

Biosynthesis of Iron-Sulfur Clusters : The Peculiar Properties of A-type Scaffold Proteins

S. Ollagnier-de Choudens¹, L. Loiseau², M. Sendra¹, Y. Sanakis³, N. Duraffourg¹,
D. Lascoux⁴, D. Marion⁵, F. Barras², M. Fontecave¹

¹Laboratoire de Chimie et Biochimie des Centres Rédox Biologiques, DBMS-CB, CEA/CNRS/Université Joseph Fourier, UMR 5047, 17 Avenue des Martyrs, 38054 Grenoble. Cedex 09, France. ²Laboratoire de Chimie Bactérienne, UPR-CNRS 9043, IBSM, 31 Chemin Joseph Aiguier, 13402 Marseille Cedex 20, France. ³NCRS Demokritos, Institute of Material Science, Ag. Paraskevi, Attiki 15310; ⁴Laboratoire de spectrométrie de masse des protéines, IBS, CNRS/CEA/UJF, 41 rue J. Horowitz, 38027 Grenoble cedex 1 ; ⁵LRMN, Institut de Biologie Structurale, UMR5075, 41 rue J. Horowitz, 38027 Grenoble cedex 1.

Iron sulfur clusters (Fe-S) are essential metal cofactors for all organisms. Proteins containing these clusters are involved in mitochondrial respiration, cell signaling pathways, in iron homeostasis, in the biological chemistry of reactive oxygen species, and they mediate novel mechanisms for enzymatic catalysis. The apo forms of these proteins can be activated *in vitro* by the addition of S²⁻ and Fe^{2+/3+} resulting in spontaneous (FeS) cluster formation. It probably does not occur *in vivo* through the same way which is not compatible with the physiological toxicity of iron and sulfide. In fact, recent characterization of gene products that are involved in cluster biosynthesis allows one to consider a range of molecular mechanisms that underlie the chemistry of cluster biosynthesis. So far, two systems are known in *E. coli*, namely the *isc* operon (Iron-Sulfur-Cluster) and the *suf* (SUIFur) operon. The latter, operates with cells under oxidative stress and iron starvation. Even though these proteins have been structurally and functionally characterized, there are still important and not completely answered questions to be addressed. Many of which concern the scaffold proteins, key proteins that deliver preformed cluster to apo-target proteins. Two types of scaffold are known: A-type (IscA, SufA) and U-type (IscU). In an effort to understand the A-type we have started to investigate the molecular mechanism of the cluster formation in SufA, the nature of its cluster and ligands, as well as the way it might be transferred to target proteins. Although we are only beginning to understand the mechanism of (Fe-S) cluster assembly, preliminary results reveal peculiar properties of this type of protein.