

Training stay: October- November 2013

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NENS STIPEND FOR TRAINING STAY

REPORT

The background K channels (K2P) TRESK and TREK2 are highly expressed in the dorsal root ganglia (DRG), accounting for the largest fraction of the resting potassium conductance in these neurons. Recent evidence supports the role of TRESK in setting up sensory neuron excitability under pathological conditions. (Tulleuda et al., 2011, Mol Pain).

The exaggerated glycolytic metabolism resulting from hyperglycemia is known to sensitize primary nociceptive neurons. This links methylglyoxal (a glycation agent overproduced in diabetes) to neuropathy and pain, but the actual mechanisms are unknown.

To test the possible effect of methylglyoxal on K2P channels, we performed whole-cell patch clamp recordings on rat and human TRESK channel, in a heterologous cell expression system. Methylglyoxal (MG) was used in different concentrations for acute as well as for chronic treatments. We also have preliminary results for the response of the human TREK-2 channel under MG treatment.

Voltage ramps from -100 to +50mV were used in order to record whole-cell currents. At times, voltage pulses from -100 to +50 were applied, to monitor a possible change in the channel's kinetics. Electrophysiological recordings were performed with a Axopatch 200B amplifier, acquired with pClamp 10.4 software (Molecular Devices). Data was analyzed with Clampfit 10.4 and Prism 5 (GraphPad Software).

Our preliminary results could help explaining the possible involvement of TRESK and TREK-2 in pain sensing and neuropathy, at the core of our initial hypothesis. Investigation should be further extended to the molecular basis of the MG effect on TRESK, but also to the connection between glycation agents and other K2P channels, in heterologous as well as in native cell expression systems.

During my training stay I learned to perform electrophysiological recordings on background potassium channels, which I found to be diverse from recordings I have previously assisted to. Also, I became more familiar to the patch clamp setup, supervised by experienced physiologists from whom I received valuable theoretical and methodological training. I gained knowledge of how to adapt protocols and analyse data. All in all, working with background potassium channels, while using a technique yet novel to me, proved to be a difficult task, but an extremely enriching experience, beyond doubt.

I intend to continue the work in my home laboratory. The adjustments for the patch-clamp setup we need to implement in order to perform recordings on K₂P channels have been established. The aforementioned results obtained in Barcelona during my training stay will be further explored to determine the involvement of K⁺ channels in diabetic neuropathy, project that entails a valuable collaboration.

I graduated from the Faculty of Biology with the clear goal of continuing my education at a top level and becoming an accomplished researcher in the field of Neuroscience. Soon, I became interested in mastering modern techniques for the study of pain and sensory transduction. Receiving a NENS stipend brought me closer to my goals and strengthened my decision of pursuing a career as a neuroscientist. Apart from having the chance to work and receive training in an internationally distinguished laboratory, the social experience I had will definitely help maintaining and establishing new connections, requisite for the research career path I have taken.



Lab photo. Jordi Pales, Jonathan Giblin, Larisa Maier, Gerard Callejo, Aida Castellanos, Xavier Gasull