**Abstract:**

Over the last decade, developments bettering the understanding of the immune system and its components have allowed for impressive advancements in treatment practices. Multiple treatments have come about to slow the progression of cancer and other compromises to the immune system. PD1-PDL-1 inhibitors are thought to possess an important component due to its immunomodulatory properties. The inhibitors act on pathways included in the adaptive immune system. An inhibitory effect acts on the interactions of the surface membrane receptors on the antigen presenting cells or T- lymphocytes. Antigens are presented to the T memory cells; the cells are then activated. The cells expand into effector and memory cells. The cells recognize antigens and T cells kill infected cells. Sometimes this response can be dampened. For example, tumor cells have certain properties that provide them with the ability to escape T cells. These types of cells can also suppress the immune system and produce a invalid interpretation of tumor antigens. The cells release immunosuppressive elements that create difficulties in regulation of foreign antigens. A crucial part of the immune system is the inhibitory pathways or “checkpoints” of the immune system. These checkpoints moderate immune tolerance and control tissue damage.

**Introduction:**

The immune system helps the body fight infections and protects against some diseases**.** Immunotherapy has been a widely known treatment for cancer. The treatment boosts the body's natural defenses to fight cancer. The benefits of treatment can stop or slow growth of cancer cells and/or can stop it from spreading throughout the body. The amount of immunotherapyresearch has increased drastically through the years. Numerous treatments have been developed, allowing treatment to become more accessible. In acknowledging the advancements of treatments, some roadblocks have come up in research. The immune system can be extremely complicated, controlled modulation of the immune system remains a major challenge. Understanding the factors involved in immunotherapy is key to accomplishing advancements in the efficiency of treatment. The immune system has two different types of defense mechanisms. Innate immunity and adaptive immunity present the system with defense against antigens. Innate immunity consists of dendritic cells, natural killer cells, macrophages, and granulocytes. Without any prior interaction with an antigen, the innate immunity will act quickly to recognize the antigen presented and produce a counteractive response. The system is the first line of defense against a pathogen, producing a response within days to weeks of exposure to a foreign antigen. The adaptive immunity generates a response based upon an antigen presenting cells activation. A better understanding of the mechanisms involved in the immune system has provided success in treatment strategies.

**Discussion/Results:**

Multiple approaches can be taken when immunotherapy is needed as a primary treatment. The uses of cytokines and vaccines are immune modifying components and a key factor in passive therapy. The term passive therapy can be described as therapy involving administration of cytokines, antibodies, and immune cells to patients in order to create a positive response while a immunological memory is not stored. Active immunotherapy encourages the immune system to generate antigen specific responses. An immune checkpoint blockade can be described as suppression of inhibitory pathways shown by cancer cells and interferes with antibodies created in the pathways involved in adaptive immune suppression. The first inhibitor to be approved by the FDA was “ipilimumab” in 2011, an inhibitor used in the treatment of metastatic melanoma. This was thought to be a breakthrough in the treatment of cancer. PD-1 and PD-L1 inhibitors are believed to have a better response in terms of manageability and controlling of related side effects. There are currently five of such inhibitors approved by the FDA: nivolumab, pembrolizumab, atezolizumab, durvalumab and avelumab. These have revolutionized management and services available in treatments. An immune checkpoint receptor called “CTLA4” also known as cytotoxic T-lymphocyte-associated antigen 4. This lowers overall T cell activation. Recent studies suggest the antagonistic CTLA4 antibodies showed a presence in melanoma. Anti-CTLA 4 treatment was the first product to provide a clear benefit in patients with cultivated melanoma. This treatment was approved by the US Food and Drug Administration in recent years. CTLA4 was the first of this class of immunotherapeutic to be given FDA approval.

