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Immuno-Oncology: the New Frontier of Cancer treatment.

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Many methods have been developed to fight cancer over the years. Many of these methods inherently contain a multitude of adverse effects that can massively impact patient outcomes post treatment. In addition to these factors, many of these treatments have plateaued in effectiveness in recent years, necessitating the construction of new treatments. Of these emerging treatment options, one particular treatment has stood above the rest in its potential applications: immuno-oncology. This field is based on the concept of harnessing the body's natural immune system to combat cancer formation and growths in the body while avoiding the dangers of traditional cancer therapies cush as radiation, chemotherapy, and surgery. Recent studies have shown the massive effects immunotherapy treatments can confer on tumors and the immune system. Immune checkpoint inhibitors act as potent new drugs that enhance the body's cytotoxic T cells efficacy in invading and attacking the tumor microenvironment. Drugs such as polyphyllin VII can prime the macrophages of the innate immune system to indirectly bolster anti-tumor defenses. Furthermore, there have been strides made to suppress pro-tumor immune components such as IL-20 to reduce or halt the growth of tumors that rely on them in organs like the pancreas. While these immune modulations are not free from consequences of their own, such as the potentially dangerous immune related adverse events they trigger, the field of immuno-oncology still stands as a bright hope for the future of oncology treatment.

Introduction

Cancer research and treatment stands as one of the most important fields of medicine in modern society. As the fields of medicine and human lifespans improve, cancer has become more and more prevalent as a threat to human health. According to the American Cancer Society (ACA), nearly 18 million people suffering from dangerous cancer were alive at the beginning of 2022 in the U.S. alone (ACA, 2023). To exacerbate this, the number of cases is expected to climb to nearly 20 million by the end of 2023. As these cancer rates continue to climb, novel and refined treatments will need to be employed to effectively fight this disease.

The alarming climb in cancer cases across the world is troubling enough on its own. As the cases of cancer have continued climbing, it has been seen that many traditional methods of cancer treatment are not ideal for long term recovery. Many of these techniques are highly intrusive and can have intense, negative

physical effects on patients. One such method is surgical removal of cancers, intended to rip cancer out at the roots. This acts as the most physically demanding method, with the potential to cause long-lasting physical harm. Others, such as the more common chemotherapy treatments and radiation therapies, confer a host of detrimental side effects upon administration, including nausea, hair loss, and a host of other issues (Arunachalam et al, 2021). Another struggle facing treatments such as these is the capacity for tumors to evolve evasive strategies to traditional methods, such as chemotherapy resistance (Chen et al, 2021). This is further compounded by the fact that many of these methods have hit a plateau of effectiveness, with few advancements made in recent years. These facts call for better, more advanced approaches of fighting cancer.

Many new methods of cancer treatment have arisen in recent years. Several of these have attempted to answer the common issues facing cancer treatment. Some, such as multidrug treatments or individualized chemotherapy, offer evolutions of traditional treatments. While these enhancements act as exciting evolutions, they are unable to always evade the pitfalls of the traditional treatment methods. Furthermore, many of these treatments can induce additional side effects even with their enhanced functions, such as multidrug treatment systems inducing multidrug immunity in cancer cells.

As research has expanded, one form of new cancer treatment has arisen that may hold the ability to evade these traditional pitfalls: the field of immuno-oncology. Immuno-oncology is the field of cancer research focused on utilizing the body's natural immune system to fight off cancerous growths. This immunotherapy, as the treatments are termed, is exciting for many reasons. To start, using the body's own immune system will allow for the avoidance of normal cancer treatment complications. Additionally, many human immune cells are already primed to fight off cancers within the body, such as Natural Killer cells and Cytotoxic T-Cell lymphocytes (Rezaeifard et al, 2021). Several studies have been completed showcasing the effectiveness of immunotherapy treatments on cancer patients, with many more coming forth on a constant basis. While immunotherapy is still a new form of treatment which must be approached with some amount of caution, it still stands as one of the most important areas of cancer research in recent history.

Recent Progress

One of the major roadblocks facing the immune system in its fight against cancer is the programmed death receptor (PD-1) found on T cells. This receptor, which is capable of inducing apoptosis in T cells, can be activated by the programmed death ligand (PD-L1) which many cancer cells evolve over time to suppress the immune system. Many modern immunotherapy treatments are able to inhibit this interaction through the use of immune checkpoint inhibitors, which are capable of blocking this interaction.

