IMPRS on Multiscale Biosystems

Deciphering the IscS interaction network in *Escherichia Coli*

PI: Silke Leimkühler (UP)
In collaboration with: Angelo Valleriani (MPIKG)
Project description:

The amino acid L-cysteine is the physiological sulfur source for the synthesis of iron-sulfur (FeS) clusters, the molybdenum cofactor (Moco), thiamin, and thionucleosides in tRNAs. In *E. coli* the L-cysteine desulfurase IscS, a PLP containing enzyme, decomposes L-cysteine to L-alanine by forming an enzyme-bound cysteine persulfide. The sulfur can be subsequently transferred to different acceptor proteins, including IscU, ThiI and TusA, which act as mediators for the synthesis of the above-mentioned biomolecules. In particular, IscU is the main scaffold protein for FeS cluster biosynthesis in which sulfur from IscS and iron from a currently unknown source are combined to form FeS clusters. These clusters, in turn can be inserted into apo-proteins, which participate in tRNA thiolation (e.g. TtcA, MiaB) or Moco biosynthesis (MoaA) among other processes. Additionally, IscS also interacts with CyaY, IscX and Ferredoxin (Fdx) but their specific role during FeS formation is still under debate. ThiI is sulfur transferase that receives sulfur from IscS and further provides it for thiamin and 4-thiouridine formation. The TusA protein was shown to function as initial sulfur donor in a complex sulfur relay system for the synthesis of 2-thiouridine and, as recently shown TusA is also involved in Moco biosynthesis. We are planning to analyze the IscS interacting network and to investigate the sulfur transfer routes for FeS cluster formation, Moco biosynthesis and tRNA thiolation. To accomplish our goals we are using different *E. coli* deletion strains grown under aerobic or anaerobic conditions to quantify the activity of Moco, FeS cluster containing enzymes and the amount of thionucleosides in tRNA. Furthermore, the influence of elevated concentrations of selected interaction partners of IscS will be investigated with respect to sulfur distribution in the cell.