[*Child's. Nerv. Syst.*, **16**, 516-521 (2000)] [Lab. of Molecular Biology]

Aberrant Expression of Neurotrophic Factors in the Ventricular Progenitor Cells of Infant Congenitally Hydrocephalic Rats.

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OBJECTS: This study was conducted to investigate the roles of neurotrophic factors in the development of hydrocephalus in HTX rats. METHODS: Expressions of BDNF, NT-3, and FGF-1 were examined immunohistochemically in the cerebral cortex and ventricular zone of 6-day-old rats with congenital hydrocephalus (HTX rats). In the ventricular zone of hydrocephalic rats, potent BDNF-like immunoreactivity (-LI) and weak but significant signals for NT-3- and FGF-1-LIs were observed. However, no significant signals were detected in non-HTX rats. A small subpopulation of ventricular cells was positive for microtubule-associated protein 2 in HTX and non-HTX rats. The positive cells in the HTX rats had neurites much longer than those in the non-HTX animals, suggesting that some ventricular cells of the hydrocephalics had ectopically differentiated into mature neurons. CONCLUSIONS: This abnormal differentiation may have been responsible for the aberrant expressions of neurotrophic factors. In contrast, the cerebral neuronal layers did not show such prominent alterations in neurotrophic factor expression.

[*J. Neurosci. Res.*, **59**, 632-642 (2000)] [Lab. of Molecular Biology]

Balance of two secretion pathways of nerve growth factor in PC12 cells changes during the progression of their differentiation, with a decrease in constitutive secretion in more differentiated cells.

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Proteins are secreted from animal cells by either a constitutive or a regulated pathway. When cDNA of NGF was introduced into PC12 cells, these cells produced and secreted active NGF, where NGF was secreted not only in constitutive but also in activity-dependent regulated way according to the results of pulse-chase and ELISA studies. The regulated secretion was caused by depolarization, cyclic AMP analogue, or beta-adrenergic agonist but not by glutamate or carbachol. Because these transfected cells differentiated into a morphology indistinguishable from that incubated with NGF protein, we next compared the secretion pathways of NGF from PC12 cells at different stages of the differentiation. NGF was secreted in both constitutive and regulated way at 2 and 7 days after the transfection of NGF-cDNA, but the constitutive secretion of NGF from the more differentiated cells of Day 7 was decreased and mature NGF tended to accumulate in the cells. These results indicate that the neurotrophin secretion mechanism is intimately regulated in the course of the differentiation of PC12 cells. Such a change in the protein secretion pathway might have an profound role in the development of neurons.

[*J. Neurosci. Res.*, **62**, 668-674 (2000)] [Lab. of Molecular Biology]

Increase in neurotrophin-3 expression followed by purkinje cell degeneration in the adult rat cerebellum after spinal cord transection.

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Changes in BDNF and NT-3 contents following thoracic spinal cord transection were investigated in the cerebral cortex, hippocampus, and cerebellum of rats. The NT-3 content became significantly elevated at 3 days after transection only in the cerebellum and gradually declined to the control level by 6 days after the injury, remaining unchanged in the cerebral cortex and hippocampus. No significant change in the BDNF content was observed in any of the regions tested. Immunohistochemical analysis showed that the labeling indicating NT-3-like immunoreactivity was intensified in both cerebellar granule and Purkinje cells 3 days after the injury. The number of Purkinje cells with aggregation of chromatin around the nuclear membrane and swelling of the cytoplasm and/or organelles gradually increased with time starting 4 days after the injury, demonstrating morphological changes indicative of necrosis. However, no abnormal morphology was found in cerebellar granule cells at any time examined. We suggest that it is reasonable that increased NT-3 stimulated the death of Purkinje cells, because 1) the degeneration was necrosis, which is known to be accelerated by neurotrophins under certain pathological conditions, and 2) the increase in NT-3 occurred prior to Purkinje cell degeneration. Therefore, our present results may imply that spinal cord injury-induced NT-3 accelerates injury rather than alleviates degeneration of Purkinje cells.

[*Antonie van Leeuwenhoek*, **78**, 203-207 (2000)] [Lab. of Microbiology]

Sibling differences in cell death of the fission yeast, *Schizosaccharomyces pombe*, exposed to stress conditions.

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Selective death of fission yeast cells of five strains was observed: one sibling, of a V-pair formed at fission, died while the other survived after being transferred to extreme or sub-lethal conditions (from pH 4.5 to pH 7.0, from 32℃ to 41℃, or to medium containing acridine orange, 200 μ g/ml). Death occurred preferentially to the sib with more fission scars or to that sib with new end derived from its mother cell which had actively grown in length. Thus, the differences between V-pair siblings in stress response related to morphology derived from fission scars and extension growth. From these observations, we rationalize the meaning of aging and rejuvenation in a yeast population with relation to scars and growth in the fission yeast *Schizosaccharomyces pombe*.