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Cycloastragenol(Telomeres Activator) and its relation with Cancer: A Brief Review

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Research Article

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Keywords: Astragalus, Cycloastragenol, Telomeres, Cancer, DNA, Apoptosis, Chemotherapy, Radiation therapy. The main theme involved in this article is to show the effect of cycloastragenol compound in curing the cancer disease. Cycloastragenol is extracted from astragalus root which is available in fewer amounts. It is an herb which is mostly grown in northern part in Asia. Cycloastragenol helps in activating telomeres. Telomeres are the caps of the DNA which decreases in size all the time when cell replicates. It is the product which helps in activating the telomeres, so that the life span increases to some extent.

ABSTRACT

INTRODUCTION

Telomeres and Astragalus

Cycloastragenol is a drug derived from Chinese herb "Astragalus Membranaceous" which helps in restoring telomeres after cell division. Astragalus is a Chinese medicinal herb improves the functioning of immune system and boosts the immunotherapy for some types of cancers ^[1].Cycloastragenol plays a vital role in telomere activation. It is promoted to kill cancer cells helps heal burns and also protects from all the heart diseases. It has the ability to stimulate the liver, circulatory system and urinary system. As there are many uses by using astragalus as a medicinal herb, there are also many flaws like dehydration, belly bloating and low blood pressure.

Normal human somatic cells have a limited life span to divide and replicate. According to Molecular Biology, all known living organisms have their development and functioning instructions written in the DNA all mammalian chromosome ends are capped by telomeres. Telomeres are ends of eukaryotic chromosomes which are biomarkers of aging. The length of telomere decreases with increased oxidative stress. Telomere length reflects the cumulative burden of oxidative stress and repeated cell replication. Telomerase and the control of telomere length are intimately linked to the process of tumorigenesis in humans. Telomeres are areas of heterochromatin composed of TTAGGG repeats located at the ends of linear chromosomes. They play a critical role in keeping genome stable and preventing premature aging diseases and the development of cancer. A family of enzymes called DNA-topoisomerases furnishes the nuclease activity involved in the regulation of DNA supercoiling They have been shown to inhibit chromosomes to form end-to-end fusions by preventing the cell from identifying telomeres as DNA-double strand breaks reported that Rsv moderately activates the human SIRT1 and TERT promoters inducing telomerase activity in HeLa-S3 cells The challenge ahead, of course, is to find out the function of these genes in telomere metabolism and their genetic organization. The high levels of morbidity and mortality of chronic non-communicable diseases (most of which highly associated

with aging) worldwide and of the possibility that short telomeres is not a universal feature of neural cancer stem cells.

Telomerase is an RNA-dependent DNA polymerase complex that contains a telomerase reverse transcriptase (TERT) and telomerase RNA ^[2]. Whenever the cell divides the length of telomeres shortens. After a few number of cell division cycles, the telomeres are steadily 'chipped away,' until they reach a critical length known as the Hay flick limit ^[3].Telomeres are the repeats of the DNA sequences and associated protein at the ends of the chromosome. These telomeres act as protective caps of the chromosome. Telomeres protect the vital information of the DNA. As we age, telomeres get shortened but if a person smokes or stress, obesity and due to the lack of exercise and even diet; the telomeres get shortened ^[4-19].

Cycloastragenol is saponin derived from astragalus, a plant which has been used as Chinese traditional herb. It is used as the medicine for over 2,000 years. T cell proliferation increases by increasing the telomere activity. Cycloastragenol is a glycone which contains carbohydrates. This compound was first identified when screen the Astragalus Membranaceous extracts which have antiaging properties ^[20-22].

Astragalus is a large genus which have nearly more than 3000 species. It is also called as huang qi or milk vetch. It is mostly grown in open places like valleys and plains especially on lime stone. The height of the plant is 30cms to 45 cms. Astragalus has anti-bacterial and anti-inflammatory characteristics, people sometimes use it for skin diseases. Medicinal uses of astragalus cure anemia, cold, diabetes, heart disease. The herb, astragalus is promoted to kill cancer cells, toxic effects of chemotherapy, heal burns and also helps to improve overall weakness. It is available in tea bags, dried slices and powder. In china, slices are mostly used in soups and mix with honey and take as medical tonic.

