A novel Alzheimer's disease drug candidate targeting inflammation and fatty acid metabolism.

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Public Summary:
BACKGROUND: CAD-31 is an Alzheimer's disease (AD) drug candidate that was selected on the basis of its ability to stimulate the replication of human embryonic stem cell-derived neural precursor cells as well as in APPswe/PS1DeltaE9 AD mice. To move CAD-31 toward the clinic, experiments were undertaken to determine its neuroprotective and pharmacological properties, as well as to assay its therapeutic efficacy in a rigorous mouse model of AD. RESULTS: CAD-31 has potent neuroprotective properties in six distinct nerve cell assays that mimic toxicities observed in the old brain. Pharmacological and preliminary toxicological studies show that CAD-31 is brain-penetrant and likely safe. When fed to old, symptomatic APPswe/PS1DeltaE9 AD mice starting at 10 months of age for 3 additional months in a therapeutic model of the disease, there was a reduction in the memory deficit and brain inflammation, as well as an increase in the expression of synaptic proteins. Small-molecule metabolic data from the brain and plasma showed that the major effect of CAD-31 is centered on fatty acid metabolism and inflammation. Pathway analysis of gene expression data showed that CAD-31 had major effects on synapse formation and AD energy metabolic pathways. CONCLUSIONS: All of the multiple physiological effects of CAD-31 were favorable in the context of preventing some of the toxic events in old age-associated neurodegenerative diseases.

Scientific Abstract:
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