Finding paves way for better treatment of autoimmune disease

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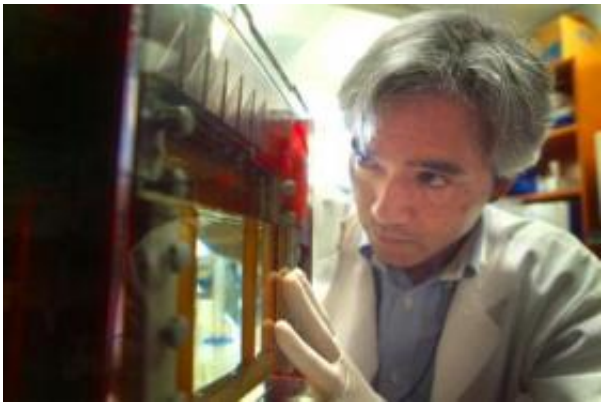

Dr. Makio Iwashima, MCG immunologist. Credit: Medical College of Georgia

A signaling molecule with an affinity for alcohol has yielded a rapid, inexpensive way to make large numbers of immune cells that work like beat cops keeping misguided cells from attacking the body.

The ability to easily make large numbers of these cells opens the door to improved treatment and a better understanding of autoimmune diseases such as type 1 diabetes and arthritis, Medical College of Georgia researchers say.

T cells are components of the immune system designed to attack invaders such as bacteria and viruses; regulatory T cells are a small subset that prevents the cells from also attacking body tissue.

Research published in the August issue of *Nature Methods* shows that, given the option, phospholipase D, which typically mixes with water, prefers alcohol. It's an apparently lethal choice for the signaling molecule that, in turn, also kills T cells that need phospholipase D to survive. Previously, it was unknown whether regulatory T cells required the molecule.

"What we have found is that if you block this enzyme, almost all T cells die after three days but the regulatory T cells can survive," says Dr. Makio Iwashima, MCG immunologist and the study's corresponding author. "After three days, we give them some food to grow and, in one week, you get about 90 percent pure regulatory cells."

The approach worked with laboratory-grade alcohol, called butanol, as well as beverage-grade ethanol.

Normally, regulatory T cells constitute about 5 percent of the T cell compartment, Dr. Iwashima says. Isolating them is doable but a long, expensive process.

When researchers gave some of the regulatory T cells to a mouse model of inflammatory bowel disease, the symptoms, including dramatic weight loss, went away. Animals showed no classic signs of inflammation, just a significant increase in regulatory cells.

MCG researchers have obtained funding from the Arthritis Foundation and the Juvenile Diabetes Research Foundation to see if the cell therapy will work as well in animal models for arthritis and type 1diabetes.

"Our prediction and our hope is that we can restore balance," says Dr. Iwashima. The usual 5- to 95-percent ratio of regulatory cells to non-regulatory T cells is lost in those with autoimmune disease, he says. However, too many regulatory cells also can be a problem, he says,

noting that cancer patients have higher levels of regulatory cells.

Regulatory T cell therapy also resolved symptoms in a model of graft versus host disease, a problem for some bone marrow transplant patients when immune cells from the donor start attacking. This finding indicates a potential role for helping transplant patients keep new organs, the researchers say.

Dr. Iwashima has an Alcoholic Beverage Medical Research Foundation grant to pursue alcohol's potential for helping isolate desirous regulatory cells. However, he cautions that his research findings are not a green light for patients with autoimmune disease to drink because of the negative health effects of regular alcohol consumption.

Dr. Iwashima and his colleagues believe the best way to optimize cell percentages is to do what the body does. In fact, they already are searching for an endogenous substance that interferes with phospholipase D.

"Ultimately, that is the most natural way, if we can find the compound in our bodies that can do the job," Dr. Iwashima says. He theorizes that this natural substance helps destroy non-regulatory T cells when the body gets too many, say after fighting a big infection, and that it may not work well enough in people with autoimmune disease.

Source: Medical College of Georgia