The scientific evidence behind astragalus root which enhance the immune system and fights against immune system. Research at The university of Texas, Anderson cancer center found that astragalus boost the immune system. The patients who take astragalus supplements have experienced a faster recovery and the survival rate has increased. Patients with breast cancer were given with a combination of astragalus and other compounds. This results in decline in mortality of 50% to 10%. They discovered that the group which receives pure astragalus extracts has a lot of improvements. In fact, the people who use astragalus will double their chances of survival.

Chinese research shows that the people who take astragalus improve the quality and conditions of the cancer patients who undergo chemotherapy. The astragalus root is stimulated for the production of interferon. Interferon is the group of proteins which are released by host cell which fights against the bacteria, viruses as such. Interferon is effective in fighting against the mutated cells and development of cancer.

Based on the research conducted at the University of Houston, astragalus root has the ability to enhance T-cells and Natural-killer cells which activate interleukin-2 which kills cancer cells and helps to relieve side effects for the people who use chemotherapy such as immunosuppression, fatigue, nausea, weight loss and many more.

In japan, the Hiroshima School of Medicine, astragalus was shown directly increase B-cells and T-cells, interleukins and antibody production. Astragalus helps in identification viral, bacterial and many other mischievous cells.

Astragalus Benefits

- 1. Wound healing.
- 2. Slow signs of aging.
- 3. Prevention of heart diseases.
- 4. Blood levels normal.

Cancer

Astragalus root is used fairly to robust at healing sickness. It has been used to treat ulcers and many other diseases. It also serves as input in cancer treatment. When cancer develops, this orderly process breaks down. As cells become more and more abnormal, cells survives even after they damage and new cells form when they are not needed. These extra cells can divide continuously and may form lump called tumor. Cancer is a tumor. Tumor is of two types: Benign tumor and malignant tumor. Benign tumor does not invade to its surrounding tissue or spreads throughout the body. Malignant tumor is that may invades to its surrounding tissue and spreads throughout the body.

Stages of Cancer

Cancer begins in one part of the body and spreads throughout the body. There are four different stages of cancer. The stage of cancer is very important for prognosis.

- 1. Stage 0: In situ
- 2. Stage 1: Localized cancer
- 3. Stage 2 and 3: Regional spread.
- 4. Distant spread.

In stage 0, the cell become cancerous cell but it can produce the tumor in that tissue. It produces in way that there is no threat to life. In the next stage, the cell gains the ability which can grow in nearby cell. In stage 2&3, cancer is larger in size and deeply grown into the cells. In stage 4, cancer spreads to other organs or parts of body. It is called metastasis. There are over 200 types of cancers.

There are few characteristics of cancer which have been proposed:

- 1. Evasion of apoptosis.
- 2. Limitless replication.
- 3. Anti-growth signaling.
- 4. Activation of metastasis.
- 5. Invasion of tissue and spread throughout the body.

Cancer is a name given to a group of diseases which are related with each other. In each and every type of cancer the cell divides continuously where no end point to it and spreads to surrounding tissues. Cancer cells differ from the normal cells in many ways. When compared with normal cell grows, become old and they die. New cell takes the place of the old one but cancer cells don't have death. They are immortal. One of the most important differences between normal cell and cancer cell is normal cell is more specialized than cancer cell i.e. normal cells mature into a very specific cell type and function. Cancer cell have a capability to ignore the cell signaling that normally passes a signals to stop dividing, it is known as programmed cell death or apoptosis ^[21-22].

Cancer cells have the ability in influencing the normal cell to form blood vessels for the supply of nutrients and oxygen for the tumor cells for which they need to grow. There are some specific categories of cancer that begins with specific cell type like carcinoma that begins with epithelial cell, lymphoma that begins with lymphocytes like B-cells and T-cells; sarcoma begins with soft tissue like muscles, leukemia that begins with blood forming tissue of bone marrow and there are many other categories like myeloma, brain and spinal cord tumor, germ cell, neuroendocrine and carcinoid tumor.

