Cells 'feel' the difference between stiff or soft and thick or thin matrix

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Cultured mesenchymal stem cells can "feel" at least several microns below the surface of an artificial microfilm matrix, gauging the elasticity of the extracellular bedding that is a crucial variable in determining their fate, researchers reported today at the American Society for Cell Biology's 50th Annual Meeting in Philadelphia.

Controlling or predicting how stem cells differentiate into cells of a specific tissue type is a critical issue in the bioengineering of artificial tissue and in stem cell medicine.

To determine how deep a cell's sense of touch can reach, University of Pennsylvania researchers placed naive mesenchymal stem cells (MSCs) on microfilm matrices controlled for thickness and elasticity and bonded to rigid glass.

Amnon Buxboim, Ph.D., of the University of Pennsylvania and colleagues constructed these artificial bedding surfaces to mimic the extracellular matrix that stem cells "feel" as they differentiate.

They used naive MSCs as prototypical adherent cells, because they are particularly sensitive to micro-environmental factors such as elasticity or hardness as they differentiate.

By a variety of measures, the researchers concluded that MSCs can "feel" to several microns into compliant matrices. The stiffer the surface, the shallower the cells could feel; the softer the surface, the

deeper they could "feel."

Because the matrices varied, the scientists were able to document significant differences between stem cells grown on varying stiffness and thickness that represent human tissue microenvironments ? such as brain tissue, which is softer than muscle, which is softer than cartilage, which is softer than pre-calcified bone.

In previous studies, the researchers discovered that as tissue cells adhered to a soft natural extracellular matrix, they pulled and deformed the surface, actions that allowed the cells to use their sense of touch below the surface.

To determine how the thickness and stiffness of the microfilm affected the form of cells grown on top, they deployed a range of methods to document significant differences between stem cells grown on thin films versus thick films.

Cell shape was measured by confocal microscopy and micro-elasticity by atomic force microscopy. Cellular responses were analyzed in terms of morphology while cytoskeletal organization was mapped using non-muscle myosin assembly. Changes in gene expression were obtained by DNA microarray-based transcriptional analysis of the genome.

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