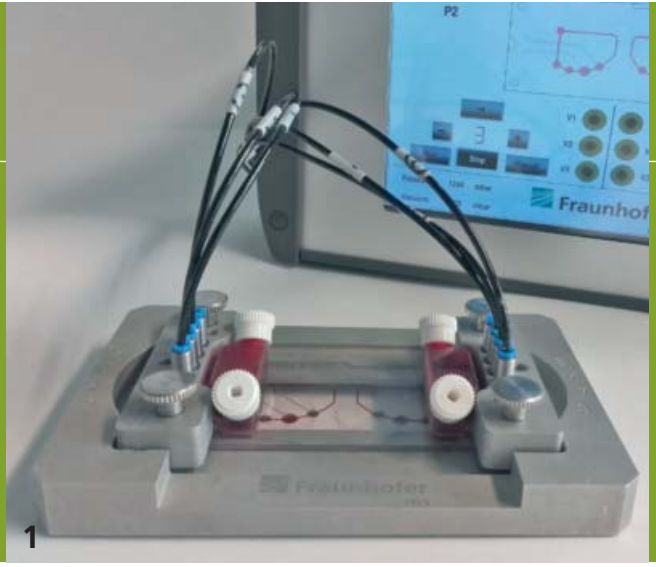


1

LASER-BASED CELL MANIPULATION IN MICRO PHYSIOLOGICAL SYSTEMS

THE TASK

Many diseases of human blood circulation and its associated organs, such as the kidney, result from damaged individual endothelial cells, which line the vascular system from the inside. Cell regeneration in interaction with the immune system plays a key role both in understanding and in curing these diseases.

Cell culture experiments in microphysiological systems are very suitable for the scientific exploration of both the underlying regeneration mechanisms and the interaction of the various cell types. Essential processes of the human body – such as blood flow of the cardiovascular system – are simulated by combining a technical pump system with the co-culture of human blood and vascular cells. The examination of the cell regeneration mechanism in such a system is carried out on vascular cells whose inner walls are damaged. Up to now the cells have been artificially damaged by means of a cannula or by chemical stimulation. These methods, however, cannot be applied to a closed cell culture system; one reason is the required high precision of the damage.

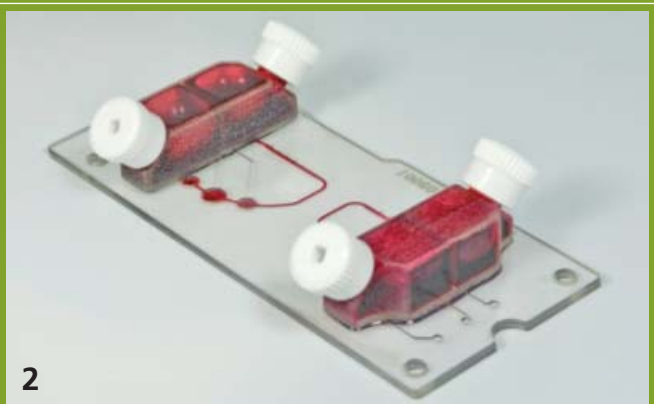
The Fraunhofer IWS Dresden had to manipulate – if possible, only partially – or damage selected cell regions in a defined manner in a closed microphysiological system that was inaccessible mechanically and from the outside. The course of the damage and the subsequent regeneration mechanisms had to be documented in parallel with images and videos.

OUR SOLUTION

A microphysiological basic platform (Fig. 1) for simultaneous cultivation of various cell types under conditions similar to those of the human body was developed at the IWS. This platform consisted of a controlling unit and a multilayer microfluidic system made of polymer films. A pump similar to the heart, cell culture segments and media reservoirs were integrated. The microfluidic platform was flexibly designed and can be adapted to several problems depending on the cell culture requirements.

A microphysiological system with a pump similar to the heart channels in which the inner surface is lined by endothelial cells, and circulating immune cells – so-called monocytes – was developed (Fig. 2) to examine the regeneration mechanisms of the human vascular system and its interactions with immunological cells. The damage induced by the laser can be traced easily by means of laser patterned position markers in the polymer film near the cell culture segments.

Laser sources with constant power were coupled into the beam path of a passing light microscope for defined selective damaging of cells. The setup developed makes it possible to optically inspect defined segments of microphysiological systems and to manipulate them intentionally by laser irradiation and monitor them on-line.



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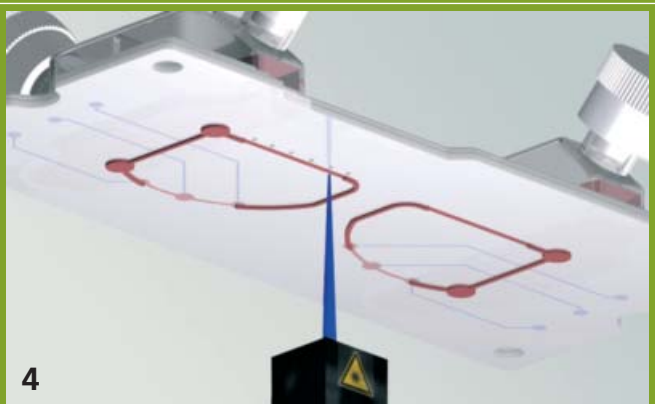


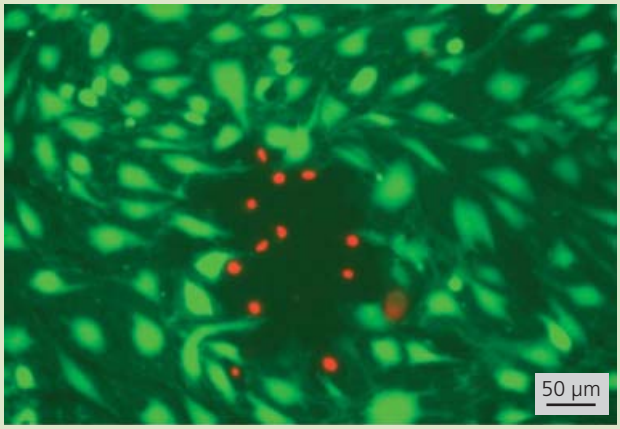
4

RESULTS

A defined cell structure in the closed vascular cell layer was damaged at several points by the microphysiological system in combination with the laser-based optical manipulation system. Based on the design of the microphysiological system, several points in the systems, which were marked before, can be damaged in a defined way (Fig. 4). The selective damage in a closed cell layer is shown in Figure 3.

Subsequent regeneration and the impact of the immune cells during this process were studied by means of time-lapse microscopy. The processes underlying the regeneration – proliferation of endothelial cells and the migration to the place of damage – can be examined with the setup and documented, and thus contribute to a better understanding of the complex interaction between immune and endothelial cells.

Selective damage (red) in a closed cell layer (green) of endothelial cells and monocytes



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As a next step, the developed system can be used to analyze how medications affect the regeneration process. These comparative studies may be based on reproducible intentional cell damaging in a defined way, by means of the technology developed.

1 Microphysiological basic system
2 Adapted microphysiological system for the co-culture
4 Laser-based damaging on a marked position in the microphysiological system

CONTACT

Dipl.-Ing. Florian Schmieder
☎ *+49 351 83391-3520*
✉ *florian.schmieder@iws.fraunhofer.de*