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RESPONSE TO LETTER

Gene Expression, Morphology, and Electrophysiology During the Dynamic Development of Human-Induced Pluripotent Stem Cell-Derived Atrial- and Ventricular-Like Cardiomyocytes [Response to Letter]

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Dear editor

We much appreciate the interest and positive comments to our study "Gene expression, morphology, and electrophysiology during the dynamic development of human-induced pluripotent stem cell-derived atrial- and ventricular-like cardiomyocytes". We had considered that induced pluripotent stem cell directed differentiation technology represents a crucial approach to investigate the maturation status of cardiomyocytes. We accordingly employed the retinoic acid (RA) and Wnt signalling with small-molecule drugs for iPS-AM and iPS-VM differentiation.[1] We validated the dynamic maturation processes of atrial and ventricular-like myocytes in terms of gene expression, morphology, and electrophysiology with diverse experimental techniques, such as qRT-PCR, immunofluorescence, flow cytometry and patch clamp. In this study, we conducted action potential recordings to assess cell maturation.

It was additionally essential to record electrophysiological properties when evaluating cardiomyocyte maturation. In our current study, the analysis of their action potentials then necessitates the utilization of voltage clamping methodology by clamping the voltage of cells under various standardized conditions. Their distinct resting potentials and action potential amplitudes can be analyzed.[2] Thus, different experimental groups can be subject to consistent voltage clamped resting potential conditions. In such experiments, the changes in Na^+ currents are in line with accelerations or otherwise in action potential depolarization, and the L-type Ca^{2+} currents, and delayed rectifier K^+ currents I_{Kr} and I_{Ks}, respectively, with Phase 2 and Phase 3 repolarization.[3] Furthermore, both the development and localization of these ion channels in the heart significantly influence their related current densities, thereby regulating the action potential waveforms. Thus, sodium channel proteins can be situated within gap junctions between, while calcium channels reside in the transverse tubules of, cardiomyocytes.[4] Thus, the maturation of electrophysiological function in cardiomyocytes is intricately linked to structure, morphology and organelles additional to ion channel maturation. A deeper exploration of the electrophysiological maturation is warranted to explore ion channels developmental influences on action potential upstroke, duration and detailed waveforms. Besides studying the temporal dynamic maturity of the underlying ionic currents, we will further investigate channel expression profiles, and corresponding ionic currents in our subsequent experiments. This could provide a more comprehensive understanding of cardiomyocyte electrophysiological maturation.

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Disclosure

The authors report no conflicts of interest in this communication.

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