

The Basics of Cancer Biology and its Genomics

Vrushali Petkar¹, Suvarna Chavan¹

¹Department of Zoology, K.J.Somaiya College of Arts, Commerce and Science Kopergaon, Maharashtra, India.

Submitted: 05-06-2022

Revised: 18-06-2022

Accepted: 27-06-2022

ABSTRACT:

Cancer incidences are dramatically increasing in society. The effect of cancer is rising constantly in all age groups. Nowadays, cancer research is more focused on the study of the progressive and novel therapeutic perspectives of cancer treatment. The researchers continuously working on the medicines of good future to treat cancer. Recently, research on cancer medicine has taken important steps towards more effective, accurate as well as less invasive treatment of cancer. Uncontrollable growth of cancer is caused by genetic as well as environmental factors. The most common risk factors for cancer include smoking, tobacco consumption, obesity, infectious diseases, chemicals as well as radiation exposure. Those risk factors can perform collectively for beginning and assisting carcinogenesis of the body. In savior conditions, they can cause death. Various therapies are used in the treatment of cancer like targeted therapy, immunotherapy, stem cell transplant, chemotherapy, surgery, hormone therapy, and radiation therapy as well as hormone therapy.

Keywords: Cancer therapy, Endometrial cancer, microsatellite instability, endocrine therapy, physiology of cancer, chemotherapy.

I. INTRODUCTION:

Cancer is a major and gradually increasing problem all over the world¹. This is the main cause of mortality worldwide and goes on increasing day by day². Our body is made up of enormous cells, which die and get replaced by new cells. Those new cells are obtained from pre-existing cells in our body. Although, in some cases, those cells divide continuously without any restriction. This continuous division of cells causes an abnormality in our body, which we called "cancer"³. Cancer is a metastatic, invasive as well as proliferative disease. It causes due to genetic defect which forms the malignant cell⁴. Uncontrollable growth of cancer is caused by genetic as well as environmental factors⁵. Several extrinsic factors like chemicals, tobacco, radiation as well as infections organisms are also responsible to cause cancer. In addition to

intrinsic factors hormones, random mutations inherited mutations, as well as immune conditions, can cause cancer. Several things are well known to rise the chance of cancer in addition to, some infections, dietary factors, the inadequacy of the physical activity, obesity as well as environmental pollutants. Those risk factors can perform collectively for beginning and assisting carcinogenesis of the body. In savior conditions, they can cause death⁶.

The process of carcinogenesis involves normal cells which are further transformed into cancer cells⁷. Cancer risk largely expanded when workers are exposed to the ionizing radiation, carcinomas chemicals, metals as well as some other particular substances are exposed in low quantity. Passive tobacco smoke rises the risk in the huge population. The people don't smoke but they are exposed to the smokers⁸. Cancer is named after the part of the body where it originated. Carcinomas are cancer that starts in the epithelial cell lining. Sarcoma starts in epidermal cell lining such as connective tissue, cartilage, muscles including bones. Lymphoma is a type of cancer that begins in the immune system cells. Leukemia is begun in cells of the bone marrow⁹. The main cancer treatments like immunotherapy, surgery, radiation therapy as well as chemotherapy¹⁰.

CAUSES OF CANCER

Many factors can cause cancer in distinct parts of the body. It can be analyzed as, mostly 22% deaths due to the consumption of tobacco, 10% deaths because of obesity, inadequate diet, absence of the physical activity, and enormous drinking of the alcohol. It includes some other facts like environmental pollutants, ionizing radiation exposure, and infection. About 15% of worldwide cancer is a result of certain infections like hepatitis B and hepatitis C, Helicobacter pylori, infection, immunodeficiency virus (HIV), human papillomavirus as well as Epstein - Barr virus. This element slightly causes the changing of genes. The inherited gene fault of the patient's parents that are causing 5-10% of cancer. Genetic factors

interaction is one of the causes of cancer along with three types of the agents that consist of:

Physical Carcinogens

Ionizing radiation like radon, ultraviolet radiation in sunlight, alpha, beta, gamma, uranium as well as X-ray radiation.

