Development and assessment of a new *in vitro* platform of human induced pluripotent stem cell-derived cardiomyocytes for evaluating the drug-induced biological phenomena predicting clinically observed cardiac effects

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Currently available human induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CMs) have been known to exert a negative force-frequency relationship as one of their immature properties. In this study, we examined whether controlling the direction of contraction process and/or supplying the higher oxygen tension may overcome such limitation of the contraction movement. We prepared one layered, higher cell-density sheets of hiPSC-CMs, and simultaneously recorded the motion vectors and field potentials. In a cell sheet under spontaneous activity, a synchronous movement consisted of multiple contractions which started from various sites. During electrical stimulation, the contraction started around the pacing electrodes and we observed the positive force-frequency relationships in contraction as well as relaxation along with the frequency-dependent shortening of the field potential durations. The use of fractional analysis of motion vectors demonstrated that contraction as well as relaxation processes consisted of fast and slow phases. Increase in oxygen tension from 20 to 95% in mixed gas accelerated the fast phase of relaxation. β-Stimulation accelerated the timing of fast phase of relaxation, whereas a tyrosine kinase inhibitor dasatinib delayed it. Thus, these observations can indicate that the currently proposed procedure may become a new tool for integrating the drug-induced biological phenomena *in vitro* extrapolating to clinically observed cardiac efficacy and adverse effects.