

Crystal structure of the mitochondrial import complex, hTIM910.

C. T. Webb^{1,2}, M. A. Gorman^{1,4}, M. Lazarou³, M. T. Ryan³, P. M. Colman¹, J. M. Gulbis¹

¹ *Structural Biology Division, The Walter and Eliza Hall Institute, Parkville, VIC, Australia*

² *Department of Medical Biology, The University of Melbourne, Melbourne, VIC, Australia*

³ *Department of Biochemistry, La Trobe University, Melbourne, VIC, Australia*

⁴ *Current address - Biota Structural Biology Laboratory, The ACRF Rational Drug Discovery Facility, Melbourne, VIC, Australia*

Over 99% of human mitochondrial proteins are synthesised from nuclear DNA and must be imported as immature precursors *via* a coordinated series of specific, tightly regulated events. Encoded topological signals ensure nascent proteins are ushered to their correct mitochondrial destination. Proteins destined for the inner or outer mitochondrial membranes contain internal targeting information. After transfer through the outer membrane's general import pore, preproteins encounter TIM910, a hetero-hexamer of two homologous polypeptides, Tim9 and Tim10. TIM910 mediates preprotein passage across and within the intermembrane space (IMS) [1]. Inner membrane carrier proteins (e.g. ADP/ATP Carriers) are transferred to the inner membrane translocase, Tim22, for insertion, whereas β -barrel proteins of the outer membrane are transferred to the sorting and assembly machinery, SAM [1]. Here we present the 3.5 Å structure of the hTIM910 complex. The structure was determined by SAD phasing using selenomethionine-substituted protein. The molecular assembly has a unique α -propeller topology in which Tim9 and Tim10 subunits alternate about a central pseudo-hexad [2]. Each subunit of the hexamer has a helix-loop-helix topology and a highly conserved "twin CX₃C motif that forms two intra-chain disulfides defining a central loop. The six loops come together to form one face of the core assembly, below which tentacle-like helices emanate. Tentacle-like protrusions in the structures of other chaperones have been implicated in substrate binding. We are combining structural and biochemical approaches to investigate chaperone-substrate interactions.

(1) Webb, C.T., Gorman M.A., Lazarou, M., Ryan, M.T., Gulbis, J.M. *Mol. Cell*, 2006, 21, 123.

(2) Dolezal, P., Likic, V., Tachezy, J., Lithgow, T. *Science*, 2007, 313, 314.