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Molecular Force Sensors

Proteins are often considered as molecular machines. To understand how they work, it is not enough to visualize the involved proteins under the microscope. Wherever machines are at work mechanical forces occur, which in turn influence biological processes. These extremely small intracellular forces can be measured with the help of molecular force sensors. Now researchers at the Max Planck Institute of Biochemistry in Martinsried have developed molecular probes that can measure forces across multiple proteins with high resolution in cells. The results of their work were published in the journal *Nature Methods*.

When proteins pull on each other, forces in the piconewton range are generated. Cells can detect such mechanical information and modulate their response depending on the nature of the signal. Adhesion proteins on the surface of cells, for instance, recognize how rigid their environment is to adjust the protein composition of the cell accordingly. To measure such tiny forces, the group of Molecular Mechanotransduction at the Max Planck Institute is developing molecular force sensors. "These small measuring instruments work along the lines of a spring scale," says Carsten Grashoff, head of the research group.

The innovative probes consist of two fluorescent molecules that are connected by a sort of molecular spring. When a force of just a few piconewton acts on the molecule, the spring stretches, and this change can be detected using a special microscopic method. "We're now able to measure the mechanics of several molecules simultaneously," Carsten Grashoff explains. In contrast to previous experiments, the scientists are not only able to determine which proteins, but also how many of them are under force at any given moment.

"In a tug-of-war, many people pull on a rope with different strengths. Some may take it easy and let the person in front do the work. Proteins work in a very similar manner. We can now determine which proteins contribute to cellular force development and what percentage of those molecules are actually involved," Grashoff explains. Moreover, the force sensitivity has been improved, with the method allowing precise measurements in the range of three to five piconewton. "As with the development of new microscopes, we are striving to attain ever better resolutions, and that is what we have achieved here," Grashoff continues.





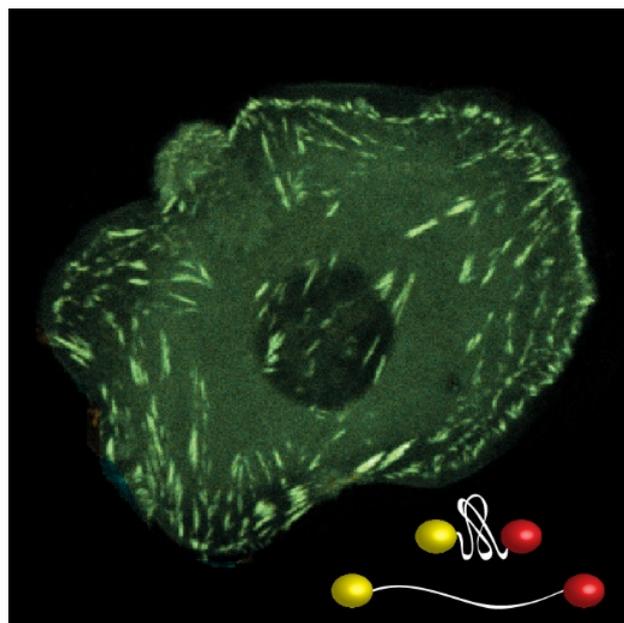
Thanks to the universal nature of cellular mechanics, the new sensors should be valuable to address a whole range of biological research questions. "Cancer research is an obvious field of application, since it has long been known that tumour cells have advantages in rigid tissues. The sensors could also give new insights into the mechanisms underlying muscle and skin diseases," Grashoff predicts.

About Carsten Grashoff

Carsten Grashoff studied applied sciences at the University of Freiberg from 1997 to 2001. After completing his diploma thesis at the Robert Koch Institute in Berlin, he gained his doctorate in 2007 from Ludwig Maximilian University in Munich. This was followed by a postdoctoral stint at the University of Virginia in the USA. Since 2011, he has headed the independent Molecular Mechanotransduction Research Group at the Max Planck Institute of Biochemistry in Martinsried. In 2014 Grashoff received the Early Career Award of the National Academy of Sciences.

About the Max Planck Institute of Biochemistry

The Max Planck Institute of Biochemistry (MPIB) belongs to the Max Planck Society, an independent, non-profit research organization dedicated to top level basic research. As one of the largest Institutes of the Max Planck Society, 850 employees from 45 nations work here in the field of life sciences. In currently eight departments and about 25 research groups, the scientists contribute to the newest findings in the areas of biochemistry, cell biology, structural biology, biophysics and molecular science. The MPIB in Munich-Martinsried is part of the local life-science-campus where two Max Planck Institutes, a Helmholtz Center, the Gene-Center, several bio-medical faculties of two Munich universities and several biotech-companies are located in close proximity. (<http://biochem.mpg.de>)





Caption:

The development of novel, fluorescence-based biosensors, which unfold in response to mechanical loads, allows the evaluation of molecular forces across specific structures within living cells.

Original Publication

P. Ringer, A. Weißl, A.-L. Cost, A. Freikamp, B. Sabass, A. Mehlich, M. Tramier, M. Rief and C. Grashoff
"Multiplexing molecular tension sensors reveals piconewton force gradient across talin-1" *Nature Methods*, September 2017

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