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Book review

Glial-Neuronal Communication in Development and Regeneration. Edited by Hans H. Althaus and Wilfried Seifert. Springer-Verlag. Berlin, Heidelberg, New York, London, Paris, Tokyo, 866 pp. 1987

The development of the nervous system includes various processes resulting from a complex interaction between the genetic programme of the stem ectodermal cells and the surrounding humoral and cellular environment. Neuroglia differentiate at that in a number of different cell types. It has been accepted for many years that the functional communication between glial and neuronal cells, suggested already in 1928 by Roman y Cajal, confines only to the participation of glia in the regulation of intercellular contents of K^+, in detoxification, nutrition and myelination of axons. Our understanding of glial cell physiology has increased greatly in the last decade. The widespread application of tissue culture techniques to examine glial and neuronal cell activity has revealed that glial cells, far from being inert or passive constituents of the brain microenvironment, are capable of participating in various physiological activities previously relegated primarily to neuronal populations. Thus, glia can participate in macromolecular, neurotransmitter and ion exchange regulation and, in turn, can influence neuronal survival, proliferation and differentiation. During ontogenesis, glial cells undertake a guiding function and provide an extracellular matrix necessary for axonal regeneration; they may also release neuronotrophic (NTF) and neurite promoting factors (NPF) which are of great importance for the reparative processes in the central and peripheral nervous system (CNS, PNS).

The book *Glial-Neuronal Communication in Development and Regeneration* succeds in bringing together authors with personal experience in these interesting aspects of present-day neurobiology, providing under the cover of a single volume of 866 pages a selection of subjects not otherwise available in one book. It represents the proceedings of a symposium under the same name held in Göttingen (FRG) in 1985. The book is divided into seven sections with three to thirteen contibutions in each section.

The first section deals with glial cell lineages. Chapter One is by S. Fedoroff and brings forward data about the phenotypic expression during development of cells from astrocytic family: radial glia, protoplasmic and fibrous astrocytes, ependimal cells, Bergmann glia, Müller's cells and pinealocytes. Good models to study reactive astrocytes and fibrous gliosis are astrocytes in primary culture, activation of Müller's cells under light-induced retinal degeneration and fetal spinal cord transplantation into injured mature spinal cord (L. Eng.). In Chapter Three the group of G. Kreutzberg presents results of ultrastructural and immunochemical study on microglia in culture supporting the concept for a common mesodermal origin of macro- and microglia and that after injury microglia might become immunocompetent (E. Rieske-Shows et ala.). Further, R. Nirsky and K. Jessen give detailed information on the antigens (GFAP, Ran_2, N-CAM, L_1) of peripheral glia (enteric glia, satellite cells, myelin-forming and non-myelin-forming Schwann cells).

The second section of the book is devoted to the receptors and antigens expressed by glial and neuronal cells during ontogenesis. It begins with a precise autoradiographic and electrophysiological study by L. Hösli and E. Hösli who demonstrate coexistence of α- and β-adrenoreceptors, together with histamine receptors on glial membranes. In Chapter Three Zanetta et al. show that complementary molecules (glycoproteins-lectins) exist on the partner cells (Purkinje cells-radial glial fibers) in the molecular layer of cerebella of young rats at the period of synaptogenesis. These complementary molecules actually participate in a recognition phenomenon which serves to eliminate components of the

surface of one of the partner cells. The reported data by F. Omlin et al. suggest that myelin-associated glyco-proteins (MAG) could be involved in mechanisms related to cell-cell recognition or cell migration too.

The last two chapters of this section analyze the role of Müller's cells in the uptake and inactivation of GABA in the synapses of retina (N. Osborn) and the developmentally regulated glial and neuronal antigens detected by monoclonal antibodies (M. Ghandour et al.)

The third section of the book examines the expression of recognition and adhesion molecules on the glial / neuronal cell surface. The first chapter by M. Albrechtsen et al. deals with biosynthesis of the neural adhesion molecules (N-CAM) in primary cultures of rat cerebellar granular neurons, cerebral glial cells and skeletal muscle cells. The properties of surface structures capable of enhancing neurite outgrowth of neuroblastoma cells and of neurons from embryonic rat brain in culture are considered by H. Rauvala et al. They present their recent attempts to solubilize and characterize membrane-bound neurite-promoting activities that might function in contact-dependent outgrowth of neurites in CNS. The last chapter by S. Carbonetto et al. is an account of the importance of the complementary interractions between the matrix adhesive molecules (located in the cellular membranes) and some components (collagens and non-collagens glycoproteins) of the extrtacellular matrix for a successful axonal regeneration in CNS.

