

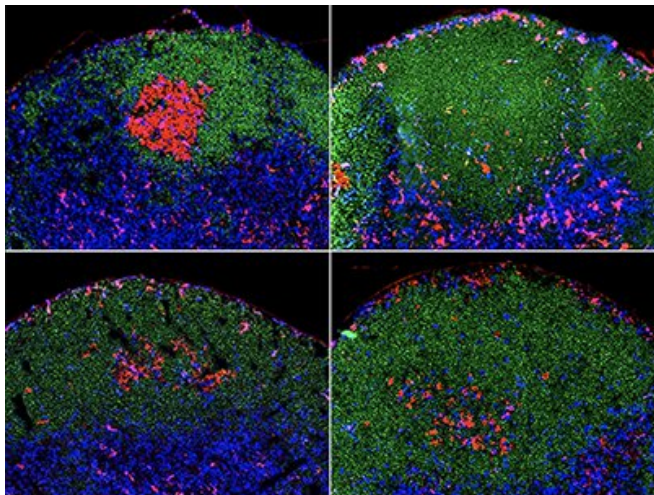
Key to powerful antibody production found

Discovery led by La Jolla Institute scientists may help with vaccines, autoimmune diseases



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By [Bradley J. Fikes \(/staff/bradley-fikes/\)](/staff/bradley-fikes/) | 8 a.m. May 2, 2016 | Updated , 1:32 p.m.



Follicular helper T cell, shown in blue, play a crucial role in the maturation of antibody-producing B cells (shown in green). Activated B cells give rise to germinal centers (shown in red), where mature B cells proliferate and produce highly specific antibodies against pathogens. Top left: normal germinal center in a mouse tonsil. All others: Germinal centers fail to form when the interaction between ICOS and TBK1 is interrupted. — *Courtesy of Dr. Kok-Fai Kong at La Jolla Institute for Allergy and Immunology and Nature Immunology.*

Another mystery in how the immune system develops powerful antibodies [has been solved](http://www.eurekalert.org/emb_releases/2016-05/ljif-lsd042816.php) (http://www.eurekalert.org/emb_releases/2016-05/ljif-lsd042816.php), according to a study led by scientists from the La Jolla Institute for Allergy and Immunology.

The study reports discovery of the molecular mechanism by which fully functional follicular "helper" T cells are generated. These helper cells assist antibody-making B cells to work to their fullest potential.

Knowledge of this pathway may help in developing more effective vaccines, and in treating autoimmune diseases, the researchers said.

The study was published Monday in *Nature Immunology*. Shane Crotty and Kok-Fai Kong of the La Jolla Institute were senior authors. Christophe Pedros, also of the institute, was first author. The study can be found online at <http://j.mp/helpericos> (<http://j.mp/helpericos>).

The importance of helper T cells has been driven home by previous work led by Crotty, who is widely recognized in the scientific community for his work on vaccines.

In 2013, Crotty led a study (<http://www.sandiegouniontribune.com/news/2013/sep/12/hiv-vaccine-study-antibodies-crotty/>) that found levels of potent "broadly neutralizing" antibodies in HIV-positive people correlated with high levels of helper cells.

In the new study, researchers found that an enzyme called TANK-binding kinase 1 associates with another molecule called Inducible T cell Co-Stimulator or ICOS to promote antibody development. ICOS was already known to play a key role, but how this molecule was recruited to the task wasn't known.

Once activated by ICOS, the helper T cells move to immune-specific tissues called follicles, where they come in contact with the B cells. Certain B cells in turn are activated and go into an area of the follicle called the germinal center, a sort of immune boot camp where these B cell develop powerful antibodies attuned to a specific pathogen. (In the case of autoimmune disorders, the B cells attack the body as if it were a pathogen).

Pharmaceutical companies are now working on drugs that target ICOS, Crotty said.

It appears to be easiest to use the ICOS pathway to treat autoimmune diseases, he said. The reason is that ICOS must be active at all times, or the T cells go away.

In the laboratory, it's easier to block a disease from beginning than to interrupt the disease process once it has established itself, Crotty said. But in real life, diseases are discovered once they've already caused symptoms.

"Then you've got to stop the disease when it's full-blown, and that's a different problem," Crotty said.

But in an experiment performed in mice, blocking ICOS prevents the helper cells from remaining fully differentiated. That in turn prevents the B cells from benefiting from their tutelage. This should help tune down the autoimmune response.

The study's science is sound, said Stacy E. Ferguson, a program officer in the Division of Allergy, Immunology, and Transplantation at the National Institute of Allergy and Infectious Diseases. Its findings can't be put to immediate clinical research in developing vaccines and autoimmune therapies, she said by email, but are broadly applicable to those fields further down the road.

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