OP04-5  The Epigenetic Factor HP1γ Facilitates Cardiac Differentiation of P19 Embryonal Carcinoma Cell

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Cell source of cardiomyocytes including pacemaker cells is important issue to develop the cell therapy of bradycardia. Currently the efficacy of cardiac differentiation from pluripotent stem cells is too low to meet the generation of biological pacemaker in replace of mechanical pacemaker. In this study, we have examined the effect of epigenetic modulator HP1γ on the capability of P19 embryonal carcinoma cells to differentiate into cardiac cells. While wild type P19 cells exhibited the capability to differentiate into cardiac cells only by treatment with chemical inducer dimethyl sulfoxide (DMSO), HP1γ over-expressing P19 cells (HP1γ-P19) facilitated them to differentiate into cardiac cells with spontaneous beating after embryoid body (EB) formation without treatment of any chemical inducer. RT-PCR analysis revealed that HP1γ-P19 EBs expressed various cardiac differentiation marker genes, cardiac contractile genes, cardiac ion channel genes being responsible for pacemaker activity and cardiac specific gap junction genes. The patch-clamp analysis indicated that the cardiomyocytes from HP1γ-P19 cells showed spontaneous action potential with cardiac specific K⁺ channel current, Ca²⁺ channel current and Na⁺ channel current, which could respond to autonomous nerve system agonists such as isoproterenol and carbachol. These data suggested that HP1γ facilitated differentiation of P19 cells into cardiac stem cells and promoted their maturation of cardiac cells involving pacemaker cells.

Keywords: cardiac differentiation, pacemaker cells, HP1γ