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[Chem Biodivers.](#) 2012 Sep;9(9):1776-93. doi: 10.1002/cbdv.201100438.

Molecular evolution, structure, and function of peroxidasins.

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Abstract

Peroxidasins represent the subfamily 2 of the peroxidase-cyclooxygenase superfamily and are closely related to chordata peroxidases (subfamily 1) and peroxinectins (subfamily 3). They are multidomain proteins containing a heme peroxidase domain with high homology to human lactoperoxidase that mediates one- and two-electron oxidation reactions. Additional domains of the secreted and glycosylated metalloproteins are type C-like immunoglobulin domains, typical leucine-rich repeats, as well as a von Willebrand factor C module. These are typical motifs of extracellular proteins that mediate protein-protein interactions. We have reconstructed the phylogeny of this new family of oxidoreductases and show the presence of four invertebrate clades as well as one vertebrate clade that includes also two different human representatives. The variability of domain assembly in the various clades was analyzed, as was the occurrence of relevant catalytic residues in the peroxidase domain based on the knowledge of catalysis of the mammalian homologues. Finally, the few reports on expression, localization, enzymatic activity, and physiological roles in the model organisms *Drosophila melanogaster*, *Caenorhabditis elegans*, and *Homo sapiens* are critically reviewed. Roles attributed to peroxidasins include antimicrobial defense, extracellular matrix formation, and consolidation at various developmental stages. Many research questions need to be solved in future, including detailed biochemical/physical studies and elucidation of the three dimensional structure of a model peroxidasin as well as the relation and interplay of the domains and the in vivo functions in various organisms including man.

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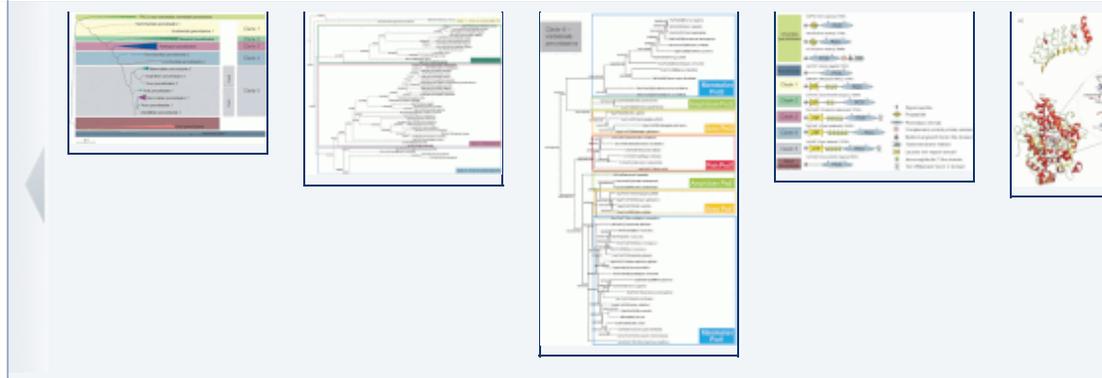
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