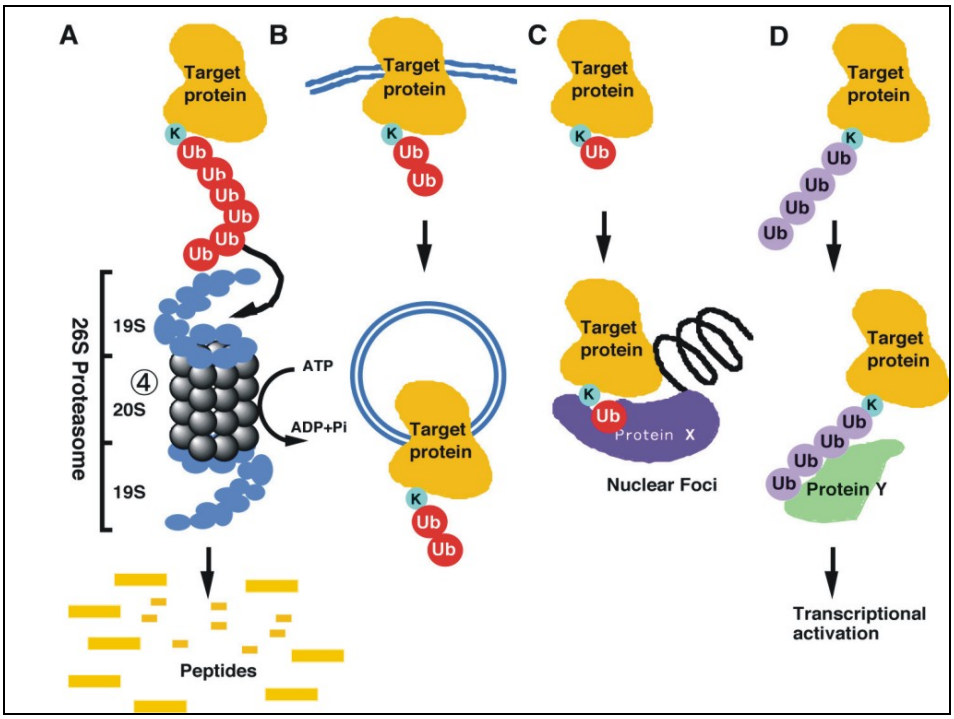
Ubiquitin research gains substantial EC support

The RUBICON Network of Excellence will work towards a better understanding of Ubiquitin-related diseases and the development of novel drugs

The European Commission has awarded a 12 Million Euro grant to foster the collaboration of European experts in the field of Ubiquitin research. A consortium of 15 leading research laboratories and five small and medium enterprises in the field are the founding members of a "Network of Excellence" on the "Role of Ubiquitin and Ubiquitin-like Modifiers in Cellular Regulation" – RUBICON. Prof. Maria Masucci, Karolinska Institutet, Stockholm, Sweden, will coordinate the Network. RUBICON plans to operate in various fields of research on Ubiquitin and Ubiquitin-like molecules to coordinate research, training activities, the joint use of state-of-the-art infrastructures, and the transfer of knowledge of basic cellular processes to drug discovery in research-industry collaborations.



An overview over the multiple functions of Ubiquitin-tagging of proteins in the cell. The addition of one or more Ubiquitin "tags" (red) to target proteins (yellow) labels the Ubiquitin-modified proteins for either (A) destruction to small peptides in the proteasome, the cell's degaradation machinery, (B) transfer into lysosome vesicles (blue) or (C) nuclear foci, or (D) interaction with other proteins (ProteinY, green) to regulate gene activity (transcriptional activation).

A pivotal role for Ubiquitin was first discovered in the analysis of protein degradation, the destruction of proteins within cells. The removal of proteins that are or no longer required in the cell is a strictly controlled process. Ubiquitin, which in itself also is a small protein, was identified as a "tag" used by cells to label molecules for destruction by the cell's "waste bin", the so-called proteasome. The elucidation of the basic mechanisms regulating the breakdown of proteins within the cell was recognised by awarding the Nobel Prize in Chemistry 2004 to three leading scientists in the field, Irwin Rose, Avram Hershko and Aaron Ciechanover. Meanwhile, it has become increasingly clear that the Ubiquitin system is highly complex,

both with respect to the number of „Ubiquitin-like“ (UbL) molecules identified and the wide array of cellular processes it controls. These include, among others, the regulation of the cell cycle, immune responses, signal transduction mechanisms, and the repair of DNA.

