infected people may develop Adult T-cell leukemia/lymphoma (ATLL). Viral-host interactions are the main players of diseases development. HTLV-I-proviral load (PVL) has been determined as an important risk marker for the development of HTLV-I-associated diseases, also HBZ as a human immunomodulator enable virus evasion from host immune responses and implicated in TCD4+ proliferation and ATLL progression. Moreover AKT1 is a primary kinase in PI3K pathway has a number of substrates that contribute to malignant transformation. Furthermore regulatory T-cells as the main source of the virus, then their functions may be impaired toward diseases progression. Thus in this study the expression of PVL, HBZ, AKT1 and Foxp3 have been evaluated. Twenty five patients with ATLL and 18 HTLV-I healthy carriers were assessed for PVL, HBZ, AKT1 and Foxp3 expression using real time PCR, TaqMan method. The data was analyzed by SPSS software. The HTLV-1 PVL were higher in ATLL than ACs (p=0.003), HBZ expression was dramatically increased in ATLL patients compare to HTLV-I carriers (P-value < 0.000), and also AKT1 expression was increased in ATLL patients compare to HTLV-I carriers (P-value = 0.058). Furthermore expression of Foxp3 had significant difference between two groups. (P-value= 0.003). Results showed that high HTLV-1 proviral load in ATLL patients compared to healthy carriers, can influence on development and progression toward ATLL. Increased AKT1 in HTLV-1-transformed cells showed AKT1 activation may be played important role in cell survival and disease progression. Results showed that viral HBZ has critical role in HTLV-I infected TCD4+ immune evasion toward oncogenesis. Furthermore the findings show that T regulatory cells are the majorly affected cells in ATLL as Foxp3 increases radically.

**Corresponding Author:** Hanieh Tarokhian (Inflammation and inflammatory disease Research Centre, Mashhad University of Medical Sciences, Mashhad, Iran)
A Retrospective Study On The Demographic Characteristics Of Non-Melanoma Skin Cancer In Iran

1. Foroughossadat Ghasemzadeh (Department Of Medical Informatics, Faculty Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran.)
2. Kobra Etminani (Department Of Medical Informatics, Faculty Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran.)
3. Ali Arab-Kheradmand (Department Of Surgical Oncology, Cancer Institute, Imam Khomeini Hospital Complex, Tehran University Of Medical Science, Tehran, Iran.)
4. Soroush Daklan (Razi Skin Hospital, Tehran University Of Medical Sciences, Tehran, Iran.)
5. Seyed Benyamin Hosseini Moini (Department Of Medical Informatics, Faculty Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran.)

Abstract

The incidence of Non-melanoma Skin Cancer (NMSC) including basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) is increasing worldwide. There are limited data on the NMSC in Iran. Herein we aimed to determine the demographic characteristic of patients diagnosed with BCC and SCC from 2013 to 2016 in the Cancer Institute, Imam Khomeini Hospital Complex, Tehran, Iran. A retrospective chart review was performed on patients with biopsy-confirmed NMSCs. The demographic characteristics were documented for BCCs and SCCs patients and a descriptive data analysis was undertaken. A total of 417 NMSCs (298 in men and 119 in women) were identified among all skin cancer patients. BCCs and SCCs were generally diagnosed in people aged 64 ≤ years old. However, three cases in women and one case in men were under the age of 20 years. BCC, SCC and mixed of them accounts for 60, 39 and 1% of cases of NMSC, respectively. Fifty cases found to have relapses more than 3 times. BCCs and SCCs were most commonly seen on the head and face. The highest incidence of NMSCs was seen in high-latitude provinces. NMSC is prevalent throughout Iran. Against general impression our results highlight the fact that both men and women are equally affected by NMSC and cases are more frequent in northern part than others. Prevention strategies are necessary to promote awareness and to decrease the burden of NMSC in Iran.

Corresponding Author: kobra etminani (Department of Medical Informatics, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran.)
Tissue Distribution And Activity Of Thioredoxin Reductase In Laryngeal Cancer And Its Healthy Margin

Abstract

Laryngeal cancer is the second common neoplastic disorder of head and neck, in which squamous-cell carcinoma (SCC) consists about 90% of cases. Due to the limitations for an early clinical diagnosis, most of cases are diagnosed in advanced stages when a more invasive therapeutic protocol is required and prognosis is poor. Therefore, finding a diagnostic or prognostic biomarker can lead to a better therapeutic intervention, leading to a better survival rate. Since thioredoxin reductase (TrxR) is reported to be involved in many steps of carcinogenesis as well as resistance to chemotherapy and radiotherapy, we aimed to investigate the tissue distribution and activity of this enzyme in laryngeal cancer, and we compared these factors with those of the healthy margins of tumors. Twenty patients with laryngeal SCC who were candidate for laryngectomy were recruited, and the tumoral stage was determined. Tumoral and normal marginal tissues were provided during surgery and handled according to standard protocols. The tissue distribution of TrxR was studied immunohistochemically, and the intensity and percentage of staining of samples were scored. The activity of TrxR was measured using Cayman Chemical Thioredoxin Reductase Colorimetric Assay Kit (Item No 10007892) that is based on the reduction of DTNB to 5-thio-2-nitrobenzoic acid (TNB) which is a yellowish compound. Considering both the intensity and percentage of cellular staining, tumoral tissues had a higher expression of TrxR compared to the normal margins (p-value =0.000). Moreover, TrxR activity was significantly higher in tumoral tissues than their healthy margins (p-value=0.03). Since most of our patients were in stage III, determination of a relationship between TrxR distribution / activity and tumor stage was not possible. TrxR might play a diagnostic or prognostic role in laryngeal SCC, leading to an earlier diagnosis and an improved survival rate.

Corresponding Author: Seyed Isaac Hashemy (Surgical Oncology Research Centre, Imam Reza Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran)
Comprehensive Perspective Of Current And Upcoming Breast Cancer Blood Biomarkers

Abstract

Breast cancer is one of the most common malignancies and the second leading cause of cancer death among women which can be prevented by early diagnosis so as to treat in pro-invasive state. In the recent years, a wide range of breast cancer bio markers has been investigated in several studies, such as genetic, epigenetic, proteomic and imaging bio markers that can be used for diagnosis, staging and prognosis of this disease. Each biomarker has its own benefit and draw-back. Although technological advances in the field of medicine has enabled us to evaluate many of these biomarkers, but still noninvasive methods has its own advantages. As breast cancer leaves some markers in the blood, analyzing the blood sample as a source of tumor markers can be counted as a noninvasive and low-cost assay for general screening which can provide valuable information for the clinical oncologist. Also, it can help in early detection resulting in saving more options for treatment. Therefore, categorizing blood breast cancer bio markers by their characteristics such as structure, function, measuring assay, specificity and efficiency could assist in choosing the appropriate bio marker for obtaining clinically relevant data about the presence or absence of the disease and its evolution as well as improving therapy. In this regard, the current review provides a brief report on blood tumor markers of breast cancer already exist in clinical practice and also upcoming bio markers, such as CA 15.3, CA 27.29, Carcinoembryonic antigen (CEA), RS/DJ-1, Tissue-type plasminogen activator (TPS), Human epidermal growth factor receptor 2 (HER-2/neu), free circulating DNA, etc. An inclusive understanding of the blood tumor markers of breast cancer, as a regularly requested test by the oncologist, which is noninvasive and economic efficient assay, may provide opportunities for enhancing the breast cancer management by helping in early detection and cancer prevention.

Corresponding Author: Seyed Isaac Hashemy (Surgical Oncology Research Centre, Imam Reza Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran)
Detection Of BRCA1 Exon 11-B Mutations Among Breast Cancer Patients In Azerbaijan

Abstract

Breast cancer is the most common cancer in women world-wide one-third of cancers in women are included. Our multi-year study on patients with this cancer represents the lower age for breast cancer patients undergoing surgery in the region. This cancer is the second leading cancer killer among women, after lung cancer. The results of a study on breast cancer cases in Iran suggests that breast cancer patients in Iran are relatively younger than their Western counterparts. More than 15 percent of healthy women with at least one first-degree relative with breast cancer; experience has shown that the risk of breast cancer in these individuals is doubled. 20 to 30 percent of breast cancer patients have a family history of this cancer. Proposed for breast cancer genes important as genetic factors include genes with high penetrance follows: BRCA1, BRCA2, P53, PTEN, STK11 / LKB1, CDH1. While others, such as ATM, CHECK2, PALB2, BRIP1 that genetic factors are considered average. BRCA1 gene are discussed in this article. The aim of this study was to evaluate mutations in exons 11-B gene BRCA1 in Azerbaijani women with breast cancer. The study also identified possible genetic problem a number of families of patients, the first data about databases this gene in the northwestern area of the country's population will bring. In this study of 30 cancer patients during surgery to lower the age of forty years and get blood samples and exons 11-B BRCA1 gene were studied. PCR and Direct sequencing methods were used for this study. There is a new Nonsynonymous mutations was first identified mutations Thr 951 Arg, which in a sample was observed. BRCA1 gene as a tumor suppressor gene the large and important role in DNA repair through recombination Homologous, maintaining stability of chromosomes, DNA damage checkpoint activation and cell cycle regulation. Therefore changes in the expression levels of BRCA1 gene can lead to vulnerability breast cells to function as oncogenes. BRCA1 gene has 24 exons and a protein with the same name during the 1863 amino acids. This gene is on the long arm of chromosome 17, paragraph 21 (21q17) .gene BRCA1 ( Breast Cancer Susceptibility) was cloned in 1996 by Miki et al. Screening for mutations in exon 22 encoder, the role of this gene in about 45% of breast cancers are hereditary and about 80 percent of eligible families both breast and ovarian cancer revealed. Mutation in the BRCA1 gene in germ cells cause susceptibility to breast and ovarian cancer . Mutations in this gene 5 to 10 percent of breast cancer cases and 20 to 40 percent of breast cancers are familial. This amount is equivalent risk about 85 to 60 percent in lifetime. In carriers of mutations in the deadly BRCA1 up to the age of 40 to 20 percent risk of developing breast cancer and 17 percent risk of ovarian cancer. This risk increases with age rises so that by the age of 80 for breast cancer risk 82 and for the risk of ovarian cancer by age 70 is 39 percent and up to 80 years of age is 54%. Reports from around the world shows that the incidence of BRCA1 mutations
from 1/8 to 13/1 and the Asian countries the rate from 0.8 percent to 8.6 percent. The results showed that there is a new mutations in exon 11-B BRCA1 gene in Azeri women with breast cancer.

