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For Immediate Release

T cells take aim at Chikungunya virus

As Chikungunya spreads into new regions, LJI scientists share a first look at how human T cells target the virus. Their findings may shed light on how viruses can trigger chronic disease.

LA JOLLA, CA—A new study, published recently in *Nature Communications*, offers the first-ever map of which parts of Chikungunya virus trigger the strongest response from the body's T cells.

With this map in hand, researchers are closer to developing Chikungunya vaccines or therapies that harness T cells to strike specific targets, or "epitopes," to halt infection. The new study also offers important clues for understanding why many people experience chronic, severe joint pain for years after clearing the virus.

"Now we can see what T cells are seeing patients with chronic disease," says LJI Assistant Professor Daniela Weiskopf, Ph.D., senior author of the new study.

This research comes as many mosquito-borne viruses, including Chikungunya, are moving into new areas of the globe.

"Historically, Chikungunya was considered an emerging virus. Now all of Latin America has been exposed," says Weiskopf. "These mosquitoes are traveling further north, and we need to know what's going on with this virus before it arrives in the United States."

T cells jump into action

Chronic Chikungunya virus disease strikes between 30 to 60 percent of those infected—usually women—and causes chronic, severe joint pain. This debilitating joint pain can last for years following the initial viral infection.

In a study out earlier this year, Weiskopf and her colleagues showed that these patients have a population of inflammatory CD4+ T cells that closely resembles the T cell signature of rheumatoid arthritis, an autoimmune disease.

"So many people, mostly women, have chronic disease following Chikungunya virus infection," says Weiskopf. "This has an impact on the workforce and impacts the economy. And there's no treatment."

Weiskopf and her colleagues are working to understand why these CD4+ T cells linger and cause problems after a person clears the virus. For this study, they investigated whether people who develop chronic disease produce T cells that naturally target a different set of epitopes on Chikungunya virus.

Would a different "flavor" of T cells be more likely to stay in the body after infection?

Weiskopf and her team used a "peptide pool" approach to assemble a map of key T cell epitopes on Chikungunya virus. The researchers broke up the virus into very small amino acid sequences, called peptides. Then they took T cells from people with chronic Chikungunya virus disease and exposed these cells to the pool of peptides.

By stimulating the T cells, the researchers discovered exactly which parts of the virus are most likely to be recognized by T cells. These "immunodominant" regions may prove to be good targets for future Chikungunya treatments.

Rimjhim Agarwal, a UC San Diego graduate student and member of the Weiskopf Lab, spearheaded experiments to learn more about these T cells. Agarwal received funding from The Tullie and Rickey Families SPARK Awards for Innovations in Immunology to take a closer look.

For her project, funded through the generosity of the Rosemary Kraemer Raitt Foundation Trust, Agarwal compared CD4+ T cells from people with chronic Chikungunya virus disease to people who cleared the virus quickly with no lasting symptoms.

Agarwal found that both patient groups had T cells that targeted the same viral epitopes. People who developed chronic disease did not recognize different proteins of the virus did not make a different flavor of T cells.

Now the question is—why do these T cells stick around to cause inflammation in some but not all people? Weiskopf and Agarwal are now looking at where Chikungunya virus might hide in the body to stimulate a long-term T cell response.

The LJI team also hopes to help other laboratories shed light on how to fight the virus. "Identifying the immunodominant T cell epitopes could seed new research into Chikungunya-specific T cell responses," says Agarwal.

Additional authors of the study, "Identification of immunogenic and cross-reactive chikungunya virus epitopes for CD4+ T cells in chronic chikungunya disease," included Calvin Ha, Fernanda H. Côrtes, Yeji Lee, Amparo Martínez-Pérez, Rosa Isela Gálvez, Izabella N. Castillo, Elizabeth J. Phillips, Simon A.

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