The PD1-PDL1 inhibitors as stated above, provide inhibition of T cell effector functions in tissues. PD1 is short for programmed cell death protein 1. In regards to tumor cells, the upregulation of ligands for PD1 can block antitumor immune responses in tumor microenvironments. It’s also understood by recent study that blocking of the PD1 pathway brings about thorough tumor regression of a plethora of tumor types. Correlation between PD1 blockade and the expression of PD1 ligands of tumor cells shows a possibility of relation. A variety of immune checkpoint receptors and ligands can be upregulated to a certain degree in tumor cells. These are highly possible components of a blockade, even more so when included in enhancing activation of antitumor immune responses like vaccines. Blockers of immune checkpoint proteins such as PD1, provide a widely varied study of possibilities and opportunities for enhancing antitumor immunity. T cell receptors or TCRs have antigen recognition properties that allow regulation of a balance between co-stimulatory and inhibitory signals. T cells are known for their ability to selectively recognize peptides derived from proteins in mostly all of the body. The cells have been a major part of therapeutic manipulation of anticancer immunity. T cells can actively acknowledge and destroy antigen expressing cells and can generate diverse immune responses. Immune checkpoints are necessary in the production of self-tolerance or prevention of autoimmunity. The checkpoints can also provide protection for damage of body tissues when the body is responding to a pathogenic infection. It’s been said, “The blockade of immune checkpoints seems to unleash the potential of the antitumor immune response in a fashion that is transforming human cancer therapeutics” (Pardoll 2012).

A new topic related to this report is called “Immunoediting”. This term refers to the altering of the immune processes to possibly change the course of tumor development. One of the most prominent instances of immunoediting in humans is from studies that show a correlation between quantity, quality, and disbursement of tumor infiltrating lymphocytes or (TILs) with patient survival. Infiltration of cytokines producing T cells CD4+ and CD8+ promote tumor control and have been seen to show a largely improved prognosis for patients with different varieties of cancer. A recent study of patients with melanoma, suggested that the presence of TILs provided a positive prognosis for patients. A study by Naito et al. showed that the presence of TILs and CD8+ T cells in colon cancer provided an important influence on the outcome of treatment. Accumulation of CD8+ T cells was thought to be a critical product in the successful prognosis of the individual. Another study involving ovarian cancer, melanoma, and colon cancer confirmed this notion and exhibited that the upregulation and location of CD8+ T cells and regulatory T cells were extremely important variables in prognosis.

CITATIONS

Pardoll, Drew M. “The Blockade of Immune Checkpoints in Cancer Immunotherapy.” *Nature News*, Nature Publishing Group, 22 Mar. 2018, [www.nature.com/articles/nrc3239](http://www.nature.com/articles/nrc3239).

Schreiber, Robert D., et al. “Cancer Immunoediting: Integrating Immunity's Roles in Cancer Suppression and Promotion.” *Science*, American Association for the Advancement of Science, 25 Mar. 2018, science.sciencemag.org/content/331/6024/1565.

Riley, Rachel S., et al. “Delivery Technologies for Cancer Immunotherapy.” *Nature News*, Nature Publishing Group, 8 Jan. 2019, [www.nature.com/articles/s41573-018-0006-z](http://www.nature.com/articles/s41573-018-0006-z).

COVER LETTER

Dear Editor,

I have completed the modified version of my Micro review document. The title of my document is “[EVOLUTION OF IMMUNOTHERAPY STRATEGIES IN MODERN MEDICINE](https://undergradsciencejournals.okstate.edu/index.php/MRCMB/author/submission/11052)”. After reviewing the comments and advice given through the peer reviews, I was able to apply changes to my document. I included many improvements to my document thanks to the constructive comments made by the reviewers. It is my hope that these changes make the manuscript acceptable for publication in Micro reviews in Cell and Molecular Biology.

Sincerely,

Chad Dillard

**Reviewer 1:**

1. The comments made were helpful and made me more mindful to create recent results and progress in study.
2. I included more recent progress in study.

**Reviewer 2:**

1. I found the comments made very useful, I included more background on adaptive immunity and allowed the reader to better understand.
2. I included more background on positives in treatment progressions.

**Reviewer 3:**

1. I found the comments made very useful, I thought this reviewer left positive comments that allowed me to make easy changes where they were needed.
2. I included more in text citations to my document.