STUDIES ON NEUROTROPHIC AND SUBSTRATE-ATTACHED NEURITE OUTGROWTH FACTORS
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Neurons require appropriate substrata on which to extend neurites and the composition of the substrata encountered in vivo is believed to regulate both the extent and direction of axon growth as well as the position at which synaptic specializations appear. In particular, three constituents of extracellular matrix—fibronectin, laminin, and factors associated with heparan sulfate proteoglycans—have dramatic effects on neurite outgrowth in appropriate circumstances. Several of these factors have been shown to exist in appropriate positions to promote neurite growth in vivo as well as in vitro. The response of neurons to such factors depends on their growth state. This presentation will focus on characterization of these neurite outgrowth promoting factors and our efforts to determine their roles in directing neuronal development. The role of ECM components in directing axon growth and guidance in vivo is poorly understood. The study of soluble factors, which contain ECM components and act when bound to a substratum, may offer insights into that role. Supported by grants from the NIH, NSF, March of Dimes, and MDA.

Functional and structural characterization of cell surface antigen L1
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Migration of granule cell neurons in the developing mouse cerebellar cortex and a Ca++ independent adhesion mechanism between cerebellar and C1300 neuroblastoma cells are inhibited by Fab fragments of antibodies to cell surface antigen L1. Both, polyclonal and monoclonal antibodies to L1 antigen react predominantly with postmitotic neurons in the central nervous system. In the peripheral nervous system the antigen is detectable on Schwann cells in addition to neurons. The antigen consists of two bands in SDS polyacrylamide gels with apparent molecular weights of 140 and 200 kilodaltons at all ages studied. Chemical deglycosylation leads to a single band of 70 kilodaltons. The antigen is immunochemically distinct from B2 glycoprotein and BSP-2 antigen which are crossreactive with N-CAM.

Development of GABA-ergic neurons in rat visual cortex: immunocytochemistry of glutamate decarboxylase (GAD)
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GAD-like immunoreactivity was visualized by PAP method using GAD antiserum S3 (Neurosci. 6:2715, 1982). In visual cortex of albinorats weakly GAD positive cells appear in a characteristic spatio-temporal sequence: in lamina I about embryonic day 18 (E18); in subplate between E20 and postnatal day 4 (P4) with a gradient from periphery to center of the visual region; in cortical plate P2 to P5. Laminas III + IV are further delayed until about P8 to P10. The number of GAD positive cells reaches adult density during the 2nd p.n. week. Pericarya and stem dendrites become GAD reactive 2 to 7 days before GAD positive axon terminals appear. Adult terminal density is attained 3 to 4 weeks p.n. In neurons GAD increases during 2 weeks after birth, but GAD density varies greatly even in adult GABA-ergic neurons. GAD reactivity was always restricted to nonpyramidal neurons. Comparisons with Golgi studies (Zoon 6: 145, 1978) and 3H-GABA autoradiography (J. Comp. Neurol. 190:187, 1980) suggest that there are 3 characteristic stages in development of GABA-ergic neurons: (1) > E16 GABA uptake (+), GAD(-); (2) > E18: uptake and GAD (+), but axons (-); (3) > E20: delayed axon development and synaptogenesis.