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Rho-associated kinase inhibitors promote the cardiac differentiation of embryonic and induced pluripotent stem cells

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Cardiac and hematopoietic stem cells (HSCs) derived from embryonic ES cells are unlimited cell source and are potentially Gused for cell transplantation of various heart and hematological diseases. Rho-ROCK signaling was implicated in regulating differentiation of various stem cells. Rho-associated kinase (ROCK) plays an important role in maintaining embryonic stem (ES) cell pluripotency. However, whether ROCK involves in modulating mesodermal differentiation including cardiac stem/progenitor cells and HSCs remains unclear. 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 murine 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 was analyzed. ROCK inhibition resulted in a drastic change in colony morphology accompanied by loss of HSC and expression of cardiac progenitor cell markers. Fasudil-induced cardiac cells were infused into a murine 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 these areas: (1) Role of 14-3-3 proteins, focal adhesion kinase and their associated downstream targets in cancer cell survival, proliferation, migration as well as tumor progression and metastasis. (2) Molecular mechanisms and signal pathways of 14-3-3 and Rho-ROCK in regulating mouse embryonic stem cell differentiation and proliferation. He has identified that inhibition of ROCK signaling contribute to neural and cardiac differentiation of mouse embryonic stem and induced pluripotent stem cells.

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