Arming the immune system to fight cancer

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In 2004, a form of cancer known as neuroblastoma claimed the life of Alexandra (Alex) Scott, a little girl who gained national attention for using her lemonade stand to raise money for cancer research. Now, the organization established in her memory, the Alex's Lemonade Stand Foundation (ALSF), has awarded the University of Maryland's Christopher M. Jewell, an assistant professor in the A. James Clark School of Engineering, a three-year, $375,000 research grant to support the pre-clinical development of a cancer vaccine technology that could give children like Alex a better chance to have a long and healthy life.

Neuroblastoma, the third most common pediatric cancer, causes nerve cells to turn into tumors. The prototype vaccine uses a unique combination of nanotechnology and immunology to "raise an army" of tumor-hunting immune cells, equip them to attack neuroblastoma, and leave them ready to reactivate if the cancer returns.

The lymph nodes are the body's immune system "command centers," packed with different types of immune cells. Each cell is equipped with a protein that responds to a particular disease or infection. Fragments of viruses, bacteria, and tumors collected in the lymph nodes are presented to these cells as antigens, molecules that provoke a response to a specific threat. When an immune cell encounters an antigen that it is designed to respond to, the cell "activates" and multiplies. These cells are then released into the blood and tissue to hunt their specific pathogens.

One type of activated immune cell, the central memory T cell, is particularly effective at infiltrating tumors. These cells start life as ordinary, inactive T cells in the lymph nodes that have the potential to become one of a number of active T cell types. Jewell's goal is to enhance the immune system's natural response by encouraging T cells to multiply and become central memory T cells specific for tumor antigens.

Jewell, a member of UMD's Fischell Department of Bioengineering, is an expert in immunomodulation, an emerging field that explores directing the body's immune system response to target a specific disease. He believes crafting a biomaterials-based vaccine that not only provides T cells with the weapons to fight neuroblastoma, but also instructions on how, will give oncologists a new, more specific treatment option that relies more on the patient's own defenses than radiation and chemotherapy.

Creating any successful vaccine is difficult. Once injected, its components are dispersed around the body. Just a fraction of the vaccine reaches the lymph nodes, and its components are often so damaged or degraded by the trip they're no longer functional. Engineered microparticle and nanoparticle vaccines face additional challenges, because they are either too large to drain into lymph nodes or become too large because they stick to cells, proteins, or other particles.

Jewell's research group is developing a unique system in which controlled-release, biodegradable polymer "depots" are injected directly into the lymph nodes. The depots protect the vaccine components inside, control when they are released, and direct what happens next.

The vaccine contains two elements: the antigen that stimulates the T cells to attack neuroblastoma cells, and "immune signals," small molecules that mimic the chemical signals immune cells use to communicate. The message, like the antigen, is another call to action: transform into central memory T cells, and multiply. Jewell hopes this approach will result in an army of central memory T cells prepared to destroy neuroblastoma tumors and capable of "remembering the enemy" later.

The cells' mission continues after the existing tumors are cleared. "Establishing these large populations of immunological memory cells could also help keep patients in remission by rapidly destroying tumor cells that might arise during relapse events," Jewell explains.

He adds that while the work is in the early stages, this technology could lead to new therapeutic technologies for treating other types of cancer.

"High risk tumors like neuroblastoma are treated with multiple therapeutic strategies with poor outcomes," says Dr. Anthony Sandler, chief of surgery at Children's National Medical Center, who is collaborating with Jewell on the project. "Cancer vaccines add another therapeutic option, but so far have had very limited success. The novel approach proposed in this work may provide the spark that stimulates effective immunity against the tumor."

"Cancer vaccines represent a new class of therapies, and biomaterials have great potential to treat cancers like neuroblastoma," says Jewell. "The ALSF's support and the clinical training we will receive through our collaboration with Children's National Medical Center have created an amazing opportunity. This investment will have a lasting impact on my lab's ability to contribute to the pediatric cancer field."

Provided by University of Maryland

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