

First contact initiative grant - Report

The European Society of Cardiology first contact initiative Grant awarded to me was utilized to carry out research under the supervision of Prof. Kanigula Mubagwa for a period of 3 months from February 2011 – April 2011. I was at the Department of Experimental cardiology, Katholieke University, Leuven, Belgium as a visiting scholar.

I was involved in identifying new Transient receptor potential (TRP) ion channels on the native isolated cardiac myocytes from pig and mouse using electrophysiology. I learned a variety of techniques including anesthetizing animals, isolating the heart and perfusing it using the Langendorff method, preparing isolated cardiomyocytes, and using the patch clamp technique to record ion currents in single cells. This adds up to his experience in using expression systems such as HEK cells. Good Results were obtained.

The work was carried out on cardiac myocytes dissociated either from control animals, from animal models of diseases (e.g. hyperaldosteronism, chronic left ventricle pressure overload by aortic constriction, ob/ob mice), of from animals with in vivo silencing or overexpression of one or several TRP genes. Electrophysiology of ion current was measured using the whole-cell patch clamp technique. TRPM7-like currents were measured in cells intracellularly dialyzed with low Mg^{2+} concentrations under conditions where the currents due to other channels are blocked using specific voltage protocols, ion substitutions or pharmacological agents. The novel cation current was studied by extracellular ACA or flufenamic acid application in cells internally dialyzed with high $[Mg^{2+}]_i$ (to block TRPM7) in addition to blocking other currents. To investigate the regulation of these channels, the standard pipette solution was modified by adding different substances or drugs that modulate signaling pathways: e.g. non-hydrolyzable nucleotides, to study the role of G proteins; ATP-free or PIP_2 -containing solutions, to study the role of phosphoinositides; etc.

In addition to the research performed; I was involved in preparing project proposal and grant application. Given below are the ISHR-ES/Servier Research Fellowship project details.

Abstract prepared for ISHR-ES/Servier research fellowship.

Regulation of cation nonselective channels and their roles in intracellular ion homeostasis in diseased myocardium.

Cation channels in cardiac ventricular cells play a pivotal role in physiologic and disease conditions. Transient receptor potential (TRP) channels represent a recently discovered superfamily of cation channels gated by diverse physical and chemical stimuli. With modern electrophysiology tools such as the patch-clamp technique Mg^{2+} -inhibited cation current in cardiomyocytes were identified. The biophysical properties of underlying channels, as well as their regulation by membrane phospholipids and by pharmacological agents led to their identification as TRPM7. Similar channels play an important role in neuronal cell death. In cardiac cells, the roles of these channels under pathophysiological conditions remain unknown. Further work is needed to determine the regulation of these channels by neuro-hormonal stimuli, and to detect the channel proteins by immunofluorescence or RT-PCR. In addition, more recent work discovered a previously uncharacterized Na^+ -permeable channel, that can be activated by the fenamate anti-inflammatory and related drugs. The protein underlying this conductance remains unknown. We would like to further investigate the regulation of the TRPM7 and of the novel channel, and their role in cardiac function under physiological or disease conditions

Fund Utilization

This award will be used for the transportation, accommodation charges and living expenses in Leuven, Belgium for a short duration.

This grant also helped me to adapt to the new environment and have hand on experience on the techniques used in the lab. Thanks for providing me with grant to perform new project and acquire more knowledge on basic cellular cardiovascular sciences.

GOWRI SHANKAR Bagavananthen Andavan.

Department of Pharmacology and Toxicology,

University of Vienna, Althanstrasse 14A,

Vienna 1090, Austria.