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MULTI-SCALE ENGINEERING MODELLING OF STEM CELL GRAFT AND HOST CARDIAC MYOCYTES

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Aim Cell therapy has potential towards aiding heart failure, the electromechanical physiology of host and graft interaction remains unknown. The study is determined to reveal the underlying mechanism with novel multiple-scale engineering modelling method.

Methods The co-culture instrumentation was designed with the recording electrode/mechanical array and larger auxiliary electrodes in the centre well, which was used for stimulation or additional recording electrodes over a larger area. The reusable acrylic barrier defines two chambers. The novel micro electrode array, micro mechanical array, bioluminescence and fluorescence imaging technology have been used to analyse the profile of graft-host interaction, in multi-scale/modality.

Results In an attempt to ensure uniformity of conduction with host cells, human embryonic stem cells (hESCs) derived cardiomyocytes (expressed Luc-eGFP) were co-cultured with HL-1 cardiomyocytes. Following the removal of the barrier on day 1, both populations of cell cultures merged together within 24 h. Electrical signals observed at this point were confirmed as originating from the host side. Between days 5 and 7, additional action potentials were observed on the graft side (N=3), beating synchronously with the host, and exhibited a lower AP amplitude propagation velocity, significantly increased ($p<0.05$) from 9.0±1.0 mm/s from the host side to graft. The propagation velocity of HL-1 cardiomyocytes is consistently observed in homogeneous HL-1 cultures, while the propagation velocity of the hESC-CM cells more closely resembles primary neonatal cardiac myocytes. Meanwhile, the bioluminescence and fluorescence imaging has shown the profiling of cell proliferation and cell fusion.

Conclusion The multi-scale engineering modelling shed light on the new hope to reveal the electrophysiological interactions between cardiac graft and host. With further validation, it would become applicable as a preclinical screening approach on cell therapy and new emerging medications.