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Reconciling Synchrotron SAXS Data with NMR Data for a Two-Domain Protein

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A preliminary structure of the protein Yih1 (Yeast impact homologue 1), a protein of partially characterised function, has been obtained by multi-dimensional NMR methods. The ~300-residue protein has two distinct domains of approximately 120 and 160 residues with an approximately 20-residue linker. However, no NOEs could be found involving contacts between the two domains. Solution-state SAXS data were recorded at the Australian Synchrotron. The structure is clearly monomeric. The NMR structure of one domain was then translated and rotated relative to the other domain until a remarkably good fit to the distinctive SAXS data was obtained. The interaction between the two domains was then, and only then, inspected and found to involve a fairly loose and not implausible association via a small hydrophobic patch and several potential salt bridges. Residual dipolar coupling measurements are in progress to determine alignment vectors of the two domains, and confirm, or otherwise, the accuracy of the SAXS model of domain association.

Cambiaghi TD, Pereira CM, Shanmugam R, Bolech M, Wek RC, Sattlegger E, Castilho BA. 2014. Evolutionarily conserved IMPACT impairs various stress responses that require GCN1 for activating the eIF2 kinase GCN2. *Biochem Biophys Res Commun* 443: 592-597 (doi: 10.1016/j.bbrc.2013.12.021).

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