Janssen Oncology

Immuno-Oncology: Fighting Cancer using the Immune System

What are Immunotherapies?

Immunotherapies are treatments that use our immune system's natural ability to fight cancer, infection and other disease.[1] Immunotherapy in the treatment of cancer is called cancer immunotherapy.[2] **Research that explores the immune response against cancer is called immuno-oncology.** In just the past few years, researchers have developed several new methods of treating cancer that increase the strength of immune responses against tumors. [2]

Immuno-oncology harnesses the power of **T cells**, a type of white blood cell that protects the body from infection. T cells work to either **fight infection** by hunting and destroying harmful substances in the body, or help our immune system to produce antibodies which **prevent infection**.[4] T cells can be adapted to respond to a specific cancer, triggering a "destroy" or "prevent" response.[5] These therapies can:

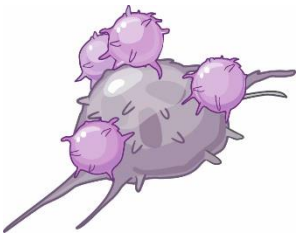
- Stop or slow the growth of cancer cells
- Stop cancer from spreading to other parts of the body (metastasis)
- Help the immune system more effectively destroy cancer cells

Monoclonal Antibodies

Monoclonal antibodies bind to a specific protein on the surface of a cancer cell, but are specific enough to not target healthy cells.[7] When introduced to the body, they can help fight cancer in a number of different ways:

- **Help the immune system destroy cancer:** The immune system doesn't always recognize cancer cells as harmful because these cells often contain a protein that blocks the "harmful" signal. Monoclonal antibodies mark cancer cells by attaching to those proteins. Because they aren't on healthy cells, these antibodies signal the immune system to respond as it normally would, targeting and destroying the cancer cells but not healthy cells.[8]
- **Prevent cancer cells from multiplying:** Growth factors in the body attach to receptors on a cell called **growth factor receptors** that tell cells to grow – including cancer cells.[9] Monoclonal antibodies can **block the growth factor receptor**, preventing the "grow" signal from reaching a cancer cell.[10]
- **Treat cancer:** Some monoclonal antibodies **carry cancer treatments** directly to cancer cells, causing the cell to die without damaging healthy cells.[11]

Checkpoint Inhibition



Within the immune system, built-in controls regulate how active T cells are in fighting infection, speeding up or slowing down activity as needed to prevent autoimmunity, which are immune responses against an individual's normal cells or tissues.[12] These controls are called **immune checkpoints.**[13] Cancer can take over these controls, preventing the body from speeding up T cells that would attack cancer cells.[14] By blocking the checkpoints – through **checkpoint inhibition** – the immune system's signals to speed up T cells are restored and the attack on cancer can continue.[15]

Cancer Vaccines or Antigen-presentation Therapeutics

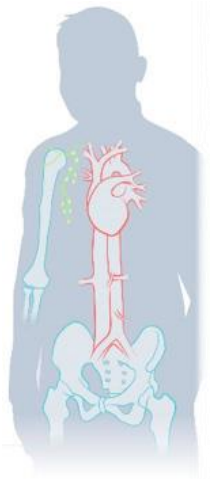
Cancer vaccines expose the body to specific antigens expressed on the surface of cancer cells, causing antigen-presenting cells to display these antigens on their surface which the immune system will recognize.[16] In turn, this triggers an immune response, targeting and destroying cancer cells expressing these antigens on their surface. Cancer vaccines can be used for prevention or treatment.

- **Prevention vaccines** are similar to those given for common childhood diseases. These help keep a healthy person – someone with no sign of cancer – from developing a specific cancer in the body by triggering the T cell responses to prevent disease if and when cancer is introduced into the body.[17]
- **Treatment vaccines** help the immune system to fight cancer by "training" T cells to recognize and attack cancer cells. Treatment vaccines can help the body to prevent a recurrence of cancer, eliminate remaining cancer cells after another treatment is complete, or stop cancer growth. These vaccines are specifically designed to target cancer cells without harming healthy cells.[18]

Our Approach to Immuno-Oncology

At Janssen Oncology, we are focused on next-generation immuno-oncology regimens that enable a highly selective attack on cancers. While the first generation mechanisms are encouraging, there is a need for new immuno-oncology approaches because most patients do not respond to the currently approved agents. With a deep understanding of the cancers we focus on, we are able to develop highly specific therapies that maximize the immune system's capacity to detect, destroy or prevent cancer. Our comprehensive approach includes a variety of methods which help to:

- **"Prime" the Immune System:** Janssen Oncology is seeking new immuno-oncology regimens to "prime" the immune system through the use of therapies which cause antigen-presenting cancer cells to express tumor-specific antigens. These are combined with **T cell modulation**, which modifies T cells to find those antigens and attack the cancer.
- **"Push" the Immune System:** Simultaneously, we are exploring **T cell redirection** – using bi-specific antibodies that bind to both cancer cells and T cells, recruiting "killer" T cells to attack cancer directly.
- **"Control" the Immune System:** The immune system naturally regulates T cell function – either activating or inhibiting it – and cancer can take control of these signals. Using **checkpoint inhibition**, we are working to boost T cell activity when cancer slows it down, helping the T cells attack the cancer. With **co-stimulation**, we are exploring ways to amplify normal T cell activity, causing it to actively seek and destroy cancer cells.
- **"Train" the Immune System:** Our deep understanding of how tumors grow and the factors which allow them to survive has fueled research to "retrain" the immune system, overriding cancer's control of the immune system's ability to destroy tumors.



Collaboration to Speed Discovery

Collaborations in immuno-oncology are essential to our strategy. In addition to experts on our own Immuno-Oncology Research group, Janssen Oncology also collaborates with more than ten leading cancer research organizations to bring new immuno-oncology agents closer to the patients who need them. Some ongoing projects include:

- **Vaccines** for a variety of cancers including lung and prostate cancer
- **T cell checkpoint** regimens to restore normal T cell function
- **T cell recruitment** regimens to help target tumors
- **Novel mechanisms** to defeat immuno-suppression created by tumors
- **Bio-specific antibodies** for highly targeted T-cell therapies
- **Biomarkers** to identify the patients who will benefit most from new therapies

With a comprehensive approach, a robust pipeline and strong understanding of how cancers form, grow and die, Janssen Oncology is focused on the future, exploring novel ways to change the paradigm of cancer treatment. Fueled by our patient-focused urgency, we are seeking new ways to bring the right treatment to the right patient faster than ever before. Our vision is focused on precision immuno-oncology and personalized regimens designed for the patient's tumor and immune profile.

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