Chemical Carcinogens

The compounds such as cadmium, n-nitrosamines, benzene, nickel, asbestos, and vinyl chloride including benzidine along with around 60 well-known vigorous cancer-causing substances and chemicals found in cigarette smoke and consumption of tobacco. Arsenic is the main chemical contaminant in drinking water and the food contaminant is the aflatoxin.

Biological Carcinogens

The Infections of some bacteria, viruses, or parasites as well as pathogens such as Merkel cell polyomavirus, hepatitis B and hepatitis C, Epstein-Barr virus, human papillomavirus (HPV), *Schistosoma* spp., in addition to *Helicobacter pylori*.

Genetics

Genetics is a general reason for cancer or tumor such as skin cancer, ovarian, prostate, breast, and colorectal cancer. The harmful compounds formed by the elevation of temperature in cooked meat also raise the risk of cancer¹¹⁻¹³.

TYPES OF CANCER

The first type is Carcinoma in which, cancer starts in the skin or tissues, it covers internal organs as well as glands that produce the solid tumor. Lung cancer, colorectal cancer, prostate cancer as well as breast cancer¹⁴. Next is Sarcoma in which, cancer starts infecting tissues that attach in support with the body, produced in nerves, lymph vessels, tendons, bones, joints, muscles, fat, cartilage as well as blood vessels¹⁵. Leukemia is a blood cancer. It shows the rapid growth of the abnormal blood cells¹⁶. Another type is Lymphoma which starts in the lymphatic system. It includes the vessel network as well as glands which help fight infections. Hodgkin lymphoma as well as non-Hodgkin lymphoma^{17,18}. Central Nervous System begins the infection in the brain as well as the spinal cord and is known as “brain and spinal cord tumors”, in addition to pituitary adenomas, primary CNS lymphomas, gliomas, vestibular schwannomas as well as meningiomas¹⁹. Multiple Myeloma is cancer that begins in plasma cells. Multiple myeloma cells are usually found to be abnormal plasma cells found in the bone marrow to

produce tumors in the bones²⁰. Melanoma is a skin cancer formed in cells (melanocytes) that synthesizes melanin. Majorly melanomas are produced in the skin, although they are formed in pigmented tissue such as the eye²¹.

NORMAL CELL TO CANCEROUS CELL CONVERSION

Cell Changes and Cancer

A body of a living organism is formed of the smallest unit known as cells. All kinds of cancer initially start in the cells. Generally, the body possesses the correct number of cells. For a specific reason, the cell generates specific signals. when the signal is absent then cells can begin to propagate unessentially and resulting in the formation of a lump which is known as a tumor. Although the several types of cancer that begin with different pathways such as blood cells, it is known as leukemia, and that does not form a solid lump.

Genes and Cell Division

All cells have the nuclei that control cells, as well as the nucleus. In the nucleus, chromosomes are present, which are formed by thousands of genes. The elongated string of the DNA is known as genes. Genes carry a coded message that notifies the cell when exactly act and divided. At the right time, cell division occurs and the cells are divided into precise same copies of it. The cell divides into two similar cells, those two cells divide into the four cells, and so on.

Gene Changes within Cells (Mutations)

During the cell division, mutation takes place because of external activity such as tobacco smoking. In Mutation the gene can be copied twice, damaged, and lost. The mutation in a cell grows unessentially. Mutation in particular genes means the cell stops forming proteins. In mutated cell division, numerous unnecessary proteins form through the cell division and develop a lump or tumor.

How Cancer Grows

The cancer cells grow continuously. Cancer cells act separately from normal cells. The cancer cells require nutrients as well as oxygen to grow as well as survive. A tumor may simply grow with nutrients as well as oxygen. It requires the blood supply to carry oxygen including nutrients for growing and multiplying. The cancer cells are distinct from the normal cells because, it divides abnormally, became evade the immune system, the avoid signals of self-destruction²².