When cancer begins, there are no symptoms. We can find symptoms when mass continue to grow. Some of the symptoms that we can find like headache, changes in testicles, cough, jaundice, body pains, indigestion, constant fatigue, unwanted weight loss, fever and abnormal lump. Causes of cancer are based on the environmental factors, genetic disorders, chemicals, Diet, exercise, radiation, hormones and physical agents. Anything that causes damage to DNA, chemicals, nuclear radiation is one of the best known examples which causes DNA damage and ultra-violet radiations which is present in sunlight, also cause DNA damage.

Symptoms

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Treatments

Most common types of treatments for cancer such as surgery, blood transfusion, photo dynamic treatment, cell transplantation, hyperthermia, laser treatment, immuno therapy, radiation therapy, chemo therapy and targeted therapy.

Surgery: Surgery is used to treat, diagnose and prevention of cancer. It is one of the best chances to cure, especially if cancer has not spread to other parts of the body.

Blood transfusion: Transfusion of the blood temporarily replaces the part of the blood when it cannot be done on his own. Blood transfusion is not a permanent solution.

Photo dynamic therapy: Photo dynamic therapy is a specialized treatment which used drugs along with light to kill cancer cells. The drug which is injected activates only after certain light falls on the drug.

Cell Transplantation: Cell transplantation is used to restore the stem cells when bone marrow has been destroyed by some diseases.

Hyperthermia: Hyperthermia means more than the normal body temperature. Normally higher body temperature is cause due to the illness but when compared to hyperthermia it refers to heat treatment. The very temperature can destroy the small area of the cells, which is tumor.

Laser treatment: Laser can be used to in two ways

1. To shrink or to destroy the tumor.

2. To activate chemical known as photosensitizing agent which only kills cancer cells.

Immunotherapy: Immunotherapy is a treatment that uses own body's immune system to treat cancer. Immunotherapy boosts the immune system in a specific way or it trains the immune system to attack only cancer cells ^[20,50,51].

Chemotherapy: Chemotherapy is a treatment which uses medicines or drug. It is one of the best treatment by which a person can have control over the cancer treatment ^[23-30].

Radiation therapy: Radiation therapy is one of the most common techniques used to treat cancer. It uses high energy particles to destroy the cancer cells ^[32-49].

Targeted therapy: Targeted drug therapy is considered as the chemotherapy, but targeted drug therapy doesn't work as chemotherapy. It takes the advantage of small difference between normal cell and cancer cell. These drugs have different side effects.

Relation with Cycloastragenol

Cycloastragenol is produced in very low level. There are few methods to purify and injected in the body which in turns activate the telomerase. Telomerase is an enzyme mainly involved maintaining or lengthening telomeres. The replication of cancer cells might stops in the presence of telomerase activity in the normal cells and tissue has important implication for the use of telomerase assay in cancer diagnosis and for the use of anti-telomerase inhibitors in cancer treatment. hTERT is a catalytic sub unit of the enzyme telomerase usually turned OFF in adult cells expect in immune, egg, sperm and mainly in malignant forming cells ^[52-79].

CONCLUSION

The evidence for using astragalus for any health condition is limited. High-quality clinical trials (studies in people) are generally lacking. Measuring telomerase is a new way to detect the cancer cells in our body. If scientist tries to know how to stop telomerase enzyme, they might able to fight against cancer by making cells age and die. Almost 90% of cancer cells have been found to have enhanced telomerase activity.

William Andrewsis one of scientists who worked on telomeres, he states that "taking telomeres inducers is safer than driving a car to work but he also acknowledges that there are some risks by taking the Cycloastragenol extract. For example, the cell which stops aging or become immortal is due to the telomerase enzyme, so there is a chance that Cycloastragenol could keep alive cancer cells that would otherwise die. The telomeres which have been linked at the ends of the DNA, gets shorter each time when they replicate. Ultimately, if they become too short, the DNA begins to diminish and cells lose their function. This is why these telomeres are known as 'the ageing clock in every cell'.

REFERENCES

- 1. <u>Valenzuela HF, et al. Cycloastragenol extends T cell proliferation by increasing telomerase activity.</u> <u>The Journal of Immunology. 2009;182:30.</u>
- 2. <u>Ip FCF, et al. Cycloastragenol Is a Potent Telomerase Activator in Neuronal Cells: Implications for</u> <u>Depression Management. Neuro signals. 2014;22:52-63.</u>
- 3. Jim English. Anti-Aging and Anti-Viral Effects of "Herbal Youth" Compound. Nutrition Review. 2013;
- 4. <u>Gutman D, et al. Possible Mechanisms for Telomere Length Maintenance in Extremely Old People.</u> Hereditary Genet. 2014;3:e111.

