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The 40 Residues that Control Folding, Cofactor Binding, Catalysis, Oligomerization and Function of 13000 Short Chain Oxidoreductase Enzymes. W. L. Duax¹, R. Huether¹, V. Pletnev², C. M. Weeks¹, T. Umland¹, Q. Mao¹, L. Gambino¹, ¹Hauptman-Woodward Inst., Buffalo, NY, ²Inst. Bioorg. Chem., RAS, Moscow.

The short-chain oxidoreductase (SCOR) family of enzymes has over 13,000 putative members in bacteria, plants, insects, and mammals that catalyze oxidation, reduction and epimerization. Over 70% (~7,900) of the putative family members belong to a single subfamily that contains the signature sequence TGxxxGIG in the $\beta 2\alpha 3$ turn of the Rossmann fold. The crystal structures of 50 of these have been reported. Although there is not one residue fully conserved, there are 40 fingerprint residues that are conserved at 70% identity or greater. We are determining the roles of each of the fingerprint residues in controlling protein folding, cofactor binding, catalysis, and function. Cofactor selectivity is controlled by two adjacent residues in the $\beta 2\alpha 3$ turn of the Rossmann fold. Seven residues may be critical to catalysis. C-H \cdots O hydrogen bonds may play a significant role in catalysis and a 3_{10} kink at the center of helix 5 and patterns of aromatic amino acid substitution on helix 5 may control dimer formation. The ϕ, ψ values of seven of the 12 Gly residues in the fingerprint fall in a region of the Ramachandran plot where the other 19 amino acids are rarely observed. Gly residues in these positions are nearly indispensable for the maintenance of the Rossmann fold. This work is supported by NIH Grant No. DK26546.