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Immune police recognize good and bad guys in the body

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Immune system police are as good at recognizing bad guys, such as bacteria and viruses, as they are our own tissue, researchers say.

The finding may cause a stir in the scientific community, which has long held that regulatory T cells or Tregs, preferentially respond to body proteins, or self antigens, rather than non-self antigens, invaders such as viruses and bacteria.

Now, Medical College of Georgia immunologists report in the September issue of Immunity that Tregs, similarly to other T cells, respond stronger and more frequently to foreign substances than to the body's own antigens.

Fortunately, the potential conflict between naïve and regulatory T cells, in which the former lead the attack against invaders and the latter try to protect invaders, usually doesn't exist, the scientists say.

That's probably because other types of immune cells come to help T cells fight an infection, says Dr. Rafal Pacholczyk, a corresponding author for the study.

"During the normal immune response, Tregs sit in the back seat and, in most cases, don't interfere," says Dr. Leszek Ignatowicz, also a corresponding author.

Still, emerging therapies to fight autoimmune diseases, such as arthritis,

multiple sclerosis and type 1 diabetes, by boosting the total number of Tregs could unintentionally upset the balance between naïve T cells and Tregs, they say.

“Regulatory cells always suppress immunity, whether it’s to a virus, bacteria or our own tissue,” says Dr. Ignatowicz.

“We have to be really careful with manipulating regulatory T cells as a whole,” adds Dr. Pacholczyk. “If we want to promote more regulatory cells in the body, we have to find a way to promote only those in which specificities are known.”

Oral insulin, which appears to boost the number of Tregs that recognize and protect insulin-producing pancreatic cells from the immune system, is a good example of how this targeted promotion may work for type 1 diabetes, they say.

To determine what antigens Tregs can recognize, Drs. Pacholczyk and Ignatowicz did side-by-side studies of antigen receptors expressed on naïve T cells and Tregs.

“Here, we could quantitatively compare proportions of how many regulatory cells or how many non-regulatory cells see non-self versus self antigens, and we found these proportions to be similar,” says Dr. Ignatowicz. “We found regulatory cells respond to cells presenting non-self antigens as frequently as naïve T cells.”

Researchers report that 70 percent of the most frequent receptors found on naïve T cells also were found on Tregs. Since receptors define what the individual T cell recognizes, it provides additional evidence that naïve T cells and Tregs see the same thing, they say.

Drs. Pacholczyk and Ignatowicz reported in the August 2006 issue of

Immunity that Tregs, like naïve T cells, learn what to recognize in the thymus. They also reported that most Tregs that mature in the thymus retain their regulatory properties and do not later convert to naïve T cells as was previously believed. This finding emphasized the role of the thymus as the primary site where Tregs differentiate and acquire their unique inhibitory functions, they say.

Although, the majority of T cells that may harm healthy body tissue are eliminated in the thymus, some errant autoreactive cells can escape and cause autoimmune disease. Tregs previously believed to primarily recognize self-tissue with the idea of protecting it are considered the antithesis of these autoreactive cells.

“It was believed that regulatory cells are baptized autoreactive cells,” says Dr. Ignatowicz. “They are like bad boys that went good,” since they also recognize self tissue but seek to protect it.

Yet scientists kept running into the reality that some regulatory cells also were recognizing – and potentially protecting – invaders such as bacteria and viruses.

The MCG scientists say because both T cell populations are educated in the thymus, it is not surprising that they recognize the same things.

Source: Medical College of Georgia