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The limitations and prospects of targeted therapy for treating cancer

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Abstract. As the living standard of people increases, people's living habits are becoming more and more unhealthy, resulting in the increasing probability of contracting cancer. However, the traditional methods are surgery and Chemotherapy. These methods cannot treat cancer completely, accompanying bad side effects. Researchers are trying their best to discover innovative methods that can enhance the cure rate of cancer, minimizing the side effects. Significant advances are being made in recent times, such as Immunotherapy, Hormone therapy, Stem cell transplants, and targeted therapy. Among these significant advances, targeted therapy is the most popular and promising technique that is highly expected by researchers. Researchers developed several ways of targeted therapy, each having its limitations and disadvantages. The main problem is that the target is not precise enough, accidentally causing the death of healthy cells. These limitations impede researchers, and the development of cancer treatments is stalled. This article mentioned the different kinds of ways to treat cancers and the specific information about targeted therapy. Lastly, the prospects of discovering a new advanced cancer therapy that can cure cancers completely are provided in the article, mentioning the limitations that confine the development of cancer therapies. This article provides a reference for future research on improving the accuracy of targeted cancer therapy and the selection of appropriate medical materials. Future research can focus on the development of medical devices that improve the accuracy of targeting and proper medical materials that can enhance the ability to treat cancer.

Keywords: Targeted therapy, limitations, accuracy.

1. Introduction

People discover and invent new things all the time, enhancing people’s living equality. However, people’s lifestyles become irregular and unhealthy, damaging their health, which also leads to unintended results; Many rare diseases appear into common ones and deliver a huge challenge to physicians to treat them. Cancer tends to get lots of attention, and the rate of having cancer in people skyrockets in a short time. Thus, researchers and physicians are paying attention to treating cancer successfully.

Trace the way back, humans have been battling cancer for centuries, with no effective treatment and no mechanism yet understood. This malignant condition lasted a long time. Therefore, researchers face great challenges in discovering an effective therapy that can completely cure cancer. As high-tech medical equipment develops, more and more techniques are being developed to cure cancer. Some common cancers went from being incurable to being a disease that has a relatively high cure rate. There

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are many ways to destroy the cancer cells. However, researchers are not satisfied with the status quo and hope to develop more advanced treatments. The prevailing methods to treat cancer are having surgeries and chemotherapy. Nevertheless, both surgeries and chemotherapy cannot eliminate cancer cells, even bringing drawbacks to patients. For instance, surgeries have a high risk and great trauma to the human body. This causes the patient's immunity and the ability to fight against other diseases to be reduced. Most importantly, it can also lead to a series of surgical complications. Most people may choose chemotherapy to treat their cancer, but chemotherapy has its corresponding flaws. While chemotherapy kills tumor cells, it also causes certain damage to the human body. Chemotherapy can lead to a drop in platelets and white blood cells, as well as hair loss and other reactions. Therefore, researchers are examining and testing new methods that can minimize the flaws and treat cancers more effectively.

Fortunately, researchers have found new therapies that can achieve their standard. One of the most promising therapies — Targeted Therapy — is being used to treat cancer. Targeted Therapy involves different tools such as NT (Nanotechnology) and ADCs. Both NT (Nanotechnology) and ADCs have their advantages which improve the effectiveness of treating cancer. The nanocarriers are small and can increase the anticancer drugs' concentration at the focal site. ADCs can reduce the systemic toxicity of drugs so that they can maximize therapeutic activity against tumor cells.

There is no perfect treatment in the world, and researchers are always perfecting existing treatments and constantly exploring new ones. To get closer to the perfect cancer treatment, researchers collect data from clinical trials and case treatments and try to make improvements. NT (Nanotechnology) and ADCs have their shortages and researchers need to optimize these treatments to compensate for these shortcomings. Delivering drugs precisely to the target is the most important step in targeted therapy. Thus, improving drug targeting has become a top priority for researchers. They should not only enhance the accuracy of delivering drugs to the target but also find more new target spots. By doing this, researchers will greatly improve the cure rate of cancer and discover more new treatments.

This paper will conduct an in-depth analysis of targeted therapy methods, and make suggestions based on the limitations and drawbacks of current targeted therapy, to provide a reference for further improvement and prospects of targeted therapy research in the future.

2. The treatments of cancer

Cancers have different kinds of treatments, including surgery, radiation, medicines, and other therapies. People use these treatments to cure or shrink a tumor or stop it from spreading. Different cancers are treated differently, depending on the tumor's location, size, and other properties. Not all methods are applicable, some cancers may only have one treatment, while others have many treatments.