As may be expected from a system involved in such a variety of essential biological functions, defects in Ubiquitin-dependent processes are associated with various pathologic conditions. Consequently, the major goals of the RUBICON Network are (i) to understand the mechanisms of post-translational protein “tagging” by Ubiquitin and UbL molecules, (ii) elucidating its role in the regulation of basic cellular processes and (iii) establishing its link to diseases, such as infectious and inflammatory conditions, cancer, and neurodegenerative disorders such as Alzheimer’s and Parkinson’s diseases.

The findings expected from the joint multidisciplinary research performed within the frame of the RUBICON Network will result in a detailed knowledge of the molecules involved in Ubiquitin and UbL post-translational modifications and the molecular dissection of their interactions. This understanding will serve as a basis for an identification of suitable targets for the development of a new generation of therapeutics directed against malfunctioning components of the Ubiquitin/UbL system. This goal can be achieved by elucidating the functions of genes and gene products and by defining the regulatory networks through which they control biological processes.

The RUBICON Network of Excellence is the ideal instrument to coordinate and structure the research activities of a multidisciplinary consortium and will provide the platform for a transfer of knowledge from academia to biomedicine and the pharmaceutical industry. Within the Network, industrial partners are working hand in hand with academic researchers both at the levels of analysis and modelling of disease mechanisms and of drug discovery. Their close link with the academic research community will minimise the time required to translate the advancement of basic research into drug discovery.

In the five years to come, major activities within RUBICON will:

Strengthen training activities: RUBICON will provide multidisciplinary training for young researchers in the biomedical field through a training programme comprising lectures and methods courses in relevant areas of research and via multi-centre research projects, which will provide postdoctoral fellows with the opportunity of a multidisciplinary training in different Network laboratories.

Facilitate access to dedicated infrastructures, research tools and data: RUBICON will facilitate the access to advanced technologies by supporting the establishment of “core facilities” and will establish shared databases to include research results of common interest and a virtual repository for reagents of common usefulness.

Optimise communication: RUBICON will provide a communications platform for the exchange of knowledge within the network and with the research community via plenary network meetings and thematic workshops. A continuous dialogue between the Ubiquitin community and pharmaceutical industry will help to increase the understanding between researchers and manufacturers and will shorten the lead time from scientific discovery to product development. A “teaching programme” will increase awareness and interest in the area of Ubiquitin and UbL modifications and associated diseases. This will include lectures for the public and seminars by RUBICON members in schools to raise the interest in natural sciences at an early stage as well as contacts with stakeholders in the field.

Spread excellence: Once the framework of primary network centres and facilities has successfully been integrated into one research community, RUBICON will be open for expansion. At that stage, access to RUBICON facilities will be opened to the scientific community and new partners offering required complementary expertise will be admitted to the consortium.

The RUBICON Network of Excellence officially started operating on January 1, 2006 and was kicked-off during a meeting at Aske Kursgård, Stockholm, in March 2006.

RUBICON Partner Institutions:

1: Karolinska Institutet , SE
2: The Netherlands Cancer Institute , NL
3: University Medical Center Utrecht , NL
4: MRC Human Genetics Unit , UK
5: University of Dundee , UK
6: Institut Pasteur , F
7: CNRS , F
8: Max Planck Institute for Biochemistry , D
9: Georg-August-Universität Göttingen , D
10: University of Konstanz , D
11: Max-Delbrück-Center for Molecular Medicine , D
12: University of Stuttgart , D
13: IFOM – FIRC Institute of Molecular Oncology , I
14: Technion – Israel Institute of Technology , IS
15: The Hebrew University of Jerusalem , IS
16: Pepscan Systems BV , NL
17: Drug Discovery Factory , NL
18: Cytomics Systems , F
19: Biomol , UK
20: Proteologics , IS

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