

# Using targeted mutagenesis to trap reaction intermediates along the Suf pathway for Fe-S cluster biogenesis

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Metals are essential cofactors for an estimated 30% of all proteins. Transition metals such as copper, iron and zinc are obligatory trace nutrients for most organisms due to their roles in broad classes of metalloproteins. However, metals can also be toxic due to uncontrolled redox chemistry or mis-metallation of the wrong protein. Therefore, elaborate metal homeostasis systems were selected throughout evolution to acquire metals from the environment, to protect them from oxygen, and to ensure their correct use in appropriate proteins. For example, mobilization and trafficking of intracellular iron pools for metal cofactor biogenesis requires that iron be directed into the most essential pathways to maintain cell viability and growth. This process is complicated by the large number of iron-containing metalloproteins that use a variety of iron cofactors such as mono- and di-nuclear iron centers, heme, and iron-sulfur (Fe-S) clusters. In many cases, there are competing requirements for iron to be used for multiple iron metalloproteins to ensure proper function of critical processes, such as central carbon metabolism. In particular biogenesis of Fe-S clusters is sensitive to disruption by reactive oxygen species, iron starvation, and other stresses. The Suf pathway is a stress-responsive Fe-S cluster biogenesis system in *E. coli* that maintains Fe-S cluster assembly during oxidative stress and iron starvation. Using a combination of genetic, biochemical, and spectroscopic approaches, we have characterized the biochemical adaptations of the Suf proteins that allow them to function under stress conditions. This presentation focuses on our recent advances in elucidating the mechanism of sulfur donation by the SufS cysteine desulfurase during Fe-S cluster biogenesis.

**Meet the Speaker, 2:15 – 3:00pm, Student Lounge, 3144**  
**Seminar, 3:35pm, ISAT 159**