With the development of biomedical technology, people have invented and discovered many therapies that stop tumors from spreading around people's bodies. Many useful therapies are used for treating cancer such as Radiotherapy, Operation, Chemotherapy, Immunotherapy, Hormonotherapy, SCT Stem Cell Transplantation, and Targeted Therapy. All of them have their pros and cons. The best treatment for the patient will be considered in individual situations.

2.1. Traditional therapies for treating cancer

Radiation therapy wipes out cancer cells and tumors with the use of high doses of radiation. When having low doses, radiation is used to look inside your body. Conversely, when having high doses, radiation therapy is used by destroying their DNA or slowing their growth. Because DNA damage cannot be repaired, cancer cells die and are broken down by the people's body [1]. However, the cancer cells won't be killed immediately by radiation therapy, and patients must wait a few days to weeks for the DNA to be destroyed and the cancer cells to die. Radiation therapy can cure cancer, preventing the tumors' growth and reappear. On the other hand, it may include side effects, causing people to lose their hair and have skin sensitivity.

Surgical procedures are used to diagnose and treat cancer. Surgery is a good way to relieve (and alleviate) the discomfort, or problems associated with cancer [2]. Cancer cells can't be completely found

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in a single operation, and often physicians send patients for staging surgery. Physicians performed staged procedures to determine the extent and speed of the cancer cells spread.

Chemotherapy is a cancer treatment that uses drugs to let cancer cells die. The main effect of chemotherapy is to stop or slow down the cancer cells' growth [3]. Physicians use chemotherapy to cure cancer, reducing the risk of cancer reoccurrence. Also, chemotherapy can be used to ease cancer symptoms, mitigating the patient's pain.

2.2. Innovative therapies for treating Cancer

With the development of medical technology, making great progress, people have developed different therapies that are innovative. People's immune systems can fight cancer with the help of immunotherapy, which uses substances made from living organisms to treat cancer [4]. There are many effective ways that physicians use immunotherapy to treat patients. Using immune checkpoint inhibitors is a prevailing way. Yet there are some side effects that immunotherapy causes, pain, swelling, soreness, itchiness, or rash may occur in patients.

Hormone therapy is a cancer treatment that uses hormones to slow down or stop the growth of cancer. It is commonly used to treat prostate and breast cancers that utilize hormonal growth. Hormone therapy can be divided into two categories: the ability to prohibit the body's ability to produce hormones, and the interference with the behavior of hormones in people's bodies [5]. Patients can take hormone therapy by mouth, injection, or surgery.

Stem cell transplantation is a treatment of high-dose chemotherapy or radiation therapy for certain cancers, blood diseases, and autoimmune diseases by destroying patients' blood stem cells. Stem cell transplantation is often unable to treat cancer directly. Instead, after receiving high doses of chemotherapy and other treatments, people's bodies regain their ability to produce new blood cells [6]. However, high-dose stem cell transplantation can cause problems with bleeding, high risk of infection, and feeling exhausted.

The last therapy is called targeted therapy, the state of the art to for cancer. Proteins that control the growth, division, and spread of cancer cells are the main targets that a cancer therapeutic approach called targeted therapy observes. [7]. Nevertheless, targeted therapy does have some drawbacks. Along with the course of therapy, targeted therapy does not affect cancer cells because of their resistance. Changes in cancer cells themselves prevent targeted therapy from interacting with them, triggering drug resistance. Alternatively, this can occur when cancer cells find new modes of growth that are independent of the target [7].

All the therapies mentioned above play a pivotal role in curing cancer. Targeted therapy is currently the most concerned form of treatment, which is the product of scientific and technological progress. Researchers continue to explore the field of targeted therapies, minimizing the limitations and optimizing the therapy.

3. Several ways of targeted therapy

Targeted therapy is a cancer therapeutic approach focused on the genetic changes or mutations that transform healthy cells into cancer cells [8]. Targeted therapies, as the name suggests, involve health providers detecting the presence of genetic changes in the body that help cancer cells grow and survive. Then, health providers use targeted therapy to treat cancer which can minimize the damage of the healthy cells. Targeted therapies can work alone or cooperate with other therapies, depending on the different types and properties of cancers. Researchers have developed several ways of targeted therapies to treat a variety of cancers.

