Structural and Functional Analysis of PDI–related Proteins

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Protein Disulfide Isomerase[PDI]–related proteins are residents of the endoplasmic reticulum and are involved in several functions, some of which include redox and chaperone activities. Their function involves several non-covalent weak interactions with specific epitopes on substrate proteins. The molecular basis of these interactions has not been understood until recently [2].

We recently elucidated the first crystal structure of such a eukaryotic PDI–related chaperone, Wind from Drosophila [1]. It has been identified that Wind binds Pipe (a 2-*O*-sulfotransferase) *in vitro*. A putative peptide binding site has been mapped on the b'-domain for substrate binding with the requirement of the integrity of a surface on the d'-domain. Crystal structures of several Wind–mutants and their complexes with the peptides mimicking the Pipe binding site were elucidated giving some clues about the binding mechanism. Further, the structure of a mammalian orthologue of Wind, Erp28 has been solved, suggesting a functional role for the structural conservation between the proteins.

[1] Ma Q., Guo C., Barnewitz K., Sheldrick G. M., Söling H. D., Uson I., Ferrari D. M., *JBC*, 2003, **278**, 44600. [2] Barnewitz K., Guo C., Sevvana M., Ma Q., Sheldrick G. M., Söling H. D., Ferrari D. M., *JBC*, 2004, **279**, 39829.

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