

A New Way to Look at Eye Complications in Diabetes

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Even though Jason DeVoss, PhD has been working in Dr. Mark Anderson's lab for less than a year, he is already making his mark by creating a promising, new ophthalmology model that may make it easier to study diabetic complications in the eye.

After receiving his training at the University of Michigan and Stanford, Dr. DeVoss joined the UCSF team that is trying to understand why the body attacks its own insulin-producing beta cells in type 1 diabetes. Specifically this group is focused on Aire, a protein that works in the thymus gland to activate the production of a wide array of self-proteins, including insulin.

To understand Dr. DeVoss' work, a lesson in basic immunology is in order. The thymus is an organ in the upper chest where T cells develop and mature. Once mature, these T cells are released throughout the body to fight infection. T cells also help to stimulate B cells, another type of immune cell. B cells, in turn, make antibodies that recognize and reject foreign proteins. Together, B and T cells respond to infection and foreign molecules in the body, triggering immunological responses that keep us healthy. However, autoimmunity can arise if these cells recognize normal self-proteins, initiating an immune attack against the body itself!

Therefore, one job of the thymus is to help reduce the chance of autoimmunity. In particular, a protein currently studied by the lab may prove critical in preventing self-recognition. The Aire protein, which is expressed by a small subset of cells in the thymus, is involved in the removal of self-reactive T cells, a process termed negative selection. As a research fellow, Dr. Anderson knocked out the Aire gene in the thymus of mice. In these Aire deficient mice, self-reactive T cells are not removed, resulting in an autoimmune attack in multiple organs such as the pancreas, salivary glands, ovaries, and stomach.

In addition to these organs, Aire knockout mice also generate an autoimmune attack against the eye, ultimately leading to blindness. It is this attack on the eye that Dr. DeVoss has chosen to focus on. From work done previously by Dr. Anderson and now continued by Dr. DeVoss, it is clear that the immune system is recognizing a particular region of the eye. The next step will be to understand what specific molecules are being targeted.

Through this process of understanding how Aire influences ocular immunity, Dr. DeVoss and his colleagues may have created a new model for ophthalmology. Unlike previous models of

retinopathy which have tried to mirror complications in diabetes and other forms of autoimmune blindness, the Aire knockout mice are a spontaneous model. This new approach may help ophthalmologists to more successfully investigate diabetic eye complications.

Before this becomes a working model for ophthalmologists, Dr. DeVoss must identify the antigens that the immune system is attacking and the cells involved. Once this is accomplished, Dr. DeVoss may have helped to make the study of diabetic eye complications much easier for researchers around the world.

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