



CECAD, University of Cologne

Press release

Scientists in Cologne identify important lysine-acetylation regulatory mechanisms for Ran protein

The team of scientists led by Dr. Michael Lammers at CECAD, the Cluster of Excellence at the University of Cologne, has discovered that the essential cellular protein Ran is fundamentally regulated by lysine acetylation. Ran belongs to the family of Ras proteins, which regulate fundamental cellular processes such as cell differentiation, cell division, and intracellular transport. Mutations in Ras-related proteins are involved in the development of various types of cancer including colorectal cancer, lung cancer, and lymphomas. Mechanisms that can switch off the functions of Ran protein are therefore of particular therapeutic interest.

Cologne, 12th August 2015. Discoveries made by scientists in Cologne lead to new perspectives in the treatment of colorectal cancer, lung cancer, and lymphomas. Dr. Michael Lammers and his research team at CECAD have identified new regulatory mechanisms for Ran protein. They have shown that all essential functions of the small GTP-binding Ran protein can be regulated by lysine acetylation. Ran is involved in many important cell processes including cell division and protein transport. Dysregulation of these processes has dramatic effects on normal cell development. Many types of tumor cells have increased concentrations of Ran or Ran-interacting proteins or Ran-regulators. Switching off Ran-function in a targeted manner, using the newly identified regulatory system, may provide novel therapeutic approaches.

The small Ran protein is a molecular switch that can be turned on or off depending on the nucleotide charge. If this switch protein is not regulated properly, there may be far-reaching effects on essential cell functions. Using high-resolution quantitative mass spectrometry, it

has recently been shown that many of many of the amino acids – the lysines – in the Ran protein can be modified by adding an acetyl group. Modifications of this type made to the folded protein, once biosynthesis is complete, essentially alter and regulate protein function. Some of the acetylation sites are to be found in highly relevant functional regions within the Ran protein.

Dr. Lammers: “With a combined synthetic biological, biochemical, and cell biological approach, we have shown that lysine acetylation regulates nearly all essential Ran functions – something that was completely unknown beforehand. For some of the sites, we have also been successful in identifying specific enzymes responsible to modify the protein in this way, adding and removing such modifications. These findings may allow us to develop novel agents for cancer therapy.”

Cancer is the second most common cause of death in industrialized nations and responsible for about 25% of all deaths. The risk of malignancy increases with age – which means that research into the development and treatment of cancer is of great economic and personal interest in an aging society. CECAD, the Cluster of Excellence at the University of Cologne, is carrying out research into aging and its associated diseases. CECAD’s vision is to develop new treatments for the entire spectrum of age-related diseases. Given this aim, the latest findings from Dr. Lammers and his team are of great import.

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