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Structural Basis of Dscam Isoform specificity

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Down syndrome cell adhesion molecule (Dscam) is a highly diverse cell surface receptor. Mutually exclusive splicing of exons arranged in three clusters results in extensive sequence variability in three immunoglobulin-like domains in *Drosophila*. Thousands of diverse Dscam isoforms are expressed in the nervous system, and each neuron carries a different set of isoforms. *In vitro* studies in flies suggest a high specificity of homophilic interactions between identical isoforms, and it is thought that this mode of interaction is essential in the formation of a brain map from single neurons. Here we report the X-ray structures of the N-terminal four domains of two different Dscam isoforms. The structures show that both isoforms assume a horseshoe configuration. Two epitopes are present on unique structural elements at opposite faces of the horseshoe. Only epitope I is engaged in homophilic dimerization, whereas the variable surface area of epitope 2 is likely involved in heterophilic recognition. Homophilic dimer formation depends on symmetric, antiparallel paring of the peptide segments from identical epitope I sequences. This suggests a structural principle in which ”peptide-complementarity” favors exclusive homotypic domain interactions as the basis for the specificity of homophilic interactions between Dscam isoforms.

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Structure of a Spherical Selfcompartmentalizing Sulphur Cycle Metalloenzyme

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Numerous microorganisms oxidise sulphur and inorganic sulphur compounds for energy conservation, thus contributing to the global biogeochemical sulphur cycle. The reaction is the basis for life in geothermally heated solfataras, acid mine drainage and bioleaching. We have determined [1], [2], the 1.7 Å resolution structure of the sulphur oxygenase reductase from the thermoacidophilic archaeon *Acidianus ambivalens*. It catalyses an oxygen-dependent disproportionation of elemental sulfur, enabling the introduction of sulphur into the biological cycle. The enzyme forms a 24-oligomer, a ferritin-resembling hollow sphere enclosing a positively charged compartment accessible *via* apolar channels gated by hydrophobic side-chain residues. A cysteine persulphide and a low-potential mononuclear non-heme iron site ligated by a 2-His-1-carboxylate facial triad constitute the active sites, which are located in a small cavity at each subunit, accessible only from the inside of the sphere. These results suggest that linear sulphur species are the actual substrates and that the iron is the site both of sulphur oxidation and reduction. The enzyme oligomerization into an enclosed reaction chamber exemplifies the formation of a proto-organelle in archaea species.

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