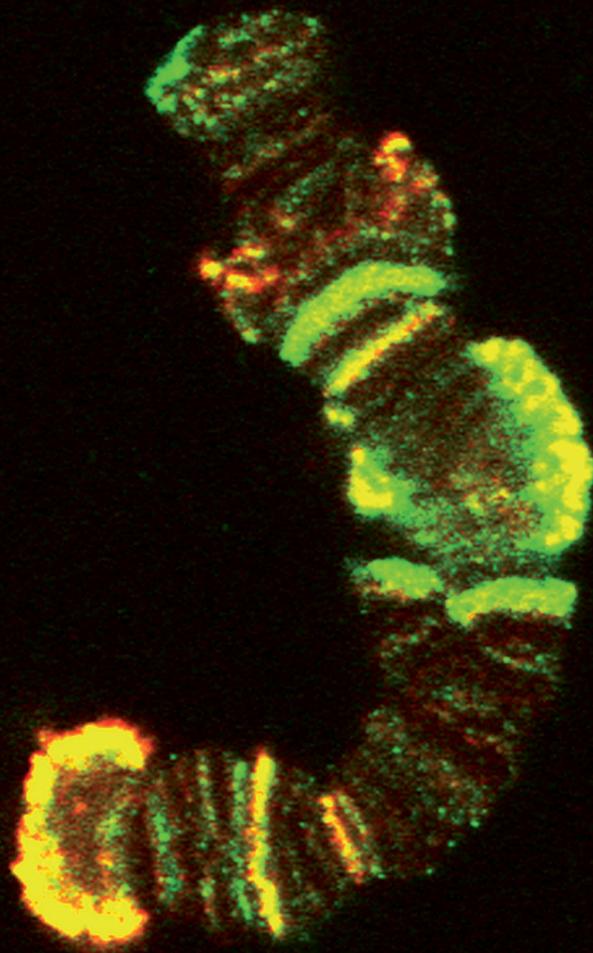


RNAQuality

Quality Control of Gene Expression –
RNA Surveillance



Scientific Goals of the RNAQuality Programme

Cells have developed multiple systems of quality control to ensure that they operate accurately. This also applies to the biogenesis and metabolism of various classes of RNAs, which only recently have been shown to be subjected to stringent surveillance mechanisms. Such systems target erroneous RNA molecules for degradation before irreversible cellular damage can occur. In particular, the presence of abnormally matured mRNA molecules might be detrimental to cells given their central role in protein synthesis. Surveillance mechanisms not only monitor RNA biogenesis in order to safeguard cells but are also implicated in the post-transcriptional regulation of wild-type transcripts and the elimination of accidentally damaged molecules. Post-transcriptional processes such as mRNA processing, export, localisation, silencing and turnover are interlinked by the use of common factors, which provide opportunities for quality control checkpoints. RNA quality control systems also modulate the clinical manifestations of many genetic disorders and hence represent promising targets for future therapeutic intervention.

Unravelling the molecular mechanisms underlying the growing number of discovered RNA quality control pathways and understanding how these systems are interconnected will be a major challenge. To address this, the ESF has launched the EUROCORES Programme RNAQuality. The Programme will focus on basic mechanisms of RNA quality control that operate at different levels of RNA biogenesis. Multidisciplinary approaches, ranging from molecular and cellular biology to structural analysis and high-throughput and computational approaches will be employed in diverse model systems.

In addition to its research component, the Programme offers a wide range of networking possibilities, providing training opportunities and establishing a platform for European researchers to join forces and to stimulate new research initiatives in this young and exciting field.

List of funded Collaborative Research Projects (CRPs)

Nuclear RNA surveillance of genome expression: From yeast to mammals

Transcription, processing and degradation of RNA, which traditionally have been studied as independent processes, are highly integrated. The complexity and speed of these reactions in vivo, together with the analytical challenges posed by the multiple alternative fates of many RNAs, requires the development of new approaches. This project aims at uncovering the mechanisms and rules governing RNA surveillance in the nucleus using a range of biological systems and methodologies, including yeast and mammalian cell genetics; yeast, insect and mammalian cell biology as well as systems biology.

Project Leader:

Torben Heick Jensen

University of Aarhus, Denmark

Principal Investigators:

Andrés Aguilera

University of Sevilla, Spain

Irene Bozzoni

CNR-IBPM, University of Rome "La Sapienza", Italy

Alain Jacquier

Institut Pasteur, Paris, France

Domenico Libri

CGM – CNRS, Gif-sur-Yvette, France

Nicholas Proudfoot

Oxford University, United Kingdom

David Tollervey

University of Edinburgh, United Kingdom

Neus Visa

Stockholm University, Sweden

The role of translational silencing complexes and mRNA degradation factors in RNA localisation in flies and mammals

It has only recently emerged that mRNA degradation factors also play an essential role in mRNA localisation and that mRNA transport is coupled to translational silencing. This project brings together two different fields that have not been connected previously: RNA localisation in oocytes and primary neurons and small RNA-guided gene silencing. Using complementary model systems, the team will combine biochemistry, genetics and cell biology approaches using advanced fluorescent microscopy techniques with proteomics to shed light on how RNA transport is linked to mRNA degradation and RNA silencing.

Project Leader:

Michael A Kiebler

Medical University of Vienna, Austria

Principal Investigators:

Gunter Meister

MPI Munich-Martinsried, Germany

Daniel St Johnston

University of Cambridge, United Kingdom

Functional and structural dissection of mechanisms targeting the exosome to cryptic and aberrant RNAs

The mechanisms underlying the recruitment of exosomes for the selective degradation of defective RNA molecules are poorly understood. This project aims at providing a structural and functional framework to understand the role of the exosome in RNA surveillance. The multidisciplinary study will combine molecular biology approaches with native mass spectrometry, structural analyses by electron microscopy and small angle X-ray scattering. The innovative combination of approaches is expected to be widely applicable in the future to decipher mechanisms involved in cellular processes in general.

Project Leader:

Bertrand Séraphin

CGM – CNRS, Gif-sur-Yvette, France

Principal Investigators:

Carol Robinson

University of Cambridge, United Kingdom

Andrzej Dziembowski

Warsaw University, Poland

Patrice Vachette

University Paris-Sud, France

Helen Saibil

Birkbeck College, London, United Kingdom

The aim of the European Collaborative Research (EUROCORES) Scheme is to enable researchers in different European countries to develop collaboration and scientific synergy in areas where European scale and scope are required to reach the critical mass necessary for top class science in a global context.

The scheme provides a flexible framework which allows national basic research funding and performing organisations to join forces to support excellent European research in and across all scientific areas.

The European Science Foundation (ESF) provides scientific coordination and support for networking activities of funded scientists currently through the EC FP6 Programme, under contract no. ERAS-CT-2003-980409. Research funding is provided by participating national organisations.

www.esf.org/eurocores

THE FOLLOWING NATIONAL FUNDING ORGANISATIONS SUPPORT THE RNAQuality PROGRAMME:

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Forschung in Österreich (FWF)**

Austrian Science Research Fund, Austria

Forskningsrådet for Natur og Univers (FNU)

*Danish Natural Science Research Council,
Denmark*

**Centre National de la Recherche
Scientifique (CNRS)**

National Centre for Scientific Research, France

Max-Planck-Gesellschaft (MPG)

Max Planck Society, Germany

Consiglio Nazionale delle Ricerche (CNR)

National Research Council, Italy

Ministry of Education and Science

Poland

Ministerio de Educación y Ciencia (MEC)

Ministry of Education and Science, Spain

Vetenskapsrådet (VR) – Medicine

*Swedish Research Council – Medicine,
Sweden*

**Biotechnology and Biological Sciences
Research Council (BBSRC)**

United Kingdom



Chironomus tentans: Co-localisation of the RNA Exosome (Rrp4) and sites of mRNA processing (snRNPs)
(Courtesy of Neus Visa and Viktoria Fager)

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