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CONTENTS

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Part III. Myelin and Demyelination

Part IV. Glial-Neuronal Interaction in Regeneration

Part V. Glial Electrophysiology and Transport

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Differential Regulation of Nerve Growth Factor and Brain-Derived Neurotrophic Factor Expression in the Peripheral Nervous System

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Whereas intact sciatic nerves of adult rats synthesize very low levels of nerve growth factor (NGF) *in vivo,* a massive increase of NGF synthesis is observed after a nerve lesion.[1] Application of interleukin 1 (IL-1) increases the level of NGF mRNA in cultured sciatic nerve explants as well as in fibroblasts isolated from the nerve.[2,3] However, the mechanisms regulating NGF synthesis in Schwann cells, the major nonneuronal cell type of the nerve, have not been clarified.

We found that forskolin (FK), a reversible activator of adenylate cyclase, rapidly increased the level of NGF mRNA without affecting its stability in highly enriched cultures of Schwann cells, whereas IL-1 and several peptide growth factors known to increase the NGF mRNA level in fibroblasts and astrocytes[4] failed to do so in Schwann cells. Forskolin was also effective in nerve explant cultures. The effects of FK were mimicked by cAMP analogs, but not by a cGMP analog or dideoxyforskolin, a forskolin derivative that does not activate adenylate cyclase. Transforming growth factor-β1 decreased the NGF mRNA levels in Schwann cells, in contrast to its effects on astrocytes.[5] A Ca^{2+} ionophore and a phorbol ester potentiated the effect of FK on the NGF mRNA level. Pretreatment of Schwann cells with H-8, an inhibitor of cyclic nucleotide-dependent protein kinases, reduced both basal and induced NGF mRNA levels, suggesting an essential role of cAMP-dependent protein kinase for NGF mRNA regulation in Schwann cells.

Brain-derived neurotrophic factor (BDNF) is a recently cloned member of the family of NGF-like neurotrophic proteins,[6] which is mainly synthesized in the central nervous system.[6,7] So far no nonneuronal cell type capable of BDNF synthesis has been identified. We found that BDNF is expressed at very low levels in the rat sciatic nerve and at much higher levels in rat Schwann cell cultures (FIG. 1). In contrast to its effects on NGF mRNA, expression of BDNF in sciatic nerve explants is not changed by administration of IL-1 (FIG. 2). Opposite to its effects on NGF mRNA, forskolin decreased the basal as well as the ionomycin-induced levels of BDNF mRNA in cultured Schwann cells. Details of the mechanisms of BDNF regulation *in vivo* and *in vitro* remain to be investigated. It is not clear why both proteins are differentially regulated.

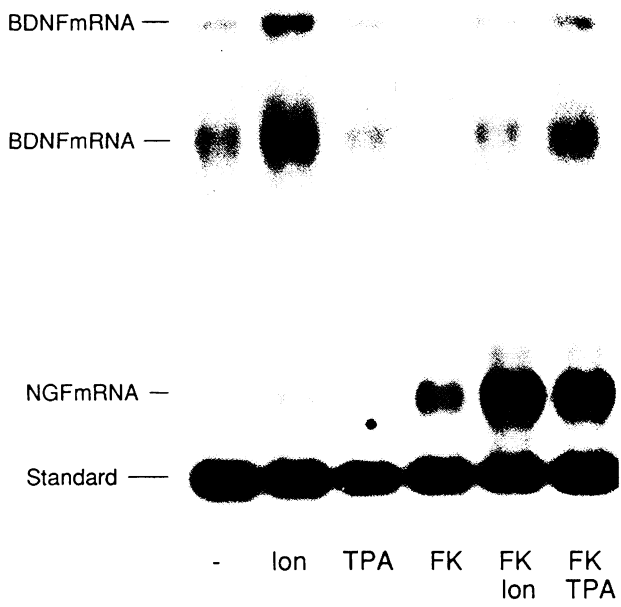

FIGURE 1. Northern blot analysis of NGF and BDNF mRNAs in cultured rat sciatic Schwann cells. Cells were incubated with 1 μg/ml ionomycin (Ion), 0.1 μg/ml TPA, and 20 μM forskolin (FK) for 3 hours.

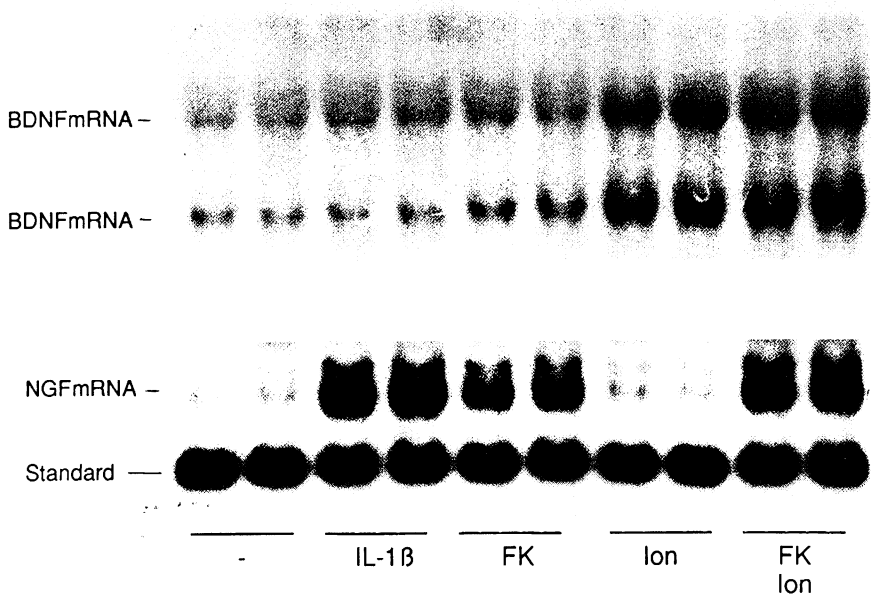

FIGURE 2. Northern blot analysis of NGF and BDNF RNAs in sciatic nerve explants. Sciatic nerve segments prepared from newborn rats (3 days in culture) were incubated with 60 U/ml IL-1β, 20 μM forskolin (FK), and 1 μg/ml ionomycin (Ion) for 3 hours. Nerve explants prepared from adult animals gave similar results.

REFERENCES

1. HEUMANN, R., S. KORSCHING, C. BANDTLOW & H. THOENEN. 1987. J. Cell. Biol. **104:** 1623–1631.
2. LINDHOLM, D., R. HEUMANN, M. MEYER & H. THOENEN. 1987. Nature **330:** 658–659.
3. LINDHOLM, D., R. HEUMANN, B. HENGERER & H. THOENEN. 1988. J. Biol. Chem. **263:** 16348–16351.
4. SPRANGER, M., D. LINDHOLM, C. BANDTLOW, R. HEUMANN, H. GNAHN, M. NÄHER-NOE & H. THOENEN. 1990. Eur. J. Neurosci. **2:** 69–76.
5. LINDHOLM, D., B. HENGERER, F. ZAFRA & H. THOENEN. 1990. Neuro. Rep. **1:** 9–12.
6. LEIBROCK, J., F. LOTTSPEICH, A. HOHN, M. HOFER, B. HENGERER, P. MASIAKOWSKI, H. THOENEN & Y.-A. BARDE. 1989. Nature **341:** 149–152.
7. HOFER, M., S. R. PAGLIUSI, A. HOHN, J. LEIBROCK & Y.-A. BARDE. 1990. EMBO J. **9:** 2459–2464.