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## Structural and functional insights into cholesterol regulation of k+ channels in vasculature and heart

Irena Levitan University of Illinois at Chicago, USA

ur research focuses on the mechanisms that underlie cholesterol regulation of ion channels with particular focus on inwardly rectifying K+ channels (Kir), which is responsible for regulating membrane potential and excitability in a variety of cells types including cardiomyocytes, smooth muscle cells and endothelial cells. We have found that an increase in membrane cholesterol paradoxically has opposite effects on two types of Kir channels expressed in cardiomyocytes, it simultaneously suppressed the activity of Kir2.1 channels responsible for the basal Kir activity and enhances the activity of cardiac KACh channels which plays a key role in the control of the heart rate. We propose that the loss of basal Kir activity together with enhanced activity of KACh should result in destabilization of the heart rate control and development of arrhythmias. In terms of the molecular mechanisms of cholesterol-induced regulation of the channels, we discovered that the channels interact with an ensemble of cholesterol molecules and identified

novel cholesterol binding sites that are specific for open and closed states of the channels. We also show that increase in membrane cholesterol *in vitro* and in vivo suppresses flow sensitivity of Kir2.1 channels, a hallmark of they function in vascular endothelium.

## **Speaker Biography**

Irena Levitan, is a professor of Medicine and adjunct professor of Bioengineering at the University of Illinois at Chicago. Her current research focuses on cholesterol regulation of ion channels and cellular biomechanics. Levitan's group provided the first comprehensive structural insights into cholesterol regulation of K+ channels and the cross-talk between cholesterol and other regulators of these channels. She was named a Guyton distinguished lecturer by the Association of chairs of Departments of Physiology for her quantitative and biophysical work on cholesterol modulation of ion channels and how this can affect integrated organ function. She is an author of more than 70 publications and a leading editor of Cholesterol regulation of Ion Channels and Receptors (Wiley, 2012) and Vascular Ion Channels (Springer, 2016).

e: levitan@uic.edu

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