**Corresponding Author:** Mohamad Ali Hossainpour-Faizi ()
Serum Chemokine Ligand 5 (CCL5/RANTES) Level Might Be Utilized As A Predictive Marker Of Tumor Behavior And Disease Prognosis In Patients With Gastric Adenocarcinoma

1. Zahra Mahdian Baygi (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad, Iran; 3. Student Research Committee, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Rana Rahimi Kakhki (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad, Iran; 2. Student Research Committee, Faculty Of Medicine, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
3. Zahra Behrooznia (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad, Iran; 2. Student Research Committee, Faculty Of Medicine, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
4. Fatemeh Hosseinnezhad (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad, Iran; 2. Student Research Committee, Faculty Of Medicine, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
5. Hosein Jalali Rad (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad, Iran; 2. Student Research Committee, Faculty Of Medicine, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
6. Maryam Ghandehari (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad, Iran; 2. Student Research Committee, Faculty Of Medicine, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
7. Pouya Ghaderi (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad, Iran)
8. Ali Shariat Razavi (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad, Iran; 2. Student Research Committee, Faculty Of Medicine, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
9. Mokhtar Ahmadi (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad, Iran; 2. Student Research Committee, Faculty Of Medicine, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
10. Sepideh Mansouri Majordi (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad, Iran; 2. Student Research Committee, Faculty Of Medicine, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
11. Kamran Ghaffarzadegan (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad, Iran)
12. Seyede Talerehe Mohaddess (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad, Iran)
13. Alireza Bari (Gastric Cancer Research Group, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Gastric cancer is the second leading cause of cancer-related deaths worldwide and the most common gastrointestinal cancer in Iran. Chemokine ligand 5 (CCL5/RANTES) is one of the most potent angiogenic factors that plays an important role in tumor growth, invasion, and metastasis. We aimed to assess the serum level of CCL5 in patients with gastric adenocarcinoma and its relation with histological grade and tumor stage, as well as the disease prognosis. Seventy-four patients with gastric adenocarcinoma that had undergone gastrectomy and 96 non-tumoral cases in which gastric cancer was ruled out by gastroscopy and biopsy were enrolled. Demographic and epidemiological characteristics and patient survival data were reviewed. Histological type, grade, and tumor stage (TNM) were determined by a single expert pathologist. Helicobacter pylori infection status and CCL5 serum level were measured by ELISA. Data were analyzed using SPSS software version 16. Patients with gastric adenocarcinoma had significantly higher serum CCL5 level compared with control group (P < .001). Higher serum CCL5 levels were associated with lower histological differentiation (P < .001), higher depth of tumor invasion (P = .022), more frequent lymph nodes involvement (P = .028), and advanced tumor stage (P = .002). The overall survival of patients with CCL5 levels higher than 70.671 pg/ml was significantly lower than those with lower than this cutoff (P = .043). Serum CCL5 levels might be utilized as a predictive marker of tumor behavior and disease prognosis in patients with gastric adenocarcinoma. Further studies to assess tissue expression of CCL5 and its gene polymorphisms are suggested.

Corresponding Author: Zahra Mahdian Baygi (Gastric cancer research group, Mashhad University of Medical Sciences, Mashhad, Iran; 3. Student research committee, Mashhad university of medical sciences, Mashhad, Iran)
Detection Of BRCA1 Exon 11-A Mutations Among Breast Cancer Patients In Azerbaijan

1. Solmaz Dianati (Islamic Azad University Ahar Branch.Faculty Of Science.Biology Department Genetics Field)
2. Mohamad Ali Hossainpour-Faizi ()
3. Nasser Pouladi ()
4. MinaAdampourezare ()
5. Azarfam Parvin ()
6. Akbar Samir (Payame Noor University Rey Branch.Faculty Of Science.Biology Department Genetics Field)

Abstract

Breast cancer is the most common cancer in women world-wide one-third of cancers in women are included. Our multi-year study on patients with this cancer represents the lower age for breast cancer patients undergoing surgery in the region. This cancer is the second leading cancer killer among women, after lung cancer. The results of a study on breast cancer cases in Iran suggests that breast cancer patients in Iran are relatively younger than their Western counterparts. More than 15 percent of healthy women with at least one first-degree relative with breast cancer; experience has shown that the risk of breast cancer in these individuals is doubled. 20 to 30 percent of breast cancer patients have a family history of this cancer. Proposed for breast cancer genes important as genetic factors include genes with high penetrance follows: BRCA1, BRCA2, P53, PTEN, STK11 / LKB1, CDH1. While others, such as ATM, CHECK2, PALB2, BRIP1 that genetic factors are considered average. BRCA1 gene are discussed in this article. The aim of this study was to evaluate mutations in exons 11-A gene BRCA1 in Azerbaijani women with breast cancer. The study also identified possible genetic problem a number of families of patients, the first data about databases this gene in the northwestern area of the country's population will bring. In this study of 30 cancer patients during surgery to lower the age of forty years and get blood samples and exons 11-A BRCA1 gene were studied. PCR and Direct sequencing methods were used for this study. There are two synonymous mutations that is new identification were reported for the first time: 2 mutation of Ser 589 Thr in the two samples was observed. BRCA1 gene as a tumor suppressor gene the large and important role in DNA repair through recombination Homologous, maintaining stability of chromosomes, DNA damage checkpoint activation and cell cycle regulation. Therefore changes in the expression levels of BRCA1 gene can lead to vulnerability breast cells to function as oncogenes. BRCA1 gene has 24 exons and a protein with the same name during the 1863 amino acids. This gene is on the long arm of chromosome 17, paragraph 21 (21q17).gene BRCA1 ( Breast Cancer Susceptibility) was cloned in 1996 by Miki et al. Screening for mutations in exon 22 encoder, the role of this gene in about 45% of breast cancers are hereditary and about 80 percent of eligible families both breast and ovarian cancer revealed. Mutation in the BRCA1 gene in germ cells cause susceptibility to breast and ovarian cancer . Mutations in this gene 5 to 10 percent of breast cancer cases and 20 to 40 percent of breast cancers are familial. This amount is equivalent risk about 85 to 60 percent in lifetime. In carriers of mutations in the deadly BRCA1 up to the age of 40 to 20 percent risk of developing breast cancer and 17 percent risk of ovarian cancer. This risk increases with age rises so that by the age of 80 for breast cancer risk 82 and for the risk of ovarian cancer by age 70 is 39 percent and up to 80 years of age is 54%. Reports from around the world shows that the incidence
of BRCA1 mutations from 1/8 to 13/1 and the Asian countries the rate from 0.8 percent to 8.6 percent. In these study, the results showed that there are two new mutations in exon 11-A BRCA1 gene in Azeri women with breast cancer.

**Corresponding Author:** Mohamad Ali Hossainpour-Faizi ()
Molecular Pathways In Gastric Cancer

Abstract

Gastric cancer is one of the most common cancers (fifth) and the third cause of cancer death in the worldwide. Mechanism of pathogenesis of gastric cancer is still unclear and rely on multiple factors includes environmental and genetics factors. The important environmental factor of gastric cancer is infection with helicobacter pylori which classified as class one of carcinogens. There are several genes and pathways that play role in gastric cancers and dysregulated during gastric carcinogenesis. Pathways which involved in normal development like Wnt/ b-catenin signaling, Hedgehog signaling, Hippo pathway, Notch signaling and oncogenic pathways such as cell cycle, NF-kB and EGFR have been found that dysregulated in gastric cancer. Epithelial mesenchymal transition (EMT) cancer, which is important during embryogenesis and tumorigenesis, have role in initiation, invasion, metastasis and progression of gastric cancer. Matrix metalloproteinase have important role in carcinogenesis and the levels of MMPs increased in many cancers as well as gastric cancer. Although surgery is the only treatment of gastric cancer but the understanding of biological processes of this pathways help to development new drugs for gastric cancer. Trastuzumab which is anti-HER2 monoclonal antibody, is effective against HER2-positive gastric cancer. There are several agents that investigates for treatment of gastric cancer in clinical trial. The molecular markers is useful to detect gastric cancer in early stages and take appropriate action for treatment and prevents from progression of cancer.

Corresponding Author: Mohammad Reza Abbaszadegan (Division of Human Genetics, Immunology Research Center, Avicenna Research Institute, Mashhad University of Medical Sciences, Mashhad, Iran)
Immune Modulation By Tumor Derived Exosomes: Role Of Engineering In Immune Stimulation

1. Adeleh Taghikhani (Department Of Immunology, Faculty Of Medical Sciences, Tarbiat Modarres University)
2. Marzieh Ebrahimi (Department Of Regenerative Medicine, Royan Institute For Stem Cell Biology And Technology)
3. Zuhair Mohammad Hassan (Department Of Immunology, Faculty Of Medical Sciences, Tarbiat Modarres University)

Abstract

Exosomes are nano vesicles and member of the larger family named Extracellular Vesicles which are released by any kind of cells such as immune cells and tumor cells. They are considerable messengers that can exchange proteins and genetic materials between the cells. Within the past decade, Tumor derived Exosomes (TEX) have been emerged as important mediators in cancer initiation, progression and metastasis as well as host immune suppression and drug resistance. Furthermore we performed a systematic search with combining the key words ‘Tumor derived exosomes’, ‘Immune suppression’ and ‘Exosome Engineering’ on Google scholar, Scopus, and ISI from English articles which studied on tumor derived exosomes and their immune function. Referring to recent progresses in understanding the role of exosome in immune suppression, tumor derived exosomes are being involved in the transmission of signals between tumor cells and immune cells (Dendritic cells, Natural Killer cells, CD4+ and CD8+ T cells, etc.) through which the efficiency against tumor antigens would decrease and consequently the regulatory responses mediated by T regulators and Myeloid-derived Suppressor Cell (MDSCs) would increase. Although tumor derived exosomes consist of tumor antigens and several Heat Shock Proteins such as HSP70 and HSP90 to induce immunity against tumor cells, they contain inhibitory molecules like Fas ligand (Fas-L), Transforming Growth Factor Beta (TGF-β) and Prostaglandin E2 (PGE2) leading to decrease the cytotoxicity and promote the regulatory effects. As mentioned above, TEX have some potential molecules which are beneficial themselves but the inhibitory molecules overcome the tumor antigens and HSPs. Some macromolecules such as miRNAs, HSPs and activatory ligands have been recognized as potent immune inducers that could be used as agents to construct a TEX based tumor vaccine. Here, we discussed emerging engineered exosomes as a novel therapeutic agent and considered the associated challenges. It is also necessary to gather research data from engineered exosomes to assess their effectiveness in immune induction In vitro and In vivo.

Corresponding Author: Marzieh Ebrahimi (Department of Regenerative Medicine, Royan Institute for Stem Cell Biology and Technology)
Double Targeting, Controlled Release And Reversible Delivery Of Daunorubicin To Cancer Cells By Polyvalent Aptamers-Modified Gold Nanoparticles

Abstract

Acute lymphoblastic leukemia (ALL) is the most common type of cancer in children. Clinical use of daunorubicin (Dau) in treatment of leukemia has been restricted because of its cardiotoxicity. Targeted delivery of anticancer drugs could decrease their off-target effects and enhance their efficacy. In this study a modified polyvalent aptamers (PA)-Daunorubicin (Dau)-Gold nanoparticles (AuNPs) complex was designed and its efficacy was assessed in Molt-4 cells (human acute lymphoblastic leukemia T-cell, target). Dau was efficiently loaded (10.5 μM)onto 1 mL of PA-modified AuNPs. Dau was released from the PA-Dau-AuNPs complex in a pH-sensitive manner (faster release at pH 5.5). The results of flowcytometry analysis indicated that the PA-Dau-AuNPs complex was efficiently internalized into target cells, but not into non-target cells. The results of MTT assay were consistent with the internalization data. PA-Dau-AuNPs complex had less cytotoxicity in U266 cells compared to Dau alone and even Apt-Dau-AuNPs complex. The PA-Dau-AuNPs complex had more cytotoxicity in Molt-4 cells compared to Dau alone and even Apt-Dau-AuNPs complex. Cytotoxicity of PA-Dau-AuNPs complex was effectively antagonized using antisense of polyvalent aptamers. In conclusion, the designed drug delivery system inherited the properties of efficient drug loading, tumor targeting, pH-dependent drug release and controllable delivery of Dau to tumor cells. Furthermore, the cytotoxicity of PADau-AuNPs complex could efficiently be antagonized using the antisense of polyvalent aptamers.

