

How oxygenases catalyze a variety of reactions?

S Ramaswamy¹, Sanaa Syed², Daniel J Ferraro³, Eric N Brown³

¹Institute Of Stem Cell Biology And Regen Medicine, Bangalore, India, ²Institute For Stem Cell Biology And Regenerative M, Bangalore, India, ³Department of Biochemistry, Carver College of Medicine, University of Iowa,, Iowa City, United States
E-mail: ramas@instem.res.in

Rieske non-heme iron oxygenases (RDO) are a well-studied class of enzymes. Our laboratory uses Naphthalene 1,2 dioxygenase (NDO) as a model to study RDOs. In our earlier work we had shown how side-on binding of oxygen to the mono-nuclear iron provides this enzyme with the ability to catalyze stereo and region-specific cis-dihydroxylation reactions 1,2. It has been shown by several others that RDOs catalyze a variety of reactions, including mono-oxygenation, desaturation, O- and N- dealkylation, sulfoxidation among other reactions. NDO itself catalyses a variety of these reactions. Work from our lab and several other laboratories have shown that the catalytic site is conserved. In order to understand the molecular basis of how this enzyme manages to do different reactions, we have determined structures of NDO with substrates that undergo a variety of reactions. Often the enzyme is also promiscuous by delivering two products (apparently two different reactions) to the same substrate – while maintaining stereo and region specificity to each product. Based on our studies we show that the orientation of the substrate controls not only regio- and stereo-specificity, but also the type of the reaction catalyzed.

It has been shown by the Lipscomb group that the substrate binds the enzyme first followed by molecular oxygen. The structures of the substrate bound NDO reveals that there is no easy path for the oxygen molecule to reach the mon-nuclear iron site in the presence of the substrate unless significant protein dynamics is involved. We have used a combination of theoretical approaches and experimental approaches to determine a few possible pathways of oxygen entry into the active site.

The results of these studies and the known published work from our and other groups together allows us to present a comprehensive structural mechanism for the reactions catalyzed by Rieske non-heme iron dioxygenases.

The work was supported by NIH when the PI was in the USA and is currently supported by grants from the Department of Biotechnology, Government of India.

(1) Karlsson, A.; Parales, J. V; Parales, R. E.; Gibson, D. T.; Eklund, H.; Ramaswamy, S. (2003) *Science*, 299 (5609), 1039–1042.

(2) Ferraro, D. J. J. D. J.; Okerlund, A. L. L. A. L.; Mowers, J. C. C. J. C.; Ramaswamy, S. J. (2006) *Bacteriol.*, 188 (19), 6986–6994.

Keywords: [Rieske oxygenases](#), [multiple reactions](#), [mono-nuclear iron site](#)