Biogenesis of iron-sulfur proteins in eukaryotes:
A complex pathway for many different cellular functions

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Iron-sulfur (Fe/S) proteins are involved in numerous important cellular pathways such as respiration, metabolism, genome maintenance, protein translation and antiviral response. The synthesis of Fe/S clusters and their assembly into apoproteins in (non-green) eukaryotes is a complex process involving more than 30 proteins located in mitochondria and cytosol (reviewed in 1-4). Biogenesis of mitochondrial Fe/S proteins is accomplished by the *iron-sulfur cluster assembly (ISC)* machinery which was inherited from bacteria during evolution. Cytosolic and nuclear Fe/S protein assembly also depends on the function of this machinery, yet additionally requires the mitochondrial *export apparatus* and the *cytosolic iron-sulfur protein assembly* (CIA) machinery. While we have a good picture of the general outline of Fe/S protein biogenesis, the detailed molecular mechanisms underlying the individual reaction steps are only now being unraveled by biochemical, biophysical, bioinorganic and structural methods. The presentation will summarize some of our recent studies concerning the basic mechanisms of cellular Fe/S protein maturation in yeast and human cells. This will include the assembly of Fe/S clusters on the mitochondrial (ISCU) and cytosolic (CFD1-NBP35) scaffold proteins as well as Fe/S cluster trafficking and insertion into target apoproteins in mitochondria (ISCA-IBA57) and cytosol (YAE1D1-ORAOV1). I will also explain how functional impairment of the ISC or CIA components results in two novel “Fe/S diseases” (reviewed in 5-6) with complex metabolic or neurodegenerative phenotypes (ISCA1) or with a liver failure combined with myelodysplastic syndrome (ORAOV1). So far, no treatment is available for any of these Fe/S diseases.

References (Reviews)

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