SPECIAL SEMINAR

Presented by the Center for Vascular and Heart Research at the Fralin Biomedical Research Institute at VTC

ENA IVANOVIC

Graduate Student
Department of Physiology
Integrative Cardiac Bioelectricity Group
University of Bern, Switzerland

In Person Seminar: Ephaptic Coupling in Cardiac Intercalated Disc Nanodomains: Insights from a Finite Element Model

Defects in cardiac conduction can lead to life-threatening arrhythmias. In pathological situations when gap junctional coupling is decreased, action potential propagation may be supported by ephaptic coupling, a mechanism during which negative electric potentials occur in the intercellular clefts of intercalated discs. In these intercalated discs, Na^+ channels form clusters that are preferentially located at the periphery of gap junction plaques in nanodomains known as perinexi, where the intercalated disc cleft is narrower. To examine the electrophysiological role of perinexi, Ivanovic and her colleagues developed a three-dimensional finite element model of a pair of longitudinally abutting cardiomyocytes. In their simulations, perinexal width greatly modulated ephaptic coupling when the Na^+ channel cluster was located inside the perinexus. The presence of a narrowed perinexus potentiated ephaptic effects due to modified patterns of Na^+ current flow, leading to more negative extracellular potentials in the perinexal cleft. Interestingly, the Na^+ current in the intercalated disc membrane of the pre-junctional cell switched from inward to outward during excitation, thus contributing Na^+ ions to the activating channels on the post-junctional intercalated disc membrane. The modulation by perinexus width mostly disappeared when the Na^+ channel cluster was located at a larger distance from the gap junction plaque, thus outside of the perinexus. However, in the absence of perinexal cleft narrowing, the close apposition of the Na^+ channel cluster and the gap junction plaque had only a minimal effect on ephaptic coupling. These results indicate that narrow perinexi are privileged sites for ephaptic coupling in pathological situations when gap junctional coupling is decreased. Therefore, perinexi might in the future be used as targets to prevent and treat cardiac arrhythmias.

WEDNESDAY, FEB. 16, 2022 at 12:00 p.m.

Room R3012, 2 Riverside Circle. Masks must be worn.
Watch live via Zoom https://virginiatech.zoom.us/s/83772660790 or at https://fbri.vtc.vt.edu/events/live-webcast.html.

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