Corresponding Author: Seyed Mohammad Taghdisi (Targeted Drug Delivery Research Center, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran)
Abstract

Breast cancer is the most frequently cancer and the second cause of mortality in women. The etiology of breast cancer is multifactorial, genetic, environmental and lifestyle factors which promotes the growth of cancer cells. By preventing cancer, the number of new cases of cancer in a group or population is lowered. Breast cancer is a preventable disease. Lifestyle changes have been shown in studies to decrease breast cancer risk even in high-risk women. Some steps that we can take to decrease our risk are: limit alcohol, control our weight, be physical active, breast-feed, ... Eating a healthy diet might reduce our risk of breast cancer. For example, eating plenty of vegetable, fruits, soy, green tea, Antioxidant, eating less fat, ... Women who have inherited changes in the BRCA1 and BRCA2 genes have a higher risk of breast cancer and for them exposure to radiation, such as chest X-rays, may increase the risk of breast cancer. Breast cancer symptoms vary widely—from lumps to swelling to skin changes and many breast cancers have no symptoms at all but In some cases, the first sign of breast cancer is a new lump or mass in the breast that you and your doctor can feel. The other possible symptoms of breast cancer include: 1) swelling of all or part of the breast 2) skin irritation or dimpling 3) breast or nipple pain 4) redness, scaliness of the nipple or breast skin. Antioxidant are nutrients that can slow oxidative damage to our body's tissues. Antioxidants can help prevent breast cancer and they are found in plant foods at bright, orange carrots and purple blueberries. The most common Antioxidants are vitamin A, C and E, betacarotene, selenium and lycopene. cancer research is the intense scientific effort to understand disease processes and discover possible therapies. As Antioxidants have anti-cancer properties, it recommended in daily diet.

Corresponding Author: elham dindarlou (elham_dindarlo@yahoo.com)
Anticancer Effects Of Chrysin On Colon Cancer Cells: Down Regulation Of Sall4

1. Malihe Bahadori (Department Of Biology, Damghan Branch, Islamic Azad University, Damghan, Iran)
2. Elaheh Amini (PhD, Department Of Animal Biology, Faculty Of Biological Sciences, Kharazmi University, Tehran, Iran)
3. Javad Baharara (Professor, Department Of Biology, Research Center For Animal Development Applied Biology, Mashhad Branch, Islamic Azad University, Mashhad, Iran)

Abstract

The SALL4/Sall4 is constitutively expressed in human and mice. SALL4 mRNA could be used as a marker for the diagnosis of different cancers. On the other hand, Chrysin has diverse biological properties. Objectives: In our study, the effects of the chrysin were investigated on the CT26 colon cancer in vitro and in vivo. Further expression of stem cell marker sall4, Bax were analyzed. Antitumor efficacy of chrysin on transplanted CT26 tumor cells in BALB/c mice was investigated. In addition, mRNA expressions of sall4, Bax were analyzed with RT-PCR. The in vivo assay revealed remarkable reduction of colon tumor volume in treated mice (8, 10 mg/kg) as compared with untreated mice. RT-PCR elucidated that chrysin attenuated tumor volume with sall4 down regulation and Bax up regulation. Consequently, it demonstrated that chrysin accomplished anticancer effect on colon cancer cells via apoptosis induction and attenuation the expression of sall4 which introduced chrysin as efficient apoptosis based therapeutic agent against colon cancer.

Corresponding Author: Malihe Bahadori (Department of Biology, Damghan Branch, Islamic Azad University, Damghan, Iran)
Breast cancer, Reasons & Prevention

1. Marziyeh Pourmand (Azad University, Zarghan, Iran)

Abstract

Breast cancer is the second epidemic cancer in the world & the second deadly cancer after lung cancer between women. Around 5-10 kinds have genetic root. Breast is organized exuding glands with the duty of producing milk & growing alternatively such as other body cells & sometimes is resting. Two groups have high risk of catching breast cancer: 1. Ones who have cancer record in their family, 2. Ones who exposed to environmental factors of Carcinogenic work. Jumping in brca 1, lorca2 gens which are two gens from genes to that their basic duty in controlling DNA healthiness & Restoration Jumps & damages of DNA which cause DNA repair & return to usual play the most important role between the known gens in breast cancer. There are a group of gens which are known as Suppressor gene of tumor & as a whole are responsible to space 1/4 of all of Inherited breast cancers. Also, the increase of Estrogen Hormone in body has an important role. Furthermore, HRT (Hormone Replacement therapy ) is in element of exposing this kind of breast. "HRT" is the replacement hormone therapy which during this a Postmenopausal woman receiving ne placement Hormone. Breast cancer has different kind which point to two of them: 1. Inflammation cancer: happen in skin & causing breast to become red & swollen & breast is becoming orange- skin like. 2. Vessel cancer: in this kind, cancer cello grow in breast vessel. In this kind, small Mass is creating in breast & also some secretions is existing from nipple. There are different ways to prevent this kind of cancer which can point to Physical exercises, reducing fat using, increasing the use of olive oil & omega3 & avoid to contact Carcinogenic work elements such as breath in insecticides, unnecessary radiators X-rays & pregnancy before age 30. We can cure breast cancer in different ways such as: Chemotherapy, Hormone therapy, biologic treatments, etc. Be careful that in addition to women, men are exposed to this kind of cancer but the risk is so low & from every 100 patients approximately 1 of them is man.

Corresponding Author: Marziyeh pourmand (Azad university, Zarghan, Iran)
Novel Non-Viral Carriers Based On Polyethylenimine For Improved Gene Delivery To Cancer Cells

1. Zahra Salmasi (Pharmaceutical Research Center, School Of Pharmacy, Mashhad University Of Medical Sciences)
2. Khalil Abnous (Pharmaceutical Research Center, School Of Pharmacy, Mashhad University Of Medical Sciences)
3. Mohammad Ramezani (Pharmaceutical Research Center, School Of Pharmacy, Mashhad University Of Medical Sciences)

Abstract

Gene therapy is emerging as the potential treatment for various forms of cancers. Despite considerable progress, there are some limitations for clinical use such as providing carriers with high transfection efficiency and minimum toxicity. The present study was designed for synthesis of carriers with enhancement in gene transfection efficiency and reduction in cytotoxicity. Novel carriers were synthesized with substitution of 10%, 30% and 50% of Polyethyleneimine 25 kDa (PEI25) primary amines with Histidine, 3-Pyridyl acetate and Piperazin. Special characterizations of carriers were performed. Particle size and zeta potential of the polyplexes was measured. Ethidium bromide exclusion assay and buffering capacity of the carriers was evaluated. Transfection efficiency and cytotoxicity of polymers was measured in murine neuroblastoma cells. Finally, In vivo experiment for determination of polyplex transfection and biodistribution was performed. The average size of polyplexes was in the range of 81–186 nm and surface charge remained enough positive. Carriers with 30% and 50% substitutions of primary amines of PEI 25 with piperazine and histidine could significantly increase transfection efficiency and decrease cytotoxicity. 24 h after intravenous administration of the polyplexes in Balb/c mice, high luciferase expression was detected in lungs and mortality was decreased compared to PEI25. These modifications of PEI 25 can significantly improve transfection efficiency and reduced cytotoxicity. Due to the high gene expression in lungs with no mortality, this modified carrier could be used for tissue-specific gene delivery in vivo.

Corresponding Author: Mohammad Ramezani (Pharmaceutical Research Center, School of Pharmacy, Mashhad University of Medical Sciences)
Abstract

Several studies indicate that public awareness is low about cancer and ways to prevent it. One way to increase awareness and prevention of cancer is increased social interaction and expanding the network of relationships in connection with this disease. This study examines construct and validate a questionnaire in order to measure social interaction that helps to prevent cancer. This method is analytical. Sampling is random and of 147 residents of Mashhad. The questionnaire is constructed from three dimensions relational, structural and cognitive that is based on Nahapiet and Ghoshal. Use of the software SPSS for the analysis of questionnaires. Methods used include item analysis (the degree of difficulty, discrimination coefficient and loop method), content validity and construct validity by confirmative factor analysis and internal consistency and reliability was reviewed by alpha coefficient for all inquiries and its dimensions. Results show confirmative factor analysis was confirmed about statements regarding dimensions relational, structural and cognitive and obtained alpha statements in various dimensions and in all statements about 0.8. Generally low the average score of respondents in the field of social interactions cancer prevention considering the standard deviation. Mean scores of social interaction index is low and there is not a significant difference in different age groups and educational. According to the results, we can say the questionnaire is a reliable and valid and the measurement tool made can weigh social interactions cancer prevention as well and help to better planning in the field of cancer prevention. This comes with increased social awareness that is the formation of networks of social relations between actors and facilitates the programs of cancer prevention.

Corresponding Author: Seyed Alireza Miranvari (PhD sociology student at Ferdowsi University of Mashhad)
The Effect Of Recovered Overtrained Exercise On Mitogen-Stimulated And Non-Stimulated Splenocytes Response

1. Zahra Gholamnezhad (Neurogenic Inflammation Research Centre, Mashhad University Of Medical Sciences, Mashhad, Iran Department Of Physiology, Faculty Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Mohammad Hossein Boskabady (Neurogenic Inflammation Research Centre, Mashhad University Of Medical Sciences, Mashhad, Iran Department Of Physiology, Faculty Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
3. Mahmoud Hosseini (Neurocognitive Research Centre, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

It has been shown that the imbalanced immune system with poor Th1 and overactive Th2 responses can result in a wide variety of chronic illness and cancer. In this study the effect of recovered overtrained exercise on Th1/Th2 balance was evaluated in rat isolated splenocytes. Twelve male Wistar rats weighing 200-250g were randomly divided into two groups: Control (n=6) and recovered overtrained (OR) (exercise plus 2 weeks recovery) (n=6). Exercised rats were summated to sever running protocol (V=25m/min, 60min/day for 6 days a week) lasted 11 weeks (exercise bouts increased in 8-11 weeks). At the end of the study; cell viability, proliferation, and interleukin 4 (IL-4) and interferon-γ (IFN-gmma) secretion in non-stimulated, concavaline A (Con A)-stimulated splenocytes were evaluated in both groups. Cell viability and proliferation of stimulated and non-stimulated splenocytes increased in the OR group compared to control group (p<0.01-p<0.001). There were not significant differences in IL-4 concentrations between non-stimulated splenocytes isolated from both groups. IL-4 concentration of Con A-stimulated cells supernatant in OR group was higher than control group (p<0.01). There were not significant differences in non-stimulated and stimulated cell IFN-gmma concentration between groups. In non-stimulated cells, IFN-gmma/IL-4 ratio of OR group was not significantly different from control group. In ConA-stimulated cells, IFN-gmma/IL-4 ratio was lower in exercise groups than control (p<0.01). The result showed that two weeks recovery restored Th1/Th2 balance, in non-stimulated splenocytes of overtrained animals. While in mitogen stimulation situation the susceptibility to chronic non-communicable diseases like cancer did not change.

