Scientists create artificial 'cells' that boost the immune response to cancer

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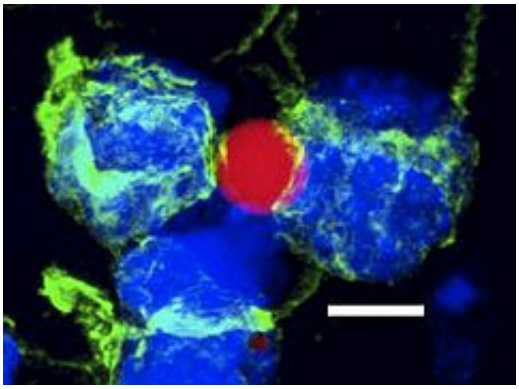

Stimulatory particles (red) bound to activated T-cells (blue) as seen by scanning electron microscopy. Scale bar = 10 μm. Credit: Yale University

Using artificial cell-like particles, Yale biomedical engineers have devised a rapid and efficient way to produce a 45-fold enhancement of T cell activation and expansion, an immune response important for a patient's ability to fight cancer and infectious diseases, according to an advance on line report in Molecular Therapy.

The artificial cells, developed by Tarek Fahmy, assistant professor of biomedical engineering at Yale and his graduate student Erin Steenblock, are made of a material commonly used for biodegradable sutures. The authors say that the new method is the first "off-the-shelf" antigen-presenting artificial cell that can be tuned to target a specific disease or infection.

“This procedure is likely to make it to the clinic rapidly,” said senior author Fahmy. “All of the materials we use are natural, biodegradable already have FDA approval.”

Cancer, viral infections and autoimmune diseases have responded to immunotherapy that boosts a patient’s own antigen-specific T cells. In those previous procedures, a patient’s immune cells were harvested and then exposed to cells that stimulate the activation and proliferation of antigen-specific T-cells. The “boosted” immune cells were then infused back into the patient to attack the disease.

Limitations of these procedures include costly and tedious custom isolation of cells for individual patients and the risk of adverse reaction to foreign cells, according to the Yale researchers. They also pointed to difficulty in obtaining and maintaining sufficient numbers of activated T-cells for effective therapeutic response.

In the new system, the outer surface of each particle is covered in universal adaptor molecules that serve as attachment points for antigens — molecules that activate the patient’s T-cells to recognize and fight off the targeted disease — and for stimulatory molecules. Inside of each particle, there are slowly released cytokines that further stimulate the activated T-cells to proliferate to as much as 45 times their original number.

“Our process introduces several important improvements,” said lead author Steenblock. “First, the universal surface adaptors allow us to add a span of targeting antigen and co-stimulatory molecules. We can also create a sustained release of encapsulated cytokines. These enhancements mimic the natural binding and signaling events that lead to T-cell proliferation in the body. It also causes a fast and effective stimulation of the patient’s T-cells — particularly T-cells of the cytotoxic type important for eradicating cancer.”

“Safe and efficient T-cell stimulation and proliferation in response to specific antigens is a goal of immunotherapy against infectious disease and cancer,” said Fahmy. “Our ability to manipulate this response so rapidly and naturally with an “off the shelf” reproducible biomaterial is a big step forward.”

Fahmy was recently awarded a five-year National Science Foundation (NSF) Career Award for work on this process and ways of engineering biomaterials to manipulate immune responses to fight cancer and other diseases. His approach incorporates signals important for T-cell stimulation in biocompatible polymer particulates, and integrates all the signals needed for efficient T-cell stimulation.

According to the NSF, devices as such these offer ease and flexibility in targeting different types of T-cells, and is expected to lead to state of the art improvements in the preparation of a new generation of therapeutic systems.

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