

Thymus teaches immune cells to ignore vital gut bacteria

April 29 2013



This image shows Anna Cebula (from left), Dr. Leszek Ignatowicz and Dr. Richard A. McIndoe, Medical College of Georgia at Georgia Regents University. Credit: Phil Jones

The tiny thymus teaches the immune system to ignore the teeming, foreign bacteria in the gut that helps you digest and absorb food, researchers say.

When [immune cells](#) recognize essential [gut](#) bacteria as foreign, inflammatory bowel disease such as [ulcerative colitis](#) and Crohn's disease can be the painful, debilitating result.

In a study published in the journal *Nature*, researchers show that the [regulatory T cells](#), or Tregs, that keep this from happening in most of us come from the tiny immune organ nestled near the heart, said Dr. Leszek Ignatowicz, [immunologist](#) in the Center for Biotechnology and Genomic Medicine at the Medical College of Georgia at Georgia Regents University.

In fact, mice born lacking T [cells](#) that were given a specific T cell type that causes colitis-like wasting disease, didn't get the disease if they also received thymus-derived Tregs.

"This essential gut-bacteria is one group that you don't want to mount an [immune response](#) against," said Ignatowicz, the study's corresponding author. "In fact, you need the Tregs' help in inducing tolerance to these bacteria if you want to treat Crohn's and other inflammatory bowel disease."

Knowing exactly where the Tregs come from is essential to making more of them, noted Dr. Richard A. McIndoe, the center's Associate Director and a study co-author. "The Tregs have to shut down the immune response. The question is: Do we have to expand the pre-existing Tregs that came to the gut from the thymus or teach peripheral naïve or effector T cells to become Tregs? "

The answer was thought to be that most immune cells learn to ignore the vital bacteria after they reach the gut. However, the new study shows that only a fraction of bacteria-friendly Tregs come from there. Since T cells don't have [license plates](#), they looked at their antigen receptors and found the Tregs in the gut had the same receptors as their precursors in the thymus. Easing the comparison was the fact that naïve T cells, which also get their education in the thymus, have mostly different receptors than thymus-educated Tregs.

They soon realized that while conversion of naïve cells to Tregs occurs more often in the gut than other organs, it was much less frequent than conventionally believed. Once in the gut, naïve cells can become Tregs or effector cells; effector cells only attack unless constrained by Tregs.

"We either have to induce effector T cells to change to Tregs or boost the number of Tregs coming out of the thymus to help patients with [inflammatory bowel disease](#)," McIndoe said. Some compounds, including vitamin A and transforming growth factor beta, already are known to aid conversion.

While T-cells mostly earn their receptors in the thymus, most don't take action until they actually see their chosen antigens, a variety of substances that can provoke an immune response. Well-educated thymus-derived Tregs can recognize antigens from the body's tissue as well as foreign antigens derived from sources like gut bacteria. Interestingly most immune cells circulating in the body are naïve T-cells that become effector cells upon their first contact with an antigen.

It was previously believed that [thymus](#)-derived Tregs primarily protect the body's own tissue but don't induce tolerance to foreign antigens like ones derived from gut's bacteria. However Ignatowicz and Dr. Rafal Pacholczyk reported in 2007 in the journal *Immunity* that Tregs could actually recognize both self- and non-self-antigens. The gut, which regularly deals with an onslaught of foreign substances such as food and drink, was a logical place to figure out where the accommodating Tregs originated, Ignatowicz said.

MCG scientists note that effector cells also are needed in the gut to recognize and eliminate harmful bacteria, such as campylobacter, a common cause of diarrhea, vomiting and abdominal cramping that can result from eating inadequately washed and cooked poultry.

Populating [gut bacteria](#) starts early, with mother's milk or formula, and is determined largely by diet as well as the environment so every individual's is different although bacteria tend to be compatible among the same species, McIndoe said.

Vaccines are likely the oldest example of using the body's natural defense system to protect against invaders. Conversely, select immune cell populations already are being used to help fight cancer. More sophisticated approaches are being developed to turn down the immune response, in the case of an organ transplant or an autoimmune disease such as lupus or arthritis.

Provided by Medical College of Georgia

Citation: Thymus teaches immune cells to ignore vital gut bacteria (2013, April 29) retrieved 26 April 2024 from <https://medicalxpress.com/news/2013-04-thymus-immune-cells-vital-gut.html>

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