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Mini Review

A Review on Anticancer Immunotherapy

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ABSTRACT

Nanoparticle-based drug delivery system is the emerging therapeutic strategy preferred for cancer patients to improve their survival alongside quality of life. Beneficial therapeutic strategies are the major goal in immunology and oncology. Nanotechnology introduces targeted site specific nano-medicine for which different phytochemical loaded nano-carriers made it easily accessible. Where chemo immunotherapy shows promising results in cancer patients it has some limitations as well. A detailed work needed to be done on immunosuppression of immune response and role of immune system in case of tumorgensis. Major hindrance arise uptill now is that immunotherapy down regulates the activity of immune system by failing to recognize tumor antigens by host cells. Certain immune checkpoints have been observed while performing immunotherapy. These immune checkpoints show immune resistance especially for T cells that recognize tumor antigens. Research shows that these checkpoints are initiated by ligand receptor interaction. Anti-tumor immunity is enhanced by binding programmed cell death protein 1 and programmed cell death ligand 1.Cytotoxic drugs are considered as potential partners in blockade of checkpoints. More interest in immunotherapy considered as valid approach for cancer treatment and its limitations can be solved by aiming to the personalized therapies.

Keywords: Chemo-immunotherapy; Biopharmaceuticals; Vaccines for tumor; Genetically modified T cell therapy; Cell signaling molecules

INTRODUCTION

The major cause of death in people worldwide is cancer and its treatment strategies are still under progress [1,2]. The clinical strategies that are considered for cancer treatment are surgery, radiotherapy, chemotherapy, immunotherapy [3]. Among these strategies for cancer treatment, the most emerging one is the immunotherapy because it works by manipulating the immune system rather than working on tumor itself [4,5]. It is hypothesized that when decipher protein receptors were blocked ,the immune system attack on cancerous cells. Antibody therapies found to be affective in patients with end stage metastasis. The first immune checkpoint blockade agent that is approved by US Food and Drug administration is Ipilimumab [6,7]. Ipilimumab is antibody that is synthesized by cloning a unique white blood cell, this then activates our immune system by effectively target CTLs associated antigen-4,whose main work is reducing the extent of immune system. These CTLs associated antigen-4 then recognize and destroy cancer cells. Major challenges that we face while clinically moving to immunotherapy is firstly immunotherapy drug act against a checkpoint protein called CTLA-4,secondly the low ability of cells /tissues to provoke immune system after administration of vaccine when disease already occur and other immune related adverse effects also witnessed [8].

LITERATURE REVIEW

Chemotherapy

Standard therapy chemotherapy, radiotherapy, surgery used for cancer treatment. If one has non-metastatic disease so cancer that hasn't spread around body, surgery remains like gold standard as cure. What chemotherapy do, it actually helps in inhibiting the rapid expansion of cancer cells. Major drawback

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of opting this treatment for cancer is that it hinder growth cells, cause hair loss , stomach discomfort and sensation of wanting to vomit and abdominal pain, swelling, distention or bloating [9].Chemotherapy fails in treating patients due to long time course of drug absorption, distribution, metabolism and excretion leading to decreased efficacy and increased patient's drug therapy toxicity. To enhance its efficacy chemotherapy is used in combination with other standard therapies [10, 11]. Antitumor efficacy is enhanced by using chemotherapy in combination with immunotherapy. Chemotherapy acts by directly killing tumor cells, on the other hand immunotherapy reactivates our immune system to act against cancer cells and destroy them. While moving to their lasting effects and time duration, chemotherapy considered a speedy action and has short action time, in contrast immunotherapy has long lasting effect against tumor. Chemotherapy deficiency like cancer stem cells as well cells that shows resistance to therapeutic chemotherapy can be easily handled by immunotherapy [11]. Gene therapy comprises of the incorporation of hereditary material into cells for a restorative reason which bring about the expression of missing protein to fix the hereditary defects or to improve their clinical status. This approach can likewise be applied to prevent disease by changing the pattern of gene expression in the host cells. The transfer of the normally functioning gene into the patient's cells is accomplished by utilizing non-viral or viral vectors.

Cancer immunotherapy

To understand how cancer immunotherapy works, we need to understand cancer-immunity cycle [6].Several steps for cancer immunity are first release of cancer antigens in body, then present these cancerous antigens to APCs, after that exposing and influencing response and activating T cells cells then interact with B cells to produce antibodies, priming of CD8 T cells generates cytotoxic T cells that are actually capable of directly killing cancerous cells [7] in Figures 1 and 2.

