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Alterations in mesenchymal stem cell contractility induced by alterations in the microenvironment: Implications for the myocardium. Embryonic stem cell differentiation is markedly influenced by the surrounding extracellular matrix, microenvironment and mechanical influences. During in vitro differentiation, mesenchymal stem cells (MSC) begin to contract, and this change can be used to assess their differentiation state. We hypothesized that the contractility of MSCs would vary as a function of the mechanics of the microenvironment. MSCs were cultured in E10-media in polydimethylsiloxane (PDMS) wells or in a custom-built microfluidic device, and the contractile behavior was compared. Cells were seeded in both small and large PDMS wells, and then mechanically stressed by high pressure, small volume expansion, and cyclic mechanical stretching. Contractility was recorded by changes in aspect ratio of cells as cells began to contract. To validate contractility as a gauge of differentiation state, MSCs were cultured in osteogenic or adipogenic conditions. In low cell density cultures, the contractility of cells was increased during a period of high pressure stress, and decreased in response to small volume expansion. This change in contractility was reversed after a 30 minute recovery. In microfluidic devices, the contractile behavior was reproducible and temporally consistent. The behaviors in small and large PDMS wells were largely independent, although the force produced per cell was inversely related to cell density in the smaller wells. Contractility was abolished in MSCs cultured in osteogenic medium and was reversed in MSCs cultured in adipogenic medium. Cells cultured in osteogenic medium had decreased contractility in small PDMS wells, and a corresponding increase in contractility in large PDMS wells. Overall, the most distinct changes in contractility were observed during pressure stress and cyclic mechanical stretching. Contractility is a unique and reproducible marker of MSC differentiation state that can be used to compare the phenotype of engineered heart tissue in vitro.

During the Iran nuclear deal talks in Lausanne, Switzerland, Secretary of State John Kerry and his French counterpart, Laurent Fabius, were careful to stay in their separate rooms during the negotiations, allowing the two top negotiators, Iran's foreign minister and the EU foreign policy chief, to talk freely as they settled on 3da54e8ca3

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