

THE CYTOKINE CYCLE

The initiating cause of Alzheimer's disease is still unknown. However, from our studies it's clear that many types of neuronal damage—from traumatic brain injury, to epilepsy, infection, or genetic predisposition—can activate brain immune cells—microglia and astrocytes—prompting them to produce IL-1 and S100 inflammatory cytokines. Initially, activated microglia can help clear dead neurons, but when activated repeatedly, their IL-1 production increases, feeding a cycle of damage-responses, each of which is characteristic of Alzheimer's, and many of which in turn activate more IL-1 production.

A β APP

IL-1 promotes the synthesis of β -amyloid precursor protein (β APP) in neurons, and also promotes the secretion of the mature β -amyloid protein outside of the cell, where it forms plaques. Though its production is driven by IL-1, β -amyloid protein can also activate microglia to produce more IL-1.

B ACETYLCHOLINESTERASE

Acetylcholine is a neurotransmitter involved in memory, and its levels are diminished in Alzheimer's patients. We showed that IL-1 drives the production of acetylcholinesterase, an enzyme that degrades acetylcholine.

C MAP KINASE p38

Tau protein expression in neurons is activated by IL-1. However, tau protein is only pathogenic in its hyperphosphorylated state, in which it causes fibrous tangles within the neuron. We showed that IL-1 also drives the activation of MAP kinase p38 (MAPK p38), which is responsible for the tau protein's hyperphosphorylation.

D α -SYNUCLEIN

Researchers recently found that α -synuclein, the protein that forms Lewy bodies in Parkinson patients' brains, is also produced by some Alzheimer's patients. We demonstrated that α -synuclein production is also activated by excessive IL-1.

