Blocking L-type Calcium Current Reduces Vulnerability to Reentry in Human iPSC-Derived Cardiomyocytes Tissue

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Background: Human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) have proven to be crucial in regenerative medicine. Many studies have analyzed the electrophysiological behavior of hiPSC-CMs for different purposes, such as cardiotoxicity tests. However, their response to drugs when coupled forming a tissue is not fully understood.

Objective: The aim of this study was to determine whether blocking L-type Ca^{+2} current (I_{CaL}) in a hiPSC-CMs tissue could be considered as a potential antiarrhythmic procedure.

Methods: A two dimensional tissue was modeled following the latest version of the unicellular hiPSC-CM *in-silico* model by Paci et al. To analyze the effects of ICaL block, the maximum conductance of I_{CaL} (g_{CaL}) was decreased (test tissue) and compared to control. Both tissues, control and test, were stimulated following a cross-field protocol to generate reentries. A phase analysis was performed and specific parameters, such as the reentrant frequency ($f_{reentry}$), wavelength of excitation, vulnerable window (VW), and cellular excitability, were evaluated.

Results: Induced reentries, where I_{CaL} was reduced by 70% showed a 7.4% decrease in $f_{reentry}$ due to the increase of the excitation wavelength. The lack of contribution of I_{CaL} in the cellular depolarization yielded a reduction of excitability that favored the meandering of the rotor tip. In control tissue, the distance travelled by the rotor tip was 0.115 cm during 386 ms in the first reentry loop, whereas in test tissue the distance increased to 1.212 cm and it took 724 ms. Furthermore, the decrease in excitability reduced the width of the VW by 52.17% from 115±5 ms to 60±5 ms.

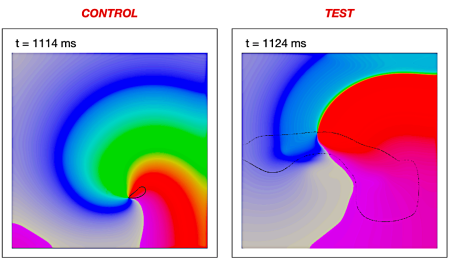

Figure 1 | Instantaneous phase maps and rotor tip movement in control (left) and test (right) tissues. The instant captured in control tissue was t = 1114 ms after de cross-field stimulus, and in test tissue was t = 1124 ms.

Conclusions: Our results suggest that blocking calcium channels could be considered as an antiarrhythmic strategy in hiPSC-CMs tissue, since meandering of the rotor tip promotes a reduction in the frequency of the reentry and the tissue excitability reduction produces a decrease in the VW width.