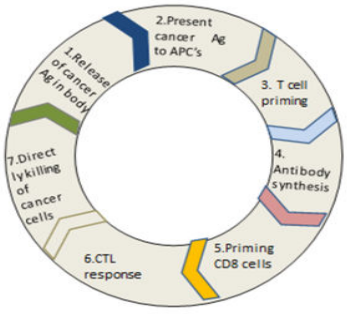

Figure 1: Cancer-immunity cycle.

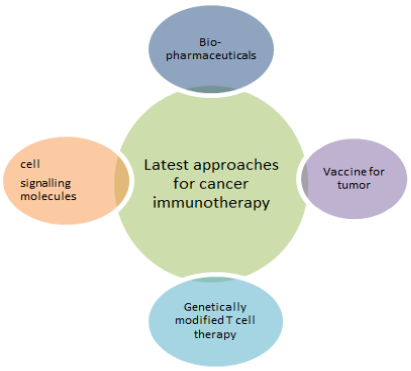

Figure 2: Latest approaches for cancer immunotherapy.

Biopharmaceuticals

Numbers of therapeutic pharmaceuticals have been approved by FDA and several are in their clinical trials. This immune checkpoint therapy actually brings major advances clinically against tumor [12]. Immune checkpoints have ability to recognize and not respond against self-produced antigens, without these checkpoints body start to attack its own cells and may lead to autoimmune disease. Blockade in these checkpoints will cause these biopharmaceuticals to reactivate immune cells and improves ability of immune cells to directly destroy cancerous cells [13]. Up till now seven immune checkpoint agents are approved by FDA, among these the first one is ipilimumab, that works by activating cytotoxic T cells to directly kill cancer cells. In last stage cancer patients, this ipilimumab along with imidazole carboxamide treatment has reduced death rate as compared to imidazole carboxamide treatment along with any injection /medical device. Another way of indirectly killing tumor cells is by reactivating T cells and blocking the binding of programmed cell death protein 1 to the programmed cell death ligand 1\.Several PD-1 antibodies are available as well several PDL-1 blocking agents are approved for treatment. Combination of PD-1 and CTLA-4 antibody developed and is used for a type of skin cancer immunotherapy [14].

Vaccine for tumor

Vaccines available for cancer are categorized into therapeutic cancer vaccines that are effective against existing tumor and other one is autologous vaccines that are specific for specific patient. Among the preventive vaccines available, HPV vaccine has the potential to prevent HPV-attributable cancers [15]. When viral infection become the cause of development of cancer in that case preventive vaccines plays important role in reducing risk. Tumor vaccines are actually a form of immunotherapy that educate our immune system how cancer cells look like so that they easily recognizable and are eliminated easily. Every person tumor has some unique antigens in that case moving to use of therapeutic vaccine for that tumor proved sophisticated way of treating it [16]. On the other side, some tumors arose as a result of mutations, in that case opting autologous vaccines is the only option left to treat it. Several other diverse vaccines that include GM-CSF, Gp-100 are under

clinical trials and are evaluated in phase 2, 3. Cancer vaccines are often used in combination with the substances that enhances the immune system's response to the presence of an antigen. It actually improves the effectiveness of a vaccine and it produces the strong immune response [17].

Genetically modified T cell therapy

Genetically modified T cell therapy proved a very effective treatment for melanoma that has spread to other parts of the body. This therapy dependent on generation of a biological process that is carried out within or on a biological tissue in an artificial environment but the condition is minimum change in natural conditions. This artificially generated biological process creates lymphocyte cultures of extremely reactive tumor cells from a type of immune cell that has moved from blood into tumor, that can easily recognize and kill cancer cells [11]. This artificially generated biological process also can be created by genetically engineered such receptors that have antigen binding surfaces to which first time occurrence of tumor antigens easily can bind. When a specific person anti-tumor culture of lymphocyte given to patient along with secreted protein and signal molecule type 2, it results in depletion of lymphocytes and rapid disappearance of a tumor in the absence of any treatment. Clinical trial of this therapy works on improving the lasting response rate alongside improving number of candidate patients that are ready to opt this treatment. This therapy has many advantages it has such lymphocytes that can easily recognize tumor antigens and has effective immune effect against tumor [18].

