Observing Living Cells in Their Three-Dimensional Environment

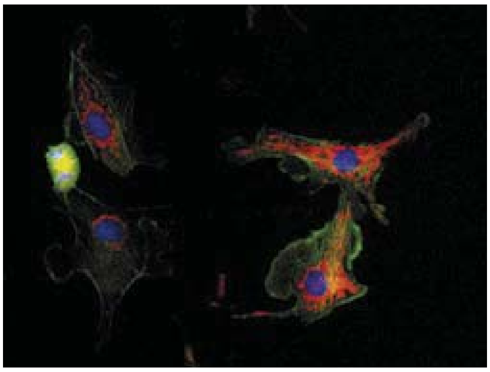
"3D-Tissue Screen" project lays foundations for further investigation of cardiac arrhythmia and Alzheimer's disease

Novel insight into the three-dimensional networks of living cells was gained within the "3D-Tissue Screen" research project. With a new microscope for live-cell imaging, the research network was able to observe complex dynamic processes in cardiac muscle cells at an unprecedented speed. This lays the foundation for a better understanding of cardiac diseases. A second microscope setup helped explore the mechanisms of Alzheimer's more precisely than before.

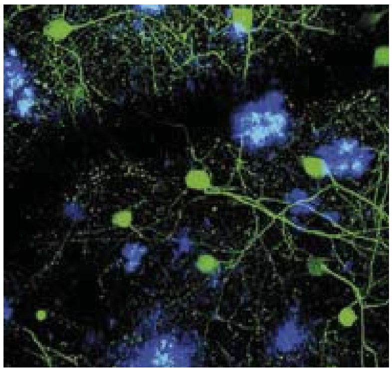
A better understanding of the causes and mechanisms of diseases is considered as a key to the development of novel, targeted therapies. Here, light microscopy is an ideal tool as it allows to study the functional interaction of molecules and structures in their native environment, i.e. in living cells and tissues. While commercial microscopes are not optimized for automated high-throughput applications in live cell research, the research network has investigated and validated several concepts as a basis for a suitable 3D reader platform. The functional model allows to keep living cells in their native three-dimensional environment by using special cell chambers, to manipulate them e.g. by electrical stimulation, and to observe their behavior in great detail. The concept is tailored for high sample throughput and combines several microscopic technologies, including laser scanning, fluorescence lifetime measurements, and marker-free quantitative phase contrast microscopy using digital holography. Under the guidance of Prof. Dr. Rainer Uhl (TILL Photonics GmbH/LMU Munich), five industrial partners and six research partners contributed their expertise. They could demonstrate the benefits of their novel solutions in a number of applications.

Understanding cardiac arrhythmia: At Saarland University, the 3D reader platform was optimized and applied for the investigation of cardiac muscle cells. Using its 3D cell model of human cardiac myocytes, the Institute of Molecular Cell Biology (MCB) explores cellular origins and mechanisms of cardiac arrhythmia in order to find novel approaches for pharmacological therapies.

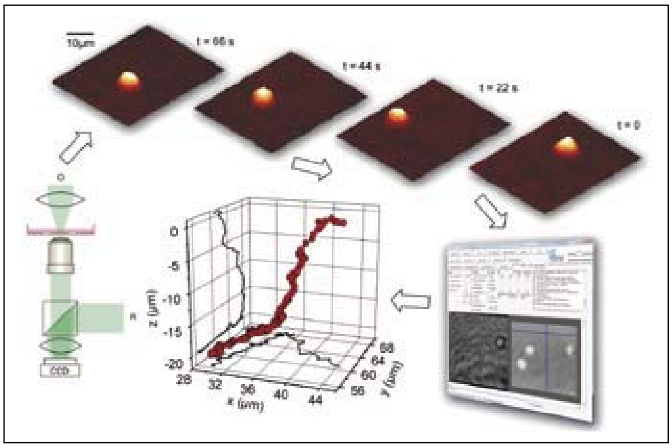
Migrating cells: The three-dimensional movement of red blood cells was observed at the Center of Biomedical Optics and Photonics at Muenster University, using the novel microscope together with a module for digital holography. This imaging procedure is especially gentle on the cells, as it does not require to treat them with fluorescence markers, and might provide further insights into the directed motion ("chemotaxis") of cancer cells in the future.



Heart muscle cells imaged with the new reader platform. (Courtesy of Saarland Univ., MCB)



Amyloid plaques (blue) between the neurons of transgenic Alzheimer's mice. (Courtesy of LMU Munich, ZNP)



Digital holographic 3D-cell tracking of sedimenting red blood cells. (Courtesy of Muenster Univ., CeBOP)

Alzheimer plaques: As an additional setup, a two-photon intravital microscope was assembled at the LMU Munich, Center of Neuropathology and Prion Research (ZNP). It enabled the scientists to study mechanisms of Alzheimer's disease more exactly than before. Now they assume that the characteristic Alzheimer plaques in the brain grow slower than expected so far.

Other applications explored in the course of the project include two-photon endoscopy for intraoperative tissue diagnostics and the investigation of plant root cells for ecological pest control. The research network is active since May 2007. While several partners successfully concluded their projects in fall 2009, the functional model and its components are still being optimized. After project wrap-up in April 2010, TILL Photonics plans to refine them into a marketable system. The German Ministry of Education and Science (BMBF) has supported the research project with about 3.3 Million Euro; another 2.2 Million Euro were invested by the involved companies.

List of the 11 project partners:
www.biophotonik.org
Project coordinator:
Prof. Dr. Rainer Uhl,
TILL Photonics GmbH,
E-mail: rainer_uhl@me.com