

Researchers identify new model of Alzheimer's as an autoimmune disease

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Scientists at the Krembil Brain Institute, part of the University Health Network, have proposed a new mechanistic model (AD²) for Alzheimer's, looking at it not as a brain disease, but as a chronic autoimmune condition that attacks the brain.

This novel research is published today, in *Alzheimer's & Dementia*.

"We don't think of Alzheimer's as fundamentally a disease of the [brain](#). We think of it as a disease of the immune system *within* the brain," says Dr. Donald Weaver, co-Director of the Krembil Brain Institute and author of the paper.

Alzheimer's disease, the most common form of dementia, impacts more than 50 million people around the world, with a new person being diagnosed every three seconds. Yet, despite more than 200 [clinical trials](#) in the past 30 years, there are no disease modifying therapeutics to prevent, halt or treat Alzheimer's.

"We need new ways of thinking about this disease, and we need them now," says Dr. Weaver. "To

date, most of the approaches in Alzheimer's research have been based upon the theory that a protein called beta-amyloid, which is supposedly abnormal in the brain, clumps up. And when it clumps up, it kills brain cells."

"But we believe beta-amyloid is right where it should be. It acts as an immunopeptide—a messenger within our immune system—so that, if we have [head trauma](#), beta-amyloid repairs it. If a virus or a bacteria comes along, beta-amyloid is there to fight it."

That's where the problem occurs, says Dr. Weaver. "Beta-amyloid gets confused and can't tell the difference between a bacteria and a brain cell and so it inadvertently attacks our own [brain cells](#). This, then, becomes what we call an autoimmune disease. The immune system is actually attacking the host, our brain."

Noted in the team's findings:

- The research team conducted a comprehensive search, looking at a wide-ranging review of both journal and patient literatures combined with their own studies, to develop a thorough mechanistic model of Alzheimer's.
- The AD² model endeavors to harmonize other mechanistic propositions (including proteopathy, synaptotoxicity and mitochondriopathy), while recognizing beta-amyloid as a physiologically oligomerizing immunopeptide and part of a much larger and broad, highly-interconnected immunopathic process.
- Within the AD² model, amino acid metabolism of L-tryptophan and L-arginine emerge as innate immunity regulators, thus pointing to new diagnostic and therapeutic approaches.

Tangible rethinking about Alzheimer's disease as an autoimmune disease, and [beta-amyloid](#) as a

normal part of our [immune system](#), opens the door to new avenues and approaches to develop innovative new therapies, says Dr. Weaver.

"We are very excited in our lab. We think that this autoimmune theory is sound and represents a significant conceptual step forward."

More information: Krembil Brain Institute researchers identify new model of Alzheimer's as an autoimmune disease, *Alzheimer s & Dementia* (2022). DOI: [10.1002/alz.12789](https://doi.org/10.1002/alz.12789)

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