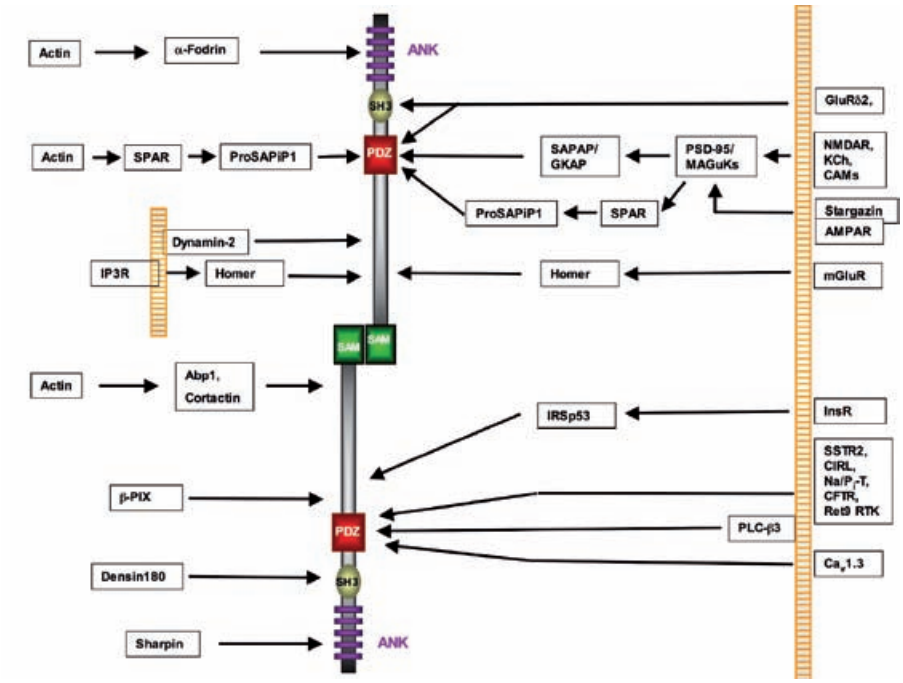
Institute of Anatomy and Cell Biology

Analysis of Synaptic Contacts: Molecular Composition and Cell Adhesion

The Team:
Head of the Institute: T. Böckers
Professor: N. Golenhofen
Group Leaders/Postdocs: B. Bartelt-Kirbach, A. Böckers, J. Bockmann, U. Fassnacht, S. Liebau, Ch. Pröpper, M. Schmeisser
PhD Students: A. Grabrucker, J. Heinrich, N. Kanwal, G. Kuh, M. Schön, T. Schmidt
Additional Members of Thesis Advisory Commitees: E. Gundelfinger (Magdeburg), A Ludolph (Ulm), U. Nienhaus (Ulm, Karlsruhe), W. Robberecht (Leuven)

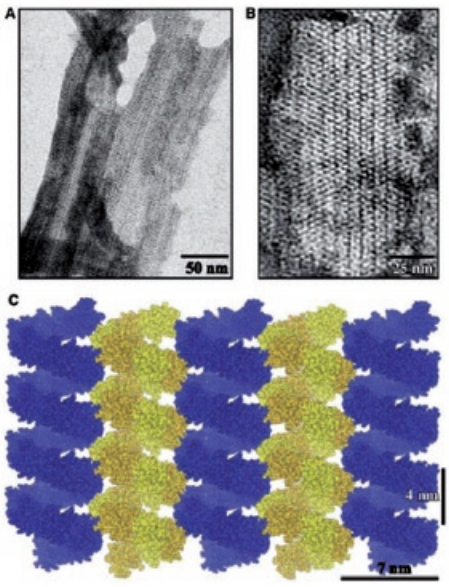
Glutamatergic synapses in the central nervous system are specific cellular junctions characterized by synaptic vesicles that are attached to the active zone of the presynapse and to an electron-dense web underneath the postsynaptic membrane known as the postsynaptic density (PSD). The pre- and postsynaptic membranes are interconnected by synaptic cell adhesion proteins (i.e. neurexin-neuroligin, cadherins) that are analysed in the laboratory (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. Andreas Grabrucker's, Jutta Heinrich's and Noreen Kanwal's projects concentrate on the role of ProSAP/Shank molecules 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. In addition, we are working on neuronal heat shock protein expression and dynactin mutations related to motorneuron degeneration (ALS). Within this context, Georges Kuh investigates the distribution of mutated dynactin fusion proteins in motor neurons and tries to identify novel dynactin interacting proteins. A wide range of methods and models including Drosophila melanogaster and transgenic mice are employed.



ProSAP/Shank molecules are multidomain molecules that assemble via their SAM domain. They are core components of the postsynaptic density and cluster several PSD molecules directly or indirectly.

The ProSAP2 SAM domain forms a sheet of fibre-like structures attached together in a side-by-side antiparallel manner. This interaction is zinc dependent.



Selected Publications:

- *Proepper Ch, Johannsen S, Liebau St, Bockmann J, Vaida B, Kreutz MR, Gundelfinger ED, Boeckers TM (2007) Abi-1, a PSD and nuclear protein, is essential for regulated dendrite morphogenesis and synapse formation, EMBO J 7, 26, 1397-1409.*
- *Liebau St, Vaida B, Storch A, Boeckers TM (2007) Maturation of synaptic contacts in differentiating neural stem cells (NSCs), Stem Cells 25, 1720-1729.*
- *Durand CM, Betancur C, Boeckers TM, Bockmann J, Chaste P, Fauchereau F, Nygren G, Rastam M, Anckarsäter H, Sponheim E, Goubran-Botros H, Delorme R, Chabane N, Mouren-Simeoni MC, Bieth E, Rogé B, Héron D, Burglen L, Gillberg Ch, Leboyer M, Bourgeron Th (2007) Mutations of the synaptic scaffolding protein SHANK3 are associated with autism spectrum disorders, Nature Genetics 39, 25-27.*
- *Wendholt D, Spilker C, Schmitt A, Dolnik A, Smalla KH, Pröpper Ch, Bockmann J, Sobue K, Gundelfinger ED, Kreutz MR, Boeckers TM (2006) ProSAP interacting protein1 (ProSAPiP1), a novel postsynaptic density protein that links the spine associated Rap-Gap (SPAR) to the scaffolding protein ProSAP2/Shank3, J Biol Chem 12, 281, 13805-13816.*
- *Baron MK, Boeckers TM, Vaida B, Faham S, Gingery M, Sawaya M, Salyer D, Gundelfinger ED, Bowie JU (2006) An architectural framework that may lie at the core of the postsynaptic density. Science 311, 531-535.*
- *Boeckers TM, Liedtke Th, Dresbach Th, Bockmann J, Kreutz MR, Gundelfinger ED (2005) C-terminal synaptic targeting elements for postsynaptic density proteins ProSAP1/Shank2 and ProSAP2/Shank3, J Neurochem 92, 519-524.*