Biology Seminar

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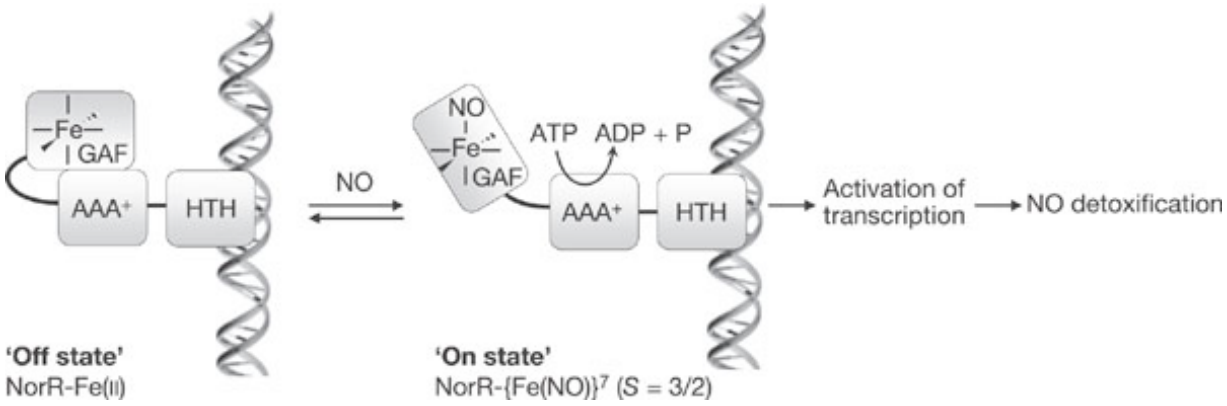
Responses to nitric oxide in *Escherichia coli*: regulatory networks and defense mechanisms

Nitric oxide (NO) is a water-soluble gaseous free radical that is reactive in biological systems, especially with the metal centers of enzymes such as cytochrome oxidase and the [Fe-S] containing dehydratases. NO has important roles as a signal molecule in eukaryotes, and is made by phagocytic cells of the innate immune system in response to infection. In some bacteria, NO is synthesized as an intermediate of the respiratory pathway denitrification, or (in the case of the enteric bacteria such as *Escherichia coli*) is made as a by-product of the reduction of nitrate and nitrite to ammonia. In both cases, the bacteria express inducible pathways for NO metabolism that protect against the harmful effects of the endogenously generated NO. The same regulatory proteins and enzyme activities are used by some pathogens to protect against the NO made by host cells.

Cultures of *E. coli* exposed to NO suffer transient growth inhibition followed by a recovery, which is due to the activities of enzymes that remove NO. Lab strains of *E. coli* express three enzymes that reduce or oxidize NO to less toxic products, and the expression of the genes encoding these enzymes is controlled by regulatory proteins designated NorR and NsrR. While NorR seems to activate a single target (the genes encoding a flavorubredoxin that reduces NO to N_2O), NsrR controls a large regulon of genes, which include those encoding two detoxification activities (the flavohemoglobin that oxidizes NO to nitrate, and the nitrite/NO reductase Nrf, which reduces both nitrite and NO to ammonia). Besides these defense mechanisms, the NsrR regulon includes genes encoding proteins with some surprising physiological roles, including aromatic amine degradation and the regulation of motility. I will review our current understanding of the mechanisms of NorR and NsrR as NO sensors, and the roles of the genes that are regulated by these proteins.



Mechanism of NO sensing and gene activation by NorR (D'Autréaux *et al*., 2005, *Nature* **437**: 769-772).

Sept 24, 2010 **2:00 PM** **ENV125 (EESAT)**