Analysis of Amino Acid coevolved sets in the Low Molecular Weight Phosphatase protein family by Molecular Dynamics

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Low molecular weight phosphatases (LMW-PTPs) are one of the three existing major types of Tyrosine Phosphatases, with important roles in intracellular signalling of processes such as cellular growth, differentiation and proliferation through interactions with various possible substrates. By utilizing our group's technique for detecting amino acid correlation on the LMW-PTP protein family multiple sequence alignment and through bibliographic revision of articles that experiment or discuss these positions, we elucidated various amino acid coevolved sets and their possible biological meanings. Coevolved residue sets corresponding to the active enzymatic site and important active site hydrogen bonds were found, as well as coevolved sets that seem to be related to the active site cavity difference in charges between Low Molecular Weight Phosphatases and a class of Arsenate Reductases that has long arisen in a group of this protein family bacterial sequences. A Proline and Glycine coevolved set that seems related to important structural enzymatic properties has also been found as well as a fifth set including a P-loop Glycine (G14) and Cysteine (C17). This Cysteine functional importance has already been established as a residue responsible for protecting the enzyme against irreversible oxidation during redox stress by the formation of a disulphide bridge with the catalytic Cysteine (C12). In contrast there is no experimental or theoretical data relating possible roles of the Glycine. An interesting proposition is that the reason this correlation is observed may be related to this Glycine's possible influence on this disulphide bridge formation. To further elaborate on this hypothesis we here report our preliminary results of a two microsecond simulation of wild-type Human cytoplasmic protein tyrosine phosphatase of the A form and a two microsecond simulation of this protein's G14A mutation in order to access the possibility of this glycine conferring the needed P-loop flexibility for the formation of the catalytic C12 and C17 disulphide bridge.