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Researchers discover new cellular mechanism that will significantly advance vaccine development

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La Jolla Institute for Allergy & Immunology (LIAI) scientists have discovered one for the textbooks. Their finding, reported Friday in the scientific journal *Immunity*, illuminates a new, previously unknown mechanism in how the body fights a virus. The finding runs counter to traditional scientific understanding of this process and will provide scientists a more effective method for developing vaccines.

"Our research grew from the question, "why do you get good antibody responses to some parts of (virus) pathogens and poor responses to other parts?" said LIAI scientist Shane Crotty, Ph.D., the lead researcher on the paper, "Selective CD4 T cell help for antibody responses to a large viral pathogen: deterministic linkage of specificities." Alessandro Sette, Ph.D., a renowned vaccine expert and director of the LIAI Center for Infectious Disease, also was a key contributor on the study. Dr. Crotty said the team studied the smallpox vaccine, considered the "gold standard" of vaccines, and found some startling answers.

"We expected one thing based on textbook knowledge and that didn't happen at all," he said. It was known previously that getting a good antibody response requires two different cells of the immune system -- B cells and CD4 T cells, both soldiers in the immune system's defensive army. Antibody responses are important because they help the body fight off viruses and they also are key to vaccine development. Surprisingly, however, Dr. Crotty said the researchers found that B cells

and CD4 T cells recognize the same piece of the virus.

"Previously, it was thought that the CD4 T cell could react to any part of the virus, but now we realize it must be specific to the same part as the B cell," he explained. "When you have a hundred different parts, this knowledge makes a big difference. It narrows down the search for the right antigens tremendously."

Scientists use knowledge of which antigens (virus pieces) trigger an antibody attack to develop vaccines. Vaccines work by exposing the individual to a milder form of a particular virus, so that the body makes antibodies to fight off the virus. Consequently, if the individual is later exposed to the actual virus, the body already has an army of antibodies built up that can fight off this stronger viral attack before it can overtake the body and cause sickness.

With the knowledge gained from the LIAI study, scientists will now be able to more easily figure out the most important viral pieces to focus on in developing a vaccine. "The fact that it requires two components to fight the (virus) pathogen is important to understand," Dr. Crotty said. "So now when we find out which viral pieces are producing a strong response from the B cells, we can cross check that against the viral pieces eliciting a good response from the CD4 T cells. The point at which these virus pieces cross – in other words where the same piece is eliciting a response from both the B cells and CD4 T cells – then we know we have found our best candidate for creating a vaccine."

Source: La Jolla Institute for Allergy and Immunology