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Public Relations

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From cell division to ageing – scientists locate main cell switches

Protein function and gene expression are often regulated by reversible modifications of already existing proteins. Scientists from the Max Planck Institute of Biochemistry and the University of Copenhagen have now been able to prove that the reversible attachment of acetyl groups influences virtually all functions of human cells and therefore has a much greater importance than previously assumed. Whether it is cell division, signal transduction or ageing – all these processes are affected by acetyl groups acting as molecular switches. Therefore, these switches may prove to be a crucial factor in the development of new therapies against diseases like cancer, Alzheimer's or Parkinson's (Science, August 14th 2009).

Proteins can be regulated by small modifications that act as molecular switches and turn certain functions on and off. One of these reversible modifications is acetylation: acetyl groups are attached to proteins and can be removed again by certain enzymes, the so-called deacetylases. This process plays a key role in many cellular processes according to the scientists' report published in the current issue of the renowned journal "Science".

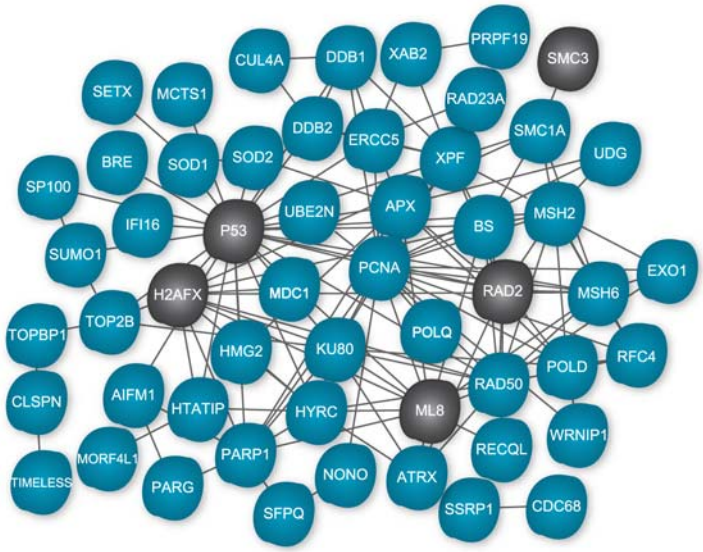
Using a specifically developed technology the scientists were able, for the first time, to search for acetylation sites in the whole protein inventory of the cell. All in all, they identified more than 3600 of these switching points in almost 1800 proteins – this proves that acetylation is much more important than previously supposed and that it has broad regulatory functions. "Our results have expanded the number of known acetylation switches by a factor of six, and give us for the first time a comprehensive insight into this type of modification", says professor Matthias Mann, director of the research department "Proteomics and Signal Transduction" at the MPI of Biochemistry.

Previously scientists believed that acetylation was mainly involved in regulation of gene expression. The new study shows that practically all cellular processes are influenced, e.g. cell division, DNA-repair or signal transduction – without acetylation cells could not survive. The significance of this process is highlighted by the example of Cdc28: This protein is necessary for the budding yeast. If the acetyl-switch of Cdc28 is defect, the yeast cell dies.

Defective protein regulation plays a role in the development of numerous diseases, therefore acetylation switches are promising target points for the development of new therapies. Especially in the treatment of cancer there are already successful medications based on the inhibition of deacetylases. Two of these drugs are presently in use against certain types of leukemia.

“Another process that is influenced substantially by acetylation is ageing”, explains Chunaram Choudhary, the first author of the study, who is now associate professor at the Novo Nordisk Center for Protein Research at the University of Copenhagen. Therefore manipulation of these molecular switches might also be a valuable tool for the treatment of age-related neurological diseases like Alzheimer’s or Parkinson’s.

Up to now, knowledge about acetylation in living cells was poor, despite its great biological and clinical significance. Due to their new technology, the scientists are now for the first time able to analyse comprehensively how acetyl-switches respond to drugs – especially with regard to the development of new medications this promises substantial progress.



Original Publication:
C. Choudhary, C. Kumar, F. Gnad, M.L. Nielsen, M. Rehmann, T. Walther, J.V. Olsen, M.Mann: Lysine acetylation targets protein complexes and co-regulates major cellular functions. Science, 14 August 2009.

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