

Exercising mesenchymal stem cells through nomadic culture on heterogeneous field of matrix elasticity

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Recently, it has been established that mesenchymal stem cells (MSCs) memorize the history of mechanical dose from culture environment, which essentially affect the lineage specifications [1]. To ensure stemness of MSCs in maintaining subculture, accumulation of such mechanical dose should be avoided in order to inhibit the lineage bias. For this issue, we have tried to develop cell culture hydrogels whose surface has heterogeneous distribution of elasticity, and to make MSCs move nomadically among different region of elasticity in a certain short duration. In this report, we have established complete design of the microelastically-patterned gels to realize the nomadic movement of MSCs and quasi-oscillatory input of mechanosignals to the MSCs so as to eliminate the history of mechanical dose (we termed such MSC as in frustrated differentiation [2, 3]). After culture of MSCs on the gels for 4days, transcriptome analysis revealed that many genes relating to cellular growth, cell death and survival as well as cellular movement were strongly up-regulated, which means the cells after nomadic culture become more vigorous like an effect of physical exercise for the cells. We will discuss mechanobiology of this phenomenon from the views of chromatin mechanics.

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