

New Therapeutic Approaches in Treating Cancer

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Introduction

After cardiovascular diseases, cancer is the second major cause of mortality in the western world accounting for 24% of all deaths. In European countries each year over three-quarters of a million people die from cancer [1]. Once cancer is diagnosed, a variety of possible treatment options can be considered. The choice of treatment depends on the type of cancer and the extent of its progress. Three basic strategies used in treatment of cancer are: surgery, radio-therapy and chemotherapy. These may be employed either alone or in combination with others [2].

Since the past two decades researchers are focusing on developing different strategies to treat cancer so that the treatment can be more effective. In this short communication we are focusing on the new approaches which have been in research for treating cancer. The approaches are described below:

Inhibition of cancer cell metabolism

Sometimes cancer cells enter a state known as senescence (programmed growth arrest). In this state, the tumour cells are inactive and no longer proliferate.

Dorr et al. [3] showed in his research work that when cancer cells enter senescence state they tend to increase energy metabolism and the cells truly crave for sugars. This is because the moment cells enter the state of senescence, they produce large quantities of protein messenger substances which are digested by cancer cells. The process of digestion is a high energy process and a block in this causes cell death. Hence inhibition of sugar metabolism causes cell death. The other targets that cause the cancer cell death are by blocking some metabolic enzymes like glucose transporter, hexokinase, pyruvate kinase M2, lactate dehydrogenase, pyruvate dehydrogenase kinase, fatty acid synthase etc. [3].

Treating with monoclonal antibodies

One approach to avoid side effects is to target specifically cancer cells and not healthy cells. In 1906, Paul Ehrlich coined the phrase "magic bullet" to describe a drug that specifically targets disease-causing organisms. His magic bullet became a reality in the 1970s with the development of monoclonal antibodies (mAbs), which are designed to adhere onto specific targets found only in cancer cells. The first mAbs, Rituximab (Rituxan/MabThera) and Trastuzumab (Herceptin), were approved in the United States in the 1990s. Till date, 12 mAbs have been approved for the treatment of cancer, the most recent being Brentuximab vedotin (Adcetris) for the treatment of lymphomas. They are highly effective in carefully chosen patients and the side effect profile is better than cytotoxics [4].

Protein accumulation in cancer cells leading to their death

Ubiquitinated protein accumulation is a novel approach to treat cancer. Both the histone deacetylase (HDAC) inhibitor, Vorinostat and the HIV protease inhibitor, Ritonavir suppress the chaperone activity of heat shock protein (HSP) 90 and increase the amount of unfolded proteins in the cell. Combining either of them with the proteasome inhibitor, Bortezomib would kill cancer cells effectively by inhibiting the degradation of unfolded proteins and thereby causing ubiquitinated proteins to accumulate in the cells [5].

Active immunotherapies

Immunotherapies also known as cancer vaccines, stimulate a patient's immune system to destroy cancer cells. In 2010, the FDA approved first of such vaccines-Sipuleucel-T (Provenge) to treat advanced hormone-refractory prostate cancer. Vaccines trigger an immune response that may protect patients against metastasis and relapse. When compared to vaccines, immunotherapies exhibit lesser side effects but may cause inflammation at the site of action in few patients [6].

Magnetic nanoparticles for cancer treatment

Delivery systems can be harnessed to modify the release of systemic cancer agents, which allows them to remain longer in circulation and enables localization. These systems increase efficacy and minimize systemic exposure, thereby reducing side effects. Drug costs are also decreased by decreasing the amount of drug that has to be loaded. Linking magnetic nanoparticles to drugs will allow external magnets to pull the drug conjugate to the region of tumour. Thereby localizing the therapy and hence reducing side effects associated with the drug [7].

Personalized medicine

Gene expression diagnostics and biomarkers can be used to stratify patients into potential responders and non-responders or to select patients who are less likely to suffer side effects. This approach will help physicians to decide which regime is to be followed. Clinical trials also can be accelerated to ensure that non-responders are not exposed to unnecessary treatments. Genes specifically expressed in cancer cells, such as PEG-3 (Parentally Expressed Gene), can improve cancer imaging, thereby increasing the chance of early diagnosis.

Treating cancer with anti-angiogenesis agents

Formation of new blood vessels inside the tumour cell is called angiogenesis. New vessels created through this process are required for tumour growth and for metastases. But tumours use an organism's normal coagulation system to grow. This in turn leads to a number of coagulation disorders (coagulopathies) in cancer patients. By shutting down the angiogenesis process cancer cells do not grow and the anticancer agent can treat the cancer cells more effectively [8]. Transmembrane receptor tissue factor (TF) is a tumour determinant. It forms a complex with factor VIIa which helps in tumour angiogenesis. TF exists in two isoforms, alternatively spliced TF (asTF) and full length TF (flTF). flTF has effect on coagulation whereas asTF is said to reduce angiogenesis without affecting thrombogenicity [9,10].

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Oncolytic adenoviruses in treatment of cancer in humans

After a century of volatile interest in treating tumours with viruses, adenovirus has been used increasingly in the past century to treat tumours.

Technical innovations have led to the generation of safer oncolytic viruses, which can also be armed to make the virus more potent. Currently, it seems that oncolysis alone is not able to cure advanced cancers due to intratumoural complexities. Thus utilization of the immunogenic effects of oncolysis for activating anticancer immunity seems useful. One approach to allow patients access to oncolytic virus therapies was the Advanced Therapy Access Program, operational between 2007 and 2011, whose lessons are now being implemented in standard clinical trials. Eventually, randomized blinded trials are needed to confirm efficacy, and several of them are ongoing with different oncolytic viruses [11].

Conclusion

Research for treating cancer has advanced rapidly in the past 70 years, from cytotoxic agents that shrank tumours but with significant systemic side effects to targeted therapies that can trigger specifically cancer cell death. Hence some of the most promising approaches have been described in this short communication which are the current area of interest among the scientists throughout the world.

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