Website address:
https://www.gesundheitsindustrie-bw.de/en/article/news/the-adhesion-of-cells-to-the-endothelium-and-to-artificial-surfaces

The adhesion of cells to the endothelium and to artificial surfaces

Professor Stefan W. Schneider from the Mannheim Medical Faculty is investigating the function of the vascular endothelium and its interaction with blood and tumour cells using microfluidics methods that enable him to measure the adhesion of cells to the walls of blood vessels under physiological flow conditions. As part of an interdisciplinary project, he is investigating the characteristics of wafer-thin surfaces covered with living cells, which are of importance for the biocompatible coating of implants and the development of biomaterials.

Prof. Dr. Stefan W. Schneider
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The decision to transform the Department of Dermatology, Venerology and Allergology at the Mannheim Medical Faculty into the internationally recognised "Mannheim Excellence Centre of Dermatology of the state of Baden-Württemberg" in close cooperation with the German Cancer Research Center in Heidelberg was closely linked with the creation of a new "Division of Experimental Dermatology". In 2008, the physiologist and dermatologist Professor Dr. Stefan Werner Schneider from the University of Münster was appointed professor of cellular differentiation and chair of the newly created division. Schneider's field of research covers the basic molecular and cell biological principles of skin diseases, in particular those related to dermato-oncological diseases, as well as the role vascular endothelial cells play in the interaction with blood cells and in the progression of tumours.

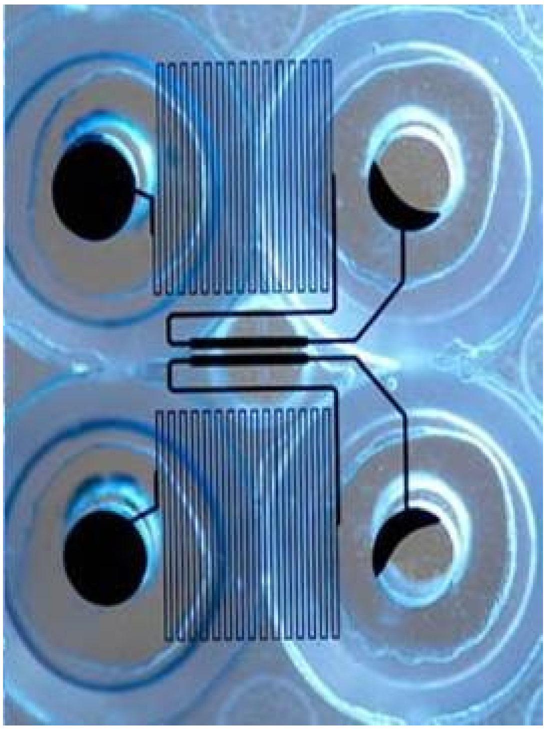
The vascular endothelium is the thin layer of cells that lines the interior surface of blood vessels, forming an interface and barrier between the blood in the lumen and the rest of the vessel wall. This unicellular layer controls the exchange of substances between circulating blood and tissue. The endothelium, which consists of innumerable blood vessels and bifurcations, has a surface area of

5,000 m2 in adults. This corresponds approximately to the size of a football field and is several thousand times larger than the surface of the human skin. Since the endothelium is microscopically thin, its total weight corresponds to only around one tenth of the weight of the human skin; however, the vascular endothelium has a similar mass as that of the liver, which is one of the largest internal human organs.

The measurement of cell flow and adhesion on the micrometre scale

Prof. Schneider has an outstanding reputation in research focusing on the functions of the vascular endothelium. Using microfluidics methods that he has partially developed in cooperation with other researchers, Prof. Schneider is able to generate the laminar flow (streamline flow, without giving rise to turbulence) of fluid of only a few microlitres in volume and measure the shear forces occurring at the surface of blood vessels. Using such standardised flow chamber systems, Schneider has been able to simulate the physical conditions that occur when blood circulates in small blood vessels only between 0.01 and 0.02 millimetres in diameter as well as measure and quantify the adhesion of tumour cells, leukocytes and thrombocytes (blood platelets) to the endothelium under near physiological conditions.

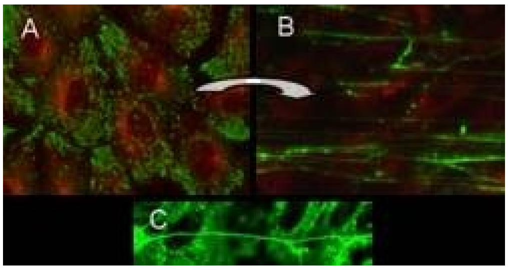
Such measurements enable researchers to gain new insights into the interactions between blood cells – for example thrombocytes and leukocytes – and vascular endothelium and contribute to improving our understanding of inflammatory processes and blood coagulation disorders. The measurements are also of great importance for analysing the interaction between tumour and endothelial cells in the bloodstream as well as for analysing the early stages of tumour progression and metastasis (the adhesion of tumour cells to the wall of the blood vessels, the penetration of the wall and subsequent infiltration of the surrounding tissue).