Corresponding Author: Zahra Gholamnezhad (Neurogenic Inflammation Research Centre, Mashhad University of Medical Sciences, Mashhad, Iran Department of Physiology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran)
The Role Of Humor In The Hope And Posttraumatic Growth Among Patients With Leukemia

1. Amir Karami (M. A. Student Of Psychology, Faculty Of Education And Psychology, University Of Sistan And Baluchestan, Zahedan, Iran)
2. Farhad Kahrazei (Assistant Professor, Faculty Of Education And Psychology, University Of Sistan And Baluchestan, Zahedan, Iran)
3. Ali Arab (Assistant Professor, Faculty Of Education And Psychology, University Of Sistan And Baluchestan, Zahedan, Iran)

Abstract

Positive psychology approach has been growing in recent years; Humor is an adaptive evolution tool that as a mechanism for coping and relieving stress plays a role in the events of stressful life and may make it easy to stand physical or psychological pain resulting from shock of a cancer diagnosis. The aim of this study was to investigate the role of humor in the hope and posttraumatic growth among patients with Leukemia. A descriptive study was correlational. For this purpose 70 patients with leukemia in the city of Zahedan were selected by available sampling method. The instrument used in this study was the sense of humor questionnaire (SHQ) (Khoshouei, Oreizy and Aghaei, 2009), hope (Snyder et al, 1991) and Posttraumatic Growth (PTGI) (Tedeschi and Calhoun, 1996). For the data analysis, correlation and stepwise regression analysis method was used. The results showed that between the total score of the humor and component enjoyment of humor (p<0.01), and sense of humor in stressful conditions (p<0.05) with hope there is a significant positive relationship. Also the results showed that the total score of humor significantly predicts hope (p<0.01), another result was that there is a significant positive relationship between the total score of the humor with posttraumatic growth (p<0.001) and the results of regression showed that the total score of the humor can significantly predict posttraumatic growth (p<0.01). Humor affects the rate of hope against this disease and strengthens this ability in patients that they can find a solution against pressures and hopefully proceed toward overcoming their problem. Also for these patients Humor plays a significant role in the positive life changes such as social relationships.

Corresponding Author: Amir Karami (M. A. Student of Psychology, Faculty of Education and psychology, University of Sistan and Baluchestan, Zahedan, Iran)
Abstract

The increasing incidence of leukemia is one of the problems of modern medical science. People with diagnosis of cancer need to keep hope during the process of treatment, diagnosis of cancer also sometimes leads to post traumatic growth. The aim of this study was to investigate the role of daily spiritual experiences in the hope and post traumatic growth among patients with Leukemia. A descriptive study was correlational. For this purpose 70 patients with leukemia in the city of Zahedan were selected by available sampling method. The instrument used in this study was the daily spiritual experiences questionnaire (DSES) (Underwood and teresi, 2002), hope (Snyder et al, 1991) and Post traumatic Growth (PTGI) (Tedeschi and Calhoun, 1996). To analyze the relationship between variables and predict hope and post traumatic growth changes, correlation and stepwise regression analysis methods were used. The results showed that among the total score of the patient in the scale of daily spiritual experiences and components of God's presence, Relation with God and Caring for others with hope and post traumatic growth there is a significant positive relationship (p<0.01) and only total score of daily spiritual experiences scale can predict hope (p<0.01). Also the total score of daily spiritual experiences (p<0.01) and component of Caring for others (p<0.05) can significantly predict post traumatic growth. According to the results, the daily spiritual experiences and relation with God and feeling guidance from God in patients with leukemia, causes that the person can better appreciate each day, also increasing spiritual experiences alongside medical therapy in patients with cancer can return a lot to society and make them hopeful to continue their lives and leads to generate positive changes in their lives.

Corresponding Author: Amir Karami (M. A. Student of Psychology, Faculty of Education and psychology, University of Sistan and Baluchestan, Zahedan, Iran)
Evaluation Cytotoxic Activities Of Schiff Base-Derived Copper (II) Complex

1. Soheyla Yadamani (Department Of Biochemistry And Biophysics, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
2. Ali Neamati (Department Of Biochemistry And Biophysics, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
3. Masoud Homayouni Tabrizi (Department Of Biochemistry And Biophysics, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
4. Mozghan Soltani (Department Of Biochemistry And Biophysics, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
5. Safar Ali Beyramabadi (Department Of Biochemistry And Biophysics, Islamic Azad University, Mashhad Branch, Mashhad, Iran)

Abstract

Breast cancer is the most common cancer among women. Usually breast cancer either begins in the cells of the lobules, which are the milk-producing glands, or the ducts, the passages that drain milk from the lobules to the nipple. Schiff base, named by the chemist Hugo Schiff, is a functional group that contains a double bond between carbon and nitrogen. Schiff bases play an important role in inorganic chemistry as they easily form stable complexes with most transition metal ions. Many studies have been reported regarding the biological activities of Schiff bases, including their anticancer, antibacterial, antifungal and herbicidal activities. Copper, is a cofactor essential for the tumor angiogenesis processes, whereas other transition metals are not. In this study, were investigated the anti-proliferation properties of copper Schiff base complex N'-N1 dipirodoxil-1-2 diaminobenzene on breast cancer cells (Tubo). Tubo cells were cultivated and treated with different concentration of copper Schiff base complex (62.5, 125, 250, 500, 1000 µg/ml). The result of MTT assay showed that the cell proliferation was decreased as time and dose dependent manner with IC50 about 125µg/ml. Morphological analysis reveals changes in treated cells such as reduction volume of cells, cell deformation and shrinkage and decrease size of cells. The results of this study use of Schiff base in cancer treatment offers some possibilities, including the possibility of destroying cancer tumors with minimal damage to healthy tissue and organs, as well as the detection and elimination of cancer cells before they form tumors.

Corresponding Author: Ali Neamati (Department of Biochemistry and Biophysics, Islamic Azad University, Mashhad Branch, Mashhad, Iran)
Study On Cytotoxic Action Of Schiff Base Manganese (II) Complex

1. Samira Yadamani (Department Of Biochemistry And Biophysics, Mashhad Branch, Islamic Azad University, Mashhad, Iran)
2. Ali Neamati (Department Of Biochemistry And Biophysics, Mashhad Branch, Islamic Azad University, Mashhad, Iran)
3. Masoud Homayouni Tabrizi (Department Of Biochemistry And Biophysics, Mashhad Branch, Islamic Azad University, Mashhad, Iran)
4. Mozhgan Soltani (Department Of Biology, Mashhad Branch, Islamic Azad University, Mashhad, Iran)
5. Safarali Beyramabadi (Department Of Chemistry, Mashhad Branch, Islamic Azad University, Mashhad, Iran)

Abstract

Cancer is the name given to a collection of related diseases. In all types of cancer, some of the body's cells begin to divide without stopping and spread into surrounding tissues. The Schiff base complexes have been used in catalytic reactions and as models for biological systems. This may be attributed to their stability, biological activity. Schiff base form an important class of organic compounds with a wide variety of biological properties. Many studies have been reported regarding the biological activities of Schiff bases, including their anticancer, antifungal, antibacterial, and herbicidal activities. Previous studies have shown that the synthesized complexes of some metals have various effects such as anti-cancer properties. The survey was conducted to investigate the antiproliferative effects of Mn2+ complex of the N'-N1 dipirodixol-1-2 diaminobenzene Schiff base. The Tubo cells were exposed with various concentrations (62.5, 125, 250, 500, 1000 μg/ml) of desired Schiff base and their morphological changes are examined using an inverted microscope. MTT assay was conducted for evaluation of anti-proliferative properties of this compound. The viability of Tubo cells was suppressed with dose-dependent manner (IC50 about 62.5 μg/ml). Morphological changes such as decrease volume of cells, changes in the shape (cell shrinkage) and reduction in the size was observed in treated cells. The Mn2+ complex of N'-N1 dipirodixol-1-2 diaminobenzene Schiff base showed antiproliferative activity on tubo cells and induced apoptosis in these cells which reveals anti-cancer properties of this compound.

Corresponding Author: Ali Neamati (Department of Biochemistry and Biophysics, Mashhad Branch, Islamic Azad University, Mashhad, Iran)
Expression Analysis Of Transcription Factor GLI3 In Esophageal Squamous Cell Carcinoma Using Real-Time PCR

1. Farzaneh Motiei Bahabadi (Department Of Biology, Islamic Azad University, Damghan, Iran)
2. Maryam Borhan Elmi (Department Of Biology, Islamic Azad University, Damghan, Iran)
3. Mohammad Hadi Sadeghian (Cancer Molecular Pathology Research Center, Faculty Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
4. Mohammad Ghodsi (Center Of Pathological And Medical Diagnostic Services, Iranian Academic Center For Education, Culture & Research (ACECR), Mashhad Branch, Mashhad, Iran)

Abstract

Sonic Hedgehog (SHH) cell signaling pathway has critical role in pathogenesis of different tumors. GLI3 gene, as a main target gene of this pathway, is correlated to different aspects of tumorigenesis in a variety of cancers. Our aim in this study was to analyze GLI3 gene expression in esophageal squamus cell carcinoma (ESCC) and to evaluate its correlation with clinicopathological factors. GLI3 gene expression analysis was performed on 49 tumors and their corresponded normal tissues of ESCC patients. After RNA extraction and cDNA synthesis, gene expression was analyzed using relative comparative Real-time PCR. GLI3 was over expressed in 8.2% of tumor samples while its under expression was detected in 4.1%. There was a significant inverse correlation between GLI3 gene expression and tumor cell metastasis into the lymph nodes; so that in lymph node metastatic tumor samples GLI3 expression was decreased while in tumor samples without lymph node metastasis the gene expression was increased. According to the role of SHH cell signaling pathway in tumorigenesis process of different cancers; expression of GLI3, as one of its target genes, in ESCC may confirm activation of this pathway in ESCC. Since GLI3 gene expression was inversely correlated to the lymph node metastasis of tumor cells, it may be introduced as a prognostic factor for ESCC metastasis.

Corresponding Author: Mohammad Ghodsi (Center of Pathological and Medical Diagnostic Services, Iranian Academic Center for Education, Culture & Research (ACECR), Mashhad Branch, Mashhad, Iran)
Hyper Methylation Of TPM-1 And TPM-2 In Colorectal Cancer

Abstract

Colorectal cancer is the third most commonly diagnosed cancer and the third leading cause of cancer death in both men and women in the US. It has low survival, poor prognosis and the highest incidence rate in all of the world. So, investigating its underlying mechanisms is essential for early detection and treatment. Several genetic and epigenetics alterations are involved in carcinogenesis of colorectal cancer. Among them, promoter hyper-methylation is an important epigenetic mechanism of gene silencing. Otherwise, down regulation of tropomyosin isoforms, a family of cytoskeleton proteins, has been shown important in colorectal cancer. So, the role of promoter hyper-methylation in tropomyosin suppression was investigated in several studies in colorectal cancer. In this review, we are focusing on the crucial role of epigenetic changes in tropomyosin in colorectal cancer. Methylase enzyme inhibition significantly increases TM1 expression. Additionally, TPM1 and TPM2 mRNA are unregulated upon inhibition of methylation. Bisulfite sequencing showed considerable cytosine methylation in metastatic cell lines that correlated with a reduced expression of TPM1 and TPM2. Nearly all of the studies suggest that epigenetic suppression of TPM1 and TPM2 may change TGF beta tumor suppressor function and cause to metastatic properties of tumor cells. Furthermore, promoter hyper-methylation of TPM1 and TPM2 genes seems to play an important role in tropomyosin down regulation in ESCC.