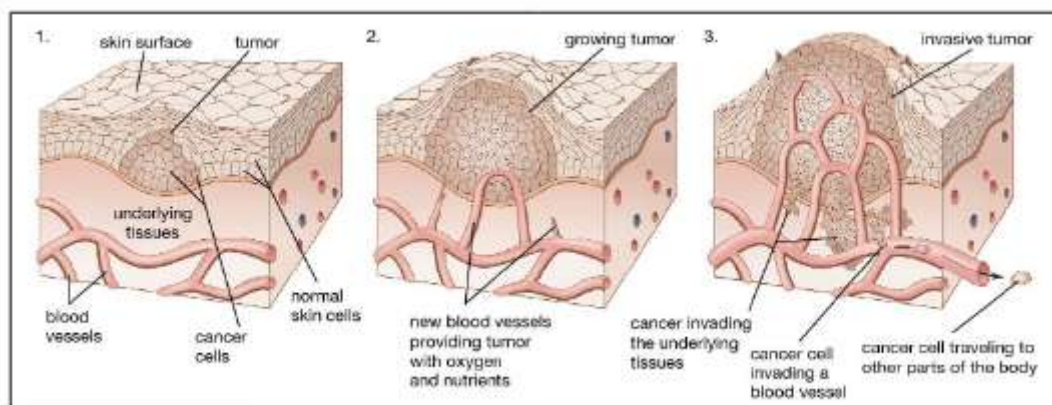


Figure 1. A visual representation of cancerous cell development²³.

REGULATION OF CANCEROUS CELLS

For the study of cancer physiology, the study of the cell cycle is required. The cell cycle consists of four steps that bring about cell growth as well as cell division to form 2 daughter cells. The phases such as G1, S, and G2 including M. A Cdk4 and Cdk6 are closely associated because of common the cyclin partner (Cyclin D). The p16, p15, p18 as well as p19 are four INK4 proteins that perform like CKIs that are cyclin-dependent kinase Inhibitors to CDK4 as well as CDK6 bringing on G1 phase arrest. It determined the CDK4/6-cyclin D interaction essential of the passage by restriction point with the exit of the G1 phase. That takes place by Retinoblastoma (Rb) Pathway. The Rb gene is the tumor suppressor gene. Rb-associated proteins like p130 as well as p107 attach with E2F complexes while in its hypophosphorylated condition with repressed E2F complexes activates target genes necessary to start of S-phase.

CDK4/6-cyclin D complex brings about phosphorylation of Rb including Rb-like proteins and thus frees E2F complexes that after transactivating other genes necessary for DNA synthesis and some cyclins like Cyclin E as well as cyclin A. The phosphorylation after hastened with cyclin an E-CDK2 complex shows the positive response exists of increase a progression in Rb phosphorylation, E2F release, gene transactivation including S-phase entry take place. Rb maintains hyperphosphorylated condition with cyclin including Cyclin B-dependent kinase complete rest of cycle then completion of the mitosis and reentry in G1 or G0 phase. The S-phase is triggered, by a degradation of the E2F. The cyclin E started and a subsequent being targeted of the destruction with phosphorylation through CDK2 then is degraded with proteolysis later ubiquitination. The increase of cyclin A-CDK2 is shown that prevent interaction in

the DNA and E2F so preventing more gene transactivation. The cyclins D-, E- as well as A-dependent kinases are inhibited with CKIs p21, p27 including p57. In the cancer cells, amplification of gene with translocation of D1 locus in the chromosome 11q13 observed that causes overexpression of the cyclin D1. A similar happens in event of the CDK4. It was determined in the heads squamous cell carcinomas including neck, bladder cancer, small-cell lung tumors, primary breast carcinoma, esophageal carcinomas, as well as hepatocellular carcinomas. The melanoma in which biliary tract including esophageal carcinomas, is a mutation it disables a CDK inhibitory role of the INK4a gene in the chromosome 9p21 described.

