Numerical Simulations Indicate I_{K1} Dynamic Clamp Can Unveil the Phenotype of Cardiomyocytes Derived from Induced Pluripotent Stem Cells

Sofia Botti, Chiara Bartolucci, Claudia Altomare, Lucio Barile, Rolf Krause, Luca F. Pavarino, Stefano Severi

University of Pavia
Pavia, Italy

Introduction: Human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) are an endless source of human CMs, resulting in a mix of atrial-like (AL) and ventricular-like (VL) cardiomyocytes. A useful tool to improve action potential (AP) measurements in hiPSC-CMs is the Dynamic Clamp (DC) technique, based on virtual inward - rectifier potassium current (I_{K1}) injection. The aim of this *in silico* study is to analyse six different I_{K1} expressions in a virtual DC procedure in order to classify hiPSC-CM AL and VL phenotypes.

Methods: The Paci2013 ionic model was used to simulate the ionic membrane currents and the AP of AL and VL hiPSC-CMs. In this computational set, the virtual DC was carried out by suppressing the native I_{K1} and testing six additional I_{K1} formulations available in the literature, using the Ten Tusscher, Grandi, Fink, O'Hara-Rudy, Koivumaki and Courtemanche ionic models, rescaled in order to obtain the same outward current peak.

Results: For each I_{K1} formulation considered, the AP morphology is absolutely non physiological for low percentages of the injected current, while it becomes physiological for higher densities. Using a mathematical criterion based on the number of AP inflections, we obtain the threshold percentages of the current density, defined as the minimal amount of injected I_{K1} required to obtain a physiological AP.

Conclusion: Keeping in mind that we are considering non-native currents, we claim that the most appropriate I_{K1} formulation is the one that minimizes the threshold percentage, i.e. the Koivumaki formulation.