

Scientists develop a new approach to treating autoimmune disease

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In autoimmune diseases, the immune system turns against the body's own tissues and organs, wreaking havoc and destruction for no apparent reason. Partly because the origins of these diseases are so obscure, no effective treatment exists, and the suffering they inflict is enormous. Now Weizmann Institute scientists have developed a method that in the future may make it possible to treat autoimmune diseases effectively without necessarily knowing their exact cause. Their approach is equivalent to sending a police force to suppress a riot without seeking out the individuals who instigated the unrest.

In healthy people, a small but crucial group of immune cells called regulatory T cells, or T-regs, keeps autoimmunity in check, but in people with inflammatory bowel disease (IBD), one of the most common autoimmune disorders, too few of these cells appear in the diseased intestine, and the ones that do fail to function properly.

The new Weizmann Institute approach consists of delivering highly selective, genetically engineered functioning T-regs to the intestine. The study was conducted by Dr. Eran Elinav, a physician from Tel Aviv Sourasky Medical Center's gastroenterology institute who is working toward his Ph.D. at the Weizmann Institute, and lab assistant Tova Waks, in the laboratory of Prof. Zelig Eshhar of the Immunology Department.

Relying on Eshhar's earlier work in which he equipped a different type of T cell to zero in on cancerous tumors, the team genetically engineered

T-regs, outfitting these cells with a modular receptor consisting of three units. One of these units directed the cells to the intestine while the other two made sure they became duly activated. As reported in the journal *Gastroenterology*, the approach proved effective in laboratory mice with a disease that simulates human IBD: Most of the mice treated with the genetically-engineered T-regs developed only mild inflammation or no inflammation at all.

The cells produced what the scientists called a 'bystander' effect: They were directed to the diseased tissue using neighboring, or 'bystander' markers that identified the area as a site of inflammation, and suppressed the inflammatory cells in the vicinity by secreting soluble suppressive substances.

The scientists are currently experimenting with human T-regs for curing ulcerative colitis and believe that in addition to IBD, their 'bystander' approach could work in other autoimmune disorders, even if their causes remain unknown. They also think the method could be valuable in suppressing unwanted inflammation in diseases unrelated to autoimmunity, as well as in preventing graft rejection and certain complications in bone marrow and organ transplantation, in which inflammation is believed to play a major role.

Source: Weizmann Institute of Science

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