3.1. The progress of several targeted therapies

CryocareTM Targeted Cryoablation Therapy is one of the targeted therapies, using extremely low temperatures to destroy tumors. During cryoablation, LPG passes through the cryoprobe and expands at the end into a gaseous probe that can produce a very low temperature, about - 190 °C, usually using nitrogen or argon gas. [9]. People required a 1cm circumferential margin to ensure complete ablation of

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the tumor with a temperature that is below - 20 °C which can induce cytotoxic cell destruction [10]. Followed by the freezing phase, the thawing phase is entered by substituting helium gas or using an internal heating needle (available in the new system) [9]. To ablate effectively, people should repeat the whole process of freezing-thawing many times. By using cryoablation, physicians can ensure that the tumors can be destroyed locally under the condition of minimally invasive surgery, reducing the destruction of surrounding healthy tissues and cells, and the recurrence rate and mortality rate, which is an efficient and progressive therapy. Cryoablation has a possible advantage in that people can observe the intracellular contents of tumor cells by using the immune system which is better than other treatments, initiating a tumor-specific immune response that helps the patient's immune system begin to react when again encountering such tumors.

Both radiofrequency ablation (RFA) and microwave ablation (MWA) are thermal ablations but vary in detail. Radiofrequency ablation (RFA) generates a current to heat a tiny piece of neural tissue by using radio waves. The areas of the nerve can be destroyed by heat, preventing the brain receive pain signals. Through the treatment of RFA, patients can feel durable relief from chronic pain, especially in areas of joints [11]. Compared to radiofrequency ablation (RFA), the ablation time of microwave ablation (MWA) with state-of-the-art equipment is shorter. Additionally, microwave ablation has higher ablation temperature and weaker thermal absorption effects than radiofrequency ablation (RFA), making tumor ablation more efficient and effective [12]. Nevertheless, these great advantages of MWA may also be its drawbacks. These effective methods are prone to damage adjacent critical structures that are harmful to the human body. Both therapies require improvement and optimization.

Additionally, high-intensity focused ultrasound ablation (HIFU), another thermal ablation technique, enables deeper tissue treatment. Because of its small wavelengths, HIFU can improve the accuracy of the target tissue and precisely control the shape of energy deposition and where it is. HIFU beams can penetrate through skin and tissues harmlessly. They have an upper size limit of approximately 3-4cm in diameter for tumors that focus on a localized area [13]. HIFU generates heat that causes a dramatic rise of temperature in exposed tissue beyond 60°C when sustained beyond 1s, causing irreversible cell death [14]. Physicians use HIFU as a treatment to fight against malignant tumors.

The last way of targeted therapy is Photodynamic Therapy (PDT). Unlike the therapeutic properties of light which have a long history, photodynamic therapy (PDT) has just developed in the last century. PDT is currently being used in clinical trials in oncology for different body parts of cancers [15]. PDT uses a photosensitizer that, a specific wavelength of light introduced after excitation, reacts with oxygen so that people can get reactive oxygen species from the target tissue, leading the cell to die. [16]. PDT has a greater selectivity than other conventional therapies, resulting in extended use.

3.2. The effects and limitations of several targeted therapies

All the therapies mentioned above have their own limitations and problems. CryocareTM Targeted Cryoablation Therapy is a minimally invasive treatment. It is usually less painful and bleeding than conventional surgery. Also, Targeted Cryoablation Therapy has a lower possibility of damaging healthy tissue near abnormal cells. However, there are still some complications that can occur. Patients may experience bleeding, cramps or pain; a fracture; or loss of sensation due to nerve damage. Symptoms such as swelling, scars, and skin infections can also occur.

Microwave Ablation (MWA) has become a dominating method that physicians use to treat cancers. Despite these technological advances and developing applications for specific tumors, the large number majority of commercial MWA applications are typically designed to create different shapes of treatment areas. Granted, this approach can also be limited, often lacking accuracy in treating tumor targets close to important structures, leaving those structures assailable to unintentional thermal damage [17]. Researchers are trying to design a new advanced technique that has the feasibility to give additional control levels of the shape of the area reference to the applicator position. This kind of technique which is called directional microwave ablation (DMWA) technology presents great prospects for expanding the clinical applicability of MWA in the treatment of tumors at challenging sites.

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While High-Intensity Focused Ultrasound Ablation (HIFU) is an innovative method that physicians use currently, it can only present short-term work. Physicians do not know how well it works in the longer term (after 10 years), lacking data and cases.

Photodynamic therapy has a drawback which limits its use. When treating cancer, one of the problems with PDT is that the parts of the body it can treat are too limited, only the parts of the body where light can reach. In this way, PDT is suitable for treating surface skin problems and some of the inner walls of the organs that can be seen through a light source. Nonetheless, it cannot treat cancers that already go deep into the skin [18]. Some problems still impede the PDT's development, especially those related to light, tissue oxygenation, and the intrinsic properties of photosensitizers [19]. To minimize the boundedness of photodynamic therapy and solve these problems, researchers need to discover improved methods that can treat all kinds of cancers, regardless of the size and the site of cancers.

