A correlation between K88 adhesion and glycosylation patterns of intestinal glycoconjugates has been investigated on tissue sections using lectinocytochemical and immunocytochemical techniques.

S.11 NEUROBIOLOGY OF GANGLIOSIDES

S11.1
The Role of Gangliosides in Brain Function: New Perspectives

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Gangliosides, sialic acid containing glycosphingolipids, are typical components of the plasma membrane of vertebrate cells, and are asymetrically located in the outer leaflet. They are contained in all the cell types present in the nervous system, and are highly concentrated in neurons, particularly in the synaptic region. Gangliosides appear to be involved in many brain functions at the cell and molecular levels (differentiation; neuritogenesis; synaptogenesis; protein phosphorylation/dephosphorylation; ion fluxes; receptors activity).

The concept of a multifunctional role for gangliosides seems the most flexible and suitable to explain their different functional implications. The oligosaccharide portions of gangliosides, protruding at the cell surface, possess a remarkable potential of interactions with external ligands of different nature. Hence, the concept that gangliosides can serve as molecular tools for appropriate interactions between the cell plasma membrane and extracellular substances (or other cells). On the other hand, the fluid character of the membrane into which gangliosides are embedded through their ceramide moieties, allows gangliosides to flow on the membrane and possibly to undergo reversible processes of lateral phase separation. This facilitates ganglioside interaction with, and modulation of, functional membrane proteins (receptors; enzymes; ion pumps; ion channels). Similar interactions with functional proteins may occur also intracellularly, provided that ganglioside soluble carriers are present and/or transport systems are operating in order for gangliosides to be available at these operational sites. By the interaction with functional proteins gangliosides may modulate events like transmembrane signalling, metabolic second messengers production, and cellular responses based on protein phosphorylation/dephosphorylation processes. A further mechanism of ganglioside action consists in the capacity to produce metabolic second messengers of sphingoid nature. This is a new issue arising from the growing body of evidence that sphingosine and ceramide, together with some derivatives, act as potent regulators of protein kinase C, other protein kinases and enzymes involved in signal transduction. On the basis of present knowledge the only conceivable link between ganglioside metabolism and formation of compounds of sphingoid nature is intra-lysosomal breakdown of plasma membrane-bound gangliosides, subsequent to endocytosis. Therefore the challenging suggestion is that external ligand binding to plasma membrane-bound ganglioside affects the rate of ganglioside endocytosis and/or their sorting to lysosomes by consequence the metabolic processing of gangliosides and the concurrent formation of second messengers of sphingoid nature can to be modified.

S11.2
Calcium-Ganglioside-Peptide Interactions as Possible Mechanism for Neuronal Functions

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On the basis of the well-known functional properties of calcium for cellular homeostasis and of the peculiar physicochemical properties of gangliosides in general, the aim of the present paper is to summarize investigations of basic interactive properties of gangliosides with respect to calcium and with functional membrane-bound proteins. With regard to this, experimental data will be presented concerning (a) the ultrastructural localization of calcium, of a calcium pump (high-affinity Ca^{2+}-ATPase) and of gangliosides in nerve fiber terminals, (b) the effect of exogenous gangliosides on Ca^{2+}-deprived cultured neurons and (c) calcium-ganglioside-peptide interactions in artificial mono- and bilayer systems. The ultrastructural data are being based on electron spectroscopical imaging (ESI) techniques, electron energy loss spectroscopy (EELS) and immunocytochemical detection of ganglioside epitopes using immuno-gold labeled monoclonal antibodies as electron dense marker.

From the experimental data obtained so far it can be concluded that gangliosides function as neuromodulators controlling the efficacy of functional membraneous proteins in order to guarantee the depolarization of the synaptic membrane always in an adaptive manner, although the environmental conditions for the membraneous constituents (temperature, pressure, ion milieu) might have changed.

S11.3
Cholinergic Neuron Specific Gangliosides — Structure and Immunohistochemical Localization in CNS

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The occurrence of cholinergic neuron specific ganglioside (Chol-1) was first described by Richardson using polyclonal antibody (anti-Chol-1) against synaptic plasma membrane of electric organ from *Torpedo marmorata* [1]. As a result of immunohistochemical staining with anti-Chol-1, the antigens were expressed specifically on the cell body and nerve terminal of the cholinergic neuron. Although Chol-1 gangliosides were thought to be functionally important molecules in the cholinergic system, their chemical structures had not been identified because they are extremely minor components. Recently, we could determine the total chemical structures of two novel Chol-1α gangliosides as GT1aα and GQ1bα [2].