Use of residue conservation analysis to identify functional and structural conserved residues of Ohr/OsmC family

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Ohr and OsmC are members of Ohr/OsmC family of proteins that display a Cys-based, lipoil dependent peroxidase activity. The hallmark motif signature of Ohr and OsmC proteins is a highly conserved pair of catalytic cysteines, whose distanced is around 60 amino acids residues. Additional conserved residues include an Arg, present in Ohr (located in the first loop between 1st and 2nd β-sheets) and OsmC (located in the third loop between 3rd β-sheet and 1st α-helix), and a Glu, located in both subfamilies in the 1st α-helix. To date, these are the only residues that were experimentally assayed. The aim of this work was to perform a structural and large sequence comparison among members of Ohr and OsmC subfamilies in attempt to identify novel functional and structural conserved residues, beyond Cys, Arg and Glu residues so far identified. For structural comparison, we used all structures from OsmC and Ohr subfamilies available in PDB database. We performed the protein sequence mining using a Hidden Markov Model (HMM) based iterative search in the Jackhammer 1.9 web server. For residue conservation, the retrieved hits were aligned using MUSCLE tool inside MEGA6 package. The final alignment file was used as input for Skyline (WebLogo generation) and Consurf tools. Remarkably, the electrostatic potential surfaces of Ohr and OsmC shares a positive character within the active site. From 14166 sequences retrieved, we identified 3270 and 1528 sequences belonging to Ohr and OsmC subfamilies, respectively. We could identify at least nine residues: Y9, D27, P37, N49, E51, E96, H122, Y127 and N134 (according 1ZB8 residue numbering) that are highly conserved among all extracted sequences and for OsmC, seven residues: G18, G20, W11, E49, P48, H56, M62 (according 1NYE residue numbering). Through this analysis, we identified new putative structural and functional conserved residues that will be now experimentally tested.

Keywords: Ohr/OsmC, thiol-dependent peroxidases, residue conservation

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