

Myocardial TRPM7 channels: Biophysical properties and involvement in cardiac diseases

Bogdan Amuzescu, Bogdan Istrate, Asfree Gwanyanya, Regina Macianskiene and Kanigula Mubagwa
University of Bucharest, Romania

TRPM7 is an ubiquitously expressed ion channel, belonging to the melastatin-related group of the transient receptor potential (TRP) superfamily, putatively involved in intracellular magnesium homeostasis and transport of transitional metal ions (iron, copper, zinc, etc.). Along with TRPM6, present mainly in intestinal and renal epithelia, where it plays an important role in magnesium transport, they form a peculiar category of channel-enzymes, featuring a functional alpha-kinase and phosphorylation sites in the C-terminal domain. Our studies led to the identification in ventricular myocytes of different species of a non-selective channel current with permeation and regulation properties virtually identical to TRPM7 in heterologous expression systems. The channel is blocked by trivalent lanthanides, has a particular current-voltage relation, requires ATP and PIP2 for activation, and is inhibited by intracellular magnesium and acidification. Recently we have identified in human atrial myocytes a current with similar permeation, block and regulation properties. In ~1/3 of patients the current was already activated at patch rupture. Our recent immunofluorescence experiments have confirmed the presence of TRPM7 in ventricular cardiomyocytes, showing a preferential location at the Z membranes of the sarcomeres and intercalated disks, and also a peri- and paranuclear staining suggestive for the rough endoplasmic reticulum and Golgi apparatus. Although earlier studies have convincingly demonstrated TRPM7 activation by free oxygen radicals during prolonged neuronal ischemia (Aarts et al. 2003 Cell 115:863-877), and an antiapoptotic effect of nerve growth factor on hippocampal neurons via downregulation of TRPM7 expression, the relevance of TRPM7 activation during myocardial ischemia is currently not understood.

Biography

Bogdan Amuzescu, MD (1991), Ph.D. (2003), has over 25 years of experience in biophysics and electrophysiology-patch-clamp. He is currently Associate Professor in the Department of Biophysics & Physiology, Faculty of Biology, University of Bucharest, and co-organizer since 2000 of a NENS-acknowledged master program in neurobiology. He wrote Over 20 original scientific papers (9 in ISI-quoted journals), several scientific books and book chapters, presentations at over 90 internal/international scientific meetings. He took part in successful completion of 8 international and 6 internal research grants. And he is a member of 6 scientific societies (e.g. Biophysical Society). Major areas of interest: membrane biophysics, neuronal & cardiac electrophysiology and pharmacology, mathematical modeling.

bogdan@biologie.kappa.ro