



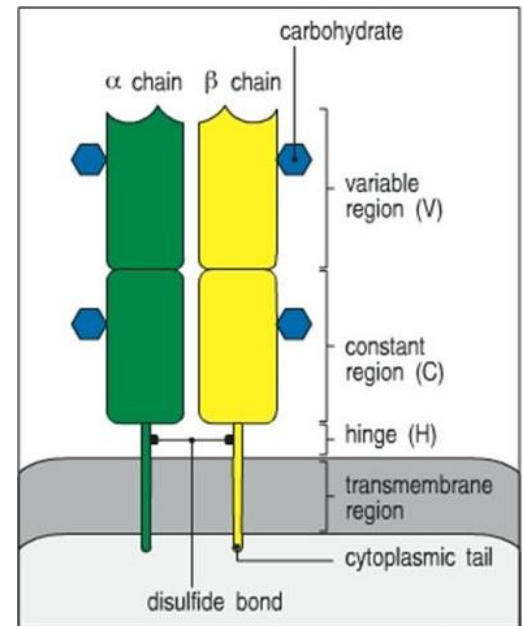
Immunotherapy: Paving the way to Designer Medicine

By: Brianna Ports

One of the most essential parts of being a scientist is understanding how to communicate with other scientists as well as the non-scientific community. Pitt Science was created with that concept in mind. Each of the presentations and events were teeming with opportunities to learn about different scientific specialties. When I attended Pitt Science I had the fortune of hearing Dr. James P. Allison from University of Texas MD Anderson Cancer Center speak on his rewarding research. I was, honestly, amazed at the leaps and bounds he has made in cancer research. Dr. Allison was one of the first individuals to identify the T-cell receptor structure, CD28 as a costimulator of T-cell activation, and that cytotoxic T lymphocyte antigen-4 (CTLA-4) acts as an immune inhibitory molecule. His research led him to the development of Ipilimumab, an anti-CTLA-4 antibody. Dr. Allison's life-long dedication to understanding the immune checkpoint blockade has landed him a well-deserved spot in Time's Top 100 most influential people this year.

When most people imagine cancer treatments, they picture chemotherapy and radiation above all else. These treatments are the "gold standard" for treating most cancers up to this point. Cancer cells are known for their ability to exponentially proliferate. This proliferation is the reason that chemotherapy is so effective. Chemotherapy drugs target cells during specific stages in their life cycle, specifically those involved with the cell cycle. Sadly, chemotherapy cannot distinguish between healthy cell growth and cancerous cell growth. Therefore, healthy cells are killed along with cancerous ones, leading to drastic side effects. There is a clear need for new treatments that are more specific and can allow cancer cells to be targeted directly. This is where Dr. Allison's research becomes essential.

Dr. Allison's discovery of the T cell receptor and its structure is foundational to immunology and immunological therapies. The T cell receptor is found on the surface of T cells, which are lymphocytes involved in cellular immunity. The key function of a T-cell receptor is to bind specific antigens which, in turn, can initiate the cell signaling needed to activate the T cell. Dr. Allison also identified CTLA-4 as an immune inhibitory molecule which can downregulate T cells by blocking CD28, a T cell costimulatory molecule which basically functions as a T-cell "on" switch (1). These discoveries have led Dr. Allison to become one of the leading Immunologists involved in immunotherapy treatments for cancer.



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Through his research, Dr. Allison has discovered that when given Ipilimumab, subjects with metastatic melanomas or prostate cancer see a decrease in tumor size. This drug essentially puts the immune system into over-drive and allows the immune system to attack the cancer cells directly. This is already an astronomical achievement. Chemotherapy is akin to setting off a bomb to destroy a target, where immunotherapies such as Ipilimumab would perform a much more targeted and less destructive "search and destroy method." Ipilimumab is the first immunotherapy discovered to be effective against metastatic melanoma, having a 22% 10-year survival rate (1).

Dr. Allison has also worked with Programmed Death-1 (PD1), which is another immune inhibitory molecule. PD1 binds to PDL1 or 2 to suppress t-cell activity. PD1 is found to be an effective treatment for melanoma, renal cell carcinomas, and non-small cell lung cancers. PD1 and CTLA-4, and many other inhibitory molecules work in a nonsynonymous fashion to inhibit T cell response (2). In studies where Dr. Allison treated metastatic melanoma subjects with both anti-CTLA-4 and anti-PD1 drugs, he found that 65% of subjects survived 2 ½ years after treatment. This study suggests that immunotherapy treatments can be used in conjunction with one another and designed based on immunohistochemical staining results.

Dr. Allison's discoveries have led directly to treatments which offer us a hope of treating cancer in a new and promising manor.

Ultimately, Dr. Allison's research has been the very foundation to which cancer immunotherapy treatments are built on. Treatments such as these have the possibility of being catered to specific cancers and cell types. Theoretically, cells could be biopsied and stained to measure for PD1, CTLA-4 and other components in the immune checkpoint blockade. Cancer treatments could then be designed for a single individual. This concept has astronomical implications.

As someone who has watched as a loved one battle with cancer, this talk and others like it can tend to really hit home. At the time I am writing this, my 17-year-old brother has just had his 6-month scans indicating that he is, thankfully, still cancer free. I have seen cancer wreak havoc on the human body and watched as the byproducts of scientific research have saved my brother's life. While my brother received chemotherapy and not immunotherapy, I have been party to many children who have been saved through these revolutionary treatments. It is amazing to me that by following his passion for science, Dr. Allison was led to discoveries that have helped families like mine. What I took away most from Dr. Allison's talk is that by doing what I love and working at the bench I can make a difference.

References

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