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Crystal Structure of Agaricus bisporus Mushroom Tyrosinase

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Supplementary Information belonging to

a)

Wangsa T. Ismaya, Henriëtte J. Rozeboom, Amrah Weijn, Jurriaan J. Mes, Fabrizia Fusetti, Harry J. Wichers and Bauke W. Dijkstra. Crystal structure of *Agaricus bisporus* mushroom tyrosinase - Identity of the tetramer subunits and interaction with tropolone.

Fig. S1. *A. bisporus* tyrosinase tetramer in the asymmetric unit of a) space group $P2_12_12$ (dimensions ~139 x 97 x 59 Å), and b) space group $P2_1$ (dimensions ~107 x 87 x 84 Å). The H subunits are coloured red and green, and the L subunits are in light blue and purple. The black balls represent the positions of the bound holmium ions (see main text for explanation).

b)

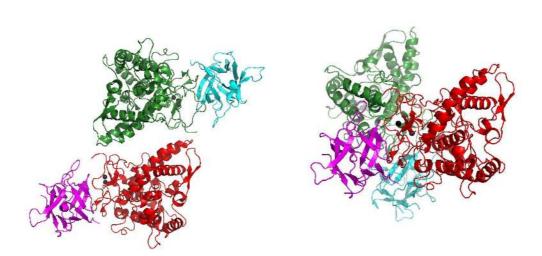


Fig. S2. Structure-based sequence alignment of tyrosinase-related type 3 copper proteins. The aligned structures and PDB database accession numbers are *Ab*Tyr, *A. bisporus* tyrosinase (PPO3, this article; PDB 2y9w); *Bm*Tyr, *B. megaterium* tyrosinase (PDB 3nm8 (1)); *Sc*Tyr, *S. castaneoglobisporus* tyrosinase (PDB 1wx2 (2)); *Ib*Cox, *I. batata* catechol oxidase (PDB 1bt1 (3)) and *Od*hcy, *Octopus dofleini* hemocyanin (PDB 1js8 (4)). Structural alignment was performed using the DALI server. The secondary structure elements are shown as squiggles (α -helix and 3₁₀-helix), black arrows (β -strands) and strict β -turns as **TT** letters at the top of

the alignment. Residues involved in copper binding are shown in cyan. Cysteines involved in the thioether bond are shown in purple. The fully conserved residues are shown in white on red background. Numbers indicate the residue numbers of AbTyr. The figure was prepared with ESPript (5).

AbTyr AbTyr	10 	β1 α1 α2 2020 20000000000 20 30 40 /GIPGEIKNRLNILDFVKNDKFFTLYVRALQ
BmTyr ScTyr IbCox OdHcy	APIQAPEISKCVVPPADLPPGAVVDNCCPPVASNIVDYKL 1 5 10 15 20 25 30 35 40	TV <mark>R</mark> KNQATLTADEKRRFVAAVL PAVTTMKV <mark>R</mark> PAAHTMDKDAIAKFAKAVE AII <mark>R</mark> KNVNSLTPSDIKELRDAMA
AbTyr	α3 <u>0000 TT 000000</u> 50 60 70 80	α4 2000000000000000000000000000000000000
IbCox	VLQARDQSDYSSFFQLGGI <mark>H</mark> GLPYTEWAKAQPQLHLYKAN ILKEKGIYDRYIAWEGAQKFHTPPGS ELKRSGRYDEFVRENEFIMSDTDSGE LMKALPADDPRNFYQQALVECAYCNGGYDQVNFPD KVQADTSDNGYQKIASYEGIPLSCHYENGT.AYA 75 80 85 90 95 100 105 110	SDRNAA <mark>H</mark> MSSAFLPWHREYLLRFERDLQSIN 1.,RTGERSPSFLPWHRRFLLDFEQALQSVD JQEIQVENSWLFFFFHRWYLYFYERILGKLI 1.,CCQHGMVTFPNW <mark>HR</mark> LLTKQMEDALVAKG
	α5 <u>2222</u> <u>2222222222</u> 19 129 139 149	$\begin{array}{ccc} \alpha 6 & \beta 2 \\ 0 0 0 0 & 160 \end{array} TT \xrightarrow{\beta 3} T$
BmTyr	GTVAQRFTTSDQAEWIQAAKDLRQPFWDWGYWPNDPDFIG PEVTLPYWEWETDAQMQDPSQ SSVTLPYWDWSADRTVR GDPSFGLPFWNWDNPGGMV SHVGTPYWDWTTT.FAN	SOIWSADFMGGNGNPIKDFIVDTG
AbTyr	α7 TT TT 2000 TT 2000 180 190 200 210	α8 122220α8 220
ScTyr IbCox	ILHYKFHPIEPTFEGDFAQWQTTMRYPDVQKQENIEGM PFAAGRWTTIDEQGNPSGGLKRNFGA PFAASTGNWPINVRVDSRTYLRRSLGGS. LYD	IIAGIKAAAPGFREWT ATKEAPTLPTRDDV VAELPTRAEV ILPPVVVDLGYNGADTDVTDQQRITDNLALM RA.QLFSFFYRQI
AbTyr BmTyr ScTyr IbCox	α9 20000 20000 2000 230 240 250 250 FNMLTK.NYTWELFSNHGAVVGAHANSLEM LNALKITQYDTPPWDMTSQNSFRNQLEGFI LSVLAISAYDLPPYNSASE.GFRNHLEGWR SVLAISAYDLPPYNSASE.GFRNHLEGWR YKQMVTNAGTAELFLGKAYRAGDAPSPGAGSIET ALALEQTDFCDFEI	NGPQLENRVHRWVGGQMGVV GV.NLENRVHVWVGGQM.AT .SPEIPIERWVGDPRNTNNEDMGNF GENAIMSWVGCSSPYGMSTI
AbTyr	η2 αll β4 200 000000000000000000 → 290 300 310 320	TT TT $\beta 5$ TT $\beta 6$ TT 330 TT
AbTyr BmTyr ScTyr IbCox OdHcy	PHAAFDPIFWMHHCNVDRLLALWOTMNYDVYV.SEGMNRE PTAPNDPVFFLHHANVDRIWAVWOIIHRNQNY GVSPNDPVFWLHHAYVDKLWAEWORRHPDSAY YSAGRDIAFYCHHSNVDRMWTIWOQLA.RDYTD. HYTSYDPLFYLHHSNTDRIWSVWQALQKYRGLPYNTANCE 355 360 365 370 375 380 385 390	QPMKNGPFGQNF.RDPMY VPTGGTP.DVVDLNETMK SDWLNAT.FLFYDENG
AbTyr	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	1000000 390
BmTyr ScTyr IbCox	QDPWQSDDLEDWETLGFSYPDFDPVKGKSKEEKSVYIND PWN.TTPEDVMNHRKLGYVYDI PWNTVRPADLLDHTA.YYTFDAL. QAVKVRIGDSLDNQKMGYKYAKT TKAHSTGATSFDYHKLGYDYDNLNFHGMTIPELEEH 425 430 435 440 445 450 455 460	WVHKHYG PLPWL HLKEIQHE

Fig. S3. Stereo figure of a superposition of *A. bisporus* tyrosinase (green; PDB 2y9w (this article)), *B. megaterium* tyrosinase (orange; PDB 3nq1 (*1*)), *S. castaneoglobisporus* tyrosinase (magenta; PDB 1wx2 (*2*)). Copper ions are in light brown and the inhibitor kojic acid from the *B. megaterium* tyrosinase structure is shown in orange.

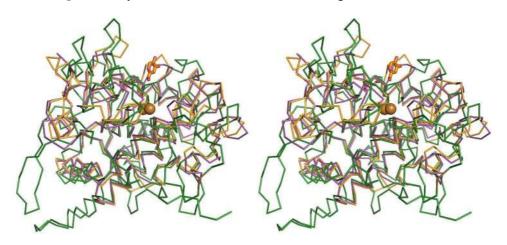
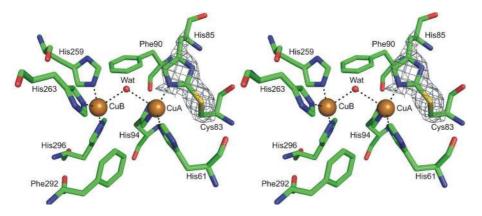


Fig. S4. Stereo figure of the geometry of the binuclear copper-binding site in space group $P2_12_12_12_2$. The ligands are colored according to atom type (green, blue, red, yellow for carbon, nitrogen, oxygen, sulfur, respectively). The brown spheres are the Cu-A and Cu-B copper ions, and the red sphere is a bound water molecule/hydroxyl ion. The electron density for the covalent thioether bond between the Cys83 S γ and His85 C ϵ 1 atoms is contoured at 2.0 σ and is shown in black mesh.



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