



New Research Finds Antibody Detects Alzheimer's Signals at Earliest Stages

Researchers at the University of Miami Miller School of Medicine have used a unique antibody (called IC 100), and other research tools, to detect inflammatory signals in early and mid-stage Alzheimer's disease in neurons and brain-specific immune cells called microglia. These findings could lead to more effective diagnostic tests, which could identify Alzheimer's at its earliest stages. IC 100 could also be used therapeutically. The study was recently published in the journal *Brain Pathology*.



Robert W. Keane, Ph.D.

“One of the key findings is that neurons are undergoing inflammation by activation of their innate immune system, the inflammasome, early in the disease process,” said Robert W. Keane, Ph.D., professor in the Departments of Physiology & Biophysics and Neurological Surgery and senior author on the paper. “This finding is exciting because we can start thinking about imaging studies to identify these neurons in patients and see if they have brain inflammation. Right now, there's no way to assess whether a patient will develop Alzheimer's disease or not.”

The research team was particularly interested in the inflammasome, the inflammatory molecules that help power each



cell's innate immune response. While this inflammatory signaling had previously been detected in some brain cells, it had never been seen in neurons during early- or mid-stage Alzheimer's. The ability to identify this inflammatory process, particularly early in disease progression, could set the stage for timely interventions to possibly slow or even stop the disease.

A Link to Early Inflammation

In the study, the team analyzed brains from people who had experienced early- or mid-stage Alzheimer's disease. Using a variety of techniques, they found inflammasome-related proteins NLRP 1, NLRP 3 and ASC were more highly expressed. Using IC 100, an antibody developed by the Keane and de Rivero Vaccari lab in 2009 and licensed to ZyVersa Therapeutics, Inc., the team found increased ASC in neurons, particularly in the hippocampus, a brain structure associated with learning and memory. These results could link early inflammation in neurons and microglia to later-stage Alzheimer's pathology.

"IC 100 is exciting because we can see the inflammation in neurons, and we can see it increase with Alzheimer's disease progression," said Regina Vontell, Ph.D., associate director of the Brain Endowment Bank and first author on the study. "We can see changes in the hippocampus and, amazingly, we can see this with the protein signals and correlate that with the clusters of amyloid and increases in phosphorylated tau in different hippocampal regions."

This research was a team effort that included Juan Pablo de Rivero Vaccari, Ph.D., Xiaoyan Sun, M.D., Ph.D., Sakir Humayun Gultekin, M.D., Helen M. Bramlett, Ph.D., and W. Dalton



Dietrich, Ph.D.

Therapeutic Potential

The same mechanisms that help IC 100 detect inflammatory proteins in neurons could also be used therapeutically. Unlike some antibodies, IC 100 gets taken into cells. In addition, Alzheimer's and other neurodegenerative diseases can generate leaks in the blood/brain barrier. While this is generally not a good result, it would allow large therapeutic molecules, like IC 100, to reach diseased parts of the brain.

“So many conditions create a leaky blood-brain barrier – Alzheimer's, Parkinson's, multiple sclerosis – and it's our hope that IC 100 will get across the barrier and get into neurons and have an impact,” Dr. Keane said. “We believe it could potentially modulate the interactions between ASC and beta amyloid and reduce that toxicity.”

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