- 5. <u>Cruz J, et al. Targeting the Telomere with T-Oligo, G-Quadruplex Stabilizers, and Tankyrase Inhibitors.</u> J Cancer Sci Ther. 2014;6:429-432.
- 6. <u>Dmitriev LF and Titov VN. DNA Replication and Telomere Shortening: Key Factors Related to the</u> <u>Production of C3-Aldehydes and the Interaction of One of them with DNA Guanine Residues. J</u> <u>GerontolGeriat Res. 2014;3:175.</u>
- 7. <u>Kenterelidou C. The Comment: The 'Telomere' of News and Public Communication. J Mass</u> <u>Communicat Journalism. 2014;4:202.</u>
- 8. <u>Saini D and Das B. Usefulness of Nucleic Acids (DNA/RNA) from Buccal Cells Isolated from</u> <u>Mouthwashes using a Modified Method. J Forensic Res. 2014;5:233.</u>
- 9. <u>Wang Y, et al. The Potential Clinical Implications of Telomerase Reverse Transcriptase in the</u> Detection and Diagnosis of Bladder Cancer. Hereditary Genet. 2014;3:131.
- 10. <u>Harari Y and Kupiec M. Genome-Wide Studies in Budding Yeast Dissect the Mechanisms that</u> <u>Maintain Telomere Length. Fungal Genom Biol 3:e113.</u>
- 11. <u>Fadri-Moskwik M, et al. Beyond Telomerase: Telomere Instability as a Novel Target for Cancer</u> <u>Therapy. J Mol Genet Med. 2013;7:91.</u>
- 12. <u>Hartwig FP. Up-Regulating Telomerase and Tumor Suppression: A Two-Step Strategy to Boost</u> <u>Hematopoietic Stem Cell Transplantation. J Stem Cell Res Ther. 2013;S3:003.</u>
- 13. <u>Kuffer A, et al. (2014) Transgenerational Effects of PTSD or Traumatic Stress: Do Telomeres Reach</u> <u>Across the Generations? J Trauma Treat 3:204.</u>
- 14. Puri N and Girard J. Novel Therapeutics Targeting Telomerase and Telomeres. J Cancer Sci Ther. 2013;5:e127.
- 15. <u>Boccardi V and Paolisso G. Malleability of Short Telomeres by Telomerase Activators: A Mini-review.</u> <u>Aging Sci. 2013;1:108.</u>
- 16. <u>Hartwig FP. Extending the Models of Tumor Suppression and Telomere Integrity Interaction: Focusing</u> on the Bone Marrow. J Bone Marrow Res. 2013;1:123.
- 17. <u>Hartwig FP. Telomere Length and Telomere-related Genetic Variations in Epidemiology: Getting the</u> <u>Context Right. J Genet Syndr Gene Ther. 2013;4:150.</u>
- 18. <u>Hartwig FP. Neural Cancer Stem Cells: Focusing on Chromosome Ends. J Alzheimers Dis</u> Parkinsonism. 2013;3:115.
- 19. <u>Uchiumi F, et al. Effect of Thujaplicins on the Promoter Activities of the Human SIRT1 and Telomere</u> <u>Maintenance Factor Encoding Genes. Pharm Anal Acta. 2015;3:159.</u>
- 20. <u>Shimodaira S. Smoking Influences the Yield of Dendritic Cells for Cancer Immunotherapy.</u> <u>Pharmaceut Reg Affairs. 2015;4:133.</u>
- 21. <u>Amit Kumar Tyagi and Sahdeo Prasad. Targeting P53 Pathway by Curcumin for Cancer Prevention</u> <u>and Treatment. Cell Dev Biol. 2014;4:e131.</u>
- 22. <u>Lina Guo, et al. The Role of Traditional Chinese Medicine in Anticancer Therapy. Med Aromat Plants.</u> <u>2014;3:e156.</u>
- 23. <u>Eskinder Ayalew Sisay, et al. Drug Related Problems in Chemotherapy of Cancer Patients. J Cancer</u> <u>Sci Ther. 2015;7:055-059.</u>
- 24. <u>Wilson IB Onuigbo. The Visionary Views of Medical Masters of Yester Years on Natures Norms Point</u> to Present prospects in the Target Therapy of Cancer. Biol Med (Aligarh). 2014;7:221.
- 25. <u>Sindhu Govindan Valiyaveedan, et al. Acquisition of Cancer Stem Cell Behavior Plays a Role in Drug</u> <u>Resistance to Combination Chemotherapy and Prognosis in Head and Neck Cancer. J Stem Cell Res</u> <u>Ther. 2015;5:261.</u>
- 26. <u>Mohammad Faizan Zahid, et al. Chemotherapy Induced Erythroid Dysplasia in a Patient with Acute</u> <u>Myeloid Leukemia. J Blood Disord Transfus. 2014;5:230.</u>
- 27. <u>Richard Kim, et al. BRCA and Pancreatic Cancer: Selection of Chemotherapy. JOP. J Pancreas.</u> 2012;13.