For example, one such study found that administering of a multidrug treatment of immune checkpoint inhibitors was capable of inducing increased infiltration of T cells into the tumor microenvironment (TME) (Ribas et al, 2020). Under this treatment, half of patients receiving a triple drug therapy remained in remission until the follow up 20.8 months after treatment. While it was found that single or double drug treatments were unable to facilitate an acceptable response, the extended period of remission and increased efficacy of T cell infiltration into the TME shows how immunotherapy can enhance natural immune responses.

Other cells of the immune system play an important role in anti-tumor defenses as well, such as the macrophages of the innate immune system. Macrophages play a role in priming cytotoxic T cells for anti-tumor function and invading the TME of lung cancer, especially since immune checkpoint inhibitors have

difficulties treating certain lung carcinomas (Yu et al, 2020). By enhancing the stimulator of interferon genes pathway (sting), which is responsible for promoting macrophage anti-tumor efficacy, with agonists such as polyphyllin VII, researchers were able to successfully enhance the immune response of macrophages and their associated cytotoxic T cells. This enhancement increased the amount of proinflammatory cytokines from the immunologically primed macrophages. This cytokine release enhanced the tumor infiltrative function of the cytotoxic T cells, ultimately allowing them to effectively enter and combat the tumor. This shows how more aspects of the immune system can be enhanced and studied in order to combat cancers even in scenarios where immune checkpoint inhibitors may be unavailable.

One other method of fighting cancer is through blocking immunological factors that may contribute to cancer. While the inflammatory response is incredibly useful in the immune response, it can lead to numerous host issues as well. Two cancers of the pancreas, cancer-associated cachexia and pancreatic ductal adenocarcinoma are associated with abnormal inflammatory responses (Lu et al, 2020). In patients suffering from these conditions, strong presence of the proinflammatory IL-20 was noted along with heavy expression of PD-L1. After administration of antibodies for the IL-20 affecting the tumor, growth of the pancreatic carcinomas was slowed, while survival rates rose significantly with prolonged survival of nearly 70% of the mouse population after 2 months, vs the near 100% mortality rate of untreated mice (Lu et al, 2020). Furthermore, combination with anti PD-L1 immune checkpoint inhibitors was found to have a massively favorable response. Ultimately, survival rate within the mice subjects was found to be massively improved upon blocking the IL-20, with several different pro-tumor functions interrupted. This reveals how one can modulate many different aspects of the immune response in the fight against cancer.

Discussion

While the field of immuno-oncology is still relatively new as a medical practice, it has already led to major strides in the field of cancer treatment. The immune system and its components provides nearly limitless potential for new frontiers in medical treatments, and every piece of new information we unlock from it allows for us to establish further headway into the field. Even with this fields comparative youth, there are already multiple routes of treatment open to cancer researchers. We have treatments capable of massively bolstering the natural anti-tumor immune response through factors such as immune checkpoint inhibitors in order to promote destruction of tumor masses (Ribas et al, 2020). This method of immunotherapy can be further supplemented through additional immune modulation, including factors such as priming innate macrophages to properly prime the immune cells against the tumor growths (Yu et al, 2020). Additionally, as our understanding of the immune system's role in tumorigeneses continues to expand, we can make efforts to suppress the immune effects that enhance tumor functions in ways such as IL-20 (Lu et al, 2020). Clearly, immuno-oncology is a varied field of research ripe with potential new treatments for the traditionally difficult cancer diagnoses.

Even with these many benefits that have been recorded, the field of immuno-oncology treatment can still present with some complications. While it is able to avoid many traditional pitfalls of cancer treatment, immunotherapy does contain many adverse effects of its own making. The chief concern rising from this field are the so termed immune related adverse events. These events are still not fully understood, but it is thought that they originate due to the actions of immune cells and components after administration of immunotherapies such as immune checkpoint inhibitors. In one study, it was found that these immune related adverse events could become

severe enough to discontinue immunotherapy treatment in upwards of 25% of cases due to drug related toxicity (Sanz-Segura et al, 2021). With studies such as these, we can see how immunotherapy still must be treated with caution as with any other form of medical treatment.

The field of immunotherapy sits as one of the newest and most promising fields of cancer treatment. The field has already delivered multitudes of methods for new medical options. Ranging from the administration of immune checkpoint inhibitors to the blockage of pro-tumor immune components such as IL-20 to much more, it is difficult not to see the boundless potential of immunotherapy. As the field of immuno-oncology continues to evolve, we may discover more drawbacks to the burgeoning field than just the immune related adverse events discovered. Additionally, we have more questions that need to be covered in relation to this field, such as how these immunological treatments will work in patients with autoimmune disorders. With all this in mind, one can confidently see why immuno-oncology is worthy of so much study.

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