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Chemical Biology and Mass Spectrometry

Research Interests

Bioinorganic chemistry of nitric oxide and hydrogen peroxide

We are interested in the numerous functions of NO in physiological processes. Much of NO signaling is mediated by S-nitrosothiols (RSNOs), and reversible S-nitrosation regulates the bioactivity of hundreds of proteins. Metal ions exert strong control over RSNO decomposition, as well as NO transfer between thiols. We are examining catalysis of these reactions by biologically important metalloenzymes such as Cu,Zn-superoxide dismutase. We are also investigating the chemistry underpinning the metabolism of NO-releasing pharmaceuticals. For example, protein-based thiols are likely involved in the bioactivation of nitroglycerin, a drug widely used in the treatment of heart disease for over a century. We are investigating the mechanisms responsible for the rapid loss with use of the therapeutic efficacy of nitroglycerin so that the enormous therapeutic potential of this and related nitro drugs can be realized.

Hydrogen peroxide is another key signalling small molecule, and we are investigating the highly-oxidizing centres produced in hemoproteins following peroxide binding to the heme. These include oxyferryl (FeIV=O) heme and amino-acid based radicals. Using native and mutant forms of the heme proteins, cytochrome c peroxidase, cytochrome c, myoglobin, prostaglandin H synthase, the bioreactivity of these centres is under investigation. We make extensive use of mass spectrometry, spectroscopic techniques (FTIR, CD, fluorescence).

Selected Publications

Q.K. Timerghazin, G.H. Peslherbe, and A.M. English (2007) Resonance Description of S-Nitrosothiols: Insights into Reactivity, Org. Letts. 9, 3049-3052.

J. Laterreur and A.M. English (2007) Hemoglobin S-nitrosation on Oxygneation of Nitrite Deoxyhemoglobin Incubations is Attenuated by Methemoglobin, J. Inorg. Biochem. 101, 1827–1835.

M. Ye and A.M. English (2006) Binding of polyaminocarboxylate chelators to the active-site copper inhibits the GSNO-reductase activity but not the superoxide dismutase activity of Cu,Zn-superoxide dismutase, Biochemistry 45, 12723-12732.

H. Jiang and A.M. English (2006) Phenotypic analysis of the ccpl and ccpl-ccp1W191F mutant strains of Saccharomyces cerevisiae indicates that cytochrome c peroxidase functions in oxidative-stress signalling, J. Inorg. Biochem. 100, 1996-2008.

H. Jiang and A.M. English (2006) Evaluation of D10-Leu Metabolic Labeling Coupled with MALDI-MS Analysis in Studying the Response of the Yeast Proteome to H2O2 Challenge, J. Proteome Res. 5, 2539-2546.