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## Alzheimer's drug discovery: Targeting synaptic glutamate uptake

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According to the amyloid hypothesis, Alzheimer dementia begins in the brain with A $\beta$  peptides accumulation and amyloid formation. However, clinical trials targeting A $\beta$  peptides and brain amyloid have failed to help anybody living with Alzheimer. Instead of repeating similar trials and errors of 25 years, we have to discover novel drug targets and better our research to prevent and treat Alzheimer. Glutamate is the synaptic signaling molecule of neurons. As soon as the glutamate signaling starts it is stopped in 0.1-2 ms by astrocytes, which take up and clear glutamate from synapses. This prevents glutamate neurotoxicity causing synapse loss and neuron cell death. Astrocytes make EAAT2 (excitatory amino acid transporter-2), the major glutamate transporter and 1% of brain protein. In Alzheimer, astrocytes are impaired in synaptic glutamate uptake. In experimental mouse models of Alzheimer, increasing EAAT2 expression slows dementia progression. Here, I describe a simple assay for drugs that activate EAAT2 in glutamate uptake. The assay targets the EAAT2 protein reconstituted in liposomes and measures glutamate uptake with Oxonol VI red fluorescent dye. By directly targeting EAAT2, the assay should limit 'off-targeting' of drugs and adverse events, which are the main problems in Alzheimer's drug discovery and clinical development. For efficacy, specificity and safety, EAAT2 activating drugs are studied in experimental *C. elegans* models of Alzheimer.

### Biography

Markku Kurkinen Obtained his PhD from University of Helsinki, Finland in 1979. He worked as an assistant Professor at Rutgers medical school, USA .He is currently working as Professor of Molecular Medicine and Genetics at Wayne State University, School of medicine, USA .His research interests reflect in his wide range of publications in various national and international journals.

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