New Compound Could Offer Therapy for Alzheimer's, Parkinson's

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An international research team has developed a compound that successfully targets and destroys aggregated proteins, leading to hopes for a new class of drugs effective against a multitude of diseases including Alzheimer's and Parkinson's.

Left: The compounds, called Molecular Tweezers, have been invented by Professors Frank-Gerrit Klärner and Thomas Schrader at the University of Duisburg-Essen, Germany, and applied to prevention of abnormal protein aggregation by Dr. Gal Bitan. The three professors are pictured together, in 2009. (Source: Breakthrough Treatment for Degenerative Diseases)

The researchers call the compound 'molecular tweezers' because it wraps around particular amino acids in the protein, not the whole aggregate, and then it both prevents the formation of toxic aggregates and also breaks down preformed ones, in a slow process. The slow cleaning is key, especially in the case of Alzheimer's, lead researcher Gal Bitan Ph.D., associate professor of neurology at the David Geffen School of Medicine at the University of California – Los Angeles, told *Bioscience Technology.*

In Alzheimer's, in addition to plaques that accumulate in the brain, there are also amyloid proteins that are deposited in the blood vessels. "It weakens the vessel walls and if that's cleared out too fast the vessel walls don't have time to rebuild, so they collapse and cause microhemorrhages and sometimes stroke," Bitan told *Bioscience Technology*. "If we can clear them slowly and gently and give them time to rebuild, then we will avoid these hemorrhages, which can be devastating."

Successful studies on animals give the researchers hope for a new class of drugs for more than 30 diseases and conditions that involve a buildup of proteins, including diabetes, cancer, spinal cord injury, and amyotrophic lateral sclerosis (ALS).

Unique compounds

These compounds are unique for two reasons. First, they target the process rather than a particular protein, making it a different type of 'precision' medicine. "It's a very different kind of precision than what has been used before because the specificity of this compound isn't for a particular protein, but for a particular abnormal process — formation of these toxic aggregates," Bitan said.

Second, the team understands exactly how the compound works. Other compounds, for example ones that have been extracted out of different foods, such as green teas, or coffee or spices, may have anti-inflammatory activities, or anti-tumor activities, but nobody knows how or why they work on the amyloid proteins, Bitan said.

“In our case, it’s a compound that was designed and used with a particular goal and we know what it does and have shown what it does. We understand the mechanism and we think this will facilitate the path forward toward clinical trials.”

High safety window

The team only tried a few compounds before finding one that was very promising, called CLR01, which Bitan says has the best safety window.

For example, mice were given a daily dose of CLR01 250 times higher than the therapeutic dose for one month and showed no negative side effects. There was a potential positive side effect however – blood cholesterol of the mice dropped by 40 percent. Currently, the compound is injected, but researchers are working to make it orally available so it could be administered as a pill.

The team would be happy to go into clinical trials, Bitan said, but first must raise enough funding to meet the Federal Drug Administration (FDA) requirements.

Currently, they are expanding the scope of research and “collaborating with a number of groups around the world to test the compound in additional animal models of different diseases.”

The research effort currently involves over 30 laboratories worldwide.

“This is a new way to think about dealing with abnormal aggregated proteins,” Bitan told *Bioscience Technology*. “We obviously can’t work on all of them and we welcome collaborators.”
