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Reactive oxygen species augment triggered activity in cardiac melanocyte-like cells

Vickas V. Patel
University of Pennsylvania, USA

Rationale: We identified a population of cardiac melanocyte-like cells (CMLCs) in mice and humans that are electrically excitable and contribute to atrial arrhythmias in response to reactive oxygen species (ROS) when missing the melanin synthesis enzyme dopachrome tautomerase (Dct). While atrial arrhythmias in Dct-null mice were partially suppressed by ROS scavengers, it is not clear if triggered activity in response to ROS differs between CMCLs and atrial myocytes.

Objective: Determine if ROS influences triggered activity in CMLCs differently than in atrial myocytes.

Methods and Results: Calcium transients and action potentials were elicited from atrial myocytes and CMCLs isolated from wild-type and Dct-null mice under whole-cell current clamp control using Fura-2, with and without 20 uM hydrogen peroxide. At baseline, delay in the calcium transient upstroke from the action potential in Dct-null CMLCs was 2.3±1.5 ms compared to 2.8±1.7 ms for wild-type CMCLs, and 4.7±2.1 ms for wild-type atrial myocytes compared to 4.5±2.5 ms for Dct-null atrial myocytes. With hydrogen peroxide, the delay in the calcium transient upstroke from the action potential in Dct-null CMLCs was 0.6±0.7 ms compared to 1.1±0.9 ms for wild-type CMCLs, and 3.0±1.8 ms for wild-type atrial myocytes compared to 3.3±2.0 ms for Dct-null atrial myocytes. Also, a significantly higher number of delayed afterdepolarizations were observed in Dct-null MCLCs versus wild-type CMLCs, and atrial myocytes had the fewest DADs in response to hydrogen peroxide.

Conclusions: Hydrogen peroxide augments intracellular calcium release and delayed afterdepolarizations more in Dct-null and wild-type CMLCs compared to atrial myocytes.

Biography

Vickas Patel completed his M.D. and Ph.D. in 1995 at the University of Colorado School of Medicine, and performed his post-graduate medical and postdoctoral training at the University of Pennsylvania and Harvard University. He is an Assistant Professor and the director of Molecular Arrhythmia Research at the University of Pennsylvania. Dr. Patel has published over 40 papers in high-impact journals, served as an editorial board member for several journals and reviewed research proposal for nationally competitive awards.

patelv@mail.med.upenn.edu