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Normal and Diseased Potassium Channels in Human Brain and Heart

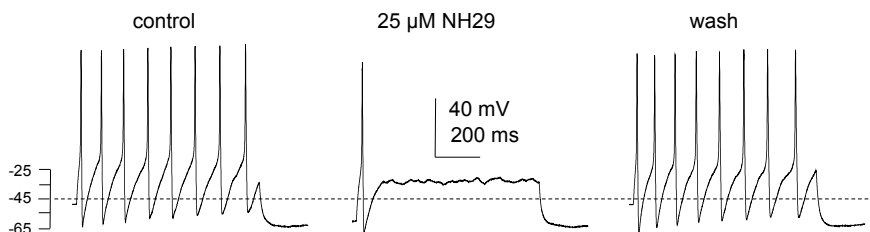
Position

Professor, Sackler Faculty of Medicine

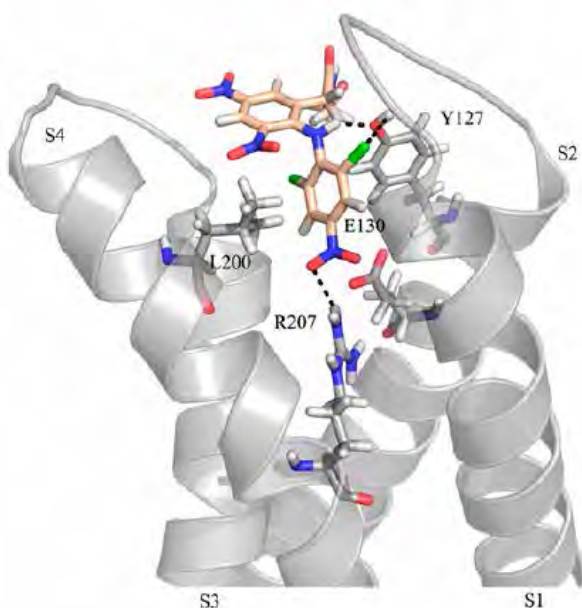
Research

Reaching an understanding in molecular terms of the mechanisms by which changes in membrane potential regulate cellular events is the main concern of our research. We focus our interest on potassium channels because they play crucial roles in many cellular functions such as shaping cardiac

and neuronal action potentials, tuning neuronal firing patterns, synaptic integration or modulating neurotransmitter release. Using the powerful combination of molecular biology, biophysics, biochemistry and electrophysiology, our research aims at elucidating the structural, biophysical and physiological attributes of potassium channels in human brain and heart and whose mutations lead to major neurological and cardiovascular disorders like epilepsy, myokymia, atrial or ventricular fibrillation.



Activation of M-type potassium channels by our homemade NH29 opener inhibits evoked spike discharge in dorsal root ganglion sensory neurons.



Docking of the NH29 gating-modifier molecule onto the voltage sensor domain of the Kv7.2 potassium channel.

Publications

Manuscripts

Peretz A, Pell L, Gofman Y, Haitin Y, Shamgar L, Patrich E, Kornilov P, Gourgy-Hacohen O, Ben-Tal N, **Attali B.** (2010) Targeting the voltage sensor of Kv7.2 channels with a new gating-modifier. *Proc Natl Acad Sci USA.* 107:15637-15642.

Strutz-Seebohm N, Pusch M, Wolf S, Stoll R, Tapken D, Gerwert K, **Attali B,** Seebohm G. (2011) Structural basis of slow activation gating in the cardiac I_{Ks} channel complex. *Cell Physiol Biochem.* 27:443-452.

Ebner-Bennatan S, Patrich E, Peretz A, Kornilov P, Tiran Z, Elson A, **Attali B.** (2012) Multi-faceted modulation of K⁺ channels by protein tyrosine phosphatase epsilon tunes neuronal excitability. *J Biol Chem.* 287:27614-27628.

Weisbrod D, Peretz A, Ziskind A, Menaker N, Oz S, Barad L, Eliyahu S, Itskovitz-Eldor J, Dascal N, Khananshvil D, Binah O, **Attali B.** (2013) SK4 Ca²⁺ activated K⁺ channel is a critical player in cardiac pacemaker derived from human embryonic stem cells. *Proc Natl Acad Sci USA.* 110:E1685-94.

Kornilov P, Peretz A, Lee Y, Son K, Lee JH, Refaeli B, Roz N, Rehavi M, Choi S, **Attali B.** (2014) Promiscuous gating modifiers target the voltage sensor of Kv7.2, TRPV1, and Hv1 cation channels. *FASEB J.* 28:2591-602.

Reviews

Kornilov P, Peretz A, **Attali B.** (2013) Channel gating pore: a new therapeutic target. *Cell Res.* 23:1067-8.

Dvir M, Peretz A, Haitin Y, **Attali B.** (2014) Recent molecular insights from mutated I_{Ks} channels in cardiac arrhythmia. *Curr Opin Pharmacol.* 15:74-82.

Grants

2013-2017 Israel Academy of Science, (ISF:1215/13). Role of SK4 Ca²⁺-activated K⁺ channels in the developing human cardiac pacemaker using embryonic stem cell-derived cardiomyocytes as a model. (PI).

2013-2017 Fields Fund for Cardiovascular Research (Co-PI).