Corresponding Author: Amir Azizi (Department of Biology, Tonekabon Branch, Islamic Azad University, Tonekabon, Iran)
Abstract

A diagnosis of childhood cancer is a formidable challenge that can put the family's stability and adaptive functioning at a great risk. Following diagnosis, families not only have to face the difficulties of helping a child cope with the physical and emotional distress of the medical treatments, they must also struggle, both collectively and individually, with the ambiguity associated with the short- and long-term prognosis of this disease and the side effects of treatment. In this article, we have tried to provide a review of a number of related articles with the purpose of collecting data on the process of adjustment to childhood cancer, short- and long-term effects on siblings in particular, and ways of more effective assessment and intervention. We have put primary focus on posttraumatic stress (PTS), one of the probable long-term effects of childhood cancer on siblings which is yet to be studied in order to investigate more closely its frequency and possible demands. Formulating assessment and intervention methods with regards to PTS and other long-term effects, as well as addressing the limitations of previous research can be considered for future works.

Corresponding Author: Kimia Alizadeh (Veterinary Medicine Student, Ferdowsi University of Mashhad)
Whole-Exome Sequencing Reveals A Novel Damaging Mutation In Seprase In A Family With Esophageal Squamous Cell Carcinoma

1. Fatemeh Fardi Golyan (Division Of Human Genetics, Immunology Research Center, Avicenna Research Institute, Mashhad University Of Medical Sciences, Mashhad, Iran. Medical Genetics Research Center, Medical School, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Morteza Moghaddassian (Division Of Human Genetics, Immunology Research Center, Avicenna Research Institute, Mashhad University Of Medical Sciences, Mashhad, Iran)
3. Mohamad Mahdi Forghanifard (Department Of Biology, Damghan Branch, Islamic Azad University, Damghan, Iran)
4. Samaneh Talebi (Division Of Human Genetics, Immunology Research Center, Avicenna Research Institute, Mashhad University Of Medical Sciences, Mashhad, Iran)
5. Mohammad Reza Abbaszadegan (Division Of Human Genetics, Immunology Research Center, Avicenna Research Institute, Mashhad University Of Medical Sciences, Mashhad, Iran. Medical Genetics Research Center, Medical School, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Fibroblast activation protein (FAP) is a serine protease gene that fame as a potential cancer therapy target and is a type II transmembrane protein with the bulk extracellular domain, including the catalytic reign and highly expressed in activated fibroblastic cells in tumors, arthritis and fibrosis. The present study is sought to identify rare germline mutations in familial esophageal squamous cell carcinoma by next-generation sequencing (NGS). The coding regions of our proband was captured by Sure Select target enrichment system. The reads are mapped against UCSC hg19 human reference genome. The dbsNP 135 & 1000G were used for population allele frequencies. The homology modeling of the novel mutation (A459D) discovered in FAP gene was performed by using the online Swiss-Prot server for automated modeling and the resulted structure has been modified and analyzed by using bioinformatics software to thoroughly study the structural deficiencies caused by the novel mutation. A rare, novel, human mutation C1367A encoding Ala459 Asp (accession number: KT988039), occurring in the blade of the β propeller domain, was identified in 2 sisters with Esophageal Squamous Cell Carcinoma (ESCC). Also thirty-five percent of the mutations we identified were novel, indicating that screening methods, which none of them found in 70 control subjects. Moreover, structural studies of the novel mutation in FAP gene disclosed abnormalities in the structure of the mutant protein which supports its malfunctioning behavior. This study is the first to fully analyzed germline mutations of Apoptosis genes in familial ESCC patients. We prefer to analyze our data with pathway-oriented method for analyzing broad of data. Additionally, structural analyses of the novel mutant protein uncovered changes in the energy level and stereo chemical properties of the FAP gene that unfortunately altered the mutant protein's functionalities.

Corresponding Author: Mohammad Reza Abbaszadegan (Division of Human Genetics, Immunology Research Center, Avicenna Research Institute, Mashhad University of Medical Sciences, Mashhad, Iran. Medical Genetics Research Center, Medical School, Mashhad University of Medical Sciences, Mashhad, Iran)
Involvement Of Intrinsic Apoptotic Signaling Pathway In 4T1 Breast Cancer Cells By Sargassum Muticum Polysaccharide Fraction

1. Mohammad Nabiuni (Department Of Cell And Developmental Biology, Kharazmi University, Tehran, Iran)
2. Elaheh Amini (Department Of Animal Biology, Faculty Of Biological Sciences, Kharazmi University, Tehran, Iran)
3. Mahnaz Fathi (Faculty Of Biological Sciences, Kharazmi University, Tehran, Iran)

Abstract

The Sargassum muticum is receiving great interest due to its beneficial biocompounds with high pharmacological potential. Meanwhile, rare information is reported on anti-cancer efficacy of polysaccharide fraction from this marine seaweed. This study was designed to evaluate the effects of S. muticum polysaccharide fraction on 4T1 metastatic breast cancer cells. The polysaccharide fraction was extracted by simple and un-expensive method. 4T1 cells were cultured in RPMI 1640 medium containing 10% FBS. The cytotoxic effects of the polysaccharide fraction of S. muticum on 4T1 cancer cells was investigated using MTT assay. Pre-apoptotic efficacy was measured by fluorescence microscopy using Acridine Orange- Propodium Iodide staining. In addition, modulation of apoptotic pathway was assessed by caspase -3, -7, -8 assays. Further, wound healing assay was performed to assess anti-invasiveness effect of S. muticum polysaccharide fraction. FTIR and phenol sulfuric acid method elucidated polysaccharide extraction. It was shown that extracted polysaccharide (15-500 µg/ml) significantly induced toxicity on 4T1 cells after 4, 48 h (as dose dependent manner). Further, AO/PI assay were recorded apoptotic DNA fragmentation subsequent to S. muticum polysaccharide fraction exposure. Caspase -3, -9 enzyme activities suggested stimulation of intrinsic apoptosis pathway in 4T1 cancer cells, suggesting pro-apoptotic potential of marine flora extracted polysaccharide. Wound healing assay demonstrated that blockage of 4T1 cell invasion in a concentration dependent manner under exposure with isolated polysaccharide. Ultimately, we believe S. muticum polysaccharide fraction can serve as a useful cancer therapy for the 43 treatment of metastatic breast cancers, but complementary investigation was required for clinical applications.

Corresponding Author: Mohammad Nabiuni (Department of Cell and Developmental Biology, Kharazmi University, Tehran, Iran)
Effective Strategies For Increasing The Hope In Patients With Cancer: A Review

1. **Marzieh Azizi** (Master Student Of Midwifery Counseling, Research Student Committee, Mazandaran University Of Medical Science, Nasibeh Nursing And Midwifery Faculty, Sari, Iran. Corresponding Author (Marziehazizi70@Gmail.Com) Phone Number: 01133111969 Mobile: 09369100142)

2. **Forouzan Elyasi** (Department Of Psychiatry, Psychiatry And Behavioral Sciences Research Center, School Of Medicine, Mazandaran University Of Medical Sciences, Sari, Iran.)

Abstract

Introduction: Patients with cancer are faced with numerous physical and psychological problems that lead to lack of hope. Hope is a complex multidimensional and strong factor in recovery and effective adaptation of patients with cancer and its complications. Enhancing the hope level in these patients is an important action and accompanied with satisfaction results. This study was conducted with the aim of assessing effective strategies for increasing the hope in patients with cancer. The present study is a narrative review in which researchers conducted their computer search in public database like Google Scholar and more specifically databases such as Web of Science, Science Direct and PubMed with using keywords such as hope, strategies, cancer, social support, counselling and selected articles from 2000 to 2016. Overall 25 articles have been searched. Researchers reviewed the summary of all articles searched, 5 articles are excluded due to non-relevance and ultimately, they applied 20 full articles to compile this review. Researchers finding regarding effective strategies for increasing the hope in patient with cancer were categorized in 3 sections. Counselling strategies such as spirituality therapy group sessions or the presence of religious leaders in a hospital or clinic, holding individual and group counseling for patients and listen to their concerns and crisis management in disappointment patients, social and familial strategies like social and family support, having sympathetic care givers, to encourage strong family connections, providing economic resources of treatment and accompany patient in treatment process, psychiatrist's therapeutic-supportive strategies such as appropriate treatment rapport with patient, acceptance patient's projection, educating problem focused coping skills and help to psychological adjustment with disease and positive reinforcement, supportive psychotherapy with the aim of increasing optimism and acceptance of the disease in patients.

Conclusion: For improvement hope strategies among hospital's personals, considering periodic education for nurses of oncology ward regarding psychotherapy styles and crisis management seems helpful. Also presence of graduated midwifery counseling who familiar with promoting hope strategies in ovary and breast cancers wards or presence of religious leaders in hospital are proposed.

**Corresponding Author:** Najibeh Mohseni (BSc in medical records, Zare hospital, Mazandaran University of Medical Science, Sari, Iran.)
Effective Strategies For Increasing The Hope In Patients With Cancer

1. Marzieh Azizi (Master Student Of Midwifery Counseling, Research Student Committee, Mazandaran University Of Medical Science, Nasibeh Nursing And Midwifery Faculty, Sari, Iran)

2. Forouzan Elyasi (Department Of Psychiatry, Psychiatry And Behavioral Sciences Research Center, School Of Medicine, Mazandaran University Of Medical Sciences, Sari, Iran.)

3. Najibeh Mohseni (BSc In Medical Records, Zare Hospital, Mazandaran University Of Medical Science, Sari, Iran.)

Abstract

Patients with cancer are faced with numerous physical and psychological problems that lead to lack of hope. Hope is a complex multidimensional and strong factor in recovery and effective adaptation of patients with cancer and its complications. Enhancing the hope level in these patients is an important action and accompanied with satisfaction results. This study was conducted with the aim of assessing effective strategies for increasing the hope in patients with cancer. The present study is a narrative review in which researchers conducted their computer search in public database like Google Scholar and more specifically databases such as Web of Science, Science Direct and PubMed with using keywords such as hope, strategies, cancer, social support, counselling and selected articles from 2000 to 2016. Overall 25 articles have been searched. Researchers reviewed the summary of all articles searched, 5 articles are excluded due to non-relevance and ultimately, they applied 20 full articles to compile this review. Researcher’s finding regarding effective strategies for increasing the hope in patient with cancer were categorized in 3 sections. Counselling strategies such as spirituality therapy group sessions or the presence of religious leaders in a hospital or clinic, holding individual and group counseling for patients and listen to their concerns and crisis management in disappointment patients, social and familial strategies like social and family support, having sympathetic care givers, to encourage strong family connections, providing economic resources of treatment and accompany patient in treatment process, psychiatrist’s therapeutic-supportive strategies such as appropriate treatment rapport with patient, acceptance patient’s projection, educating problem focused coping skills and help to psychological adjustment with disease and positive reinforcement, supportive psychotherapy with the aim of increasing optimism and acceptance of the disease in patients. For improvement hope strategies among hospital’s personals, considering periodic education for nurses of oncology ward regarding psychotherapy styles and crisis management seems helpful. Also presence of graduated midwifery counseling who familiar with promoting hope strategies in ovary and breast cancers wards or presence of religious leaders in hospital are proposed.

Corresponding Author: Marzieh Azizi (Master Student of Midwifery counseling, Research student Committee, Mazandaran University of Medical Science, Nasibeh Nursing and Midwifery Faculty, Sari, Iran)
Study Of Methylation Status In PTEN Gene In Iranian Breast Cancer Patient

1. Soheila Asoudeh Moghanloo (Department Of Medical Biotechnology. National Institute Of Genetic Engineering And Biotechnology, Shahrake Pajoohesh. 15th Km, Tehran-Karaj Highway, Tehran, Iran)
2. Fatemeh Asoudeh (Department Of Cellular And Molecular Biology, Varamin (Pishva) Branch, Islamic Azad University, Tehran, Iran.)

