

## W0451

**Functional Diversity from a Simple Protein Fold.** M.L. Hackert, J.J. Almrud, W.H. Johnson<sup>†</sup>, C.P. Whitman<sup>†</sup>, Dept. of Chemistry and Biochemistry, and <sup>†</sup>College of Pharmacy, The Univ. of Texas at Austin, Austin, TX 78712.

The tautomerase superfamily is represented by 4-Oxalocrotonate tautomerase (4-OT), 5-(carboxymethyl)-2-hydroxymuconate isomerase (CHMI), and macrophage migration inhibitory factor (MIF). 4-OT and many other proteins in this family are hexameric, while other members are trimeric or dimeric. However, all members of this enzyme superfamily share a simple folding unit represented by the 4-OT monomer that is remarkable for its small size (62 a.a.) and simple ( $\beta$ - $\alpha$ - $\beta$ ) fold. Some subunits, like those of CHMI and MIF, are nearly twice as large as the 4-OT subunit and probably arose by gene duplication. Members of this superfamily also share a key mechanistic feature - an active site amino-terminal proline, which sometimes has an unusually low  $pK_a$ , as the general base in keto-enol tautomerization.

Several new members of the 4-OT family have been identified and representative structures determined, although the function of many of these proteins remains unknown. Within the superfamily, dehalogenase and decarboxylase activities are now known in addition to the tautomerase, isomerase and MIF activities noted previously. The functional diversity in the 4-OT superfamily suggests that nature used these short sequences as building blocks to create new structures and activities. A summary of these results will be presented.