MedicalXpress

Autoimmune disease—retraining white blood cells

December 17 2012

Symptoms of an autoimmune disease disappeared after a team of scientists retrained the white blood cells. This method is extremely promising for treating diseases such as type I diabetes and multiple sclerosis.

How can the immune system be reprogrammed once it goes on the attack against its own body? EPFL scientists retrained T-cells involved in type I diabetes, a common autoimmune disease. Using a modified protein, they precisely targeted the white blood cells (T-lymphocytes, or T-cells) that were attacking pancreatic cells and causing the disease. When tested on laboratory mice, the therapy eliminated all signs of the pathology. This same method could be a very promising avenue for treating multiple sclerosis as well. The scientists have just launched a start-up company, Anokion SA, on the Lausanne campus, and are planning to conduct clinical trials within the next two years. Their discovery has been published in the journal *PNAS* (*Proceedings of the* National Academy of Science).

To retrain the rebellious white blood cells, the researchers began with a relatively simple observation: every day, thousands of our cells die. Each time a cell bites the dust, it sends out a message to the immune system. If the death is caused by trauma, such as an inflammation, the message tends to stimulate white blood cells to become aggressive. But if the cell dies a programmed death at the end of its natural life cycle, it sends out a soothing signal.

In the human body there is a type of cell that dies off en masse, on the order of 200 billion per day – red blood cells. Each of these programmed deaths sends a soothing message to the immune system. The scientists took advantage of this situation, and attached the pancreatic protein targeted by T-cells in type I diabetes to red blood cells.

"Our idea was that by associating the protein under attack to a soothing event, like the programmed death of red blood cells, we would reduce the intensity of the immune response," explains Jeffrey Hubbell, co-author of the study. To do this, the researchers had to do some clever bioengineering and equip the protein with a tiny, molecular scale hook, that is able to attach itself to a red blood cell. Billions of these were manufactured and then simply injected into the body.

Complete eradication of diabetes symptoms

As these billions of red blood cells died their programmed death, they released two signals: the artificially attached pancreatic protein, and the soothing signal. The association of these two elements, like Pavlov's dog, who associates the ringing of a bell with a good or bad outcome, essentially retrained the T lymphocytes to stop attacking the pancreatic cells. "It was a total success. We were able to eliminate the immune response in type I diabetes in mice," explains Hubbell.

Minimizing risks and side effects

Co-author Stephan Kontos adds that the great advantage of this approach is its extreme precision. "Our method carries very little risk and shouldn't introduce significant side effects, in the sense that we are not targeting the entire immune system, but just the specific kind of T-cells involved in the disease."

The scientists are planning to conduct clinical trials in 2014, at the earliest. To demonstrate the potential of their method, they plan to first test applications that would counteract the immune response to a drug known for its effectiveness against gout. "We chose to begin with this application before we tackled diabetes or multiple sclerosis, since we knew and were in control of all the parameters," explains Hubbell.

Currently, the researchers are also testing the potential of this method in treating multiple sclerosis. In this disease, T-cells destroy myelin cells, which form a protective sheath around nerve fibers. They are also studying the potential of their method with another kind of white blood cell, B-lymphocytes, that are involved in many other autoimmune diseases.

Provided by Ecole Polytechnique Federale de Lausanne