Abstract

PTEN tumor suppressor gene encodes a protein that plays a role in increasing the level of phosphorylation. PTEN gene mutation effects of tumorigenic properties is unknown. PTEN gene is disabled by genetic and epigenetic mechanisms such as hypermethylation. CpG island hypermethylation is another route to tumour suppressor gene inactivation however, the literature regarding PTEN hypermethylation in cancer is controversial. To evaluate the frequency of methylation of PTEN gene in patients with Breast cancer, the methylation specific PCR using exon 7 (MS-PCR) PCR and restriction enzyme (PER) was dependent. After examining 50 patients with Breast cancer by MS-PCR and PER hypermethylation in 42% and 48%, respectively, were found. Background check pathologic tissue samples of cancer patients showed that the PTEN gene inactivation may be performed in the early stages of cancer and epigenetic factors influencing the progression of cancer. We show that methylation of the PTEN CpG island is a rare event in cancer cell lines and that apparent methylation most likely originates from homologous regions of the PTENP1 pseudogene promoter.

Corresponding Author: Soheila Asoudeh Moghanloo (Department of Medical Biotechnology. National Institute of Genetic Engineering and Biotechnology, Shahrake Pajoohesh. 15th km, Tehran-Karaj Highway, Tehran, Iran)
Abstract

Cancer is a group of diseases with abnormal growth of cells, the ability to infest to adjacent and dispose tissues and the patient's final death. Types of cancer are causing 14 percent all of death in around of the world and every year more than 10 million people in worldwide diagnosed with cancer. Cancers are second agent of death in developed countries and as the third in developing countries in progress. Generally, 80-90 percent of cancers are related to environment and lifestyle, which role of the diet is between 30-35% of deaths from cancer, therefore, it is estimated that at least one-third of all cancer is preventable. This is moment of the importance of attention to the preventive and therapy aspects of nutrition in cancer. Accordingly, this paper is designed with aim of review and compare of the nutritional measures of traditional medicine with modern medicine on cancer. This paper is written to overview method and to practice of library. In traditional medicine resources, is often the first speech of principles of sanitation, or “SETTEHYE ZARORIYEH” ( 6 principles of preservation of health ) with the title of “devise of eating and drinking” (how to consume foots and drinks) started and it is paid to detail to the quantity and quality and role and the importance of nutrition of correct and healthy in the category of disease prevention and health preservation. In addition, with the introduction of foods of eligible of property of “TARYAGHIYAT” (or antioxidant) such as; vegetables and fruits or avoiding from overused of SOWDAZA materials, such as salt beef profits, it has been pointed more than before to the role of nutrition in cancer prevention. In the category of nutritional therapy for cancer patients as well as, along with cleansing the body, With the expression of general principles, such as; The use of food and drinks of eligible of the sufficient moisture and with the ability to produce of healthy phlegm in the body and to convert the quality of the blood to a blood of relatively watery diluted, That be away from “EHTERAGHI materials” (or oxide); is provide the base of the diet of cancer patients. therefore, the consumption of meat of chicken, lamb, capricorni, fresh fish of river Along with Cook vegetables and collective, Such as; squash, purslane, barley in it, and as well as, consuming drinks, such as; medical Beer, syrup of violets and morning glory recommends for them. In modern medicine resources, as well as, for cancer prevention, has been recommended than to adhere to diets containing of fresh vegetables and fruits and antioxidants (Such as; garlic, onion, pepper, radish and green tea) and reduction of fat intake to less than 30% of calories, the limitation of the consumption of red meat and salt and pickles and also pay attention to how to cook food, along with other preventive measures, such as exercise. In the category of treatment of cancer patients, also, Besides of the attention to physical mobility, are referenced to weight control, appetite stimulant factors, to consume of plenty of fluids (water, fruit juice, soup), low-fat dairy products, muscle of meat, poultry and fish; that in the text of the article has been paid to express them. With regard to the immense consistent of nutritional principles related to cancer In the school of traditional medicine with modern medicine, It seems that the integration and to work of its recommendations, along with the new medicine recommendations, Not only can promote cancer prevention in the
community. But can also be very helpful in health promotion of the cancer patients.

Corresponding Author: Mahdi Zarvandi (Mashhad University of Medical Sciences, School of Traditional Medicine, Students' Research Office, Mashhad, Iran())
Comparison Of Dendritic Cell Differentiation Markers In Patient Suffering Leukemia With Normal Healthy One

1. **Hajar Rajaei** (Department Of Stem Cells And Developmental Biology, Royan Institute For Stem Cell Biology And Technology. Tehran-Iran)
2. **Marzieh Ebrahimi** (Department Of Stem Cells And Developmental Biology, Royan Institute For Stem Cell Biology And Technology. Tehran-Iran)

**Abstract**

Generating potent dendritic cells (DCs) in vaccination concept has been the focus of many researches and it is of great interest to produce desired mature DCs against tumor antigens of the patients. To this end, maturity process must be performed efficiently. But in some situations and cases, monocytes derived from peripheral blood cells (PBMCs) might not express the maturity markers even in the presence of maturity induction materials like lipopoly saccharide. To compare the maturity process between monocytes (MOs) derived from control and cancer bearing person, PBMCs of healthy and patient suffering leukemia were isolated and the flow cytometric data of both samples were compared. PBMCs were isolated using ficoll paque and after 2 hr adherence cell culture, the MOs received IL-4 and GMCSF for 5 days in complete RPMI supplemented with L-glutamine, non-essential acid amine, penicillin streptomycin and 10% fetal bovine serum. After that LPS was added for 2 days. The markers of HLA-DR, CD86, and CD83 were checked on monocytes on first day, 5th day and 7th day in both normal one and the leukemia sample. The flow cytometric analysis showed mean fluorescence intensity (MFI) of 97.1, 508 and 2908 in CD86, MFI of 55.3, 659 and 727 in HLA-DR, MFI of 3.92, 51.1 and 126 in CD83 in normal person. While MFIs of these markers in the person undergone leukemia were 4.64, 23.6 and 279 in CD86, 26.4, 3.32 and 3.27 in HLA-DR and 2.56, 2.27 and 5.42 in CD83 respectively on 1st day, 5th day and 7th day in the presence of IL-4, GMCSF and LPS. Overall, maturity induction in MOs derived from patients suffering cancer for clinical use might not occur efficiently even in the presence of tumor antigens.

**Corresponding Author:** **Hajar Rajaei** (Department of Stem Cells and Developmental Biology, Royan institute for stem cell biology and technology. Tehran-Iran)
MIR-15B AS Circulating Biomarkers For Diagnosis Of Malignant Melanoma

1. Parisa Sahranavardfard (Department Of Stem Cells And Developmental Biology, Cell Science Research Center, Royan Institute For Stem Cell Biology And Technology, ACECR, Tehran, Iran.)
2. Esmaeil Ebrahimie (Department Of Genetics And Evolution, School Of Biological Sciences, The University Of Adelaide, Adelaide, South Australia, Australia)
3. Alirezha Ghanadan (Pathology Department, The Cancer Institute Of Iran, Tehran University Of Medical Sciences, Tehran, Iran)
4. Amirmader Emani Razavi (Iran National Tumor Bank, The Cancer Institute Of Iran, Tehran University Of Medical Sciences, Tehran, Iran.)
5. Forough A. Sayahpour (Department Of Stem Cells And Developmental Biology, Cell Science Research Center, Royan Institute For Stem Cell Biology And Technology, ACECR, Tehran, Iran.)
6. Azam Samadian (Department Of Stem Cells And Developmental Biology, Cell Science Research Center, Royan Institute For Stem Cell Biology And Technology, ACECR, Tehran, Iran.)
7. Marzieh Ebrahimi (Department Of Stem Cells And Developmental Biology, Cell Science Research Center, Royan Institute For Stem Cell Biology And Technology, ACECR, Tehran, Iran.)

Abstract

Circulating microRNAs in serum and other body fluids, as a valuable source of cellular data, also can serve as cancer diagnostic and prognostic biomarkers. Therefore, finding biomarkers for early and non-invasive diagnosis of malignant cancers such as melanoma can affect in tumor therapy. In this study we investigated the expression of 7 microRNAs in the serum of patients with melanoma. The seven microRNAs that regulate EMT phase in melanoma were chosen based on searching on miRTarBase, miRWalk, and miRCancer databases. The expression level of selected MicroRNAs was quantified by Real-time PCR in serum of 10 melanoma pateints and 6 normal donors. The expression level of each microRNA was normalized against U6 snRNA expression and was calculated using the 2-ΔΔCT method. Among the seven selected microRNAs (miR-205, miR-141, miR-203, miR-15b, miR-22, miR-9, miR-155), the miR-15b (fold change= 1.6, p value = 0.05) was significantly up-regulated and miR-155 (fold change= 2.8, p value = 0.002) was down-regulated in patients with melanoma compared to control group samples. The most of patients was in stage II with metastatic to dermal lymph nodes. The data presented at this study suggested that the high level of miR-15b (as targeting for CDK4 and SMAD3) together with low level of miR-155 (its target ZEB1) might serve as novel biomarkers in the non invasive diagnosis of malignant melanoma, although more studies are needed to confirm our findings. Support: This work was supported by grants funded by Royan Institute

Corresponding Author: Parisa Sahranavardfard (Department of Stem Cells and Developmental Biology, Cell Science Research Center, Royan Institute for Stem Cell Biology and Technology, ACECR, Tehran, Iran.)
Economic Evaluation Of The Cost Of Mammography Compared With In Comparison To The Cost Of Treating Patients With Breast Cancer By The Insurance

1. Fatemeh-Sokhanvari (Isfahan University Of Medical Sciences)
2. Farzaneh.Hajahmadi (Isfahan University Of Medical Sciences)
3. Fatemeh.Moradi (Isfahan University Of Medical Sciences)
4. Hamid.Torkzadeh (Isfahan University Of Medical Sciences)

Abstract

Breast cancer is the most common cancer that women are affected. In Western countries, it is more common in women over 50 years of age, but in our country, patients are younger and in many cases due to lack of awareness of symptoms in patients who have advanced stages. It should be noted that no matter how breast cancer is detected early, treatment is easier, more successful and less costly for the patient and the insurance organizations too. According to studies, mammography is the best and most accurate diagnosis and screening method. If the woman has not breast problem, for early diagnosis the first mammography done at the age of 35-39 years. In Western countries regarding disease incidence and available resources, mammography done in 40-49 years every 1-2 years and then to 65 years and depending on the doctor's opinion done every year. According to previous studies, the most cause of the lack of Iranian women for mammography has been the high cost. Since most of the cost, pay the patient in the form of out of pocket which is expensive for the majority of society. Cooperation with insurance pay a larger share of this amount. is not only effective Health equity but also the interest of insurance organizations. The data showed that the cost of mammography is 900,000 rials in mammography center that the insurance organization stopay only 280,000 rials and the remaining 620,000 rials will be paid by the patient in the form of out of pocket. Review the medical expenses to the surgery are as follows. Price lumpectomy, about 15000000 million rials that comes with at least two days in hospital with Hotelling 2700000 Rials per night will be equivalent to 20400000 rials. That the insurer does not pay the £8992000 That the insurer pay onl y 8992000 rials. If that is the patient in low Stage and looking early mammography detected. In contrast, patients who are diagnosed late will have to do a mastectomy or radical mastectomy. The cost of mastectomy was 25000000 rials. Meanwhile, the need for a longer stay in hospital for at least three days Hotelling hospital added to this amount. That is a total equivalent to 33100000 rials. The amount of the share of the insurer is exceeds 15238000 rials. Radical mastectomy is spending more and more stay. Surgery cost in this case is 280000000 rials. Which, along with that least four days in hospital would be equal to 34984000 rials and The insurer must pay the amount of 17984000 rials. On the other hand, if the insurance organization pay the premium to the 50% of mammography cost, Including 20 patients for mammography in the early detection of a lumpectomy, paid by the insurance (209840000 + 9000000 would be 218840000 rials. When compared with the cost paid prior to mastectomy for 20 patients was equivalent to 304.76 million Rials. And the radical mastectomy for 20 patients at 359.78 million Rials. There are significant differences in terms of rials. In conclusion, it is noteworthy that according to the medical costs of patients with high-stage breast cancer in a large financial burden on the shoulders of insurance organizations. By raising share of insurance not only can...
mammography. By raising share of insurance organization in the cost mammography not only did to
cure for more patients and thus implement health equity The issue of the economic interest of
insurance organizations as well. This should be supported by health authorities and insurance
organizations.

