

A nervous system drug-by-design

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Working like an architect, Prof. Hagit Eldar-Finkelman of Tel Aviv University's Sackler School of Medicine is "building" a new drug, L803-MTS, to treat a number of central nervous system (CNS) diseases like Alzheimer's. In pre-clinical studies, it also shows promise against Parkinson's, Huntington's and diabetes.

L803-MTS is based on the physical structure of the GSK3 protein, which plays a causative role in insulin resistance and Type II diabetes. Working with chemists, biotechnologists and 3-D modelists, Prof. Eldar-Finkelman and her colleagues built — like engineers constructing a building — a drug that locks onto the GSK3 protein, rendering it harmless and unable to wreak havoc inside the body.

Recent research findings on the L803-MTS drug have been published in the *Journal of Molecular Biology* (2008) and *Current Pharmaceutical Design* (2009, currently in press).

An innovative approach

Since Prof. Eldar-Finkelman linked GSK3 to insulin resistance in diabetes more than ten years ago, a race has been on among drug manufacturers to find a drug that can potentially turn off the harmful effects of GSK3. But rather than build on existing drugs, Prof. Eldar-Finkelman and her colleagues worked from the ground up. "I decided to take a completely different approach from all the big drug companies rushing to find the ultimate drug," says Prof. Eldar-Finkelman. "I designed my own."

Pre-clinical results have been positive, and the new drug does not exhibit dangerous toxic side effects, a problem with existing formulations. While L803-MTS cannot reverse the onset of a CNS disease once it has started, Prof. Eldar-Finkelman believes it can slow down the devastating effects of CNS diseases, like impaired memory and depression, or [insulin-resistance](#).

"Ours is the first lab that showed the importance of GSK3 as a target in Type II [diabetes](#), and was among the first to introduce a specific inhibitor against the GSK3," she says. "Our approach became so popular that today many pharmaceutical companies, big and small, are competing to work on a GSK3 inhibitor."

A new competition

With seed money from Ramot, Tel Aviv University's technology transfer arm, Prof. Eldar-Finkelman has taken her basic research to the next step, seeking a strategic partner to guide the research through the clinical process and eventual commercialization.

"One important thing to note is that our drug acts differently than other compounds," she says. "Most GSK3 inhibitors are developed on the basis of ATP competitors. Ours are substrate competitors, meaning that they bind to a different site at the surface of the protein. This strategy is completely different, and yields a better and safer compound."

Prof. Eldar-Finkelman is now conducting additional pharmacological and toxicological tests on the new compound. She believes it will be a lead compound for treating CNS disorders, "because it was based on rational drug design. We started from scratch and thought through the design of a specific compound that would be safe and effective. Our aim is to slow the progression of CNS diseases, but the new drug might also be used as a preventative therapy," she adds.

Source: Tel Aviv University ([news](#) : [web](#))

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