

α -DsbA's: Structure determination of novel oxidoreductases

M. Kurz¹, B. Heras¹, I. Iturbe-Ormaetxe², S. O'Neill², R. Beiko¹, P. Frei³, R. Glockshuber³, J. Martin¹

¹ *Institute for Molecular Bioscience, University of Queensland, Brisbane, QLD, Australia*

² *School of Integrative Biology, University of Queensland, Brisbane, QLD, Australia*

³ *Institut für Molekularbiologie und Biophysik, ETH Zürich, Zürich, Switzerland*

A crucial step in protein folding is the formation of disulfide bonds between cysteines. In bacteria, Dsb (DiSulfideBond) proteins are involved in this process, with the key player being DsbA. Dsb proteins are found in a wide range of bacteria, yet most studies have focused on *E. coli*. Recent data indicates that DsbA is involved in the pathogenicity of virulent bacteria and therefore is a potential target for drug design. We aimed to evaluate the function and structure of two DsbA-like proteins (α -DsbA and α -DsbA2) from *Wolbachia pipientis*. This endosymbiotic α -proteobacteria infects a range of invertebrate hosts causing sex distortion effects, and has potential applications in the control of insect transmitted diseases such as malaria. Comprehensive biochemical and structural characterisation of the DsbA-homologues of *Wolbachia* will be important to aid our understanding of disulfide bond formation in bacteria other than *E. coli*. In addition, structural studies could form the basis for the development of inhibitors with antimicrobial activity. Additionally, we use bioinformatics to investigate DsbA's from the entire bacterial kingdom to establish rules to classify Dsb protein sequences. This will help to gain insight about function of DsbA proteins before structure determination. We solved the structure of α -DsbA - believed to represent the first *W. pipientis* protein structure - and found significant differences compared to two other DsbA structures that have been solved. We also undertook a comprehensive biochemical, mutational and functional analysis of α -DsbA and α -DsbA2, to understand the specific role of these proteins in *Wolbachia pipientis*. The results enable us to compare and contrast the function and structure of the *Wolbachia* proteins with the prototype *E. coli* DsbA.