Crystal Structure of the Noncatalytic Domains of Protein Disulfide Isomerase ERp72

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The synthesis of proteins in the endoplasmic reticulum (ER) is limited by the rate of protein folding and, in particular, the rate of correct disulfide bond formation. This process is carried out by protein disulfide isomerases, a family of ER proteins, which includes general enzymes such as PDI that recognize unfolded proteins, and others, including ERp72, that are selective for specific proteins. During infection, this quality control machinery is hijacked by viral toxins that pose as misfolded proteins to get translocated through ER into cytoplasm. A recent study demonstrated that cholera toxin is retained in the ER by ERp72, while PDI promotes its translocation. Here, we determined the structure of ERp72 using small-angle X-ray scattering (SAXS) and X-ray crystallography. The structure shows striking similarity to another protein disulphide isomerase, ERp57, and provides the basis for understanding substrate specificity by ERp72.

Acknowledgements: This work was supported by grants from the Canadian Institutes of Heath Research to K. Gehring and D. Y. Thomas.

Key words: X-ray structure, ERp72, protein disulphide isomerase, viral infection.