The fourth section of the book is concerned with the glial / neuronal metabolic interractions. The elevation of K^+ concentration under neuronal activation or after application of monoamine transmitter substances increases the glycogen turnover in the glial cells of leech segmental ganglia (V. Pentreath et al.). In Chapter Two A. Schousboe et al. discuss the mechanisms through which neurons might modify the active uptake of GABA and glutamine in astrocytes. It is followed by the report of M. Tytell supporting the hypothesis that a protein transfer does occur from the surrounding glia into the axoplasm in squid giant axon through phagocytosis of the glial processes by axons. In the last chapter F. Mugnaini and M. Fiori consider the possibility that a glial-neuronal (satellite glia-afferent axonal terminals) competition may exist for apposition to neuronal surfaces during the establishment of intracellular contacts in avian cilliary ganglion.

The fifth and the longest section of the book contains a number of diverse chapters examining the influence on glial / neuronal cells by hormones, gangliosides, trophic factors and informational substances. The first three chapters deal with the problems of the effect of serum-containing media on the survival and maturation of neurons in culture (R. Balazs et al.), the role of glycolipid- and glycorpotein synthesis for neurite outgrowth (E. Yavin et al.), glial / neuronal communication (cell migration, interaction with extracellular matrix) during ontogenesis of cerebellum (G. Moonen et al.). Chapter Four by Ch. Richter-Landsberg and B. Jastorff is a review of the role of nerve growth factor (NGF) and cAMP analogues on neuronal differentiation in PC12 cells. Further, K. Unsicker and R. Lietzke provide a concise, well-written chapter updating the previous summaries on the neuronotrophic (NTF) and neurite-promoting factors (NPF) in developing chromaffin cells. The authors' concept is that chromaffin cells may be considered as modified neurons that are both targets and storage sites of NTF and NPF. The next five chapters take the reader into detailed reviews of the functional role of astrocytes during development of the nervous system and their interactions with neuronal cells in mature brain. In Chapter Seven the group of Seifert describes a model for biological testing and discrimination of different activities (for neuronal survival, neurite initiation and elongation) of a factor isolated from astroglial-conditioned medium which has a specific trophic effect only for hypocampal neurons (S. Beckh et al.). Conditioned medium from astrocyte cultures derived from the cerebellum of 7-day-old rats contains an autoregulative growth factor which stimulates the cell division of cerebellar and cerebral astrocytes to quantitative variable degree (A. Michler-Stuke). In Chapter Ten G. Fischer presents a method for serum-free cultivation of astrocytes and points the factors specifying the cellular heterogeneity, proliferation and differentiation in culture. This is followed by an article of the group of M. Sensenbrenner who describes their data on the biochemical characterization of an astroglial growth factor (AGF) isolated from bovine brain (B. Pettmann et al.). This factor is composed actually of two activities (AGF_1 and AGF_2) which are identical to the acid- and basic fibroblast growth factors, respectively. AGF is localized in the nuclei of neurons and could play a role in the regulation of glial proliferation in ontogenesis, as well as in reactive gliosis after brain injuries. The remaining chapters are on the effect of epidermal growth factor on glial cell development in aggregating cell cultures as a function of developmental stage and culture conditions (P. Honegger and B. Guentert-Lauber), the trophic and metabolic coupling batween astroglia and neurons (S. Varon et al.), the effect of muscle-derived substances on survival and neurite outgrowth of spinal cord neurons and identified motoneurons in culture (Ch. Henderson).