- 28. <u>Yibin Feng, et al. Cancer Chemotherapy: Time for New Solution. Chemotherapy (Los Angel).</u> 2014;3:130.
- 29. <u>Bassam Abdul Rasool Hassan. Role of Cancer and Chemotherapy in the Incidence of</u> <u>Thrombocytopenia. Pharm Anal Acta. 2013;4:e157.</u>
- 30. <u>Stella Capriglione. Pelvic Recurrence of Breast Cancer Presenting as Ovarian Carcinoma: Case</u> <u>Report. Chemotherapy. 2013;2:116.</u>
- 31. <u>Ravez S, et al. Synthesis and Anti-proliferative Activity of 2-amino-4-Anilinoquinazoline Derivatives.</u> <u>Med chem. 2014;5:067.</u>
- 32. <u>Elizabeth M Nichols, et al. Radiation Therapy in the Elderly with Early Stage Breast Cancer: Review</u> and Role of New Technology. J Nucl Med Radiat Ther. 2014;6:204.
- 33. <u>Rajesh Kumar, et al. A Survey on the Quality Assurance Procedures Used in Intensity Modulated</u> <u>Radiation Therapy (IMRT) at Indian Hospitals. JCST. 2010;2:166-170.</u>
- 34. <u>Bijaya K. Nayak, et al. Synergistic Effect Between Curcumin (diferuloylmethane) and Radiation on</u> <u>Clonogenic Cell Death Independent of p53 in Prostate Cancer Cells. JCST. 2010;2:171-181.</u>
- 35. <u>Ricard Mesía, et al. (2009) Management of Cutaneous Toxicity and Radiation Dermatitis in Patients</u> with Squamous Cancer of the Head and Neck Undergoing Concurrent Treatment with Cetuximab and <u>Radiotherapy. JCST.2009;1-028-033.</u>
- 36. <u>Astrid Dalhaug, et al. Scylla or Charybdis: Case Report on Radiation Tolerance of the Spinalcord. J</u> <u>Nucl Med Radiat Ther. 2011;2:114.</u>
- 37. <u>Rasha Hamdy Hamed and Eman Elzahaf. Low Dose Weekly Paclitaxel Versus Low Dose Weekly</u> <u>Cisplatin with Concomitant Radiation in Locally Advanced Head and Neck Cancers. JCST. 2011;3-168-172.</u>
- **38**. <u>David R. SotoPantoja, et al. Therapeutic Targeting of CD47 to Modulate Tissue Responses to</u> <u>Ischemia and Radiation. J Genet Syndr Gene Ther. 2011;2:105.</u>
- 39. <u>Nicolaas A.P. Franken, et al. Radiosensitization with Chemotherapeutic Agents and Hyperthermia:</u> <u>Effects on Linear-quadratic Parameters of Radiation Cell Survival Curves. J Cancer Sci Ther. 2012;S5-002.</u>
- 40. <u>Hubert Fornalik, et al. Aspirin and Warfarin are Associated with Improved Overall Survival in Medically</u> <u>Inoperable Endometrial Cancer Patients Treated with Radiation Therapy. Gynecol Obstet (Sunnyvale).</u> <u>2012;S4-002.</u>
- 41. <u>Makoto Emoto. Low-Intensity Ultrasound Irradiation for Human Cancer- A New Therapeutic</u> <u>Application. J Ecosys Ecograph. 2012;2:e107.</u>
- 42. <u>Radha Malapati, et al. Late Mid trimester Pregnancy, Advanced Bulky Cervical Cancer, Radiation</u> <u>Therapy, and Physician's Moral Distress: A Management Dilemma. Gynecol Obstet (Sunnyvale).</u> <u>2012;2:114.</u>
- 43. <u>H Lomas, et al. Post Chemoradiation PET SUV is highly Predictive of Overall Survival in Esophageal</u> <u>Cancer. J Nucl Med Radiat Ther. 2012;3:125.</u>
- 44. <u>Sourav Guha. et al. (2012) Intensity Modulated Radiation Therapy (IMRT) in the Treatment of</u> Squamous Carcinoma of the Oropharynx: An Overview. JCST. 2012;4-077-083.
- 45. <u>ArunaTuraka. Intensity Modulated Radiation Therapy for Thyroid Cancer: Is it Beneficial? J Nucl Med</u> <u>Radiat Ther. 2012;3:e102.</u>
- 46. Joshua Bauml, et. al. A Pragmatic Evaluation of the National Cancer Institute Physician Data Query (PDQ)®-Based Brief Counseling on Cancer-Related Fatigue among Patients Undergoing Radiation Therapy. J Palliat Care Med 2012;2:125.
- 47. <u>NiranjanBhandare and William M Mendenhall. A Literature Review of Late Complications of Radiation</u> <u>Therapy for Head and Neck Cancers: Incidence and Dose Response. J Nucl Med Radiat Ther.</u> <u>2013;S2-009.</u>

