You are invited to attend a seminar by Professor Peter Ruben

Acidosis and temperature: twin arrhythmogenic triggers in Long QT3 and Brugada Syndromes

Despite substantive advances in understanding the underlying molecular mechanisms, inherited arrhythmias remain a major cause of morbidity and mortality, including sudden cardiac death. Long QT and Brugada Syndromes (LQTS and BrS), in particular, contribute to these statistics and often go undetected until a catastrophic event occurs. Many of the cardiac voltage-gated, sodium channel (NaV1.5) mutations underlying LQTS and BrS have been characterized biophysically. Although the defective channel properties account, in most cases, for the possibility of arrhythmogenesis, the events that trigger these pathophysiological behaviours remain unknown.

Professor Peter Ruben and his research team at Simon Fraser University (BC, Canada) studied three NaV1.5 mutations and found one, E1784K, associated with LQT3 and BrS. NaV1.5 E1784K is acutely sensitive to changes in pH and temperature. Low pH is reported to block currents through NaV1.5, depolarizing voltage dependence of activation, and destabilizing fast inactivation. In the E1784K mutant, these effects are significantly exacerbated.

In a computer model of cardiac action potential, such changes are predicted to affect epicardial action potential (AP), independent of the endocardial AP. This creates a large transmural dispersion of repolarization, an elongated AP consistent with LQTS, and a coved and elevated ST segment, consistent with BrS. In another series of experiments, increased temperature also exacerbated persistent currents through NaV1.5 E1784K, thereby elongating the modeled cardiac AP. At higher temperatures, use-dependent inactivation was elevated, thus reducing channel availability.

Overall, their findings led Professor Ruben’s research team to suggest low pH and elevated body temperatures, such as those associated with prolonged exercise, may act independently, and possibly in concert, as arrhythmogenic triggers.

Event Details

Date: Friday 21 August 2015
Time: 12pm
Venue: Confucius Institute,
Building 202, Level 4, Room 2
RMIT Bundoora campus west
Clements Drive (off Plenty Road)
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RSVP

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