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Institute of Anatomy and Cell Biology

Stem Cell Biology and Proteins of Synaptic Contacts: Functional Characterization of iPSC Cells and Synapses in the Context of Neuropsychiatric Diseases

Head: Tobias M. Böckers

Stem cells are considered a very valuable tool for dissecting developmental aspects and investigating pathomechanisms, and can be used for cell-based therapies. Stem cells are characterized by their abilities of symmetrical cell division and their potential to give rise to different cells in organisms. Pluripotent, embryonic stem cells of the blastocyst's inner cell mass can even generate all the cells of an organism. Since the first generation of the so-called induced pluripotent stem cells (hiPS) by Yamanaka, pluripotent stem cells can be reprogrammed from several kinds of somatic cells. This offers the chance of investigating stem cells and their differentiated progeny in disease-specific settings. In this respect, we generated iPSC cells from patients with defined genetic defects that either lead to developmental defects in the central nervous system or cause neurodegeneration. In our
studies including stem cell biology, we are investigating human and patient-specific iPS cells of several neurological disorders such as ProSAP/SHANK-related autism spectrum disorders (Leonhard Linta), LRRK2-related M. Parkinson (Stefanie Raab), developmental defects of the nervous system related to dysfunctional translation initiation (Maira Bertolessi), developmental disorders related to mutations in an RNA Polymerase (Moritz Klingenstein) as well as neurodegeneration (ALS).

In addition, we concentrate on glutamatergic synapses of the central nervous system that are specific cellular junctions characterized by an electron-dense web underneath the postsynaptic membrane known as the postsynaptic density (PSD). 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, Michael Schmeisser and Noreen Kanwal’s projects 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. This is followed up by Stefanie Pfänder in human neurons derived from induced pluripotent stem cells (iPS). In addition, we are working on drugs influencing synapse number and maturity (Patrick Udvardi) as well as on neuronal heat shock protein expression.

Selected Publications: