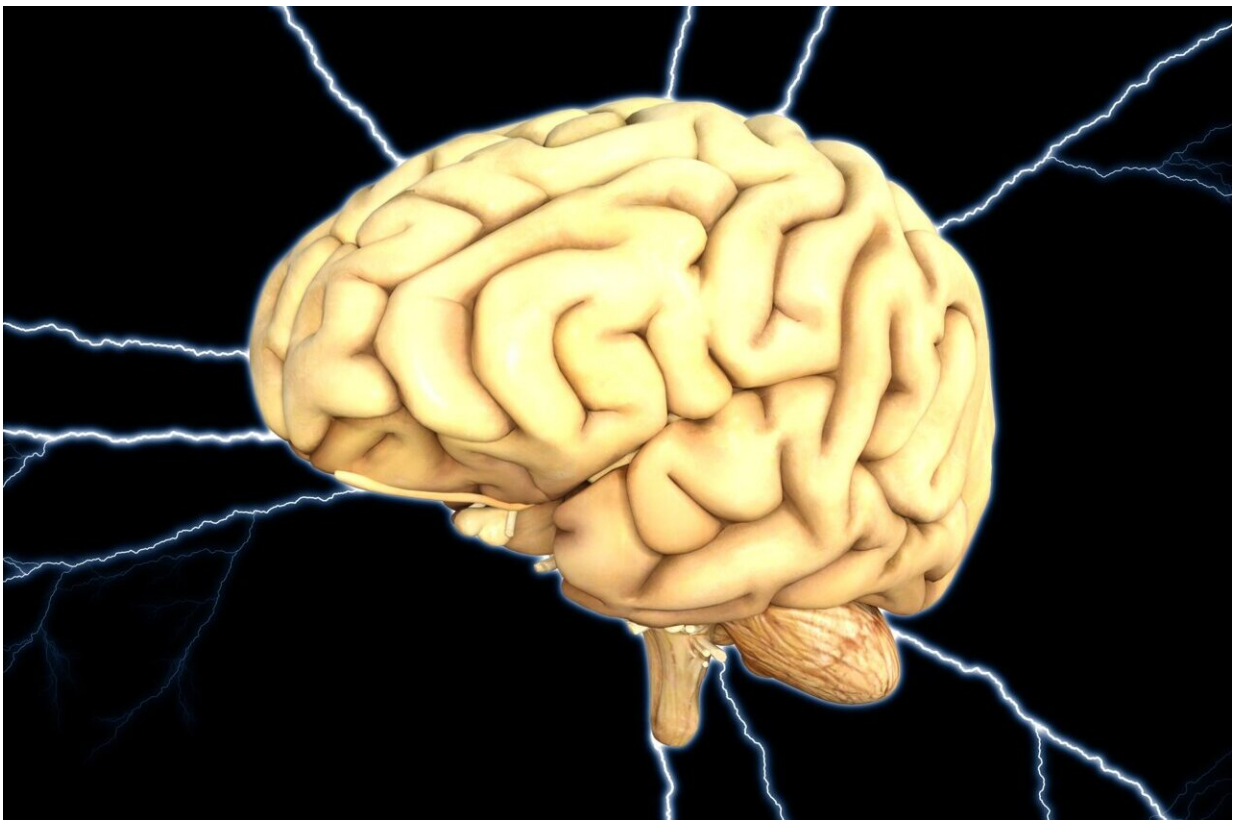


Researchers develop a molecule that inhibits degenerative processes related to Alzheimer's disease

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Credit: Pixabay/Pete Linforth.

Researchers at the Technion—Israel institute of Technology, in collaboration with researchers from CNRS, recently published findings

about the development of an artificial molecule that may inhibit the development of Alzheimer's disease. The molecule breaks down the toxic chemical complex Cu–A β , thus inhibiting the cell death that is thought to be related to Alzheimer's. The study was led by Professor Galia Maayan and doctoral student Anastasia Behar from the Schulich Faculty of Chemistry, in collaboration with Prof. Christelle Hureau from the Laboratoire de Chimie de Coordination du CNRS, Toulouse, France.

Copper ions are a key component of the structure and function of various cells in the body. But their accumulation can lead to cell toxicity, causing dangerous conditions such as oxidative stress, cardiovascular disorders, and degenerative diseases of the brain, including Alzheimer's.

One of the mechanisms involved in the development of Alzheimer's is the formation of free radicals that damage the brain [cells](#). These are oxidizing agents formed, among other things, by Cu–A β , a complex of [copper](#) and [amyloid beta](#). It is already known that the breakdown of this complex, and the removal of copper from the [amyloid](#), prevents [cell death](#), followed by the inhibition of the disease. The extraction of the copper is done by chelation—using molecules that bind the [copper ions](#) and extract them from the amyloid.

However, this is not a simple challenge, because the chelators must meet several critical chemical and kinetic conditions, including stability and resistance to oxidation-reduction reactions. It is also important that the chelator does not bind zinc ions during the copper extraction process, as they are also essential for neuron function (but do not cause toxicity when they are bound to the amyloid); if the chelator does not bind the zinc, it can continue to bind the copper ions, but if it binds zinc, copper binding will be inhibited.

The Technion and CNRS researchers report in the *Angewandte Chemie*

International Edition on the successful development of a new artificial chelator that meets all these requirements. The chelator, called P3, is a peptide-like water-soluble synthetic molecule that performs its task selectively; it strongly binds copper and forms the complex CuP3, extracting the copper from the amyloid. By doing so, it inhibits and even suppresses the formation of harmful oxidizing agents, without creating new oxidation processes. Although it binds [zinc ions](#) and even extracts them from the amyloid faster than it extracts the copper ions, the binding to zinc is weaker, making the zinc-amyloid complex unstable, so in practice P3 mostly binds copper ions. by creating a new, stable complex, and inhibits the formation of harmful oxidizing agents (NO ROS), thereby neutralizing amyloid toxicity.

More information: Anastasia E. Behar et al, A Water-Soluble Peptoid Chelator that Can Remove Cu²⁺ from Amyloid- β Peptides and Stop the Formation of Reactive Oxygen Species Associated with Alzheimer's Disease, *Angewandte Chemie International Edition* (2021). [DOI: 10.1002/anie.202109758](#)

Provided by Technion - Israel Institute of Technology

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