Structural Determination of the hTIM10 Complex

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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 TIM10, a hetero-hexamer of two homologous polypeptides, Tim9 and Tim10. TIM10 mediates preprotein passage across and within the intermembrane space (IMS). Inner membrane carrier proteins (*e.g.*AAC) 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]. Tim9 and Tim10 share a twin CX_3C consensus sequence, similar to a zinc finger motif. Whilst disulphide formation appears to be necessary for hexamer formation and function, there is evidence that zinc binding occurs in the cytosol prior to import, oxidation occurring later in the IMS [2].

Initial electron density maps have been calculated using SAD phasing, and I am on the way to determining the structure of the human TIM10 complex. The structure will illuminate how this key intermediate functions in the context of translocation.

[1] Koehler C.M., *Annu. Rev. Cell Dev. Biol*., 2004, **20**, 309. [2] Lu H., Allen S., Wardleworth L., Savory P., Toktlidis K., *J. Biol. Chem*., 2004, **279**, 18952.

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