Corresponding Author: Fatemeh-Sokhanvari (Isfahan University of Medical Sciences)
C-FABP-PPARγ-VEGF Signaling Axis Promotes Tumorigenicity In Castration Resistant Prostate Cancer

1. Farzad Seyed Forootan (Royan Institute Of Biotechnology)
2. Youqiang Ke (University Of Liverpool)
3. Shiva Seyed Forootan (University Of Liverpool)
4. Kamran Ghaedi (Royan Institute Of Biotechnology)

Abstract

In previous work, it is suggested that the excessive amount of fatty acids transported by C-FABP may have facilitated malignant progression of prostatic cancer cells through a C-FABP-PPARγ-VEGF axis to increase angiogenesis and through another C-FABP-PPARγ route to inhibit apoptosis. To further functionally characterised the C-FABP-PPARγ-VEGF axis, we have, in this work, investigated the molecular mechanisms involved in its tumorigenicity promoting role in prostate cancer. Suppression of PPARγ in highly malignant prostate cancer cells produced a significant reduction in their proliferation rate (up to 53%), invasiveness (up to 89%) and anchorage-independent growth (up to 94%) in vitro. Knockdown of PPARγ gene in PC3-M cells significantly reduced the average size of tumours formed in nude mice by 99%. Tumour incidence was reduced by 90% and the latent period was significantly prolonged by 3.5 fold. The results in this study also showed that C-FABP promoted VEGF expression and angiogenesis through PPARγ which was activated by the stimulation of the fatty acids transported by C-FABP. Further investigations showed that PPARγ up-regulated VEGF expression through acting with the PPAR-responsive elements in the promoter region of VEGF gene in prostate cancer cells. Although androgen can modulate VEGF expression through Sp1/Sp3 binding site on VEGF promoter in androgen-dependent prostate cancer cells, this route, disappeared as the cells gradually lost their androgen dependency; was gradually replcaced by the C-FABP-PPARγ-VEGF axis. These results suggested that the C-FABP-PPARγ-VEGF axis, rather than androgen modulated route, may be a more important novel therapeutic target for treatment of castration resistant prostatic cancer.

Corresponding Author: Farzad Seyed Forootan (Royan Institute of biotechnology)
Breast cancer is the most common invasive cancer in females worldwide. Metastatic breast cancer (MBC), that is also called stage IV or advanced breast cancer, is breast cancer that has spread from breast to other organs in the body. Despite advances in early diagnosis, prevention, and treatment, it is still the second-leading cause of cancer-related deaths in women, therefore it is essential to improve the care of MBC patients, since even today it remains an incurable disease. Taxanes are highly active chemotherapeutic agents which are used in the treatment of early-stage and metastatic breast cancer. Docetaxel and paclitaxel are one of the most active agents for the treatment of breast cancer. These first-generation taxanes are intensely hydrophobic, therefore; solvents are required for its parenteral administration. Nanoparticle albumin-bound paclitaxel (Nab-paclitaxel) technology, that was initially developed more than a decade ago, allows for the transportation of such hydrophobic drugs with no need of potentially toxic solvents. Nab-paclitaxel can be administered without premedication, in a shorter infusion time and there is no need for a special infusion set. Furthermore, this technology allows the selective delivery of greater amounts of anticancer drug to tumors, by exploiting endogenous albumin pathways and decreasing the incidence of serious toxicities. The aim of this study was to determine the effect of Nab-paclitaxel on metastatic breast cancer treatment. This article indicated that Nab-paclitaxel can be effective on treating the metastatic breast cancer.
Abstract

Many studies have been done on anti-cancer properties of crocetin, extracted from saffron. Different assumptions for anti-cancer activity of crocetin is intended such as inhibition of the synthesis of nucleic acid, induced apoptosis and anti-oxidant properties of this compound. In the present study, the effects of crocetin on the inhibition of MRP2-mediated multidrug resistance in the human ovarian cancer cell line A2780 and its Cisplatin resistant derivative, A2780/RCIS cells, has been evaluated. Cytotoxic effect of crocetin and DMSO (as the control sample) was evaluated using MTT assay and IC50 was calculated. The effects of crocetin on MRP-2 activity have been evaluated by doxorubicin efflux assay. Briefly, cells in exponential growth were exposed to 10 μM Dox in the absence or presence of MRP-2 specific inhibitor (furosemide 1 mM) and Crocetin at 25-400 μM for 1 h at 37º C (accumulation phase). The supernatants were replaced with fresh medium in the absence or presence of furosemide and incubated for 3 h at 37º C (efflux phase). The supernatants were removed and assayed spectrofluorometrically for Dox content at excitation and emission wavelengths of 480 nm and 600 nm, respectively. The results showed that crocetin inhibited the proliferation rate of the A2780 and A2780/RCIS cells with an IC50 value of 174 μM and 340 μM, respectively. DMSO showed no significant toxicity on these cell lines. Furosemide at 1 mM was not toxic for A2780/RCIS cell. Exposure of A2780/RCIS to Crocetin inhibited Dox efflux uptake by inhibition of MRP2 transporter in a dose dependent manner. Crocetin at 25, 50, 100 and 200 μM, inhibited Dox efflux by 58%, 72%, 98% and 100% in compared with furosemide. The presence of Furosemide in the sample showed no influence on the absorption or emission spectra of Dox. These findings proposed that Crocetin can inhibit MRP2-mediated drug efflux in human ovarian cancer cells.

Corresponding Author: Navid Neyshaburi (School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran; Biotechnology Research Center, Mashhad University of Medical Sciences, Mashhad, Iran)
Hemocompatibility And Anticancer Activity Evaluation Of Two Antimicrobial Peptides, Plantaricin CS And Snakin Z

Abstract

Plantaricin CS and Snakin Z are two peptides that purified from innate immune systems of two different species. The aim of this study is investigation of hemocompatibility and anticancer activity of these two peptides. Human red blood cells (RBCs) were treated with different concentration of peptide in two methods: radial diffusion assay and spectrophotometric assay. For in vivo assay, the mean of hematocrit, RBCs and White Blood Cells (WBCs) was assessed after treatment of 48 rats (24 rats for each peptide) with different concentrations of peptides (5, 15, 45, 135 and 400 µg/ml) for two weeks. The cytotoxicity of these two peptides was also evaluated on two cancerous cell lines: Ovarian cancer (OVCAR3), Breast cancer (MCF-7) by MTT assay. In in vitro, two peptides have low hemolytic activity on RBCs. According to data, these peptides have significant cytotoxicity at concentrations higher than 135 µg/ml on examined cancerous cells. The sequence of activity was Snakin Z and > Plantaricin CS. According to the hematologic parameters, no significant changes were observed in the groups treated with Plantaricin CS in all concentration; but Snakin Z showed significant toxicity on all blood cells. This peptide decreases the RBC, WBC and Hematocrit as 4.1 RBC×1000000/µL, 12 WBC×1000/µL and 16% in concentration of 400 µg/ml, respectively. According to this study, both of peptides showed hemocompatibility and anticancer activity in values that they have biological activities. So it’s suggested that Snakin Z and Plantaricin CS may be suitable pharmaceutical agents for development of new drugs for cancer therapy.

Corresponding Author: Hadi Zare-Zardini (Hematology and Oncology Research Center, Shahid Sadoughi University of Medical Sciences and Health Services, Yazd, Iran)
Application Of Nanotechnology In Cancer Therapy And Cancer-Related Infections In Children

1. Hadi Zare-Zardini (Hematology And Oncology Research Center, Shahid Sadoughi University Of Medical Sciences And Health Services, Yazd, Iran)
2. Maryam Boyerhasani (Department Of Biology, Falavarjan Branch, Islamic Azad University, Isfahan, Iran.)

Abstract

Most of mortality throughout the world occurs due to cancer diseases. Nanostructures are the new compounds that have become one of the most important technologies for utilizing in different fields over the past two years especially in medicine. In between, nanotechnology has the potential to cancer detection and therapy. This study is a review of prospects in applications of nano-materials for cancer detection and treatment. We have summarized the nano-materials (metal nanospheres, nanorods, nanoshells and nanotubes) in medical applications targeting cancer. We also discuss advancements in established nanoparticle technologies such as liposomes, polymer micelles, and functionalization regarding tumor targeting and controlled release strategies as well as drug delivery. This paper will discuss the therapeutic applications of different nano-materials with a major focus on their applications for the treatment of cancer and cancer-related diseases in children.

Corresponding Author: Hadi Zare-Zardini (Hematology and Oncology Research Center, Shahid Sadoughi University of Medical Sciences and Health Services, Yazd, Iran)
A Review Of Medicinal Plants Effective In The Treatment Of Apoptosis Of Cancer Cells

1. Niloufar Karami (Department Of Biology, University Of Science And Arts, Yazd)
2. Ameneh Javid (Department Of Biology, University Of Science And Arts, Yazd)
3. Bibi Fatemeh Haghirosadat (Bio-Engineering Sciences Faculty Of Science And Technology Of Tehran University)

Abstract

Medicinal herbs in various fields of medicine, industry, food and agriculture applications. In the field of medicine and therapy for the treatment of cancer researchers hope many medicinal plants. Plants, herbs, and ethnobotanicals have been used since the early days of humankind and are still used throughout the world for health promotion and treatment of disease. Plants and natural sources form the basis of today’s modern medicine and contribute largely to the commercial drug preparations manufactured today. About 25% of drugs prescribed worldwide are derived from plants. Still, herbs, rather than drugs, are often used in health care. For some, herbal medicine is their preferred method of treatment. Today, natural antioxidants are the focus of considerable attention and efforts are ongoing for the replacement of synthetic ones. In addition, these natural antioxidants can be formulated as functional foods and can help prevent oxidative damage from occurring in the body. Due to the side effects of drugs and chemicals in countries around the world, including developed countries are thinking about changing pattern of drug use of chemical plant. Some active drug substances which are very important in the pharmaceutical industry, is impossible to artificially produce only natural as Astkhrajand plants. Although synthetic medicines to improve patients more quickly and has an adverse effect on the human body Mshkhsand but most of them can have side effects. In this study, we report and review of some medicinal plants effective in the treatment of cancer or other diseases discussed.

