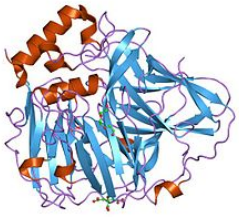
Multicopper oxidase

In molecular biology, **multicopper oxidases** are enzymes which oxidise their substrate by accepting electrons at a mononuclear copper centre and transferring them to a trinuclear copper centre; dioxygen binds to the trinuclear centre and, following the transfer of four electrons, is reduced to two molecules of water.[1] There are three spectroscopically different copper centres found in multicopper oxidases: type 1 (or blue), type 2 (or normal) and type 3 (or coupled binuclear).[2][3] Multicopper oxidases consist of 2, 3 or 6 of these homologous domains, which also share homology with the cupredoxins azurin and plastocyanin. Structurally, these domains consist of a cupredoxin-like fold, a beta-sandwich consisting of 7 strands in 2 beta-sheets, arranged in a Greek-key beta-barrel.[4] Multicopper oxidases include:

- Ceruloplasmin EC 1.16.3.1 (https://enzyme.expasy.org/EC/1.16.3.1) (ferroxidase), a 6-domain enzyme found in the serum of mammals and birds that oxidizes different inorganic and organic substances; exhibits internal sequence homology that appears to have evolved from the triplication of a Cu-binding domain similar to that of laccase and ascorbate oxidase.
- Laccase EC 1.10.3.2 (https://enzyme.expasy.org/EC/1.10.3.2) (urishiol oxidase), a 3-domain enzyme found in fungi and plants, which oxidizes different phenols and diamines. CueO is a laccase found in *Escherichia coli* that is involved in copper-resistance.[4]
- Ascorbate oxidase EC 1.10.3.3 (https://enzyme.expasy.org/EC/1.10.3.3), a 3-domain enzyme found in higher plants.
- Nitrite reductase EC 1.7.2.1 (https://enzyme.expasy.org/EC/1.7.2.1), a 2-domain enzyme containing type-1 and type-2 copper centres.[5][6]

In addition to the above enzymes there are a number of other proteins that are similar to the multi-copper oxidases in terms of structure and sequence, some of which have lost the ability to bind copper. These include: copper resistance protein A (copA) from a plasmid in *Pseudomonas syringae*; domain A of (non-copper binding) blood coagulation factors V (Fa V) and VIII (Fa VIII);[7] yeast Fet3p (FET3) required for ferrous iron uptake;[8] yeast hypothetical protein YFL041w; and the fission yeast homologue SpAC1F7.08.

Multicopper oxidase (type 1)



crystal structures of e. coli laccase cueo under different copper binding situations

Identifiers	
Symbol	Cu-oxidase
Pfam	PF00394 (http://pfam.xfam.org/family?acc=PF00394)
Pfam clan	CL0026 (http://pfam.xfam.org/clan/CL0026)
InterPro	IPR001117 (https://www.ebi.ac.uk/interpro/entry/IPR001117)
PROSITE	PDOC00076 (https://prosite.expasy.org/PDOC00076)
SCOP2	1aoz (http://scop2.mrc-lmb.cam.ac.uk/search?t=txt;q=1aoz) / SCOPe (https://scop.berkeley.edu/pdb/code=1aoz) / SUPFAM (http://supfam.org/SUPERFAMILY/cgi-bin/search.cgi?search_field=1aoz)
Membranome	253 (http://membranome.org/protein_superfamilies/253)
Available protein structures:	
Pfam	structures (http://pfam.xfam.org/family/PF00394?tab=pdbBlock) / ECOD (http://prodata.swmed.edu/ecod/complete/search?kw=PF00394)
PDB	RCSB PDB (https://www.rcsb.org/search?q=rcsb_polymer_entity_annotation.annotation_id:PF00394%20AND%20rcsb_polymer_entity_annotation.type:Pfam); PDBe (https://www.ebi.ac.uk/pdbe/entry/search/index?pfam_accession:PF00394); PDBj (https://pdbj.org/searchFor?query=PF00394)

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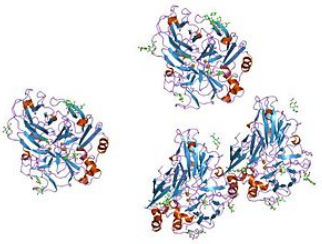
PDBsum	structure summary (https://www.ebi.ac.uk/thornton-srv/databases/cgi-bin/pdbsum/GetPfamStr.pl?pfam_id=PF00394)

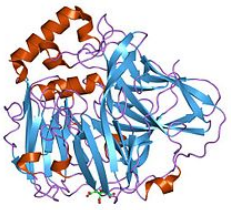
Multicopper oxidase (type 2)



active laccase from trametes versicolor complexed with 2,5-xylidine

Identifiers	
Symbol	Cu-oxidase_2
Pfam	PF07731 (http://pfam.xfam.org/family?acc=PF07731)
Pfam clan	CL0026 (http://pfam.xfam.org/clan/CL0026)
InterPro	IPR011706 (https://www.ebi.ac.uk/interpro/entry/IPR011706)
SCOP2	1aoz (http://scop2.mrc-lmb.cam.ac.uk/search?t=txt;q=1aoz) / SCOPe (https://scop.berkeley.edu/pdb/code=1aoz) / SUPFAM (http://supfam.org/SUPERFAMILY/cgi-bin/search.cgi?search_field=1aoz)
Available protein structures:	
Pfam	structures (http://pfam.xfam.org/family/PF07731?tab=pdbBlock) / ECOD (http://prodata.swmed.edu/ecod/complete/search?kw=PF07731)
PDB	RCSB PDB (https://www.rcsb.org/search?q=rcsb_polymer_entity_annotation.annotation_id:PF07731%20AND%20rcsb_polymer_entity_annotation.type:Pfam); PDBe (https://www.ebi.ac.uk/pdbe/entry/search/index?pfam_accession:PF07731); PDBj (https://pdbj.org/searchFor?query=PF07731)
PDBsum	structure summary (https://www.ebi.ac.uk/thornton-srv/databases/cgi-bin/pdbsum/GetPfamStr.pl?pfam_id=PF07731)

Multicopper oxidase (type 3)



crystal structures of e. coli laccase cueo under different copper binding situations

Identifiers	
Symbol	Cu-oxidase_3
Pfam	PF07732 (http://pfam.xfam.org/family?acc=PF07732)
Pfam clan	CL0026 (http://pfam.xfam.org/clan/CL0026)
InterPro	IPR011707 (https://www.ebi.ac.uk/interpro/entry/IPR011707)
SCOP2	1aoz (http://scop2.mrc-lmb.cam.ac.uk/search?t=txt;q=1aoz) / SCOPe (https://scop.berkeley.edu/pdb/code=1aoz) / SUPFAM (http://supfam.org/SUPERFAMILY/cgi-bin/search.cgi?search_field=1aoz)

Available protein structures:	
Pfam	structures (http://pfam.xfam.org/family/PF07732?tab=pdbBlock) / ECOD (http://prodata.swmed.edu/ecod/complete/search?kw=PF07732)
PDB	RCSB PDB (https://www.rcsb.org/search?q=rcsb_polymer_entity_annotation.annotation_id:PF07732%20AND%20rcsb_polymer_entity_annotation.type:Pfam); PDBe (https://www.ebi.ac.uk/pdbe/entry/search/index?pfam_accession:PF07732); PDBj (https://pdbj.org/searchFor?query=PF07732)
PDBsum	structure summary (https://www.ebi.ac.uk/thornton-srv/databases/cgi-bin/pdbsum/GetPfamStr.pl?pfam_id=PF07732)

CMulti-copper polyphenol oxidoreductase laccase

crystal structure of protein cc_0490 from caulobacter crescentus, pfam duf152	
Identifiers	
Symbol	Cu-oxidase_4
Pfam	PF02578 (http://pfam.xfam.org/family?acc=PF02578)
InterPro	IPR003730 (https://www.ebi.ac.uk/interpro/entry/IPR003730)
Available protein structures:	
Pfam	structures (http://pfam.xfam.org/family/PF02578?tab=pdbBlock) / ECOD (http://prodata.swmed.edu/ecod/complete/search?kw=PF02578)
PDB	RCSB PDB (https://www.rcsb.org/search?q=rcsb_polymer_entity_annotation.annotation_id:PF02578%20AND%20rcsb_polymer_entity_annotation.type:Pfam); PDBe (https://www.ebi.ac.uk/pdbe/entry/search/index?pfam_accession:PF02578); PDBj (https://pdbj.org/searchFor?query=PF02578)
PDBsum	structure summary (https://www.ebi.ac.uk/thornton-srv/databases/cgi-bin/pdbsum/GetPfamStr.pl?pfam_id=PF02578)