- 48. <u>ArunaTuraka. Dose Response to Radiation Therapy for Primary Ocular Lymphomas. OMICS J</u> <u>Radiology. 2013;2:e118</u>.
- 49. <u>Aaron H Wolfson. Image-Guided Whole Abdominal Radiation Therapy in Gynecologic Cancers. OMICS</u> J Radiology. 2013;2:134.
- 50. <u>Cheena Chawla P and Anil Chawla. The Promise of Onco-immunology: Integrating Immunotherapy</u> with Conventional Cancer Treatments. J Integr Oncol. 2014;3:124.
- 51. <u>Talwar GP. et al. Immunological Approaches for Treatment of Advanced Stage Cancers Invariably</u> <u>Refractory to Drugs. J Clin Cell Immunol 2014;5:247.</u>
- 52. <u>Yoshihito Ohhara, et al. Circulating Tumor Cells as Prognostic Marker in Japanese patients with Kras</u> <u>Wild-type Metastatic Colorectal Cancer Receiving Panitumumab after Progression on Cetuximab. J</u> <u>Cytol Histol 2014;5:204.</u>
- 53. Jennifer Wu. IL-15 Agonists: The Cancer Cure Cytokine. J Mol Genet Med. 2013;7:85.
- 54. Igor Astsaturov. Development of Cures in the Era of Genomic Medicine. J Develop Drugs. 2012;1:e104.
- 55. <u>Rajendra Sharma. Cancer Chemoprevention: Prevention is Better than Cure. J Cancer Sci Ther.</u> <u>2012;S3-e001.</u>
- 56. Adnan Smsr, et al. Could Serum Testosterone Level and Body Mass Index Predict Psa Relaps in Prostate Cancer Patients undergoing Radical Surgery? J Cancer Sci Ther. 2011;S1-007.
- 57. <u>BL Milner, et al. CD133/EpCAM Cancer Stem Cell Markers of Tumor Stage in Colorectal Cancer Cells.</u> J Tissue Sci Eng. 2015;6:143.
- 58. <u>Poirier AL, et al. Report on the First Stages in the Translation of Measures of Health-Related Quality</u> of Life at the End of Life. J Palliat Care Med. 2014;4:178.
- 59. <u>Dieudonne Njamen, et al. The Efficacy of Some Comestible Natural Products in Treatment of Cancer.</u> <u>Altern Integ Med 2014;3:158.</u>
- 60. <u>Desai NS and Mohini Gore. Computer Aided Drug Designing Using Phytochemicals- Bacoside A3 and</u> <u>Myricetin and Nitric Oxide Donors-S-Nitroso N-Acetylpenicillamine and Nitroglycerin as a Potential</u> <u>Treatment of Pancreatic Cancer. J Comput Sci Syst Biol. 2012; 5:001-008.</u>
- 61. <u>David L Vesely. Cardiac Hormones for the Treatment of Prostate Cancer. J Cancer SciTher. 2011;S1-001.</u>
- 62. <u>Christine D Craig, et al. Cognitive Impairment in Gynecologic Cancers: A Systematic Review of Current</u> <u>Approaches to Diagnosis and Treatment. J Palliat Care Med. 2013;3:144.</u>
- 63. <u>ChangxiongGuo and DaotaiNie. Are Lipoxygenases Valid Targets of Cancer Prevention and</u> <u>Treatment? J Carcinog Mutagen. 2012; S1-008.</u>
- 64. <u>http://omicsonline.org/abstract/Harnessing_Novel_Biomarkers_Of_Human_Embryonic_Stem_Cells_For_Cancer_Diagnosis_And_Therapy/</u>
- 65. <u>AduGyamfi M, et al. Efficacy of Supportive Histo-morphological Features in Prostate Cancer</u> <u>Diagnosis. Med Surg Urol. 2014;3:142.</u>
- 66. <u>Arnon Blum, et al. Virchow Node and Gastric Cancer Clinical Diagnosis is Still Important. J Clin Case</u> <u>Rep. 2014; 4:412.</u>
- 67. <u>Raffaele Pezzilli, et al. Lymphocytes and Pancreatic Cancer: The Effects of These Cells on Diagnosis</u> <u>and Patient Survival. JOP. J Pancreas. 2011;12.</u>
- 68. Md. ZillurRahman. Breast Cancer: Diagnosis Advanced. Surgery Curr Res. 2014; 4:e112.
- 69. <u>Marolt U, et al. Generating Aptamers for Cancer Diagnosis and Therapy. ClinExpPharmacol.</u> <u>2012;2:111.</u>
- 70. <u>David R Baldwin and Richard B Hubbard. Lung Cancer: Early Diagnosis and Screening. J Cancer</u> <u>SciTher. 2012;S7-002.</u>
- 71. <u>Wataru Heshiki, et al. Constitutive Activation of Caspase-3 in Non-Apoptotic Oral Squamous Cell</u> <u>Carcinoma Cells. J Cancer Sci Ther. 2015. 7:075-080.</u>

