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dr. christiane menzfeld

phone: +49 89 8578-2824

menzfeld@biochem.mpg.de
www.biochem.mpg.de/news
@MPI_Biochem

Two molecular machines caught in the act with the electron microscope

Scientists at the MPI of Biochemistry have for the first time succeeded in determining the structure of the interaction of two large molecular machines. In cooperation with researchers from the Heidelberg University, they investigated the interaction between the ribosome and the exosome. Ribosomes use ribonucleic acid (RNA) as blueprint for the production of proteins. The exosome in turn is responsible for the degradation RNA. The study of the interaction of two molecular machines using cryo-electron microscopy provides a better insight into the physiological functioning of such machines. The study was published in *Science*.

Ribosomes, the protein factories of the cell, assemble protein building blocks into long chains based on a construction manual, the messenger RNA or mRNA. These chains are later folded into the protein. Faulty mRNA or RNA that is no longer needed must be degraded. This task is performed by the exosome. Previous studies have investigated the destructive function of the exosome, which – comparable to a destruction worker – completely degrades the RNA. In contrast, the now published study had a closer look at the precision work, i.e. the constructive function, of the exosome.

The exosome's precision work

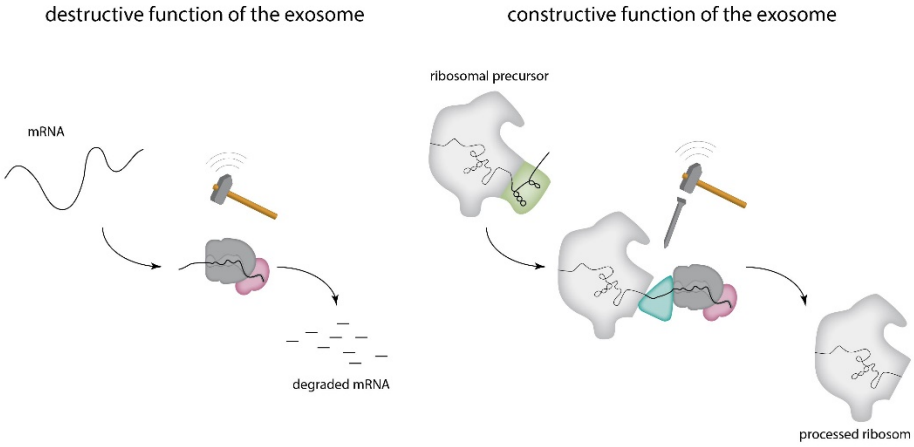
Ribosomes themselves are large protein complexes that must be produced in the nucleus. During this maturation process, the exosome binds to a precursor of the ribosome and selectively degrades a protruding part of the ribosome. A team of scientists led by Elena Conti, director of the "Structural Cell Biology" department at the Max Planck Institute of Biochemistry, and the University of Heidelberg have now been able to structurally investigate this interaction of exosome and ribosome. "This is comparable to the work of a stonemason who uses a hammer and chisel to remove stone in a targeted manner, thus creating a precise structure," explains Sebastian Falk, one of the first authors of the study alongside Jan Schuller.

Exosome and ribosome caught in the act

The researchers studied the two molecular machines by using the method of cryo-electron microscopy (cryo-EM), which was awarded the nobelprize in 2017. To this end, exosome and ribosome were shock-frozen together at very low temperatures. The scientists calculated the

structure from the cryo-EM data and combined it with crystal structures from previous studies from the Conti department to generate a model.
Exosome expert Elena Conti explains: “One of my long-standing goals was to capture a snapshot of the exosome with a cellular substrate.” Now, Conti and her team have essentially caught the exosome and ribosome as they interact and function together. "This study is the culmination of many years of hard biochemical and structural work," adds Conti.

A new area of structural biology
Previous studies in the field of structural biology have always focused on individual molecular machines. “We now succeeded for the first time to visualize two molecular machines together. Thus, we no longer looked at them individually in isolation, but investigated their interaction. With this we take the physiological environment into account, marking this study as the beginning of a new area in the field of structural biology”, Conti explains the significance of this publication.



Caption
The exosome is a barrel-shaped molecular machinery through which the mRNA is threaded before it is completely degraded at the bottom by a nuclease. In addition to the degradation of RNA, the exosome also has a function in the production process of the ribosomes. The exosome deliberately degrades a part of the precursor ribosome.
Sandra Schuller © Max Planck Institute of Biochemistry

Original publication:
J. Schuller, S. Falk, L. Fromm, E. Hurt, E. Conti: Structure of the nuclear exosome captured on a maturing preribosome, Science, März 2018
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About Elena Conti

Professor Elena Conti studied Chemistry at the University of Pavia in Italy. She received her PhD in Protein Crystallography at Imperial College, London in 1997. After a Postdoctoral fellowship in John Kuriyan's lab at The Rockefeller University, New York, USA, she was appointed Group leader at the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany in 1999. There she focused her research interest on mechanisms of RNA export to the cytoplasm and the structure and function of the molecular machines involved. Conti has followed the fate of RNA in the cytoplasm since then. She was appointed Director and Scientific Member at the Max Planck Institute of Biochemistry, Martinsried near Munich, Germany in 2006 where she leads the department of "Structural Cell Biology". Since 2007, she is Honorary Professor at the Ludwig Maximilian University in Munich. Conti received numerous awards, among others the Gottfried Wilhelm Leibniz Prize 2008 and the Louis-Jeantet Prize for Medicine 2014. More information you find here.

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, about 800 employees from 45 nations work here in the field of life sciences. In currently about 35 departments and 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 in close proximity to the Max Planck Institute of Neurobiology, a Helmholtz Center, the Gene-Center, several bio-medical faculties of the Ludwig-Maximilians-Universität München and the Innovation and Founding Center Biotechnology (IZB). (http://biochem.mpg.de)

Contact:

Prof. Dr. Elena Conti
Structural Cell Biology
Max-Planck-Institut für Biochemie
Am Klopferspitz 18
82152 Martinsried
E-Mail: conti@biochem.mpg.de
www.biochem.mpg.de/conti

Dr. Christiane Menzfeld
Public Relations
Max-Planck-Institut für Biochemie
Am Klopferspitz 18
82152 Martinsried
Tel. +49 89 8578-2824
E-Mail: pr@biochem.mpg.de
www.biochem.mpg.de