[Neuroscience, **57**, 495-499 (1993)] [Lab. of Molecular Biology]

Memory Impairment and Neural Dysfunction after Continuous Infusion of Anti-Nerve Growth Factor Antibody into the Septum in Adult Rats.

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The relationship between nerve growth factor (NGF) and senile dementia of the Alzheimer type is of interest. We demonstrate here that the oral administration of idebenone, a simulator of NGF synthesis *in vitro*, produced recovery of reduced NGF content in aged rat brain. Twenty-one-day successive administration of idebenone produced significant recovery of reduced NGF content in the frontal cortex and parietal cortex of aged rats. These results suggest that NGF content in the brain is low in aged rats and that oral administration of idebenone leads to a recovery of this reduction.

[Biochem. Biophys. Res. Commun., **193**, 198-203 (1993)] [Lab. of Molecular Biology]

NGF Level Is Not Decreased in the Serum, Brain-Spinal Fluid, Hippocampus, or Parietal Cortex of Individuals with Alzheimer's Disease.

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Although the cause of Alzheimer's disease (AD) is unknown, nerve growth factor (NGF) has gained attention as a therapeutic agent for the disease. Because NGF maintains the magnocellular cholinergic neurons that are damaged in AD, research interests have been focused on the change in NGF level in patients with AD. This is the first reported study in which human NGF levels were accurately measured and compared between normal and AD samples. We measured NGF levels using enzyme immunoassay (EIA) system for human NGF and found no difference in NGF level in serum, brain-spinal fluid, or brain (hippocampus and parietal cortex) obtained from normal people and patients with AD. These results suggest that a decrease in the NGF level is not a causative factor of AD.

[Biochem. Mol. Biol. Int., **30**, 615-621 (1993)] [Lab. of Molecular Biology]

Stimulation of Nerve Growth Factor Synthesis/Secretion in Mouse Astroglial Cells by Coenzymes.

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We examined the effect of coenzymes such as PQQ, pyrroloquinoline quinone; TOPA, 3-(2,4,5-trihydroxyphenyl)-DL-alanine, and lipoic acid on nerve growth factor (NGF) synthesis in mouse astroglial cells, BALB c/3T3 cells, and WS-1 cells in culture. These coenzymes had a stimulating effect on NGF synthesis without causing cytotoxicity. Especially PQQ showed the strongest activity of promoting NGF synthesis in astroglial cells, whereas lipoic acid had the strongest effect on BALB c/3T3 cells. The activity may not due to the catechol ring or 1,4-benzoquinone ring, but due to the oxidative or reductive activity. These results suggest that these coenzymes may play a role in NGF synthesis and neuronal survival through the stimulating effect of the NGF synthesis in brain and such compounds are good candidates as NGF inducers.