Cell signaling molecules

Cell signaling molecules have ability that they boost up patient body's integrated response to an antigen, mediated by lymphocytes by triggering autophagy effects and by indirectly creating antitumor effects. Cell signaling molecules different types have been used in treatment of cancer clinically. First cell signaling molecule that was introduced to market was interferon alpha, used for treatment of cancer of blood and bone marrow and the melanoma cells that have spread from primary site to other parts of body. Cell signaling molecules type interferon alpha has the ability that it causes the change in body's immune system. This type of cell signaling molecules actually prompt the expression of major histocompatibility factor 1 and 2 by antigen presenting cells. It triggers natural killer cells to differentiate T cells [19,20].

CONCLUSION

Well the other type of cell signaling molecule interleukin 2 plays multi role, what it do it plays role in differentiating and proliferating the T cells and effective in treating the cancer that spread to other parts of body as well RCC. Tumor necrosis factors kill tumor cells directly and granulocyte macrophage colony stimulating factor have ability that they enhance growth of specialized cells that are involved in detection, phagocytosis and destruction of bacteria/ white blood cell type that has small granules/dendritic cells that plays important role in adaptive immune response. Patients that were once refectory to all treatments, for example metastatic melanoma has really benefitted from immunotherapy. Patients that once could not be treated can now receive immunotherapy that reaps really durable and long term responses like they will be cancer free for a very long time. The downside is that not everyone will respond to this and the patients that do respond they get really durable and sustained responses.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

REFERENCES

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. Ca-Cancer J Clin.2019;69(1):7-34.
2. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians. 2018;68(6):394-424.
3. Miller AB, Hoogstraten BF, Staquet MF, Winkler A. Reporting results of cancer treatment. Cancer. 1981; 47(1): 207-214.
4. Waldmann TA. Immunotherapy: past, present and future. Nature medicine. 2003;9(3): 269-277.
5. Jiang T, Zhou C. The past, present and future of immunotherapy against tumor. Transl Lung Cancer Res. 2015; 4(3): 253.
6. Pardoll DM. The blockade of immune checkpoints in cancer immunotherapy. Nat Rev Cancer. 2012;12(4): 252-264.
7. Tain YL, Hsu CN, Chan JY. PPARs link early life nutritional insults to later programmed hypertension and metabolic syndrome. Int J Mol Sci. 2015;17(1): 20.
8. Chen G, Emens LA. Chemo immunotherapy: Reengineering tumor immunity. Cancer Immunol, Immunother. 2013;62(2): 203-216.
9. Cook AM, Lesterhuis WJ, Nowak AK, Lake RA. Chemotherapy and immunotherapy: Mapping the road ahead. Curr Opin Immunol. 2016;39: 23-29.
10. Galluzzi L, Senovilla L, Zitvogel L, Kroemer G. The secret ally: Immunostimulation by anticancer drugs. Nat Rev Drug Discov. 2012;11(3):215-233.
11. Egilmez NK, Harden JL, Rowswell-Turner RB. Chemoimmunotherapy as long-term maintenance therapy for cancer. Oncoimmunology. 2012;1(4):563-565.
12. Chen DS, Mellman I. Oncology meets immunology: The cancer-immunity cycle. immunity. 2013;39(1):1-10.
13. Sharma P, Allison JP. The future of immune checkpoint therapy. Science. 2015;348(6230):56-61.
14. Markham A, Duggan S. Cemiplimab: First global approval. Drugs. 2018;78(17):1841-1846.
15. Sankaranarayanan R. HPV vaccination: The most pragmatic cervical cancer primary prevention strategy. Int J Gynecol Obstet. 2015;131:S33-35.
16. Schlom J. Therapeutic cancer vaccines: current status and moving forward. J Natl Cancer Inst. 2012;104(8):599-613.
17. Schwartzentruber DJ, Lawson DH, Richards JM, Conry RM, Miller DM, Treisman J, et al. Gp100 peptide vaccine and interleukin-2 in patients with advanced melanoma. NEJM. 2011;364(22):2119-2127.
18. Dudley ME, Rosenberg SA. Adoptive cell transfer therapy. Semin Oncol. 2007;34(6): 524-531.
19. Wang Z, Wu Z, Liu Y, Han W. New development in CAR-T cell therapy. J Hematol Oncol. 2017;10(1):1-1.

20. Berraondo P, Sanmamed MF, Ochoa MC, Etxeberria I, Aznar MA, Pérez-Gracia JL, et al. Cytokines in clinical cancer immunotherapy. Br J Cancer. 2019;120(1):6-15.