- 72. <u>Ana Paula de SouzaPardo. Side-by-Side Epigenetics and Genetics Share Importance in Cancer</u> <u>Development. Human Genet Embryol. 2015;</u>
- 73. Jain T, et al. Theranostics: A Way of Modern Medical Diagnostics and the Role of Chitosan. J Mol Genet Med 2014; 9:159.
- 74. <u>Cestmir Altaner. Pro-drug Gene Therapy for Cancer Mediated by Mesenchymal Stem/Stromal Cells</u> <u>Engineered to Express Yeast Cytosinedeaminase: Uracilphosphoribosyltransferase. J Stem Cell Res</u> <u>Ther. 2015; 5:264.</u>
- 75. Byrne C, et al. Predicting Risk of Anastomotic Leak in Patients Undergoing Neo-adjuvant Radiotherapy and Low Anterior Resection for Rectal Cancer. J Gastrointest Dig Syst. 2015; 5:255.
- 76. <u>IvanaSpasevska, et al. Advances in Bispecific Antibodies Engineering: Novel Concepts for</u> <u>Immunotherapies. J Blood DisordTransfus. 2015; 6:243.</u>
- 77. <u>Moshe Lapidot, et al. Involvement of Heparanase in Empyema: Implication for Novel Therapeutic</u> <u>Approaches. JClin Cell Immunol. 2015; 6:290.</u>
- 78. <u>Sarah K Baird.Mesenchymal Stem Cells: How can we realize their Therapeutic Potential in Cancer</u> <u>Therapy? J ClinExpPathol. 2015; 5: 206.</u>
- 79. <u>Hoda Sbeity and Rafic Younes. Review of Optimization Methods for Cancer Chemotherapy Treatment</u> <u>Planning. J ComputSciSystBiol. 2015; 8: 074-095.</u>