Focus of the PhD-Project (Dr. Andreas Beck)

Investigation of TRP proteins in astrocytes

Transient receptor potential proteins (TRPs) are a family of cation channels shown to be involved in membrane depolarization and Ca^{2+} signaling of many cell types. Since the first member was found in photoreceptor cells of *Drosophila melanogaster,* plenty of homologues were detected in all kinds of animal species, even in yeast. Most TRPs act as physiological sensors in response to physical or chemical environmental changes. According to their structural homology they are divided into seven groups of which the TRPC (canonical), TRPM (melastatin-receptor) and TRPV (vanilloid-receptor) proteins are the most abundant. Some of them are highly expressed in the brain, mainly in neuronal cells, where they seem to be involved in membrane potential changes and shaping action potentials, and thus modeling the release of and the response to neurotransmitter. But there are also TRP proteins suggested to be in non-neuronal brain-derived cells such as astrocytes and microglia. The functional proof and characterization of these TRP proteins in astrocytes is the focus of the present PhD-project.

Methods:

To reach our goals, we are going to use diverse molecular techniques (e.g. PCR, western-blot), fluorescent Ca^{2+} imaging and whole-cell patch clamp to proof the presence of TRP proteins in cultured mouse cortical astrocytes. Those and further functional assays might enable us to characterize and elucidate the physiological function of TRP channels in these cells.

Selected publications:

- Nelson PL, Beck A, Cheng H (2011): Transient receptor proteins illuminated: Current views on TRPs and disease. *Vet J.*; 187: 153-164. (*Review article)*
- Chang Y, Schlenstedt G, Flockerzi V, Beck A (2010): Properties of the intracellular transient receptor potential (TRP) channel in yeast, Yvc1. *FEBS Lett*.; 584(10): 2028-2032. *(Review article)*
- Cheng H, Feng JM, Figueiredo ML, Zhang H, Nelson PL, Marigo V, Beck A (2010): Transient receptor potential melastatin type 7 channel is critical for survival of bone marrow derived mesenchymal stem cells. *Stem Cells Dev*.; 19(9): 1393-1403.
- Lange I, Penner R, Fleig A, Beck A (2008): Synergistic regulation of endogeneous TRPM2 channels by adenine dinucleotides in primary human neutrophiles. *Cell Calcium*; 44(6): 604-615
- Beck A, Penner R, Fleig A (2008): LPS-induced down-regulation of I_{CRAC} but not I_{CAN} in cultured mouse microglial cells. *J. Physiol.*; 586(2): 427-439.

- Starkus J, Beck A, Fleig A, Penner R (2007): Regulation of TRPM2 by extra- and intracellular calcium. *J. Gen. Physiol.*; 130(4): 427-440.
- Cheng H, Beck A, Launay P, Gross SA, Stokes AJ, Kinet JP, Fleig A, Penner R (2007): TRPM4 controls insulin secretion in pancreatic beta-cells. *Cell Calcium*; 41: 51-61.
- Takezawa R, Cheng H, Beck A, Ishikawa J, Launay P, Kubota H, Kinet JP, Fleig A, Yamada T, Penner R (2006): A pyrazole derivative potently inhibits lymphocyte calcium influx and cytokine production by facilitating TRPM4 channel activity. *Mol. Pharm.*; 69(4): 1413-1420.
- Beck A, Kolisek M, Bagley LA, Fleig A, Penner R (2006): Nicotinic acid adenine dinucleotide phosphate (NAADP) and cyclic ADP-ribose (cADPR) regulate TRPM2 channels in T lymphocytes. *FASEB J.*; 20(7): 962-964.
- Kolisek M, Beck A, Fleig A, Penner R (2005): Cyclic ADP-ribose and hydrogen peroxide synergize with ADP-ribose in the activation of TRPM2 channels. *Mol. Cell*; 18(1): 61-69.
- Beck A, Zur Nieden R, Schneider HP, Deitmer JW (2004): Calcium release from intracellular stores in rodent astrocytes and neurons *in situ*. *Cell Calcium*; 35(1): 47-58.
- Beck A, Lohr C, Berthold H, Deitmer JW (2002): Calcium influx into dendrites of the leech Retzius neuron evoked by 5-hydroxytryptamine. *Cell Calcium*; 31(3): 137-149.
- Beck A, Lohr C, Deitmer JW (2001): Calcium transients in subcompartments of the leech Retzius neuron as induced by single action potentials. *J. Neurobiol*.; 48(1): 1-18.