CDK4 mutations prevent an interaction with the p16 noticed in the melanoma. The INK4a locus homozygous deletions are identified with accounted for the nasopharyngeal carcinomas, gliomas, mesotheliomas, sarcomas, acute lymphocytic leukemias, bladder as well as ovarian tumors. A G1 checkpoint is mainly dependent on p53 this is the tumor suppressor gene. A p53 gene is regarded as a main designed tumor suppressor gene. That accumulates while cell exposure to the ultraviolet light, gamma-irradiation including chemotherapeutic drugs causes the genotoxic stress. That regulates the several genes it included of cell-cycle arrest in G1 with DNA repair later detecting the damage of DNA before genomicstakes place. Whether later fails, p53 can trigger the death of a cell through apoptosis. Therefore, p53 is commonly referred to as "the guardian of the genome" that restricts the multiplication of the faulty genome of the daughter cells²⁴.

CANCER TREATMENTS AND TYPES

Types of cancer treatments include Surgery, Targeted Therapy, Immunotherapy, Chemotherapy, Radiation therapy, Hormone Therapy, Stem Cell Transplants as well as medications²⁵⁻²⁷.

Surgery

That prevents or decreases the spread of diseases including removing cancer from the body, a surgeon can remove the lymph nodes. The surgeon generally used small and thin knives known as scalpels. Surgery usually needed cuts in skin, muscles, as well as frequently bone. Surgeries are mainly useful for solid tumors; this is a local treatment reason that is enclosed in one area²⁸.

Radiation therapy/Radiotherapy

The therapy is used for a large quantity of radiation and is useful for cancer treatment by killing the cancer cells, shrinking tumors, and slowing their growth. Radiopharmaceuticals are radioactive medications that are useful for a treat the pain it spread in the bones, external beams are useful for a treat pain, bladder control, loss of the bowel, as well as problems breathing through shrinking tumors²⁹.

Chemotherapy

Chemotherapy used medicines or drugs for the treatment of cancer. In this therapy, chemicals are used for the treatment of cancer to stop and slow down the cancer cells' growth or kill the cancer cells along with shrinking the tumors, it causes pain as well as another problem although has serious difficulties³⁰.

Immunotherapy

The immune system is boosted by this therapy through medications and other treatments. For example, the adoptive cell as well as checkpoint inhibitors treatment. The immune system formed the WBC as well as tissues of the lymph nodes which helps the body to fight against diseases and infections by increasing its strength. Also known as biological therapy, which described the use of substances formed from living organisms for the treatment of cancer. Certain immunotherapies are immune system boosters and also help the immune system recognize cancer cells and destroy them by marking that cells³¹.

TYPES OF IMMUNOTHERAPIES

Checkpoint Inhibitors

It is a type of drug which used to boost the immune system for the treatment of cancer. However, the drugs do not directly target the

tumor cells, but the drug-breaking capability of the cancer cells prevents the attack on the immune system. It releases brakes carried by the t cells³².

Adoptive Cell Transfer

The T cells can fight cancer and remove the tumor. The t-cells can be grown in huge batches in the laboratory. It takes 2-8 weeks for them to grow, later the cells get inserted back into the body via vein with the help of a needle.

Monoclonal Antibodies

It is an immune system protein that is formed in the laboratory. It can bind particular targets of the cancer cells. The monoclonal antibodies marking on cancer cells because the immune system simply finds and destroys them³³.

Targeted Therapy

In this therapy, the target cells can grow, divide, spread, and also boost the immune system. For example, monoclonal antibodies, as well as to small-molecule drugs. The targeted therapy is useful for the treatment of cancer through the interference of particular proteins. It assists tumor growth along with spread in the body³⁴.

Hormonal or Endocrine Therapy

The therapy in which hormone is used for the treatment of cancer, like prostate as well as breast stop or slow growth of that hormones. Hormone therapy can be used in distinct ways at different times. It included, before surgery to shrink a cancerous tumor (neoadjuvant therapy), and after other cancer treatments to decrease the chance of cancer coming back. It is known as adjuvant therapy, which destroys the cancer cells to prevent it comes back after the treatment³⁵.

Stem Cell Transplant

The therapy restores blood-producing stem cells in cancer patients that are damaged through chemotherapy and radiation. The stem cells can generate distinct cells types cells that are required for health, the important types of the blood cells like RBC for transport of oxygen, WBC to protect the body against infections, and Platelets used in the blood clotting. It generally does not directly act against cancer except the certain kind of leukemia including numerous myelomas, although that useful for a patient to reproduce the stem cells later in the treatment including the large quantity of the radiation as well as chemotherapy.

