

Immunity research hints at cures

MCG doctors find connection between gene, protective cells

By **Tom Corwin** | *Staff Writer*

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A gene that helps keep the immune system from attacking the body itself also is playing a dual role in promoting regulatory cells that could help prevent diseases such as type 1 diabetes and possibly even cancer, according to Medical College of Georgia researchers.

In a study published today in the journal *Nature Medicine*, a research team led by Qing-Sheng Mi and Jin-Xiong She found a ground-breaking role for the gene *Aire*, also known as autoimmune regulator gene, by studying mice that were specially bred to lack it. The mice develop a disease similar to a rare human disease called autoimmune polyglandular syndrome type 1, one of the few known to result from a single gene defect, said Dr. She, the director of the Center for Biotechnology and Genomic Medicine at MCG.

"From that sense, it is an extremely valuable model for scientists to understand how autoimmunity works and how we can come up with new treatments," Dr. She said. "That's really why the studies of such autoimmune diseases can be very useful and very important."

The immune system uses T cells to recognize and attack viruses and other invaders, Dr. She said. But occasionally the body produces what's known as autoreactive T cells, which mistakenly attack the body's own proteins. This can lead to autoimmune diseases such as type 1 diabetes and multiple sclerosis, Dr. She said. *Aire* plays an important role in getting rid of them, a process called negative selection, Dr. Mi said.

"So it gives a signal to the T cells that are involved in negative selection, then the cells can kill the autoreactive T cells that (promote) autoimmune development," he said.

This happens in an organ called the thymus, where T cells are processed, but some autoreactive T cells inevitably escape the thymus into the body, where they can be kept under control by regulatory T cells, Dr. She said. One type of those regulatory cells is a type of natural killer T cell; Dr. Mi was part of a Canadian team that found that mice with a model of type 1 diabetes were deficient in those natural killer T cells.

Scientists had been trying for years since to prove a link between the natural killer T cells and the *Aire* gene, but this is the first time it has been done, Dr. She said.

"(It) controls the production of both bad T cells and good T cells," Dr. She said. "This is really the critical protein that regulates how the immune system works."

Aire has long been known to have a role in the thymus but "this is something else entirely," said Leonard Sigal, a clinical professor of medicine and pediatrics at the Robert Wood Johnson Medical School at the University of Medicine and Dentistry of New Jersey, who has written about *Aire*. The finding could have implications for more than just autoimmune disease, he said.

"There may be roles for the results of this kind of research in understanding the pathogenesis (disease development) of not only autoimmune disease but also malignancy (cancer)," said Dr. Sigal, who was not involved in the research. "When you think about it, the immune response against a malignancy you want to encourage, whereas the immune response against self you want to suppress. So it's two sides of the same coin."

The MCG team has been working with a chemical that helps promote the killer T cells, which the Canadian team used to help prevent the development of type 1 diabetes in their mice, Dr. Mi said. Some clinical trials already have begun in breast cancer and type 1 diabetes, he said. The chemical, referred to as alpha-GalCer, was first derived from a kind of sea algae, Dr. She said. Because it does seem to have a very specific response from those certain kinds of immune cells, that could be important, Dr. Sigal said.

"Instead of shooting blindly, you've got a specific target," he said. The MCG team will continue working on which genes Aire also regulates, Dr. She said, in the hopes of finding even more specific targets and from there, potential therapies for the more common autoimmune diseases.

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Diabetes, MS

The immune system can sometimes go awry and attack the body's own cells, which can result in autoimmune diseases such as type 1 diabetes and multiple sclerosis. Type 1 diabetes accounts for 5 percent to 10 percent of the estimated 20.8 million people in the U.S. that had diabetes in 2005, according to the Centers for Disease Control and Prevention. About 400,000 people have MS, according to the National Multiple Sclerosis Society.