Pneumatically driven microfluidics system ("Bioflux") that enables the standardised testing of small volumes under shear flow on endothelial layers and functionalised surfaces.

The researchers of the Division of Experimental Dermatology specifically combine basic cell biology and cell dynamics research with biophysics and medical technology developments. The microfluidics measurements carried out by Professor Schneider and his team involve the use of small air-pressure driven flow chambers for controlling the continuous flow of fluid. In addition, in cooperation with researchers from the Institute of Biophysics at the University of Augsburg, Schneider's team also uses a contact-free surface acoustic wave-driven system (SAW) to control the flow of very small volumes of fluid. On his website (external link: www.umm.de/1426.0.html), Professor Schneider describes the different flow chamber systems used to simulate the different conditions under investigation. The systems enable the researchers to directly investigate cultured endothelial cells and functionalised surfaces under flow conditions using microscopes and molecular biology methods. The "artificial blood vessels" also enable the researchers to simulate pathophysiological flow conditions such as stenoses (narrowing of blood vessels, in particular those associated with arteriosclerosis), bifurcations or turbulent flow.

Communication and interaction between tumour cells and endothelium in the bloodstream



Endothelial cells under flow: A: Prior to stimulation, vWF (von Willebrand factor, green) is found inside the Weibel-Palade bodies (WPB). B: vWF is released within seconds of stimulation and stretched (green – extracellular vWF; red – intracellular vWF). C: The strongly adhesive vWF threads form a network structure.
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Under physiological conditions, the vascular endothelium maintains the blood flow; when activated by malignant tumour cells, vascular endothelial cells play a central role in the mechanisms that contribute to the inflammation-induced activation of coagulation. Within just a few seconds of their activation, the endothelial cells release (a process known as exocytosis) the content of special storage granules (Weibel-Palade bodies, WPB) into the blood, including different inflammation factors such as interleukin 8 and a large polymeric protein known as von Willebrand factor (vWF) that plays a key role in the coagulation of blood.

Exposed to the shear flow of the blood, released vWF proteins form thread-like structures up to one millimetre long that adhere to the surface of the endothelial cells where they are able to bind thrombocytes as well as tumour cells. The adhesion of the vWF proteins to the endothelial cells enables the tumour cells to invade the surrounding tissue, a process known as extravasation. The researchers from Mannheim are investigating the adhesion and migration behaviour of tumour cells and their interaction with vWF under flow conditions that mimic the physical conditions that prevail in the microenvironment of tumour-activated endothelial cells. Life cell imaging involves the use of high resolution microscopy methods such as reflection interference contrast microscopy (RICM) and fluorescent microscopy.

Biocompatible surface coating of medical devices and implants

In a DFG (German Research Foundation)-funded project, in which the Mannheim researchers are working with physicists and medical doctors from the University of Augsburg and the two universities in Munich, Professor Schneider focuses on the “quantitative evaluation of static and dynamic cell adhesion and cell activity on antibacterial DLC layers for biomedical application”. DLC (diamond-like carbon) are wafer-thin materials that display some of the typical properties of diamond (hardness, wear resistance, slickness); they are highly chemically resistant and are physiologically harmless. They are particularly suitable for protecting medical instruments and implants (e.g. stents) against corrosion as they do not release allergy-causing ions (such as nickel) and can be sterilised using routine sterilisation methods.

Researchers at the Institute of Physics at the University of Augsburg use plasma immersion ion implantation methods to produce such antibacterial, biocompatible coatings that are subsequently cultured with different living cells. In order to be able to precisely measure the adhesion of the cells to different implant surfaces, the researchers have developed a biochip on which the cells are exposed to a precisely defined fluid flow generated by surface acoustic waves (SAW). The growth of the cells and the antibacterial efficiency of the modified DLC coatings are investigated biologically and biomechanically by Professor Schneider’s team at the Mannheim Medical Centre. In addition to being used in biomedical applications, the novel biochip is also suitable for the rapid screening of biomaterials.

Further information:
Prof. Dr. med. Stefan Werner Schneider
Head of "Experimental Dermatology"
Department of Dermatology, Venerology and Allergology
Mannheim Medical Centre and Mannheim Medical Faculty of Universität Heidelberg
Theodor-Kutzer-Ufer 1-3
68167 Mannheim
Tel.: +49 (0)621/ 383 6902
E-mail: stefan.schneider(at)medma.uni-heidelberg.de

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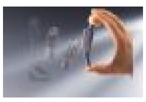

Implants of the future: bioactive, corrosion-resistant and antibacterial