The Entrepreneurial University.

Technische Universität München

News Release

Munich, Feb. 19, 2010

Activation of heat shock protein explained:

Symmetrical protein activated by break in symmetry

Mucoviscidosis, a disease better known as cystic fibrosis, is the most common hereditary metabolic disease in Europe. The defective regulation of the heat shock protein Hsp90 by the partner protein Aha1 is a trigger of the disease. Scientists at the Technische Universität München (TUM) have succeeded in explaining the mechanism behind this reaction. They have reported their findings in the current edition of the journal Molecular Cell.

Every cell contains thousands of proteins. To control the life cycle of the cell, from division to death, the activities and lifespan of these proteins must be regulated. The heat shock protein Hsp90 plays a central role in this process. Hsp90 is a chaperone, a kind of “quality controller” that tests and monitors the quality and activity of numerous important signal proteins. If the cell is subject to a high level of stress, for example due to heat or oxygen deprivation, the production of this protein increases in order to limit the damage for other proteins.

The enormous complexity of the regulatory system of a cell is demonstrated by the fact that Hsp90 is also regulated by partner proteins. As evidenced by the example of cystic fibrosis, the disease also known as mucoviscidosis, this regulation is crucially important for the organism. It is known that this disease is reinforced considerably by the interaction between Hsp90 and a partner protein called Aha1. However, precisely how Aha1 influences the functioning of Hsp90 was unclear up to now.

Hsp90 is a protein composed of two identical symmetrical subunits. It was previously assumed that the two halves also work symmetrically, that is two Ah1 proteins are needed for its activation. At the TUM’s Department of Chemistry, a team of biochemists headed by Professor Johannes Buchner working in cooperation with Professor Horst Kessler’s group succeeded in explaining the mechanism for the activation of Hsp90 by its partner protein Aha1.

Surprisingly, the break in the symmetry of Hsp90 plays an important role in this process: The activation mechanism of Hsp90 works asymmetrically. The docking of an Aha 1 protein to two binding sites of an Hsp90 is sufficient to completely activate Hsp90. The researchers hope that in the long term the understanding of this mechanism could lead to the development of new approaches to the treatment of cystic fibrosis and other diseases, like cancer.

Technische Universität München Corporate Communications Center 80290 München www.tum.de

Dr. Ulrich Marsch	Head of Corporate Communications	+49.89.289.22779	marsch@zv.tum.de
Dr. Andreas Battenberg	Press Relations	+49.89.289.12890	battenberg@zv.tum.de
Patrick Regan	International Press Relations	+49 89 289 22743	regan@zv.tum.de

The Entrepreneurial University.

Technische Universität München

Publication:

Asymmetric Activation of the Hsp90 Dimer by Its Cochaperone Aha1 Marco Retzlaff, Franz Hagn, Lars Mitschke, Martin Hessling, Frederik Gugel, Horst Kessler Klaus Richter and Johannes Buchner Molecular Cell 37, 344–354, February 12, 2010, DOI: 10.1016/j.molcel.2010.01.006

Contacts:

Prof. Dr. Johannes Buchner
Technische Universität München
Department of Chemistry
Lichtenbergstraße 4
D-85748 Garching

Phone: +49 89 289 13341
Fax: +498928913345
Email: Johannes.Buchner@ch.tum.de
Website: http://www.chemie.tu-muenchen.de/biotech/index.html