Comparison of ten Tusscher-Panfilov and Tomek Rodriguez-O'Hara Rudy for Modelling Brugada Syndrome and IV Amiodarone Administration

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Background: Brugada syndrome (BrS) is a genetic channelopathy and one of the leading causes of ventricular fibrillation (VF), which can be refractory to defibrillation shocks, requiring pharmaceutical assistance. Ten Tusscher-Panfilov 2006 (TT06) is a popular model for modelling ventricular arrhythmia; Tomek Rodriguez-O'Hara Rudy with dynamic chloride (ToR-ORd-dynCl) is a more recent model that aims for higher drug modelling accuracy. The models were compared in the context of attempted VF termination with acute IV amiodarone administration in single-cell BrS models for studying single-cell pharmacological VF termination dynamics.

Methods: Reduced sodium (GNa), increased transient outward (Gto), and combined (GNa&Gto) BrS models were created in epicardial TT06 and ToR-ORd-dynCl models. Ion channel conductances were tuned such that the action potentials match observed Brugada phenotypes. A dynamic restitution protocol was applied to find the lowest cycle length before loss of action potential dome in each model. Models were then rapidly paced for 100 beats. An IV bolus of amiodarone was then applied by further altering INa,INaL, and ICaL conductances based on literature and clinical observations of acute amiodarone therapy. Models were then paced for a further 100 beats at varying cycle lengths to simulate the effects of amiodarone at different pacing rates post-administration and to find the lowest stable rate.

Results: TT06 required significantly higher Ito increases in both the Gto (4.5x multiplier) and GNa&Gto (6.6x multiplier) models to create the BrS phenotype, compared to ToR-ORd-dynCl (2.6x and 2.7x, respectively). IV bolus amiodarone decreased action potential duration by a mean of -27.3ms in ToR-ORd-dynCl and -1.3ms in TT06. TT06 stabilised at higher pacing rates post- vs pre-amiodarone (190ms vs 225ms) compared to ToR-ORd-dynCl (185ms vs 190ms).

Conclusion: TT06 and ToR-ORd-dynCl can both capture BrS phenotypes, but TT06 requires more extreme conductance changes, with models behaving differently post-amiodarone administration.