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Department of Chemistry

Seminar

9:45 a.m. Thursday, March 3 • 331 Smith Hall

Assistant Professor

F. Wayne Outten

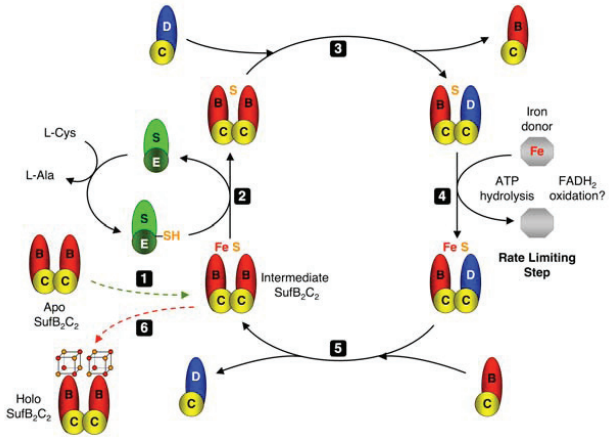
Department of Chemistry and Biochemistry
University of South Carolina

The Suf Fe-S cluster assembly pathway: In vivo and in vitro characterization of a multi-protein factory for metal cofactor biosynthesis

Research interests: Microbial metal metabolism, bio-inorganic chemistry, microbial physiology, and microbial genetics; biochemical mechanisms of Fe-S cluster assembly; characterization of transition metal acquisition, trafficking, and storage systems during environmental stress; metal homeostasis during biofilm formation in micro-organisms.
Website: http://www.chem.sc.edu/faculty/wayne_outten/default.html

Abstract

Iron-sulfur (Fe-S) clusters are key iron cofactors in biological pathways ranging from nitrogen fixation to respiration. Due to the toxicity of ferrous iron and sulfide to the cell, *in vivo* Fe-S cluster assembly is carried out by multi-protein biosynthetic pathways. Fe-S cluster assembly proteins traffic iron and sulfide, assemble nascent Fe-S clusters, and correctly transfer Fe-S clusters to the appropriate target metalloproteins *in vivo*. The gram-negative bacterium *E. coli* contains a stress-responsive Fe-S cluster assembly system, the SufABCDSE pathway, that functions under iron starvation and oxidative stress conditions that compromise Fe-S homeostasis. Through a combination of *in vitro* protein-protein interaction and Fe-S cluster assembly assays with *in vivo* co-expression analysis, we discovered that the SufS cysteine desulfurase transfers persulfide sulfur from SufE to a $SufBC_2D$ complex and that $SufBC_2D$ functions as a novel Fe-S scaffold system to assemble nascent Fe-S clusters.[1] We also determined that SufA interacts with $SufBC_2D$ in order to accept Fe-S clusters formed de novo on SufB, thereby acting as a Fe-S shuttle protein. Recently we found that SufB, SufC, and SufD, co-expressed with the SufS-SufE sulfur transfer pair *in vivo*, purify as two distinct complexes ($SufBC_2D$ and $SufB_2C_2$) that contain Fe-S clusters and $FADH_2$. These studies also showed that SufC and SufD are required for *in vivo* Fe-S cluster formation on SufB. Furthermore, while SufD is dispensable for *in vivo* sulfur transfer, it is absolutely required for *in vivo* iron acquisition. Finally, we demonstrated for the first time that the ATPase activity of SufC is necessary for *in vivo* iron acquisition during Fe-S cluster assembly.[2] Clearly the Suf interact to function as a dynamic multi-protein assembly line for mobilizing iron and sulfide to build and transfer Fe-S clusters.



Current model for Suf Fe-S cluster assembly. Individual Suf proteins are labeled as A, B, B, D, S, or E.

[1]The SufBCD Fe-S scaffold complex interacts with SufA for Fe-S cluster transfer. Chahal HK, Dai Y, Saini A, Ayala-Castro C, and Outten FW. *Biochemistry*. **2009**. 48(44): 10644-10653.
Native *Escherichia coli* SufA, coexpressed with SufBCDSE, purifies as a [2Fe-2S] protein and acts as an Fe-S transporter to Fe-S target enzymes. Gupta V, Sendra M, Naik SG, Chahal HK, Huynh BH, Outten FW, Fontecave M, and Ollagnier de Choudens S. *J Am Chem Soc*. **2009**. 131(17): 6149-6153.
[2]SufD and SufC ATPase activity are required for iron acquisition during in vivo Fe-S cluster formation on the SufBCD complex. Saini A, Mapolelo DT, Johnson MK, and Outten FW. *Biochemistry*. **2010**. 49(43): 9402-9412.

Host: Regents Professor Lawrence Que Jr.
Refreshments will be served prior to the seminar.