Types of Stem Cell Transplant

Allogeneic transplant in which, stem cells from the other as blood relations and another person, Autologous transplant which is an autologous transplant, stem cells collected from the patient for themselves, Syngeneic transplant in

which, stem cells obtained from similar twins whether the patient is one^{36,37}.

Different types of medications

There are different types of cancer medications. It consists of alkylating agents, plant alkaloids as well as antimetabolites. Doctors use the cancer medications on their own and in composite with another treatment, like radiation therapy. A great medication includes a combination that is mainly based on several components which affect disease progress as well as a person's complete health³⁸.

RECENT TREATMENT OF CANCEROUS CELLS

Endometrial cancer (EC) is a general gynecologic malignancy and it has the greatest amount of mismatch repair-deficient/microsatellite instability-high (dMMR/MSI-H) condition in tumors; until 30% of complete ECs categorized like dMMR/MSI-H. A main function of MSI is to repair the fault of DNA mismatch repair (MMR) genes by mismatched bases. The loss of MMR proteins (MSH2, MSH6, MLH1 including PMS2) is because of epigenetic silencing and genetic mutation which is related to errors in DNA replication of microsatellite areas. The screening with immunohistochemistry (IHC) is useful for identifying the MMR protein condition, besides dMMR (absent any MMR proteins) and MMRp (present the total MMR proteins).

Microsatellite instability (MSI) is a hallmark of dMMR that may be noticed with further next-generation sequencing (NGS) or PCR. The molecular description in the ECs is determined by four subgroups of EC in related prognostic implication: The POLE-mutated tumors are associated with desirable prognosis, the MMR-deficient tumors are associated with prognosis of intermediate, including MMR-proficient as well as p53-mutated tumors related to faulty prognosis. But dMMR is probably the inferior endometrioid histologic subtype, the MMRp tumors, which incorporate a larger number of the ECs (~70%), contain several histologic subtypes related to low prognosis with a restricted choice of treatment. The Dostarlimab (JEMPERLI) is humanized monoclonal antibody of the IgG4-k, it has a great affinity for PD-1, causing inhibition of the attached with PD-L1 as well as PD-L2. In the USA, dostarlimab is accepted as monotherapy for adult patients with dMMR recurrent, and EC is proceeded and later the platinum-carrying regimen³⁹.

II. CONCLUSION:

In this paper, we focused on the study of cancer, its origins, spread, development, multiplication, and therapeutic analysis of it. Along with the physiological study of cancer we have given various emerging therapeutic methods for the treatment of cancer. This paper gives a brief idea about the Microsatellite Instability (MSI) method of cancer treatment. This article will help to understand the physiology of cancer and its Therapeutic agents alone with newly developing testament methods.

III. ACKNOWLEDGMENT:

The authors gratefully acknowledge Dr. B. S. Yadav, principal of the K. J. Somaiya College of Arts, Commerce, and Science in Kopargaon, and Prof. Prajakta Deshpande, Department of Zoology at the H. P. T. Arts, and R. Y. K. Science College in Nashik, Maharashtra, India, for their insightful comments that significantly enhanced the quality of this Research article.

REFERENCES

- [1]. Lekha, G. S., Aparna, S., Kasirajan, N., & Kanagarajan, A. (2018). Diagnosis and Treatment of Cancer—Siddha Perspective. *J Res Sid Med*, 1(1), 3-14.
- [2]. Noh, C. I. C., & Rahman, M. S. (2017). Immunotherapy for the treatment of cancer: a review. *Borneo Journal of Medical Sciences (BJMS)*, 3-12.
- [3]. Hegde, M. V., Mali, A. V., & Chandorkar, S. S. (2013). What is a cancer cell? Why does it metastasize?. *Asian Pacific Journal of Cancer Prevention*, 14(6), 3987-3989.
- [4]. Rossi, F., Noren, H., Jove, R., Beljanski, V., & Grinnemo, K. H. (2020). Differences and similarities between cancer and somatic stem cells: Therapeutic implications. *Stem Cell Research & Therapy*, 11(1), 1-16.
- [5]. Reddy, S., Ramesh, S. and Anupalli, R.R. (2019). A Mini-Review on Breast Cancer-Risk factors, Treatment and Prevention. *Journal of Emerging Technologies and Innovative Research (JETIR)*. 6(3).
- [6]. Mathur, G., Nain, S., & Sharma, P. K. (2015). Cancer: an overview. *Acad. J. Cancer Res*, 8(1).
- [7]. Ridhowati, S., Zakaria, F. R., Syah, D., & Chasanah, E. (2014). Sea cucumber as an anticancer agent and Its development for functional food products. *Squalene Bulletin*

