

BEYOND THE LOOKING GLASS: CANCER IMMUNOTHERAPY ADVANCES DUE TO INFECTIOUS DISEASE RESEARCH

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POSSIBLE SHARED IMMUNOLOGICAL MECHANISMS UNDERLIE INFECTIOUS DISEASES AND CANCER

Why does the model created for vaccine development work for a wide range of infectious diseases but fall short when it comes to cancer? Until recently, it has been widely held that cancer has little in common with infectious diseases, and that its treatment and prevention should therefore be of a different standard. David Raulet, Laurent Coscoy, Daniel Portnoy and Russell Vance all believe that this has the potential to be a notion of the past. These scientists founded the Immunotherapeutics and Vaccine Research Initiative (IVRI) on the idea that communication between the fields of cancer research and immunology research can spark revolutions in both fields, ultimately translating to innovative new cancer treatments.¹¹ Looking for a new treatment plan for either cancer or infectious diseases is arduous because each subtype comes with a unique set of virulence factors that must be overcome. However, the researchers of IVRI believe that there are enough similarities

between the two fields to bridge this gap.

Cancer evolves rapidly in response to its environment in order to evade our immune response, and since tumors are composed of our own cells, it is more difficult for the immune system to attack the cancer. Our immune system is able to identify most pathogens by pathogen-associated molecular patterns, or PAMPs. A variety of molecules can act as PAMPs, from the lipopolysaccharides on the outer membrane of bacteria to the flagella that allow bacteria to move. Since PAMPs have molecular features that our own cells do not possess, this allows our immune cells' receptors to identify and bind them, and signal for immune response.⁷ Abnormalities in our own cells are sometime referred to as pseudo-PAMPs and trigger similar immune responses.

Tumors wreak havoc wherever they are present, killing neighboring cells and creating genomically unstable progeny. This is how our immune system is able to find tumors.¹¹ This genomic instability, coupled

with the PAMP-like scenarios previously mentioned, causes an immune system reflex, initiating tissue repair and healing responses through inflammation. Too often, however, inflammation becomes chronic and can lead to cellular damage, proliferation, and formation of new blood vessels which can help the cancer spread. According to Dr. Russell Vance, “[a]n interesting way to think of cancer is as a chronic infectious disease—the consequence of the unresolved presence and growth of a ‘foreign’ body.”¹⁰ With this concept in mind, immunotherapy researchers hope to enhance our own immune response to prevent the spread of malignant cells.

IVRI's faculty director, Dr. David Raulet, hopes to accomplish this goal using Natural Killer (NK) cells. NK cells use specific methods to recognize cancerous cells, one of which is by upregulating proteins through activated stress pathways. In Dr. Raulet's words: “[t]he cells essentially say ‘Kill me! I'm stressed out!’ The NK cell

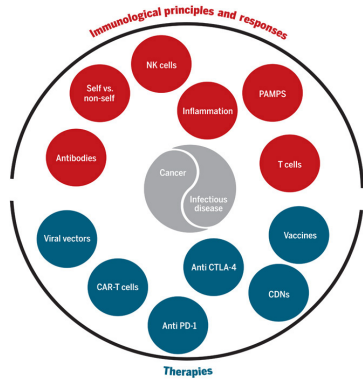


Figure 1: A figure demonstrating exactly how much overlap there is between infectious diseases and cancer. The image includes some of the shared immunological principles, responses, and therapies.¹⁴

kills that cell and then calls on the rest of the immune system to come help out.^{7,8}

One critical component in the recognition of pathogens by the immune system is the major histocompatibility complex (MHC). The MHC is an assembly of proteins that displays fragments of pathogens on its surface for targeting by the immune system. Some cells undergoing malignant transformations may downregulate their MHCs to reduce immune recognition and confer selection of such cells; however, they can be combated through the strategy of increasing the number of modified NK cells in the bloodstream, which have been mutated to allow their attack on endogenous can-

cerous cells. This is where immunotherapy comes in. Immunotherapy is the treatment (or prevention) of disease using supplements to our own immune system. Most immunotherapy overlooks any and all pre-conceived notions about how to approach cancer and instead goes back to the basics: improving our immune response to eliminate abnormalities within our bodies. If NK cells from either the patient or a donor are injected into the patient's blood, it is possible to increase the number of NK cells in the bloodstream and enable these new NK cells to have tumor-attacking capabilities.⁴

Perhaps the approach that is most indicative of the leaps and bounds made in cancer immunology is the Listeria-based

vaccine. *Listeria monocytogenes* is a pathogen that elicits a strong immune response. To generate a vaccine strain, the virus is attenuated with mutations so that its immunogenic capabilities are retained without any toxicity. The patient's immune system begins rapid production of T-cells to combat the potential infection and this response can be engineered to target the types of cells found in a tumor. Although this research is still in the clinical trial stage, the Listeria vaccine has been shown to cure mice with late-stage pancreatic cancer. Researchers are now wondering if the Listeria vaccine could be applied to other pathogens, such as HIV or tularemia, that we have yet to develop sound treatments for.¹¹

