

Summary

In the present study, two different IgSF-members have been investigated addressing different aspects. The first part of the study deals with the analysis of human pathological missense mutations of L1CAM. Carriers of these mutations exhibit multiple severe neurological symptoms, which has been combined using the acronym CRASH-Syndrome. Here, different *in vitro* assays were utilized to give insights into molecular mechanisms causing the CRASH-Syndrome. The cell surface expression of mutant L1 proteins and their impact on homophilically mediated neurite outgrowth was tested. Analysis of 25 pathological missense mutations revealed dramatic effects on the surface expression of mutant L1 proteins in CHO cells. In detail, mutations that are predicted to affect the structure of individual extracellular domains are more likely to affect intracellular processing and/or ligand binding than those mutations affecting surface properties of the molecule. Furthermore, different L1-mutations have been overexpressed in primary neurons and their effects on the homophilically mediated neurite outgrowth was examined. Here, the results were conclusive with respect to the cell surface expression in CHO cells.

In the second part, the mouse homologue of the recently described IgSF-member Neurotractin has been characterized. For this, the cDNA of mouse neurotractin (mNTRA) was cloned and specific antibodies have been generated. Western Blot Analysis of the spatiotemporal distribution showed a developmentally regulated increase of mNTRA in different brain regions. Immunohistochemistry, using antibodies against mNTRA, identified its expression on different neuronal subpopulations in the cerebellum, olfactory bulb, cortex, and the hippocampus. Moreover, the subcellular distribution of mNTRA has been localized to presynaptic terminals using immunocytochemistry of primary neurons, and a biochemical approach using brain tissue of adult mice. Functional studies were performed examining the influence of mNTRA on neurite outgrowth. Here, a positive effect on the neurite length of hippocampal neurons and a clear choice behaviour of outgrowing hippocampal explants for mNTRA was observed. This implies for mNTRA a function as an attractive guidance cue for the neurite outgrowth of hippocampal neurons.

In order to analyse a potential plasticity-dependent regulation of mNTRA *in vivo*, entorhinal cortex lesions with mice were performed. Immunohistological examinations showed an upregulation of mNTRA in the deafferented hippocampus, and most interestingly, on reactive astrocytes in the denervated outer molecular layer of the dentate gyrus. The spatiotemporal expression regulation of mNTRA after lesion, corresponds with the timing of regenerative

axon sprouting in the outer molecular layer. Thus, the attractive influence of mNTRA *in vitro*, and the regulation after entorhinal cortex lesion, leads to the assumption of an *in vivo* function of mNTRA in regenerative axon sprouting.

Finally, mNTRA-deficient mice have been generated, for a detailed analysis of the *in vivo* function for mNTRA in future studies.