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For Immediate Release

A new timeline for Parkinson's disease

LJI scientists discover that T cells may allow for early detection of Parkinson's cases—years before motor symptoms development

LA JOLLA, CA—Your T cells work hard to fight disease. Unfortunately, "friendly fire" from T cells can sometimes harm the body's healthy tissues.

For people with autoimmune disease, T cell reactivity is a big problem. Haywire T cell responses lead to autoimmune diseases such as type 1 diabetes, rheumatoid arthritis, and inflammatory bowel disease.

In recent years, scientists at La Jolla Institute for Immunology (LJI) have discovered that T cells may also contribute to the development of Parkinson's disease. Researchers in the laboratory of LJI Professor Alessandro Sette, Dr.Biol.Sci., have found that many people with Parkinson's disease have T cells that target key proteins, called alpha-synuclein and PINK1, on vulnerable brain cells.

Earlier this year, Sette and his colleagues published a study in *npj Parkinson's Disease* that sheds light on exactly which subtypes of T cells target alpha-synuclein. Their findings offered further clues that T cell reactivity plays a role in Parkinson's disease. Still, the scientists didn't have a timeline to show *when* T cells might contribute to disease development.

"We can see these reactive T cells in people after they develop Parkinson's, but what happens before that?" says LJI Visiting Scientist Emil Johansson, Ph.D., a researcher in the Sette Lab and co-author of the study.

Now we have answers. In a new *npj Parkinson's Disease* paper, Sette and his colleagues show that potentially harmful T cell reactivity is highest during the "prodromal" period in Parkinson's—the years before patients receive a diagnosis.

"This T cell immunity could be a marker for early Parkinson's treatment, even before people show symptoms," says Sette, who was senior author on the new paper. "And there's reason to think that treating Parkinson's in the very early stages can lead to a better outcome."

How the study worked

The prodromal period in Parkinson's disease can last for decades before a person develops noticeable symptoms such as tremors and cognitive impairments.

Because prodromal Parkinson's disease is very difficult to detect, the LJI team studied T cell reactivity in research volunteers at high risk of developing Parkinson's disease. These volunteers had genetic risk factors for Parkinson's and some had symptoms such as disrupted REM sleep cycles and loss of sense of smell, which can be early signs of Parkinson's disease development.

The researchers used a technique called Fluorospot to learn more about T cells found in blood samples from these study volunteers. This technique revealed which volunteers had high levels of T cells that reacted to alpha-synuclein or PINK1—and when those T cell numbers were highest.

Sette and his colleagues found that potentially harmful T cells show up early on, well before the onset of noticeable motor symptoms, such as tremors. "You can see that T cell reactivity before diagnosis," says Sette.

In fact, T cell reactivity to PINK1 was at an all-time high before diagnosis.

Sette warns against jumping to conclusions. Parkinson's is a complex disease, and the new research doesn't prove that T cells are actually driving the inflammation associated with Parkinson's disease.

"Parkinson's disease is associated with the destruction of nervous system cells. Does that destruction cause autoimmunity—or is the autoimmunity the cause of the disease? That's the chicken-and-the-egg of inflammation in Parkinson's disease," says Sette.

"Certainly, the fact that this T cell reactivity is highest when patients are closest to a diagnosis is intriguing," he adds. "The finding suggests T cells could have something to do with it."

Next steps for helping patients

The new research may guide the development of early diagnostic tools. In the meantime, LJI scientists are looking for ways to block inflammation and protect brain cells.

As Johansson explains, some T cells actually help dial back inflammation to protect our tissues. "We want to see if there are specific T cells that are protective," says Johansson. "Could they interfere in inflammation and maybe reduce the number of autoimmune T cells?"

Sette and his colleagues are also working to understand the role of T cells in other neurodegenerative diseases.

"We are very interested in diseases such as Alzheimer's, for example, where a lot of progress has been made toward identifying people in very early stages of the disease progression," says Sette.

Additional authors of the study, "T cell responses towards PINK1 and α-synuclein are elevated in prodromal Parkinson's disease," included first author Antoine Freuchet, Gregory P. Williams, Tanner Michealis, April Frazier, Irene Litvan, Jennifer G. Goldman, Roy N. Alcalay, David G. Standaert, Amy W. Amara, Natividad Stover, Edward A. Fon, Ronald B. Postuma, John Sidney, David Sulzer, and Cecilia S. Lindestam Arlehamn.

This study was supported by LJI & Kyowa Kirin, Inc. (KKNA- Kyowa Kirin North America), the Swedish Research Council (grant references 2024-00175), Aligning Science Across Parkinson's (ASAP-000375), and the Michael J. Fox Foundation.

DOI: 10.1038/s41531-025-01001-3

About La Jolla Institute

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