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Press release

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Super Resolution Microscopy for Pharmaceutical Industry: Patents granted for 3D complex labeling

Mechanism of action of drugs in body cells becomes transparent - The LIMON 3D microscopy (LIght MicroscOpical Nanosizing) of Prof. Dr. Dr. Christoph Cremer opens new possibilities for pharmaceutical research. 3D molecular complexes so-called biomolecular machines, targets of drugs can thus be studied in vivo. "By means of these issued patents, our super resolution microscopy is especially important for molecular biotechnology and the pharmaceutical industry, with emphasis on target identification and personalized medicine," according to Dr. Andrea Nestl, innovation manager of the Technology Licensing Office (TLB) and responsible for the patent management and the commercialization.

Biomolecular machines (BMM) are highly complex nanostructures consisting of several large molecules and which are responsible for basic functions in the body cells. Depending on their functional status they have a defined 3D structure. Examples of biomolecular machines are nucleosomes which enable the DNA, a two meter long carrier of genetic information, to fold in the body cells in a space of a few millionth of a millimeter in diameter only. Therefore, the DNA can serve as an information and control center.

By using Professor Christoph Cremer`s LIMON 3D in combination with LIMON complex labeling it is possible for the first time to make hidden proteins or nucleic acids of a 3D-molecule complex of the so-called biomolecular machines visible without destroying the complex. Up to now, the problem in most cases was that the complex had to be destroyed for detailed analysis of the individual macromolecules therein. Alternatively, virtual computer simulation models or expensive nuclear magnetic resonance methods were used to visualize the three-dimensional structure of such complexes.

The issued LIMON patent family allows the identification and the spatial positioning of individual components of the complex in its original native i.e. in a biologically relevant composition.

Besides the usual labeling of a macromolecule with a single fluorescent molecule, LIMON offers the option to label the target molecule with a variety of fluorescent markers of the same type in order to highlight several different areas. This is especially important for the investigation of such complexes in which not all binding sites for labeling probes are accessible, and thus it is difficult to visualize the individual partners.

“The pharmaceutical industry can trace in this way the interactions of biomolecular machines with pharmaceutically active compounds specifically and answer fundamental mechanistic questions about drugs”, according to Dr. Andrea Nestl, responsible for the development of patenting and marketing strategy on behalf of the University of Heidelberg. The mechanism of drug action in the cells becomes thus transparent, and the expensive development of drugs, which reaches the region from 500 million up to 2 billion U.S. dollars and usually lasts for 10 to 12 years, can take place in less time, and additionally, it is less cost-intensive.

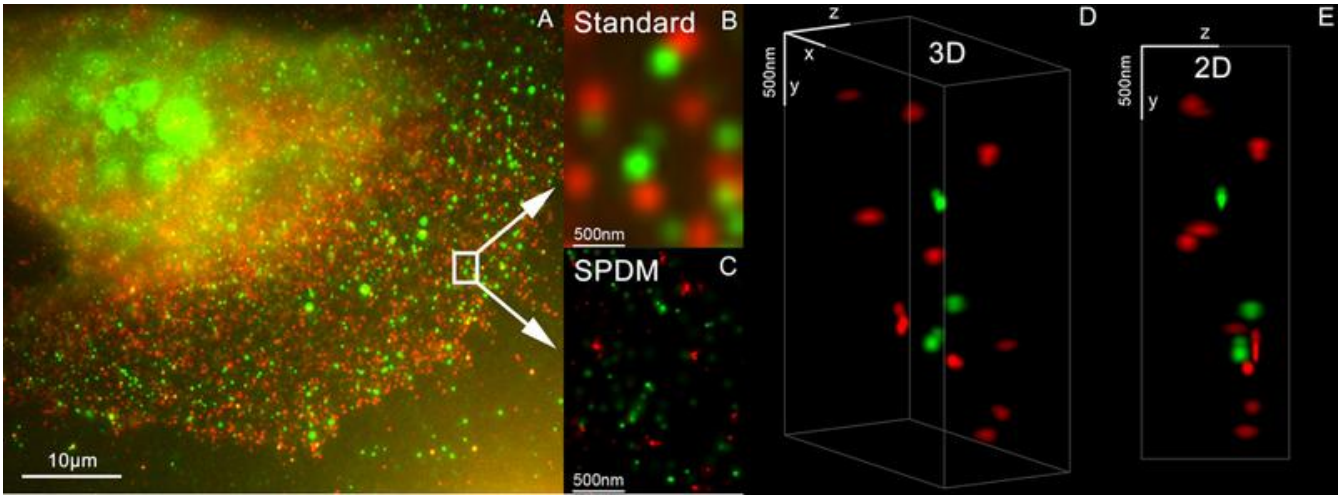
The 3D Super Resolution Microscopy LIMON is an excellent tool for the development and validation of therapeutically active substances. As an example for the importance in pharmaceutical industry by using LIMON, it was possible for the first time to investigate in detail the gene product which is responsible for 20 percent of inherited metastatic breast cancer. The aim is the patient-specific optimization of the existing Herceptin therapies.

Due to individual genetic equipment patients with an identical diagnosis often respond very differently to treatment with the same medicine. Personalized medicine considers and takes into account all diagnostic possibilities for characterizing the personal particularities. Thus the Super Resolution Microscopy LIMON patents will offer a significant contribution. The results of this breast cancer study were recently published in the notable Journal of Microscopy (Rainer Kaufmann, Patrick Müller, Georg Hildebrand, Michael Hausmann and Christoph Cremer: Analysis of Her2/neu membrane protein clusters in different types of breast cancer cells using localization microscopy Journal of Microscopy 242: 46-54 (2011).

To realize the 3D LIMON Super Resolution Microscopy Professor Christoph Cremer combines two of his 2D Super Resolution Microscopy methods: the localization microscopy SPDM (Spectral Precision Distance Microscopy) and the structured illumination SMI (Spatially Modulated Illumination), both patented by TLB as well. The main LIMON patents are issued in Europe and in the USA. With this European divisional patent application the third member of the LIMON patent family is being granted.

Christoph Cremer is full Professor and Chair of Applied Optics and Information Processing at the Kirchhoff Institute of Physics, and the Institute of Pharmacy and Molecular Biotechnology (IPMB), both at the University of Heidelberg, and he is group leader in the field of Super Resolution Microscopy at the Institute of Molecular Biology gGmbH (IMB) at the University of Mainz. In addition he is scientific member of the US-American Jackson Laboratory in Bar Harbor / Maine. Professor Christoph Cremer is longtime coordinator of the BMM-network "Biomolecular Machines / Biomolecular microscopy" of the Rhine-Neckar bioregion, where numerous working groups in Heidelberg participated in the in the fields of medicine, mathematics / computer science, chemistry, pharmacy, physics and biology. Objective target is the quantitative analysis and modeling of "biomolecular machines" outside the cell and within the living cell itself.

URL for press release: http://www.tlb.de/uploads/tx_mmtecdocs/Super_resolution_microscopy_Cremer_2011.pdf



In pharmaceutical research, target identification and personalized medicine the super resolution microscopy method LIMON (combination of SPDM and SMI) will play an important role in the future. Picture: 3D nanoscopy of breast cancer with Her3 and Her2, target of the breast cancer drug Herceptin