

Abstract

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Omega-3 essential Fatty acids modulate initiation and progression of neurodegenerative disease.

Palacios-Pelaez R, Lukiw WJ, Bazan NG.

Diater Laboratorios, 28918, Leganes, Madrid, Spain.

BACKGROUND: The significance of the selective enrichment in omega-3 essential fatty acids in photoreceptors and synaptic membranes of the nervous system has remained, until recently, incompletely understood.

FINDINGS: While studying mechanisms of cell survival in neural degeneration, we discovered a docosanoid synthesized from unesterified docosahexaenoic acid (DHA) by a 15-lipoxygenase (15-LOX), which we called **neuroprotectin D1** (NPD1; 10R,17S-dihydroxy-docosa-4Z,7Z,11E,13E,15E,19Z hexaenoic acid). This lipid mediator is a docosanoid because it is derived from the 22 carbon (22C) precursor DHA, unlike eicosanoids, which are derived from the 20 carbon (20C) arachidonic acid (AA) family member of essential fatty acids. **We discovered that NPD1 is promptly made in response to oxidative stress,** as a response to brain ischemia-reperfusion, and in the presence of neurotrophins. NPD1 is neuroprotective in experimental brain damage, in oxidative-stressed retinal pigment epithelial (RPE) cells, and in human brain cells exposed to amyloid-beta (Abeta) peptides. We thus envision NPD1 as a protective sentinel, one of the very first defenses activated when cell homeostasis is threatened by imbalances in normal neural function.

SUMMARY: We provide here, in three sections, recent experimental examples that highlight the specificity and potency of NPD1 spanning beneficial bioactivity during initiation and early progression of neurodegeneration: (1) during retinal signal phototransduction, (2) during brain ischemia-reperfusion, and (3) in Alzheimer's disease (AD) and stressed human brain cell models of AD.

CONCLUSIONS: **From this experimental evidence, we conclude that DHA-derived NPD1 regulation targets upstream events of brain cell apoptosis, as well as neuro-inflammatory signaling, promoting and maintaining cellular homeostasis, and restoring neural and retinal cell integrity.**

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