Corresponding Author: Niloufar Karami (Department of Biology, University of Science and Arts, Yazd)
Improvement Of Antitumor Activity Of Doxorubicin By Coformulation Of Crocetin And Doxorubicin In PLGA Nanoparticles

1. Maryam Hashemi (Nanotechnology Research Center, School Of Pharmacy, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

The current study reports investigation of codelivery by PLGA nanoparticles (NPs) loaded with crocetin (Cro), a natural carotenoid acid that is found in the crocus flower, and Doxorubicin (DOX). Double emulsion/solvent evaporation method was used for preparation of PLGA nanoparticles containing Dox and Cro. Characterizations of prepared NPs were investigated by atomic force microscopy (AFM) and dynamic light scattering analysis. In vitro Cytotoxicity of DOX and Cro loaded PLGA NPs (PLGA-DOX-Cro) on MCF-7 cell line was evaluated using MTT test. Flow cytometry experiments were implemented to distinguish cells undergoing apoptosis from those undergoing necrosis. Furthermore the expression of caspase 3 was examined by western blot analysis. Results: The prepared formulations had size of 150-300 nm. Furthermore, PLGA-DOX-Cro nanoparticles inhibited MCF-7 tumor cells growth more efficiently than either DOX or Cro alone at the same concentrations, as quantified by MTT assay and flow cytometry. Studies on cellular uptake of DOX-Cro-NPs demonstrated that NPs were effectively taken up by MCF-7 tumor cells. This study suggested that DOX-Cro-NPs may have promising applications in breast cancer therapy.

Corresponding Author: Maryam Hashemi (Nanotechnology Research Center, School of Pharmacy, Mashhad University of Medical Sciences, Mashhad, Iran)
Effect Of Iranian Traditional Medicine Remedy On Chemotherapy Induced Nausea And Vomiting In Breast Cancer; A Double Blind, Randomized, Cross Over Clinical Trial

1. Sadegh Shokri (School Of Persian And Complementary Medicine, MUMS, Mashhad, Iran)
2. Mohammad Nazari (School Of Persian And Complementary Medicine, Mashhad University Of Medical Sciences(MUMS), Mashhad, Iran)
3. Ali Taghizadeh (Surgical Oncology Research Center, MUMS, Mashhad, Iran)
4. Mojtaba Mousavi Bazzaz (Department Of Community Medicine, Faculty Of Medicine, MUMS, Mashhad, Iran)
5. Hasan Rakhshandeh (Center Of Medicinal Plants, School Of Medicine, MUMS, Mashhad, Iran)

Abstract

Chemotherapy induced nausea and vomiting (CINV) is the most unfavorable side effect and has negative effect on quality of life and continuation of chemotherapy. Despite finding new drugs, the problem still is remain. For controlling of this complication, Persian medicine offer different options. One of them is Persumac, an Iranian traditional medicine remedy. The general objective of study was considering effect of Persumac on resistant CINV. The specific objectives were to assess the effect of Persumac on number and severity of nausea and vomiting in CINV. This randomized, double blind, cross over clinical trial was carried out on 69 patients with breast cancer and resistant CINV who received outpatient high emetogenic chemotherapy in Imam Reza hospital, Mashhad, Iran from Octobr 2015 to May 2016. Persumac (prepared from Rhus Coriaria and Bunium Persicum boiss) and lactose as placebo were used. Data collection was performed by a three-section questionnaire covering the demographic characters, number and severity of nausea and vomiting and drug status consumption. 80 of 93 eligible patients in stage I(without intervention), complete the study in stage II(Intevention) and 11 of them declined participation for stage III(cross over). Determining of P value of carry over, period and treatment effects demonstrated that confounding factors were not affected the results obtained before and after cross over. The mean severity of nausea in acute phase was in stage 1: 4.83 ± 1.40, stage 2: 4.54 ± 2.0 and stage III: 4.15 ± 0.92 in group 1 (first Persumac and then lactose in cross over) and in group 2 (first lactose and then Persumac in cross over)was respectively 4.83 ± 1.40, 4.54 ± 2.0, 4.15 ± 0.92 with p value of carry over effect: 0.03 and period effect: 0.22. Except severity of nausea in acute phase, the mean number and severity of nausea and vomiting scores significantly decreased in acute and delayed phase of CINV. In summary, the findings showed that, Iranian traditional medicine remedy may help for controlling of refractory CINV. The functional importance of these findings is that another option is provided to the therapists for CINV controlling. Additional research in this area and different cancers, patients with more various features and more complete methodology and tools could be provide appropriate design for new research on this topic.

Corresponding Author: Hasan Rakhshandeh (Center of Medicinal Plants, School of Medicine, MUMS, Mashhad, Iran)
The Role Of Thrombin As A Potent Proinflammatory Signaling Molecule In Cancer Pathogenesis

1. Safieh Ebrahimi (Department Of Medical Biochemistry, School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Seyedmahdi Hasanian-Mehr (Department Of Medical Biochemistry, School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Blood coagulation and inflammation are closely intertwined pathways. Thrombin, a multifunctional serine protease in plasma, regulates numerous pathophysiological processes related to coagulation and inflammation. Thrombin through activation of protease-activated receptors (PARs) initiates proinflammatory signaling responses in in vitro and in vivo systems. Proinflammatory signaling function of thrombin increases release of proinflammatory cytokines and chemokines, triggers vascular permeability, promotes leukocytes migration, and induces adhesion molecules expression. Thrombin as a potent signaling molecule is strongly implicated in a number of proinflammatory disorders including severe sepsis, neurodegenerative disorders, cardiovascular disease, and of special interest in this review cancer. Tumor cells express high level of tissue factor (TF) which upon binding to factor VIIa triggers more thrombin generation in the tumor microenvironment. Thrombin contributes to the malignant phenotype by enhancing tumor cell adhesive and metastatic properties. Thrombin activation of PARs leads to upregulation of various adhesion molecules, such as the GPIIb-IIIa integrin, P-selectin, and CD40 ligand, these adhesion molecules are required for tumor cells migration and adhesion between tumor cells, platelets, endothelial cells, and the extracellular matrix which lead to tumor progression(8). Thrombin also contributes to the malignant phenotype by induction of various growth factors, chemokines, and cytokines secretion that promote the stimulation of proliferation, differentiation and migration of cancer cells. Moreover, thrombin is involved in angiogenesis by inducing inflammatory cytokines that could enhance the angiogenic process in human malignancies. Taken together, Thrombin through increasing vascular permeability, platelet activation and overexpression of adhesion molecules, proinflammatory cytokines, chemokines and proangiogenic factors regulates tumor cell proliferation, differentiation, migration and angiogenesis. A deeper understanding of the major signaling pathways involved in thrombin-induced - inflammation could thus lead to the design of agent to regulate the proinflammatory signaling function of thrombin and have great clinical significance in terms of the treatment of cancer. This review summarizes the acquired knowledge on mechanisms of thrombin-mediated proinflammatory responses in cancer for a better understanding and hence a better management of this disease.

Corresponding Author: Seyedmahdi Hasanian-Mehr (Department of Medical Biochemistry, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran)
Determinants Of Mammography Screening Behavior Among Employed Women In South Khorasan, Iran 2016

1. Mitra Moodi (Social Determinants Health Research Center, Birjand University Of Medical Sciences, Birjand, Iran)
2. Fatemeh Haghighi (Medicine School, Birjand University Of Medical Sciences, Birjand, Iran.)
3. Mahyar Mohammadifard (Medicine School, Birjand University Of Medical Sciences, Birjand, Iran)
4. Zoya Tahergorabi (Social Determinants Health Research Center, Birjand University Of Medical Sciences, Birjand, Iran)
5. Sodabeh Eshaghi (Noncommunicable Disease Center, Birjand University Of Medical Sciences, Birjand, Iran.)
6. Maryam Miri (Health Education & Health Promotion, Social Determinants Health Research Center, Birjand University Of Medical Sciences, Birjand, Iran)

Abstract

Breast cancer is the most malignancy among women in the world. Early diagnosis is so important for facilitating effective treatment, reducing mortality rate and increasing life expectancy. Mammography is an appropriate and effective method of early detection of breast cancer. The aim of this research was to identify factors associated with mammography screening behavior in Birjand female employers. This cross-sectional study was conducted on 680 employed female aged 40 years and older in 49 different governmental organization of south Khorasan. Eligible women were 40 years of age and older which had no history of breast cancer. Data were collected using a valid and reliable questionnaire. The obtained data were analyzed by SPSS (version16) using Logistic Regression test at the significant level of $\alpha = 0.05$. Mean of age, marriage age and the first pregnancy age was 46.24±4.12, 22.68±4.69 and 24.18±5.15 years, respectively. 88% had university education, 93.8% married and 5.1% history of breast cancer in family. 27.1% women reported having had of least one mammogram in their lifetime. Logistic regression analysis indicated that women with history of breast cancer in family members had most likely mammogram choice (OR: 2.69, $P = 0.008$). As the rate of mammography screening among employed women in South Khorasan is low, it is necessary design comprehensive and appropriate educational intervention about breast cancer screening methods especially mammography. Also, finding indicated that perceived threat is the most important determinant factor of mammography screening behavior.

Corresponding Author: Mitra Moodi (Social Determinants Health Research Center, Birjand University of Medical Sciences, Birjand, Iran)
Experimental And Molecular Docking Study Of Novel Heterocyclic Compounds Against FLT3 Receptor Tyrosine Kinase

1. Mohammad Hossein Tanipour (Department Of Medical Biochemistry, School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
2. Mostafa Akhlghi Bagherjeri (Department Of Medical Biochemistry, School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
3. Hassan Ostadi (Department Of Medical Biochemistry, School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)
4. Mohammad Saadatmandzadeh (Faculty Of Sciences, Department Of Chemistry, Ferdowsi University Of Mashhad, Mashhad, Iran)
5. Baratali Mashkani (Department Of Medical Biochemistry, School Of Medicine, Mashhad University Of Medical Sciences, Mashhad, Iran)

Abstract

Cancers, including Leukemia, are major causes of human mortality. Leukemia is the most common cancer diagnosis in children who are younger than 15 years. Acute Myeloid Leukemia (AML) have been recognized as a prevalent type of leukemia by 25-30% of all. Internal tandem duplications (ITD) and point mutations in the tyrosine kinase domain (TKD) of the FLT3 receptor (FMS-Like Tyrosine kinase) are the most common genetic alterations in AML. Small Molecules Inhibitors (SIMs) of the mutated kinases are considered as one of the most promising molecular strategies to combat with such genetic defects. A set of 8 novel heterocyclic compounds composed of a common core (7,7-dimethyl-7,8-dihydro-6H-tetrazolo[1,5-b][4,1,2]benzothiadiazin-6-one) structure and different substituents used in this study. Two murine cell lines of FD-FLT3-WT and FD-FLT3-ITD dependent to human FLT3 receptor were used for doing cellular examinations. Cytotoxicity evaluation was performed using Resazurin reagent for both cell lines in the presence of various growth factors (FLT3 ligand and GM-CSF) for the FD-FLT3-WT line to achieve IC50. The interactions of the inhibitor compounds and the homology models FLT3 were evaluated by molecular docking method using GOLD and Accelrys Discovery Studio software. The D8 compound with the amino substituent could result in the IC50 values of 14.28 and 0.93µM, respectively, in two cell lines of FD-FLT3-ITD and FD-FLT3-WT. However, two D1 and D2 compounds were effective against the FD-FLT3-ITD line, but not on the FD-FLT3-WT cell line. Also, the docking results indicate these compounds were docked with more favorable energy at the active forms of the receptor (homology models built based on 1PKG and 2GQG). In both experimental and in silico studies, compounds D1, D2 and D8 were considered as the best compounds of this category due to their specific activity and potent receptor-ligand interactions.

Corresponding Author: Mohammad Hossein Tanipour (Department of Medical Biochemistry, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran)