

KOLLOQUIUM

Institut für Molekulare
Biowissenschaften
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Science in progress

Tuesday, May 28th, 2024, 12:00, Biocentre, lecture hall B3

Raphael Trischler and Jan-Niklas Tants

Jan-Niklas Tants

Molecular mechanisms of Roquin-RNA complex formation

mRNA *cis*-regulatory RNA elements recruit *trans*-acting factors to control transcript half-lives. The immune-regulatory protein Roquin binds and remodels constitutive and alternative decay element (CDE and ADE, respectively) stem-loops (SLs) and initiates mRNA decay. Binding to SLs is mediated through the core ROQ domain, which is flanked by two HEPN-domains that create a second RNA-binding site (extended ROQ). The interaction of core ROQ with SL elements has been long studied, but how both RNA binding sites recognize and remodel target RNA structures in a concerted manner remains elusive. We here use optical tweezer experiments and NMR spectroscopy to analyze folding pathways of the ADE of the crucial T cell co-receptor Ox40. We reveal stabilization of the apical RNA SL through Roquin binding. Further, we give evidence for additional interaction of extended ROQ with single-stranded RNA which requires partial unwinding of RNA duplexes in lower stem regions. We propose the expanded region to steer regulation by context-encoded specificity and suggest plasticity of stem structures as a determinant for full-length Roquin RNP formation. Our work reveals a previously unknown mechanism of a dual-function RNA binding surface and revises our previous model of Roquin RNA targets and their recognition. This study illustrates a powerful methodological toolbox to capture RNA folding intermediates and their role in RNP formation.

Raphael Trischler

Novel metabolic features of human gut microbes

The gut microbiome is a highly complex community, not only involved in the digestion of nutrients but also playing a role in the development of diseases as well as contributing to human health. Acetogenic bacteria are key players in the metabolic web in the gut due to their role in the hydrogen and carbon dioxide cycle. Some acetogens such as members of the species *Blautia* produce succinate, a compound often associated with the human well-being. However, only little is known about the physiology of different *Blautia* species. The key feature of acetogenic bacteria is the fixation of carbon dioxide with hydrogen as electron donor. The first reaction is the reduction of CO₂ to formic acid, but many gut acetogens do not have a formate dehydrogenase. Thus, formate seems to be as important in interspecies electron transfer as hydrogen. *Blautia* species can not only grow autotrophically but also heterotrophically. During growth of *Blautia schinkii* on glycerol not acetate, but ethanol was produced. Homoethanogenesis from glycerol might be involved in the development of a non-alcoholic fatty liver disease. *myo*-Inositol is also part of the human diet and again, an unusual product spectrum was observed: 3-hydroxypropionate was produced. The pathway for *myo*-inositol degradation will be presented. In summary, the gut acetogens show very unusual metabolic features that can contribute to human health but also to the development of diseases.

Science in progress represents talks of institute members. Either post docs or advanced PhD students present and discuss their recent data.