- of Marine and Fisheries Postharvest and Biotechnology, 9(2), 85-96.
- [8]. Nataru, S., Pulicherla, Y., & Gaddala, B. (2014). A review on medicinal plants as a potential source for cancer. *Int J Pharm Sci Rev Res*, 26(1), 235-48.
- [9]. Mounica, U., Pooja, S., Senthil, J., and Janakidevi, V. (2020). Anticancer Activity of Some Medicinal Plants: A Review. 4(6).
- [10]. Mansoori, B., Mohammadi, A., Davudian, S., Shirjang, S., & Baradaran, B. (2017). The different mechanisms of cancer drug resistance: a brief review. *Advanced pharmaceutical bulletin*, 7(3), 339.
- [11]. Saini, A., Kumar, M., Bhatt, S., Saini, V., & Malik, A. (2020). Cancer causes and treatments. *International Journal of Pharmaceutical Sciences And Research*, 11, 3109.
- [12]. Quazi, M. A., & Molvi, K. I. (2014). Management of Cancer with Herbal Remedies. *International Journal for Pharmaceutical Research Scholars*, 3(3), 45-51.
- [13]. Anand, P., Kunnumakara, A. B., Sundaram, C., Harikumar, K. B., Tharakan, S. T., Lai, O. S., & Aggarwal, B. B. (2008). Cancer is a preventable disease that requires major lifestyle changes. *Pharmaceutical Research*, 25(9), 2097-2116.
- [14]. Abbas, Z., & Rehman, S. (2018). An overview of cancer treatment modalities. *Neoplasm*, 1, 139-157.
- [15]. Burningham, Z., Hashibe, M., Spector, L. and Schiffman, J.D. (2012). The Epidemiology of Sarcoma. 2(1):14. DOI: 10.1186/2045-3329-2-14
- [16]. Chapalamadugu, U., Ojochenemi, D. A., & Chatakonda, R. *Asian Journal of Research in Pharmaceutical Sciences and Biotechnology*.
- [17]. Word, Z. H., & Matasar, M. J. (2012). Advances in the diagnosis and management of lymphoma. *Blood and Lymphatic Cancer: Targets and Therapy*, 2, 29-55.
- [18]. Montes-Moreno, S. (2011). Hodgkin's lymphomas: a tumor recognized by its microenvironment. *Advances in hematology*, 2011.
- [19]. Nabors, L. B., Ammirati, M., Bierman, P. J., Brem, H., Butowski, N., Chamberlain, M. C., & Ho, M. (2013). Central nervous system cancers. *Journal of the National Comprehensive Cancer Network*, 11(9), 1114-1151.
- [20]. Gerecke, C., Fuhrmann, S., Striffler, S., Schmidt-Hieber, M., Einsele, H., & Knop, S. (2016). The diagnosis and treatment of multiple myeloma. *Deutsches Ärzteblatt International*, 113(27-28), 470.
- [21]. Gupta, A. K., Bharadwaj, M., & Mehrotra, R. (2016). Skin cancer concerns in people of color: risk factors and prevention. *Asian Pacific journal of cancer prevention: APJCP*, 17(12), 5257.
- [22]. Saini, A., Kumar, M., Bhatt, S., Saini, V., & Malik, A. (2020). Cancer causes and treatments. *International Journal of Pharmaceutical Sciences And Research*, 11, 3109.
- [23]. Britannica, T. (2020). Editors of Encyclopaedia. Argon. *Encyclopedia Britannica*.
- [24]. Xuereb, J., & Blundell, R. (2008). The role of cell cycle regulation in cancer.
- [25]. Patil, S. A., Shinde, K. S., Choudhary, H. B., Patekar, R. R., & Rede, S. D. (2021). The novel approach in various types of cancer treatments. *World Journal of Advanced Research and Reviews*, 10(3), 403-411.
- [26]. Suryadev, Y.Y., Kumar, V.A., Kumar, Y.R., Vimal, Y. and Piyush, Y. (2017). Targeted Cancer Therapy. 1(1):11-17
- [27]. Chu, D. T., Nguyen, T. T., Tien, N. L. B., Tran, D. K., Jeong, J. H., Anh, P. G., ... & Dinh, T. C. (2020). Recent progress of stem cell therapy in cancer treatment: molecular mechanisms and potential applications. *Cells*, 9(3), 563.
- [28]. Shabgah, A. G., Navashenaq, J. G., Mahboobi, M., & Sedighian, H. (2014). Immunotherapy is an optimal manner for cancer treatment. *Biosciences Biotechnology Research Asia*, 11(3), 1167-1178.
- [29]. Baskar, R., Lee, K. A., Yeo, R., & Yeoh, K. W. (2012). Cancer and radiation therapy: current advances and future directions. *International journal of medical sciences*, 9(3), 193.
- [30]. Mustapha, A., Ismail, A., Abdullahi, S. U., Hassan, O. N., Ugwunnaji, P. I., & Berinyuy, E. B. *Cancer Chemotherapy: A Review Update of the Mechanisms of Actions, Prospects, and Associated Problems*.
- [31]. Smith, A. J., Oertle, J., & Prato, D. (2014). Immunotherapy in cancer treatment. *Open Journal of Medical Microbiology*, 4(03), 178.

