MechCell – Mechanobiological control of cell functions and cell differentiation

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The interdisciplinary project MechCell is scheduled to investigate mechanical influences on biological cell cultures and single cells.

In vivo cells are stimulated mechanically by other cell types in their local environment and by motion of the organism they live in. In static culture environments, like cell culture plates, cells are not stimulated mechanically. They do not need to react on such stimuli and loose natural properties. Mechanobiology describes the inclusion of forces into cells and cell cultures and the comparison to static cultures. The understanding of mechanical interactions on cellular scale is essential. Four topics are under investigation: Mechanical forces in cell cytoskeleton, differentiation of stem cells, influence of shear stress to the differentiation of epithelial cells, and the influence of surface textures on cell growth.

1. Mechanical forces in cell cytoskeleton

To measure the mechanical forces in the cytoskeleton of cells an electromagnetic tweezers is used to pull magnetic particles which were taken up by a cell. The cell integrates these particles into its cytoskeleton so that they can be used as indicator for internal forces. The particle is pulled periodically by the magnetic field gradient and moves back due to the cytoskeleton. The optically observed movements of the particles are used to calculate the forces. The measurements can be compared with measurements of cells without natural cytoskeleton. Figure 1 shows the measurement setup with the cells in culture medium, the electromagnetical tweezers with water cooling tubes and the microscope for optical observation. A detailed description of the first experimental results is published in [1].

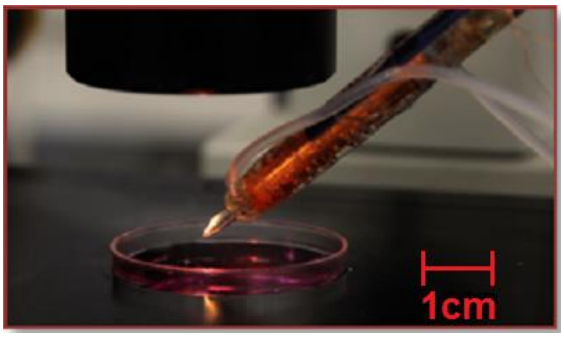

Fig. 1: Electromagnetic tweezers to move magnetical particles which were taken up by cells. The particles are hold by the cytoskeleton of the cells, moved by the tweezers and observed optically.

2. Differentiation of stem cells

Adhered cells and cell cultures can be stretched by deformation of flexible substrates they are adhered to. Especially stem cells react on such stimuli. They have the possibility to differentiate to several types of adult cells. For example MSCs (mesenchymal stem cells) can differentiate to bone cells (osteoblasts) or fat cells (adipocytes) due to different chemical preparation of their culture medium as well as due to different mechanical stimulation. We design micro titer plate-like culture vessels made of PDMS (Polydimethylsiloxane) including a flexible membrane array at the bottom (fig. 2). Membrane bending can be carried-out by pneumatic actuation.

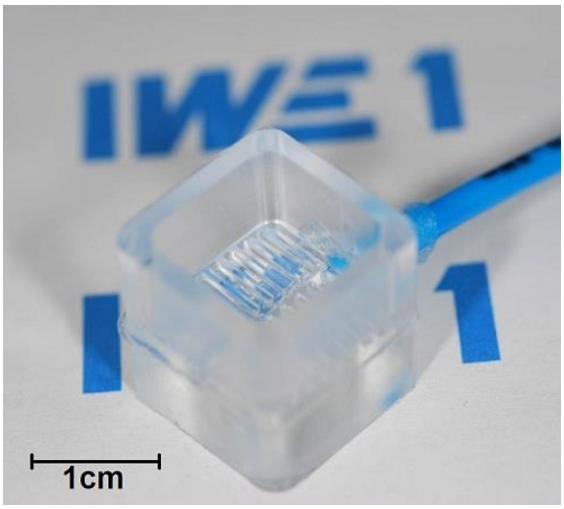

Fig. 2: Culture cavities made of PDMS with stretchable bottoms. Compressed air stretches the bottoms periodically. Adhered cells are also stretched.

The membrane bulging is nearly one-dimensional due to the membranes aspect ratio. The adhered cells are stretched with the deformation of the membrane. A simulation of the deformation is shown in figure 3. Adjusting the air pressure makes it possible to set the stretching of adhered cells to physiological and pathological values. The periodicity of the stimuli can be set at the control unit for the pressure valves.

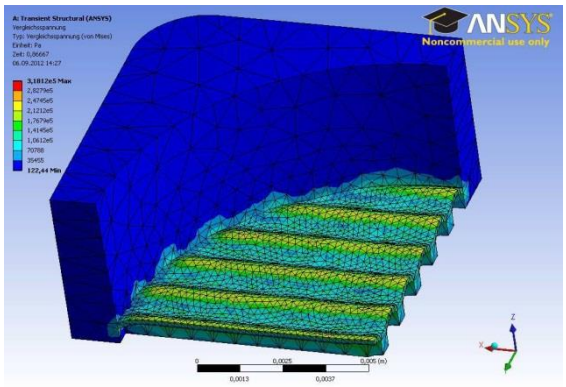

Fig. 3: FEM simulation of membrane bending due to pressure load.

3. Shear stress on epithelial cells

Endothelial cells living in the inner wall of blood vessels are loaded with shear stress from the blood flow. Shear stress aligns the cells parallel to the direction of flow. To mimic a blood vessel a PDMS-shaped culture vessel is designed with two parallel channels separated by a porous membrane. At the bottom of the upper channel a monolayer of endothelial cells is cultivated on the membrane. The bottom channel can be used to apply cell derived mediators to simulate an inflammation.

Fig. 4: Fluidic vessel made of PDMS to load adhered cells with shear stress due to flow of the liquid culture medium.

4. Influence of surface texture on cell growth

The structure and texture of biological environments of cells also influence the growth of cells, their adherence and their properties. In a first approach, we fabricated of trenches by reactive ion-etching with defined line and spaces in the mm-range in biocompatible polyimide films. (see figure 5). First culture experiments using mesenchymal stem cells show a dependency of cell growth of the texture of the underlying surface.

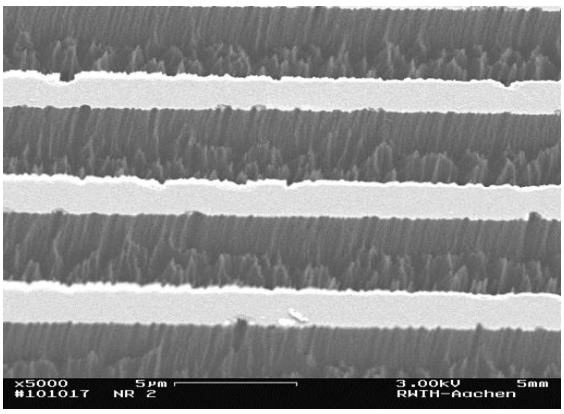

Fig. 5: Scanning electron microscope picture of a micro structured polyimide surface to investigate the influence of surface properties on cell development and growth.

References

[1] L. Ramms, G. Fabris, R. Windoffer, N. Schwarz, R. Springer, C. Zhou, J. Lazar, U. Schnakenberg, Th. Magin, R. Leube, R. Merkel, B. Hoffmann: Keratins as main component for the mechanical integrity of keratinocytes. PNAS 110 (46) 18513-18518 (2013)

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