The sixth section of the book summarizes the current undestandings of the mechanisms of axonal regeneration. It begins with there chapters outlining the structural and functional plasticity of CNS and PNS by neural tissue transplantation technique (B. Bregman and P. Reiner; O. Isacson et al., I. Zimmer et al.). Recently, it has been demonstrated by the group of Aquayo that the fate of transected neuron depends only on the type of the surrounding glia (other cells and matrix) irrespective of the cell

body's location in CNS or PNS. Thus, successful axonal regeneration occurs only in the environment of peripheral glia (Schwann cells and extracellular matrix) or of glia from immature CNS. In Chapter Four K. Crutcher examines the mechanism of axonal outgrowth of sympathetic neurons (with cell bodies located in PNS) into CNS-tissue (hypocampus). The results support an already generally accepted view that axonal growth in the mature nervous system requires a peripheral environment. The astrocytes, forming an important element of the neuronal environment, proliferate after trauma in all vertebrates. However, the generated astrocytic scar in fish and amphibia is permissive for growing axons, whereas in birds and mammals it is not. The deficiency of the astroglial/axonal interaction in avian and mammals might be due to the occurence of orthogonal arrays of particles only in the cell membranes of these species (H. Wolburg). Chapter Sixth by R. Lindsay et al. is a very good account of studies using tissue culture manipulations, cell marketing techniques and plasma clot method to follow the development of grafted neurons and glia in brain. The next chapter is concerned with models to study reactive gliosis after mechanical trauma or administration of neurotoxicants (kainic acid, trimethyltin). The treatment of lesioned rats with cytosine arabinoside or immunosupressant prior to lesioning greatly reduces the proliferative response of glia cells (M. Billingsley et al.). Further, H. Müller and E. Shooter report that the expression of the 37 kDa protein (apolipoprotein E) during development, as well as after injury of the PNS and CNS suggests that it plays a role in *de novo* nerve growth and in nerve repair, probably related to lipid metabolism and transport. The 37 kDa protein/apo E is expressed by macrophages in the PNS and astrocytes in the CNS of newborn rats, indicating a previously unexpected common function of these ontogenetically unrelated cell types in nerve development. In the last chapter a cell separation method is described which allows the simultaneous isolation and cultivation of neurons and oligodendrocytes from the same brain of young adult rats (A. Stoykova et al.). Mature CNS neuronal cells show low regenerative capabilities for neurite outgrowth in culture which increase considerably when cocultivated with oligodendroglial cells.

The final section of the book deals with the mechanisms of myelination and remyelination by oligodendrocytes in CNS and by Schwann cells in PNS. The removal of galactocerebrosides from the Schwann cell surface during the initial stages of myelinogenesis can prevent the myelination without significantly altering the other Schwann cell functions: formation of basal lamina and axonal ensheatment (B. Ranscht et al.). K. Jessen and R. Mirsky demonstrate that galactosocerebrosides appear to be a ubiquitous component of the mature Schwann cell membranes, irrespective wheather they form myelin or not. This suggests that the role of glycolipids in axon-glia interactions is more general than currently envisaged and cannot be restricted to myelination only. This is followed by a very good account of the molecular organisation of the cell membrane in normal and pathological axons (S. Waxman). This section also has a chapter from N. Ratner et al., presenting evidence from culturing of neurons and Schwann cells that the burst of Schwann cell proliferation during development is regulated by a molecule (heparin sulfate proteoglicans?) on the neuronal surface. In Chapter Five R. Bansal et al. take the reader into detailed review of oligodendroglial differentiation in primary culture of dissociated fetal rat brain. Although oligodendrocytes undergo the main normal mylein-related differentiation, the synthesis of galactolipids, MBP, PLP, CNP proceeds at a lower level and the cells fail to complete the process with the elaboration of normal in vivo levels of myelin membranes. The chapter by S. Szuchet provides a good reading material on the mechanism of remyelination: a process of deposition of myelin on an axon that has lost its former myelin. The mature oligodendrocytes grown in pure culture synthesize myelin components and form multilamellar profiles with the ultrastructural and biochemical features of normal myelin. The process occurs in the absence of neurons and is designated by the term myelin palingenesis (reformation). In the last chapter H. Althaus et al. describe an in-vitro system to study remyelination. Oligodendrocytes isolated from mature pig brain can be cultivated for several weeks in monolayer culture and enwrap with their new-formed processes the added carbon fibers. Several morphological and biochemical criteria provide evidence that this material represents in part mature myelin.

In conclusion, this is an important and useful book for beginners as well as advanced neurobiologists with interest in the neuro/glial interractions in development and regeneration of nervous system. The contributions are up-to-date, written by recognised authorities in their respective fields who point to problems of importance in the direction of future research.

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