[Naunyn-Schmiedeberg's Arch. Pharmacol., **349**, 401-407 (1994)] [Lab. of Molecular Biology]

Oral administration of idebenone induces nerve growth factor in the brain and improves learning and memory in basal forebrain-lesioned rats.

ATSUMI NITTA, YUTAKA MURAKAMI, YOSHIKO FURUKAWA*, WARARU KAWATSURA, KYOZO HAYASHI, KIYOFUMI YAMADA, TAKAAKI HASAGAWA, TOSHITAKA NABESHIMA

We demonstrate that the oral administration of idebenone, a potent *in vitro* NGF synthesis stimulator, induced an elevation of NGF, its mRNA and choline acetyl transferase activity, in basal forebrain lesioned rats, but not in intact rats. Idebenone also ameliorated the behaviroral deficits in habituation, water maze, and passive avoidance tasks in these animals. These results suggest that idebenone stimulated NGF synthesis *in vivo* and ameliorates the behavioral deficits which were accompanied with the recovery of the reduced choline acetyltransferase activity in the basal forebrain-lesioned rats.

[Brain Res., **641**, 350-352, (1994)] [Lab. of Molecular Biology]

Etoposide induces programmed death in neurons cultured from the fetal rat central nervous system.

MITSUNARI NAKAJIMA, KUMIKO KASHIWAGI, JUN OHTA, SHOEI FURUKAWA*, KYOZO HAYASHI, TAKUJI KAWASHIMA, YOKICHI HAYASHI

The effects of etoposide on the death of neurons cultured from the central nervous system (CNS) of fetal rats were examined. The neurons died in the presence of etoposide, and this effect was prevented by inhibition of protein synthesis and/or RNA synthesis. Furthermore, DNA degradation, including a ladder-like pattern, became evident in these neurons 3 h after incubation with etoposide, whereas cell death commenced after about 6 h. These results indicate that etoposide-treated CNS neurons require new protein and RNA synthesis to undergo an active death program, and that nuclesomal fragmentation of DNA mediates the etoposide-induced programmed cell death.

[Neurosci. Lett., **176**, 161-164 (1994)] [Lab. of Molecular Biology]

Nerve growth factor and epidermal growth factor rescue PC12 cells from programmed cell death induced by etoposide:distinct modes of protection against cell death by growth factors and a protein-synthesis inhibitor.

MITSUNARI NAKAJIMA, KUMIKO KASHIWAGI, JUN OHTA, SHOEI FURUKAWA*, KYOZO HAYASHI, TAKUJI KAWASHIMA,YOKICHI HAYASHI

A rat pheochromocytoma cell line (PC12 cells) died within 24 h in the presence of etoposide (1-40 μg/ml), an inhibitor of topoisomerase II. This cytotoxic effect was prevented by either nerve growth factor (NGF) or epidermal growth factor (EGF). Cycloheximide and actinomycin D also suppressed the cell death as well. These results indicate that prevention of etoposide-induced programmed cell death by both NGF and EGF is mainly due to inactivation of molecules involved in the death processes rather than suppression of specific protein synthesis.