

# Abstract

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## A role for docosahexaenoic acid-derived neuroprotectin D1 in neural cell survival and Alzheimer disease.

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**OBJECTIVE AND METHODS:** Deficiency in docosahexaenoic acid (DHA), a brain-essential omega-3 fatty acid, is associated with cognitive decline. Here we report that, in cytokine-stressed human neural cells, DHA attenuates amyloid-beta (Abeta) secretion, an effect accompanied by the formation of NPD1, a novel, DHA-derived 10,17S-docosatriene.

**RESULTS:** DHA and NPD1 were reduced in Alzheimer disease (AD) hippocampal cornu ammonis region 1, but not in the thalamus or occipital lobes from the same brains. The expression of key enzymes in NPD1 biosynthesis, cytosolic phospholipase A2 and 15-lipoxygenase, was altered in AD hippocampus. NPD1 repressed Abeta42-triggered activation of proinflammatory genes while upregulating the antiapoptotic genes encoding Bcl-2, Bcl-xl, and Bfl-1(A1). Soluble amyloid precursor protein-alpha stimulated NPD1 biosynthesis from DHA.

**CONCLUSIONS:** These results indicate that NPD1 promotes brain cell survival via the induction of antiapoptotic and neuroprotective gene-expression programs that suppress Abeta42-induced neurotoxicity.

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