2-YIA-39 YIA

Development of a novel functional assay to evaluate drug effects using human iPS cell-derived cardiomyocytes.

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Preclinical predictions using cell assay system is a major issue in drug development. With advances in iPS cell technology, human iPS cell-derived cardiomyocytes (hiPSC-CMs) are a valuable tool to characterize the pharmacological effects of drugs on heart cells. However, current approaches to evaluate cardiac contractile function *in vitro* are limited to low-throughput methods. We here test middle-through put and noninvasive assay system with motion field imaging (SI8000 system, Sony corporation) using high speed video image of hiPSC-CMs.

Human iPSC-CMs were kept at 37° C, 5% CO_2 and beating cells were recorded as sequential phase-contrast images. Motion vectors of hiPSC-CMs were analyzed by the SI8000 system. After the measurement, tissue-types (atrial or ventricular) were determined by immunostaining using anti-MLC2a and anti-MLC2v, respectively, and compared the motion vector traces. Contraction and relaxation velocities in atrial-like myocytes were faster than those in ventricular-like myocytes. Application of 100 nM isoproterenol induced the same trends on contractile functions in each cell-type of hiPSC-CMs, but beta2-antagonist blocked the effects only in atrial-like myocytes, indicating that the statistical comparison of these data allows us to identify tissue-types of hiPSC-CMs. Our results suggest a substantial potential to increase accuracy of pharmacological assessment.