COLLOQUIA IN CELLULAR SIGNALLING

Venue: Medical University Vienna, Center for Physiology and Pharmacology, Institute of Pharmacology, Waehringerstrasse 13a, 1090 Vienna, "**Leseraum**".

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Friday **06.06.2014 11:00 s.t.** **Alain Labro (host: W. Sandtner)**

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"Reconcile Kv3.1 high threshold activation and fast deactivation with action potential repolarization; role for voltage sensor relaxation"

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Abstract:

The shape of the action potential (AP) can be tuned by expressing a selected subset of voltage-dependent potassium (Kv) channels. Members of the Kv3 family have been linked to high-frequency AP firing because of their high threshold of channel gate opening and fast closure kinetics. Although fast closure prevents the membrane from being repolarized to strongly (affecting subsequent AP generation), the probability of incomplete membrane repolarization increases. We show here that Kv3.1 channels bypass this problem by displaying a very steep voltage dependence in their channel kinetics and having very fast voltage-sensor domain (VSD) relaxation that develops before channel opening and slows down VSD return upon repolarization. Therefore, upon short membrane depolarizations the Kv3.1 channel displays a previously uncharacterized resurgent (hooked tail) current upon membrane repolarization (in the voltage range between -30 and 0 mV). This resurgent current disappeared when the membrane depolarization was sufficiently long to open the channels completely. This unique Kv3 behavior could be transferred onto the Shaker channel by transplanting the S3S4 linker of the VSD and is not linked to an underlying inactivated state as is the case for the hERG channel. We conclude that the presence of a resurgent current in Kv3 channels is an important feature for high-frequency AP firing as it secures complete membrane repolarization during the falling phase of the AP that normally works as a negative feedback mechanism on channel closure.