

Atomic Model of Microsomal Glutathione Transferase 1 from Electron Crystallography

Peter J Holm^{a,b}, Priyaranjan Bhakat^b, Caroline Jegerschöld^b, Nobuhiko Gyobu^c, Kaoru Mitsuoka^c, Yoshinori Fujiyoshi^c, Ralf Morgenstern^a and Hans Hebert^{a,b}, ^a*Karolinska Institutet, Sweden.* ^b*Lund University, Sweden.* ^c*Kyoto University, Japan.* E-mail: peter.holm@mbfys.lu.se

The integral membrane protein microsomal glutathione transferase 1 (MGST1) possesses glutathione and peroxidase activity thus protecting the organism from toxic substances. We have determined the atomic model of MGST1 at 3.5 Å resolution by electron crystallography of 2-dimensional crystals from two different two-sided plane groups making it the first membrane enzyme solved to atomic resolution by this technique. The MGST1 homotrimer is constructed by 12 trans-membrane helices forming three all alpha-up-down 4-helix bundles with a fold strikingly similar to the cytochrome c oxidase subunit I suggesting divergent evolution from a common structural ancestor. The MGST1 model reveals inter-subunit interaction and strengthens previous suggestions of global conformational changes upon glutathione (GSH) binding. Furthermore a possible location of the putative hydrophobic binding site is suggested.

Keywords: **microsomal glutathione transferase 1, membrane protein structure, electron crystallography**