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The involvement of Rho-associated kinase inhibitors in regulating cardiac differentiation of embryonic stem cells

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Cardiac and hematopoietic stem/progenitor cells derived from Embryonic stem cells are unlimited cell source and are potentially used for cell transplantation of various heart and hematological diseases. Rho and Rho-associated kinase (ROCK) signaling was implicated in regulating differentiation of various stem cells and ROCK plays an important role in maintaining embryonic stem (ES) cell pluripotency. We have previously reported that suppression of ROCK signaling induced embryonic stem cells different into neural lineages. In this study, we examined whether ROCK signaling is involved in modulating mesodermal differentiation including cardiac stem/progenitor cells and hematopoietic stem cells (HSCs). To determine whether ROCK is involved in ES cell differentiation into cardiac and hematopoietic lineage, we evaluated the effect of ROCK inhibitors, Y-27632 and fasudil on mouse ES and induced pluripotent stem (iPS) cell differentiation. Cells were cultured in hematopoietic differentiation medium in the presence or absence of ROCK inhibitor and colony formation as well as markers of HSCs and ES cells were analyzed. ROCK inhibition resulted in a drastic change in colony morphology accompanied by loss of HSC and increase of cardiac progenitor cell markers. Fasudil-induced cardiac cells were infused into a mouse acute myocardial infarction model. They preserved left ventricular function. These findings provide new insights into the signaling required for ES cell differentiation into cardiac lineage or HSC and suggest that ROCK inhibitors are useful in directing iPS cell differentiation into cardiac progenitor cells for cell therapy of cardiovascular diseases.

Biography

Jun-Yang Liou has his expertise in molecular signaling in regulating cell proliferation and differentiation. His research interests focus on areas like: (1) Gene regulation and siganl transduction in regulating cancer cell survival, proliferation, migration and invasion; he has identified several regulators involved in tumor progression and metastasis. (2) Molecular mechanisms and signal pathways in regulating mouse embryonic stem cell differentiation and proliferation. He has identified that inhibition of ROCK signaling contributes to neural, hematopoietic and cardiac differentiation of mouse embryonic stem and induced pluripotent stem cells.

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