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P11-01

Development of *in vitro* assay for drug-induced myocardial hypertrophy

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Cardiac hypertrophy is a risk factor of ischemic heart disease or cardiac dysrhythmia. Myosin light chain-2 (MLC-2) is known as a marker protein of myocardial hypertrophy. As an assay for drug-induced myocardial hypertrophy, a transcription assay using MLC-2 promoter/Luciferase vector transfected rat primary cardiomyocytes had been established. We investigated to apply H9c2 cells, a rat heart myoblast cell line, to this assay, and compared its utility with rat primary cardiomyocytes.

MLC-2/Luciferase vectors were transfected to H9c2 cells or rat primary cardiomyocytes for 24hrs using lipid-mediated gene transfer, FuGENE6. Transfected cells were treated with phorbol 12-myristate 13-acetate (PMA), norepinephrine (NE) and endotheline-1 (ET-1) for 48hrs. PMA, NE and ET-1 stimulation increased the transcription of MLC-2 in H9c2 cells ($\geqq 1\,\mu$ g/ml). In rat primary cardiomyocytes, an increase of MLC-2 transcription was noted in PMA ($\geqq 10\,\mu$ g/ml), however could not reproduce with NE and ET-1. These results indicate that this H9c2 cells system is useful to detect potential of myocardial hypertrophy of drugs.

P11-02

Investigation of Drug-induced APD Prolongation in Guinea Pig Papillary Muscles under the Condition of Low Extracellular Potassium and Magnesium concentrations

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Drug-induced QT prolongation is concerned because of the relation to torsades de pointes (Tdp) in the worst. Hypokalemia and hypomagnesemia are the risk factor of Tdp and QT prolongation. We studied the effect of drugs, which prolong QT interval, on the action potential in guinea pig papillary muscles with microelectrode technique under the low extracellular potassium and magnesium concentrations. Guinea pig papillary muscles were isolated from the right ventricle. After the preparation was stabilized for 1 to 2 hours, normal K^+(4.7 mM) and Mg^{2+}(1.3 mM) or low K^+(2.7 mM) and Mg^{2+}(0.3 mM) Tyrode solution was perfused and the action potentials were recorded. Effects of cisapride, erythromycin and probucol on APD_{90} were evaluated at 30 min after drug perfusion. The decrease of K^+ and Mg^{2+} concentrations enhanced the effect of drug-induced APD prolongation.

These results suggest that the microelectrode techniques with low K^+ and Mg^{2+} concentrations might be useful to evaluate the effect of drug-induced QT prolongation.