

Blocked signals to immune cells extend their life and contribute to progression of lupus

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Immune cells that would normally die in healthy people accumulate in bodies of patients who have lupus and contribute to the disease, according to new Saint Louis University research published in the Feb. 15 issue of *Immunity*.

The finding is important because it tells us more about how lupus develops and suggests a strategy for treating the autoimmune disease, said Harris Perlman, Ph.D., associate professor of molecular microbiology and immunology at Saint Louis University and senior author of the study.

“We want to eliminate those hyperactive immune cells that lead to continuation of the disease but maintain infection-fighting white blood cells,” Perlman said. “This will restore the balance of cells in the immune system, which has become very skewed in lupus patients.”

It is estimated that between 1.5 and 2 million Americans have some form of lupus, which can damage the kidneys, heart, joints, skin, lungs, blood vessels, liver and nervous system.

In those who have an autoimmune disease such as lupus, the cells in the immune system become confused. Instead of attacking only infected cells or foreign bodies, they turn ultra-vigilant and attack the body’s own normal cells and tissues, causing inflammation, pain and injuries.

Perlman and his team have discovered the double whammy for lupus

patients. They harbor a higher than normal number of immune cells that carry too much of the pro-survival or anti-apoptotic proteins that tells them to keep living past their prime.

Normally these cells should undergo “apoptosis,” a natural process by which cells die so they don’t spread infection or take away nutrients from healthy cells. The signal to die can come from inside the cell itself or from outside the cell.

Perlman and his colleagues found that the communications system that tells immune cells that it’s time to die gets turned off in lupus patients and causes immune cells to accumulate in the body. This failure to delete these cells allows the disease to progress, Perlman said.

Perlman’s research team took blood from 14 lupus patients and 14 healthy people. Patients with lupus produced more immune cells with too much of the proteins that prolonged cell life. The more of these immune cells patient had, the more severe was his or her disease.

The team used that knowledge to create mice that had a defect in the two known “death pathways” that signal when they’re supposed to die. They showed that these mice displayed high numbers of immune cells that would normally die and that all of the mice developed very severe lupus.

“We showed it in patients and reproduced the result in mice,” Perlman said. “Now we can use this mouse model to do pre-clinical trials for therapies to fight lupus.”

The next step, Perlman said, is to test a therapy that blocks proteins that prevent cells from dying by mimicking the action of proteins that tell immune cells it’s time to die.

“We want to deliver a treatment that will target those proteins that keep

these immune cells alive. This could induce a type of remission in patients,” Perlman said.

“We need to tilt the balance toward the normal cells – cells that don’t want to attack the body but function correctly so the patient can fight infection and have a normal life. We want to kill those cells that lead to the continuation of disease.”

Source: Saint Louis University

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