- [32]. Esfahani, K. (2020). Roudaia L. Buhlaiga N. Del Rincon SV Papneja N. Miller WH Curr. Oncol, 27, S87-S97.
- [33]. Zhang, H., & Chen, J. (2018). Current status and future directions of cancer immunotherapy. J Cancer 9: 1773–1781.
- [34]. Hosseinzadeh, E., Banaee, N., & Ali Nedaie, H. (2017). Cancer and treatment modalities. Current Cancer Therapy Reviews, 13(1), 17-27.
- [35]. Abraham, J., & Staffurth, J. (2008). Hormones in cancer. Practical Clinical Oncology, 23.
- [36]. Zhang, C. L., Huang, T., Wu, B. L., He, W. X., & Liu, D. (2017). Stem cells in cancer therapy: opportunities and challenges. Oncotarget, 8(43), 75756.
- [37]. Barrachina, L., Remacha, A. R., Romero, A., Vázquez, F. J., Albareda, J., Prades, M., & Rodellar, C. (2017). Priming equine bone marrow-derived mesenchymal stem cells with proinflammatory cytokines: implications in immunomodulation–immunogenicity balance, cell viability, and differentiation potential. Stem Cells and Development, 26(1), 15-24.
- [38]. Falzone, L., Salomone, S., & Libra, M. (2018). Evolution of cancer pharmacological treatments at the turn of the third millennium. Front Pharmacol. 2018; 9: 1300.
- [39]. Oaknin, A., Gilbert, L., Tinker, A.V., Brown, J., Mathews, C., Press, J., Sabatier, R., Malley, D.M.O., Samouelian, V., Boni, V., Duska, L., Ghamande, S., Ghatage, P., Kristeleit, R., Leath, C., Guo, W., Im, E., Zildjian, S., Han, X., Duan, T., Veneris, J. and Pothuri, B. (2021). Safety and antitumor activity of dostarlimab in patients with advanced or recurrent DNA mismatch repair-deficient/microsatellite instability-high (dMMR/MSI-H or proficient/stable (MMRp/MSS) endometrial cancer: interim results from GARNET-a Phase I, single-arm study. DOI: 10.1136/jitc-2021-003777