# Modulation of Schwann Cell Phenotype by TGF-β1: Inhibition of P0 mRNA Expression and Downregulation of the Low Affinity NGF Receptor

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*ABSTRACT* The phenotype of a fully differentiated, mature Schwann cell is apparently largely determined by Schwann cell-axon interactions. In vitro, elevation of intracellular cAMP levels in Schwann cells induces a phenotype which resembles that of a mature, i.e., axon-related, Schwann cell. Therefore, an important role for cAMP as a second messenger of axon-Schwann cell interactions in vivo is assumed.

However, the effects of cAMP on Schwann cells are not restricted to induction of features of a mature phenotype. For example, elevation of intracellular cAMP levels results also in a markedly increased synthesis of nerve growth factor (NGF) mRNA, which is barely detectable in intact sciatic nerves of adult animals. Furthermore, since cAMP induces myelin gene expression in cultured Schwann cells, additional regulatory mechanisms have to be postulated for the induction and maintenance of a mature non-myelinating Schwann cell phenotype.

Here we show that a soluble protein "growth factor" can partially induce a non-myelinating mature Schwann cell phenotype in vitro. Treatment with transforming growth factor β1 (TGF-β1) results in a marked and rapid downregulation of the low affinity NGF receptor (NGFR) on cultured Schwann cells without induction of P0 gene expression. In contrast, in agreement with previous studies, an increase in P0 mRNA levels and a reduction in NGFR mRNA levels are observed after cAMP elevation. Downregulation of NGFR mRNA after cAMP elevation is much slower when compared with the effect of TGF-β1, suggesting the involvement of different intracellular mechanisms. Consistent with this hypothesis, we did not observe an induction of mRNA coding for TGF-β isoforms after cAMP elevation in cultured Schwann cells which constitutively synthesize TGF-β1 mRNA. 

## INTRODUCTION

The peripheral nerve contains a major type of glial cell, the Schwann cell, which in intact nerves of adult animals expresses one of at least two different mature phenotypes: it is either myelinating or non-myelinating. The maturation process underlying this phenotypic diversification is not well understood. Anastomosis and transplantation experiments have demonstrated a decisive role of axonal influence for the determination of the mature Schwann cell phenotype and a high degree of phenotypic plasticity (Aguayo et al., 1976; Spencer, 1979; Weinberg and Spencer, 1975a).

Both mature Schwann cell phenotypes express a set of common antigenic markers. These include galacto-

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