Press Release

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Freiburg, 09.12.2016

Watching Individual Proteins at Work

Research team presents new approach for observing structures and movements of complex molecules

Scientists at the University of Freiburg and the Technical University of Munich have developed an approach for gaining new insight into the dynamics of complex molecules, using the heat shock protein Hsp90 as an example. Hsp90 consists of several functional and structurally independent domains. Among other things, they interact with regulators of cellular metabolism, such as the protein p53. Up to now, scientists have only managed to produce either high-resolution static images or low-resolution moving images of complex molecules like Hsp90. Now the team in Freiburg and Munich has succeeded in producing high-resolution moving images of Hsp90 at work with the help of fluorescence. In the process, the scientists discovered that substrate proteins can control the movements of Hsp90. The researchers present their work in the current issue of the journal *Nature Methods*. “We are convinced that our method will soon be an indispensable tool in structural biology for analyzing proteins,” says Prof. Dr. **Thorsten Hugel** from the University of Freiburg’s Institute of Physical Chemistry.

The molecular chaperone Hsp90 helps regulate many fundamental processes in human cells. Among other things, it plays a crucial role in the folding of simple amino acid chains to form functioning proteins with a defined structure. To enable Hsp90 to fulfill its duties, the individual domains need to cooperate with different proteins. Hugel and his team aim to produce a dynamic image of this cooperation among proteins in real time. They are

thus working on developing new methods for imaging and analyzing the relevant processes at high speed.

Scientists have previously limited their focus to just a few of the states Hsp90 can assume – for instance open and closed. The results of the Freiburg and Munich researchers demonstrate that this focus needs to be extended to include a dynamic perspective: The goal is to describe possible structural ensembles in greater detail, especially with regard to the temporal dimension (see illustration).

Thorsten Hugel has been receiving a 1.9-million-euro Consolidator Grant from the European Research Council (ERC) since the start of the year to conduct his research. In addition, the physical chemist is an associated member of the University of Freiburg's Cluster of Excellence BIOSS Centre for Biological Signalling Studies.

Original publication:

Björn Hellenkamp, Philipp Wortmann, Florian Kandzia, Martin Zacharias, Thorsten Hugel: Multidomain structure and correlated dynamics determined by self-consistent FRET networks. In: Nature Methods.
doi:10.1038/nmeth.4081
www.nature.com/nmeth/journal/vaop/ncurrent/full/nmeth.4081.html

Article in the university newspaper *uni'leben* on Thorsten Hugel's research on HSP90:

www.pr2.uni-freiburg.de/publikationen/unileben/unileben-2016-1/page1.html#/6

Caption:

Dynamic ensemble: The illustration shows an ensemble of possible structures the molecular chaperone Hsp90 can assume within its open state. The newly developed method allows scientists to determine not just the structure of such ensembles but also their dynamics, i.e., the timescale of the structural changes they undergo.
Source: B. Hellenkamp, F. Kandzia, and W. Schürmann

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