Poster Presentation

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Nitric oxide synthase and possible redox partners in Bacillus cereus

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Nitric oxide synthase (NOS), a BH4-dependent heme-enzyme, is the only enzyme that specifically produces NO in mammals. NO is produced by the NOS homodimer in two multistep reaction cycles involving electron transfer from a reducing domain to the heme active site. The importance of NO in mammals is due to its function in signalling, vasodilation and immune response. Some bacterial species also contain NOS-encoding genes, but these bacterial NOSs are differently organized – they contain no reducing domain – and their functions and mechanism are not fully resolved [1]. Bacterial NOSs are potential drug targets, because of their role in protection against antibiotics and oxidative stress in some pathogenic bacterial species (e.g. Bacillus anthracis) [2]. Flavodoxins (Flds) have been shown to be relevant redox partners for bacterial NOSs [3], but the specificity of the interaction between NOS and Flds remains poorly understood. We have investigated the NOS protein system in Bacillus cereus, whose genome encodes NOS and two Flds, by combining crystallographic and spectroscopic methods. So far the structures of the two Flds have been solved to 0.98 Å and 2.75 Å resolution, while NOS has been solved to 2.9 Å resolution. An important part of the study has been to investigate the effect of synchrotron X-ray radiation on the oxidation state and structure of the Flds, due to their radiation sensitive cofactor flavin mononucleotide (FMN). The high-resolution (0.98 Å), oxidized structure of one Fld indicates that X-rays induce structural changes around the FMN cofactor. Another important part of the study has been to gain further insight into the specificity and flexibility of the interactions between ferredoxin/flavodoxin-NADP+ reductases, Flds and NOS in Bacillus cereus, as well as the possible mechanism of bacterial NOSs.

[1] *J. Sudhamsu, B. Crane, Trends in microbiology, 2009, 17, 212-218,* ***[2]*** *I. Gusarov, K. Shatalin, M. Starodubtseva et al, Science, 2009, 325, 1380-1384,* ***[3]*** *Z. Wang, R. Lawson, M. Buddha et al, Journal of Biological Chemistry, 2007, 282, 196- 202*

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