3D Laser Lithography in Biotechnology and Medical Engineering

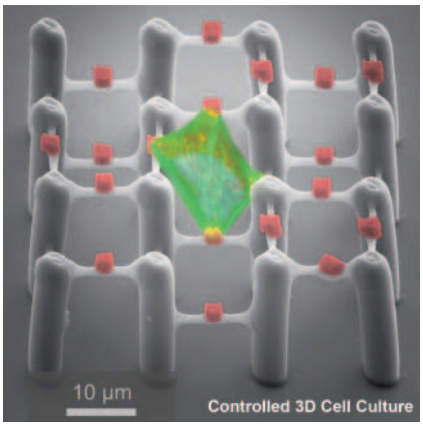
Cell Cultivation in the Third Dimension

There are limits to classic cell cultivation in a Petri dish. This is because in natural tissue, cells in an organism are normally in an extracellular matrix. A Petri dish cannot simulate these real environmental conditions. A remedy is provided by the described method, which has been utilized by scientists at the Karlsruhe Institute of Technology (KIT). Using 3D laser lithography, freely structured and flexible structures can also be created in a three-dimensional, reproducible way. This means that cells can colonize a specially reproduced spatial matrix.

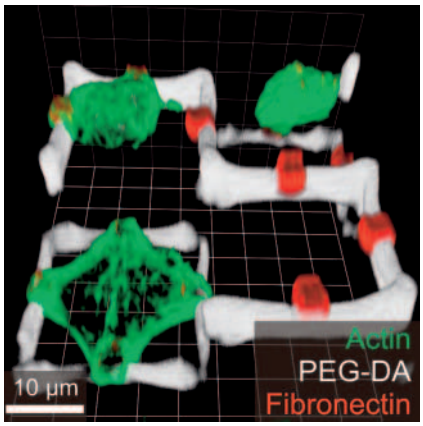
The structure itself consists of 25 µm high posts that are connected with thin rungs at different heights. This basic structure consists of a protein-repellent polymer. In addition, "handholds" or "docking sites" made of a protein-binding photopolymer are located in the middle of the rungs for the cells. Cells can attach here in a defined manner. Such a matrix opens up numerous new possibilities. In this way, the influence of the physical environment (stiffness and architecture) on stem cell differentiation or cell migration can be investigated. Forces can be measured, and reactions to various stimuli can be observed and analyzed. The results include findings on tissue regeneration or the influence of active pharmaceutical ingredients on wound healing, for example.

Nanoscribe GmbH has developed a laser lithography system that can be used to realize complex three-dimensional structures in a fully automatic and reproducible way with a previously unavailable design flexibility on submicrometer scales with structure widths of up to 150 nm and sizes of up to 1 mm. This makes it possible to create microstructures for small pumps and needles or to equip surfaces with particular biometric characteristics. Important keywords in this connection are gecko, lotus or salvinia effect. A typical area of application for 3D laser lithography is also the creation of three-dimensional structures for cell biology.

The driving force of the laser lithography system from Nanoscribe is the P-563 nanopositioning system from PI. This works with travel ranges of up to 300 x 300 x 300 µm³, with repeatability in the nanometer range. Highly linear capacitive sensors integrated in the positioning system provide the precise actual value acquisition that is necessary to move the sample precisely and repeatably in relation to the laser focus. These sensors directly detect the motion and thereby allow a higher phase reliability and bandwidth than indirect systems. A digital controller from PI provides the necessary path control.



Three-dimensional structure: cells dock on the "handholds" (Photo: B. Richter and M. Bastmeyer, Zoological Institute, Karlsruhe Institute of Technology (KIT))



This makes it possible to investigate the influence of the physical environment (stiffness and architecture) on stem cell differentiation or cell migration. (Photo: B. Richter and M. Bastmeyer, Zoological Institute, Karlsruhe Institute for Technology (KIT))

The fine adjustment of the sample is performed by the piezo system that has been integrated in the laser lithography system by Nanoscribe. (Photo: Nanoscribe)