UNIVERSITY OF CALIFORNIA
MERCED | SCHOOL OF ENGINEERING

Friday, October 11th, 2019
10:30 to 11:45
COB 110

Relationship between electrical excitability and contractility in intact mouse hearts

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Abstract

In the heart, a Ca^{2+} influx through L-type Ca^{2+} channels triggers Ca^{2+} release from the sarcoplasmic reticulum (SR). In most vertebrates, this influx occurs during the ventricular action potential (AP) plateau phase 2. However, in murine models, the influx through L-type Ca^{2+} channels happen on the early repolarizing phase 1. This work aims to assess if changes in the open probability of K^+ channels defining the outward current (Ito) during phase 1 can modulate Ca^{2+} currents, Ca^{2+} release from the SR and systolic pressure during the cardiac cycle in intact perfused beating hearts. Pulsed local field fluorescence microscopy (PLFFM) and loose patch photolysis (LPP) was used to test the hypothesis that a decrease in Ito will enhance Ca^{2+} influx and SR Ca^{2+} release. A reduction in the phase 1 repolarization rate increases the amplitude of Ca^{2+} transients due to an increase in Ca^{2+} influx through L-type Ca^{2+} channels. Furthermore, 4-AP-induced changes in APD_{30} and the amplitude of Ca^{2+} transients were larger in epicardium than endocardium. Ito activation with NS5806 resulted in a reduction of Ca^{2+} currents amplitude that led to a reduction of SR Ca^{2+} release. Finally, to experimentally evaluated the model prediction, we expressed Cav 1.2 Ca^{2+} channels in xenopus oocytes. The oocytes were AP voltage clamped with AP waveforms recorded from dog or human hearts. Interestingly, this experimental approach shows that during an epicardial AP, the Ca^{2+} influx also occurs during phase 1.

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Biography

My laboratory has been involved in the development of new optical, spectroscopic and electrophysiological techniques for studying key aspects of striated muscle physiology. Along my career have been interested in studying the relationship between electrical excitability and Ca^{2+} dynamics on intact beating hearts. Recently, my laboratory developed state-of-the-art techniques called Loose Patch Photolysis and Florescence Local Field Optical Mapping that allows the measurements of Ionic Currents and Ca^{2+} spatial distribution in the intact heart.

Degrees

Doctor in Biological Sciences (Biophysics). University of the Republic (PEDECIBA) Republica Oriental del Uruguay. 1993
Electronic Engineer (Bioelectronics). Universidad Tecnológica Nacional, Argentina. 1990

Recent Publications

Ramos-Franco J, Aguilar-Sanchez Y**, Escobar AL.** (2016) Intact Heart Loose Patch Photolysis Reveals Ionic Current Kinetics During Ventricular Action Potentials. Circ Res.

Aguilar-Sanchez Y, Fainstein D, Mejia-Alvarez R, **Escobar AL.** (2017) Local Field Fluorescence Microscopy: Imaging Cellular signals in intact hearts. J Vis. Exp.

Lopez-Alarcon M, Rodriguez A, Felice JI, Medei E, **Escobar AL.** (2019) Phase 1 repolarization rate defines Ca^{2+} dynamics and contractility on intact mouse hearts. J Gen Physiol.

Bazmi M, **Escobar AL.** (2019) How Ca^{2+} influx is attenuated in the heart during a "fight or flight" response. J Gen Physiol

Aguilar-Sanchez Y, Rodriguez A, Argenziano M, **Escobar* AL**, Ramos-Franco J*. (2019) Transmural Autonomic Regulation of Cardiac Contractility at the Intact Heart Level. Frontiers in Physiology * corresponding authors.