Institute of Anatomy and Cell Biology

Proteins of Synaptic Contacts: Functional Characterization and Elucidation of their Possible Role in Neuropsychiatric Diseases

Head: Tobias Böckers

Glutamatergic synapses in the central nervous system are specific cellular junctions characterized by synaptic vesicles that are attached to the active zone of the presynapse and to an electron-dense web underneath the postsynaptic membrane known as the postsynaptic density (PSD). The pre- and postsynaptic membranes are interconnected by synaptic cell adhesion proteins (i.e. neurexin-neurexin, cadherins) that are analyzed in the laboratory (PhD project Thomas Schmidt). PSDs are composed of a dense network of several hundred different proteins that creates a macromolecular complex serving a wide range of different functions. Prominent PSD proteins, such as members of the MaGuk or ProSAP/Shank family, build up a dense scaffold that creates an interface between clustered membrane-bound receptors, cell adhesion molecules and the actin-based cytoskeleton.
The synaptic rearrangement (structural plasticity) is a rapid process and is believed to underlie learning and memory formation. The characterization of synapse/PSD proteins is especially important in light of recent data suggesting that several mental disorders have their molecular defect at the synapse/PSD level. Anna Lena Jansen and the PhD projects of Jutta Heinrich and Noreen Kanwal concentrate on the role of ProSAP/Shank molecules and interacting proteins within the PSD. The self-assembly of these proteins is zinc dependent and zinc seems to play a key role in the local rearrangement of structural PSD components (PhD project Michael Schmeisser). In addition, we are working on those drugs influencing synapse number and maturity (PhD project Patrick Udvardi) as well as on neuronal heat shock protein expression and dynactin mutations related to motoneuron degeneration (ALS). Within this context, Georges Kuh investigates the distribution of mutated dynactin fusion proteins in motor neurons and identifies novel dynactin interacting proteins. A wide range of methods and models, which includes Drosophila melanogaster and induced pluripotent stem cells (hiPS) as well as transgenic mice, are also employed.