

Appealing the death sentence for brain cells

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A new drug candidate discovered by Tel Aviv University researcher Prof. Illana Gozes may lead to an effective treatment against the debilitating Alzheimer's disease. This compound could also treat a number of diseases where patients suffer from cognitive deficits, such as schizophrenia and Parkinson's, by limiting damage to the brain.

The new drug candidate, known as AL-108, was found to protect American patients with mild cognitive damage against memory loss by protecting the skeleton and transport system of brain cells. The new drug candidate has passed its Phase II clinical studies in U.S. Food and Drug Administration approved clinical trials. AL-108 is currently being developed by the Canada-based Allon Therapeutics Inc.

An Emphasis on Living Brain Cells

"My logic is that if you try to protect a dead cell, it won't work. We need to protect the living cell between the death sentence of having Alzheimer's and actual cell death," says Prof. Gozes. Her discovery, now the drug candidate AL-108, provides nerve cell protection. Publications reporting on the efficacy of AL-108 in animal models have appeared in the *Journal of Pharmacology and Experimental Therapeutics*, *Journal of Molecular Neuroscience*, the *Journal of Biological Chemistry* and many more.

Prof. Gozes, a co-founder of Allon Therapeutics and the company's Chief Scientific Officer, targeted support cells in the brain known as glia, which make up the majority of cells in the brain and are those that facilitate brain repair. She hypothesized that proteins produced by glia, and responsive to brain injury, may be able to repair the damage caused by neurodegenerative diseases such as Alzheimer's.

Like Train Rails Without Ties

Prof. Gozes and her team discovered a protein (ADNP) involved in brain repair, but if developed

into a drug it would be too large to cross the blood-brain barrier. Cutting the protein into fragments, Prof. Gozes determined a small portion of the protein (NAP) provides potent neuroprotection by protecting nerve cells against severe oxidative stress and the toxicity associated with diseases such as Alzheimer's. AL-108, the drug candidate under development now, is an intranasal formulation based on NAP.

What happens in the nerve cells of Alzheimer's brains can be likened to a derailed train, says Prof. Gozes. The nerve cell skeleton — the microtubules — are like the rails, and a protein called "tau" functions like the ties between the rails. In Alzheimer's, the ties fall off, the tracks fall apart and nerve cells die. AL-108 however, seems to prevent this process from accelerating.

AL-108, which could be ready in as early as 5 years, targets the microtubules and protects against amyloid plaques — a characteristic of Alzheimer's disease. AL-108 also seems to be able to maintain brain microtubule functioning, preventing memory loss and the deterioration of other cognitive functions, such as learning abilities, in those whose mental functioning has already started to decline.

"It's important to stress that these are drug candidates in clinical development in North America for now, and will not be ready for several years," says Prof. Gozes, who co-founded Allon Therapeutics with Tel Aviv University's technology transfer arm Ramot.

Source: American Friends of Tel Aviv University

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