Session 12: Cellular Biophysics in Diseases (Cancer, Rare Diseases, Infectious Diseases)

Session chairs: Laszlo Matyus (University of Debrecen, Hungary) & E. Ada Cavalcanti-Adam (University of Bayreuth, Germany)

O-12.1 Invited speaker

Molecular pathology of ion channels in diseases and their pharmacological targeting

Gyorgy Panyi [1]

[1] University of Debrecen, Debrecen, Hungary

Several pathological conditions are associated with ion channel malfunctions. Among these loss-of-function (LOF) mutations of the gene encoding the voltage-gated K+ channel KCNQ2 leads to hyperexcitability syndromes, such as benign familial neonatal seizures. We have characterized two novel LOF mutations of Kv7.2, S113F in the extracellular S1-S2 loop and A306V in the water filled cavity of the pore. We found that the peak current density is substantially reduced in the S113F mutant and that A306V mutation resulted in non-functional channels. Linking S113F with the wild-type subunits in concatamers showed that the presence of a single mutant subunit confers the LOF phenotype to the tetramers, whereas the WT/A306V heteromers showed novel, inactivating K+ current phenotype.

Voltage gated K+ channels can be pharmacologically targeted with high selectivity using peptide toxins isolated from venomous animals. Inhibition of the Kv1.3 K+ channel is a promising therapeutic approach in certain autoimmune diseases (e.g. multiple sclerosis) mediated by effector memory T cells. We have recently identified and characterized sVmKTx, a selective Kv1.3 inhibitor peptide which is the derivative of the potent Kv1.3 inhibitor peptide Vm24. We have also generated an mCherry-conjugated Vm24 that can serve as a tool to identify Kv1.3 channel expressing cells.