Each of these therapies has limitations and boundedness, causing low efficacy in cancer treatment. Researchers spend time discovering new methods or advanced technologies to break these impediments. Fortunately, researchers have found some technologies that have great contributions to the treatment of cancers.

4. The Prospects of Cancer Treatments

Researchers introduce some new advanced technologies in cancer treatment which may reduce the limitations of previous therapies. The two emerging technologies are nanotechnology and antibody-drug conjugates. These two technologies show their advantages, giving hope to patients.

The use of nanotechnology is likely to play a pivotal role in the human cure of cancer. Nanotechnology is any device or product that is manufactured or modified by manipulation of matter at the nanoscale [20]. Nanocarriers are creative and huge progress in the fusion of nanotechnology with cancer therapy [21]. These tiny carriers have huge advantages that go beyond the limitations of previous conventional treatments. The development trajectory of nanocarrier targeting cancer cells is mainly manifested by two pathways: active and passive targeting. Active targeting of surface modifications involving nanocarriers with specific targeting ligands binds to receptors on the surface of modified cancer cells, promoting both precision and enhanced cell conjugation [21]. Instead, passive targeting utilizes the unique properties of tumor cells, facilitating the accumulation of nanocarriers in the microenvironment around tumors. Nanotechnology offers targeted therapies for cancer cells and tumors, guides the surgical resection of tumors, and directly and selectively improves the efficacy of radiotherapy-based therapy.

Another useful technology is antibody-drug conjugates (ADCs), which is a fast-growing field of cancer therapy. Nine different antibody-drug conjugates (ADCs) are approved for cancer treatment and there are also many still in clinical development. Antibody-drug conjugate (ADCs) consists of three main components: antibodies, linker, and payload. These three component characteristics determine the clinical characteristics of the ADCs [22]. Researchers use antibody-drug conjugates to find more suitable targets that enhance the effectiveness of medication, also addressing resistance and tumor heterogeneity. The potential of ADCs is tremendous, while still having some challenges to be overcome such as drug resistance, and intratumor and intertumoral heterogeneity.

Microneedles are a useful instrument that physicians use when they use several therapies to treat cancers. Microneedles (MNs) are tiny needle-like structures that are administered through the skin layer. They are non-invasive and have less or no significant pain in the skin parts applied [23]. Physicians use microneedles to target where the cancer cells are located. A group of researchers has developed a breakthrough "smart needle" probe that uses light to determine the location of cancer tissue or cells almost instantly, offering doctors a lot of convenience. The optical biopsy utilizes the Raman spectroscopy technique, which requires a low-power laser to illuminate the tissue before it can measure the light scattered by the tissue. By knowing that light scattering is different between healthy and diseased tissues, health professionals can detect a problem in a few seconds [24]. By using this kind of needle, physicians can diagnose the cancer in a few seconds, reducing the anxiety of patients.

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Also, physicians often use microneedles to deliver drugs to treat cancers. Microneedles have a greater advantage than subcutaneous needle injections because microneedles cause nearly painlessness at the site of administration and contribute to better flux control and local administration. Most importantly, the specific drug delivery system of microneedles helps to prevent damage to healthy cells and improves the accuracy of targeting cancer cells.

The introduction of these technologies has greatly increased people's confidence in the cure for cancer. The occurrence of new technologies enhances the accuracy of targeting cancer cells and increases the cure rate of cancers. However, these technologies are immature, and still in the process of continuous development. Researchers will encounter other limitations and obstacles, letting them keep discovering new medical instruments and developing advanced cancer-treating therapies.

5. Conclusion

Although targeted therapy can avoid damaging healthy tissues and cells unintendedly, there are still many limitations and deficiencies that researchers need to address. These limitations --- the lack of precision in targeted therapies, the boundedness of environmental conditions, and the damage of healthy cells --- have prevented a complete cure of cancer. Researchers should search for new methods of targeted therapy which is more advanced and developed, enhance the accuracy of targeting cells, and find more new targets that can be implemented. For CryocareTM Targeted Cryoablation Therapy, researchers should find solutions to alleviate the side effects that occur after patients have this treatment. For Microwave Ablation (MWA), researchers need to take a precise look at directional microwave ablation (DMWA) technology which can increase the accuracy of targeted therapy. Researchers also need to collect more clinical traits that use High-Intensity Focused Ultrasound Ablation (HIFU) to treat cancers in order to know its long-term work. With the finding of proper photosensitizers, photodynamic therapy results in a wide applicability. Only through continuous improvement of existing treatments can people obtain more suitable and efficient treatments, curing the cancer completely.

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