Until just a few years ago, cancer and infectious diseases were considered to be two completely different entities. However, recent findings have led to a paradigm shift that has revolutionized this notion and opened doors in the field of cancer immunotherapy. As Dr. Russell Vance admits, "We were surprised to find the amazing number of similarities between our immune responses [to cancer and infectious diseases]. Historically, tumor biology and infectious disease biology were considered very different fields, and now we are able to appreciate all of the overlap."¹⁰ These innovative approaches have the potential to not only revolutionize the field of immunotherapy but also offer new treatment options to cancer patients worldwide. The more we are able to learn about the nature of tumors and how to treat cancer, the closer we come to eventually curing the disease.

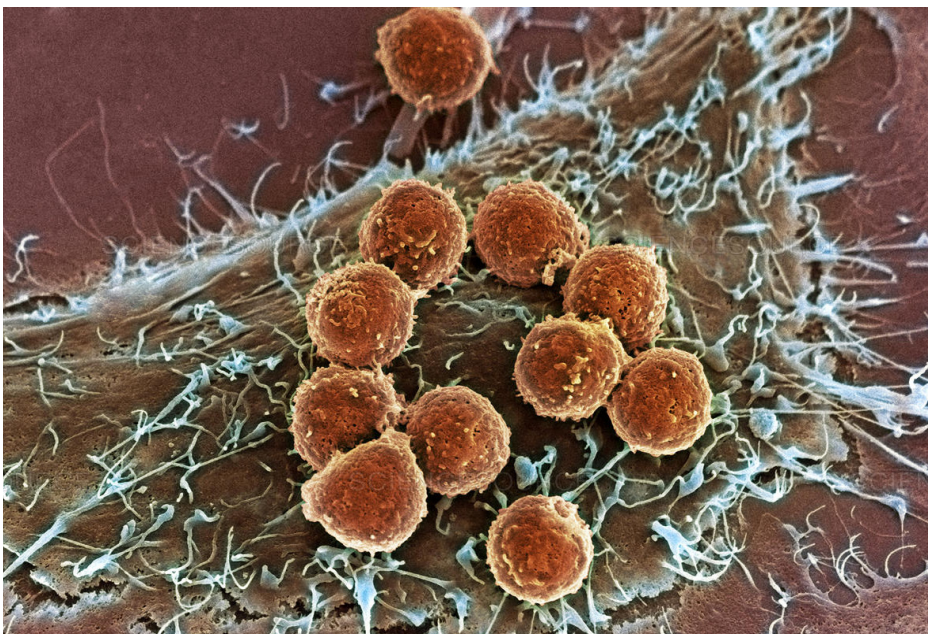


Figure 2: A T-lymphocyte latches onto a malignant tumor. The T-cell identifies a pseudo-PAMP on the surface of the tumor and binds to it, triggering an immune response.¹³

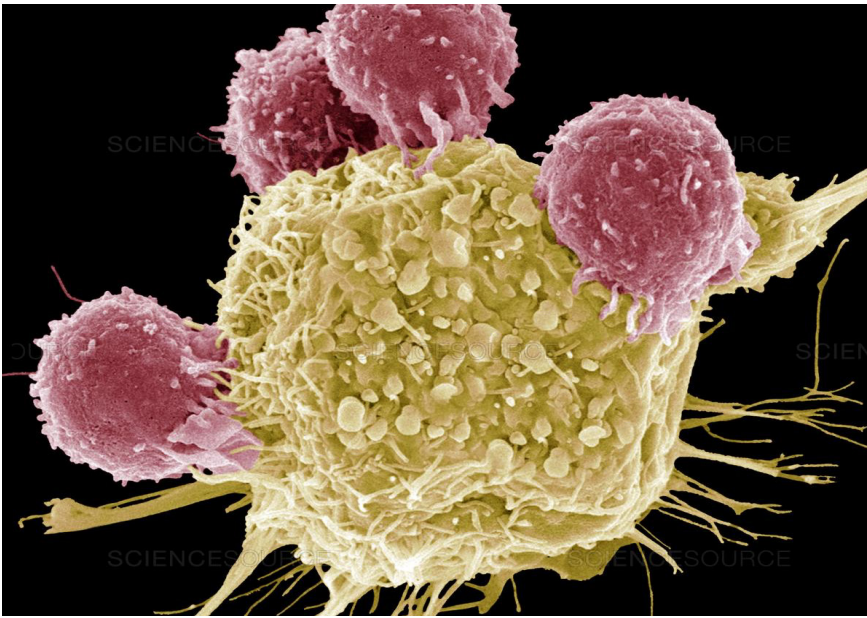


Figure 3: T-lymphocytes latching onto a malignant cell.¹⁵

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IMAGE SOURCES

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