MOLECULAR BIOLOGICAL AND BIOCHEMICAL ANALYSIS OF GLYCOPROTEIN SYNTHESIS RELATED TO PLASTIC CHANGES IN THE GOLDFISH CNS

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Using radioactive valine and fucose as precursor molecules, incorporation studies have repeatedly demonstrated the functional involvement of glycoproteins in various forms of neuronal plasticity. Ependymin is an example of such a CNS specific secretory glycoprotein which was first identified in the ependymal zone of goldfish brain. Intracerebroventricular injections of anti-ependymin antisera interfere with the consolidation of plastic adaptations that range from classical conditioning and learning of a motoric task to activity-depending sharpening of receptive fields during regeneration of the retino-tectal projection in goldfish (1).

cDNA cloning techniques revealed that the 195 amino acids of the ependymin sequence are preceded by a hydrophobic stretch of 21 residues and a cleavage site for signal peptidase, in concordance with earlier reports on secretion of this glycoprotein during functional regeneration, long-term potentiation and memory consolidation. Several point mutations and two N-glycosylation sites in the primary structure result in the expression of a family of closely related polypeptides carrying one (31 kDa variants) or two (37 kDa variants) N-linked carbohydrate chains. Ependymins comprise 3-sulfated glucuronic acid amongst their sugar moieties and display the L2/HNK-1 epitope, a carbohydrate structure involved in cell-cell and cell-substrate adhesion. Indeed, ependymins provide a good substrat for growing axons of goldfish retinal ganglion cells in vitro (in collaboration with J.T. Schmidt, Albany, and C.A.O. Stürmer, Tübingen).

Recently, 2-deoxygalactose, a metabolic inhibitor of the incorporation of fucose in a 1-2 glycosidic linkage to galactose, was shown to interfere with memory consolidation following active shock avoidance conditioning of goldfish (in collaboration with R. Jork, Magdeburg). Because ependymins are known to incorporate radioactive fucose, posttranslational modifications of these cell adhesion molecules may provide molecular mechanisms implicated in neuronal plasticity.

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1) For references see: Schmidt R. (1989): Glycoproteins involved in long lasting plasticity in the teleost brain. *In* H. Rahmann (ed.): *Fundamentals of Memory Formation: Neuronal Plasticity and Brain Function. Prog. Zool.*, **Vol. 37**, pp. 327-339.