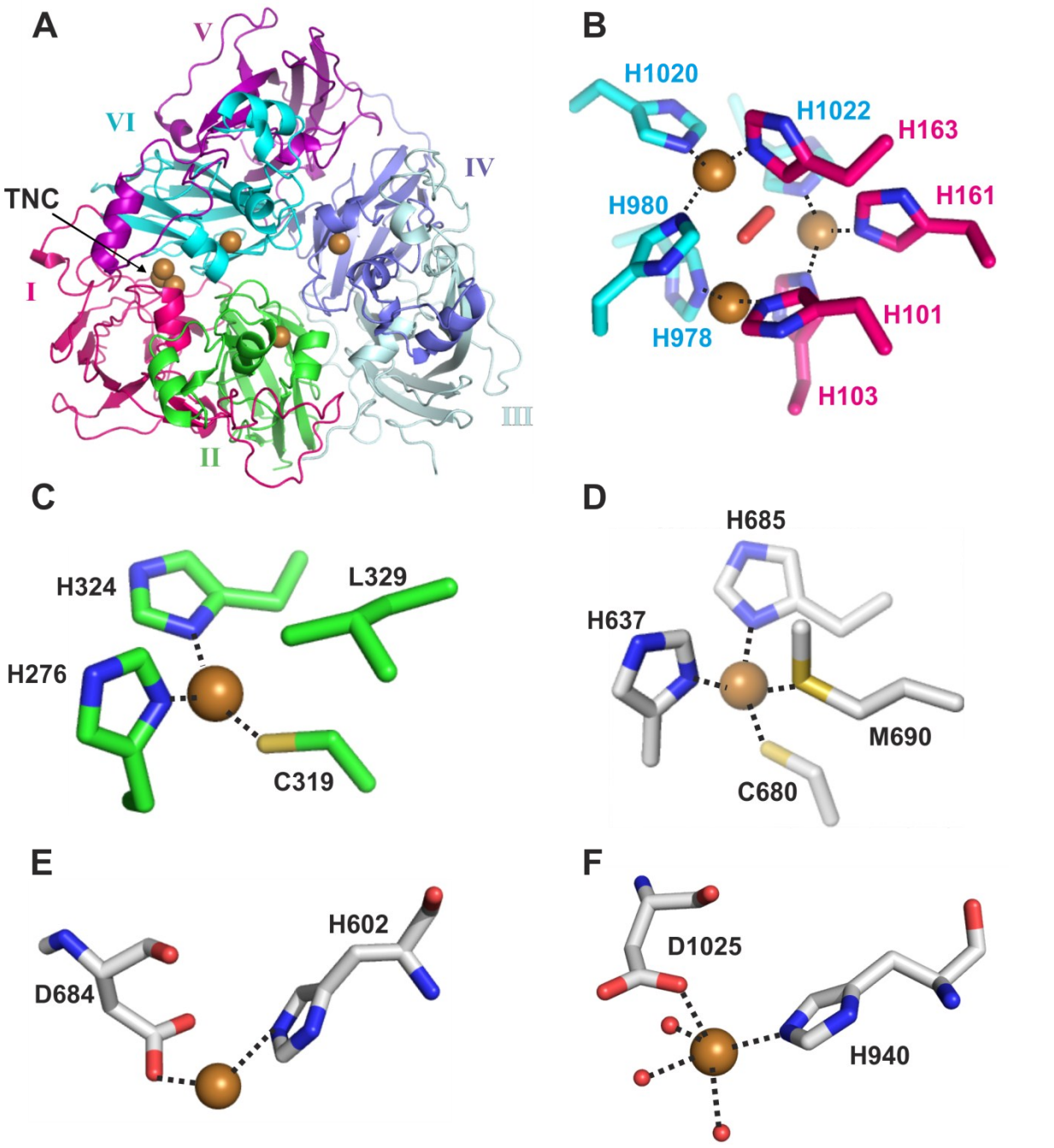
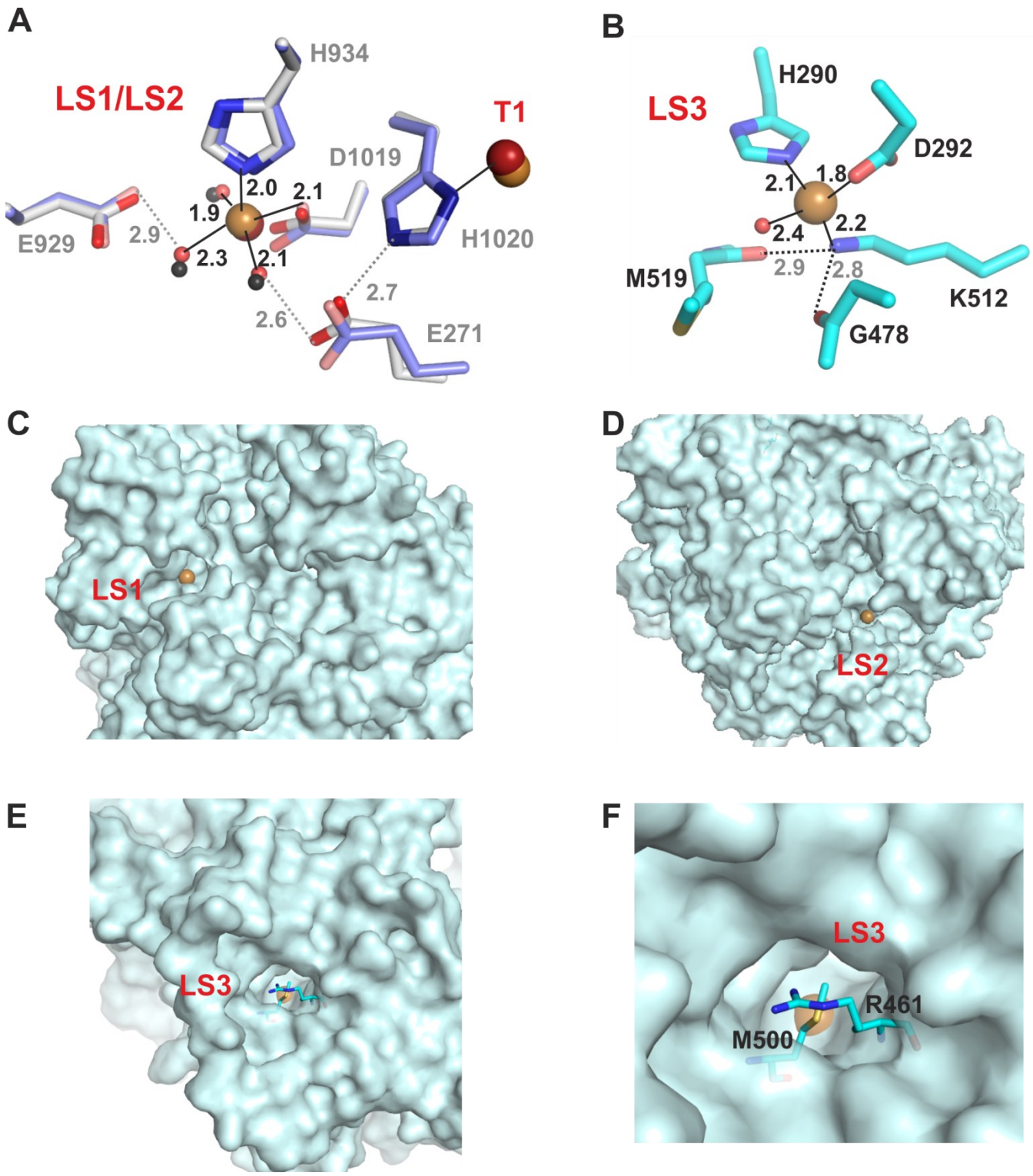
Electronic Supplementary Material (ESI) for Metallomics.



Supplementary Figure S1. Structural organization of human Cp. (A) Cartoon representation of overall domain structure of Cp (pdb code 4enz). Domains are marked in Roman numerals and colored as follows: I in dark pink, II in green, III in pale cyan, IV in blue, V in magenta and VI in cyan. Copper ions are shown as yellow-orange spheres. Trinuclear center is labeled by TNC. (B) The trinuclear center of hCp. Histidines are shown in stick representation. Dyoxygen is shown as red stick. Carbon atoms of histidines are colored corresponding domain color. Nitrogen atoms are colored blue, copper ions are colored yellow-orange. (C,D) Mononuclear copper binding centers, (C) in domain II, (D) in domain IV. Residues are shown in stick representation. Copper ion is shown as yellow-orange sphere. (E,F) Labile copper binding sites. (E) in domain IV (pdb code 1kcw), (F) in domain VI (pdb code 2j5w). Residues are shown in stick representation. Nitrogen and oxygen is colored blue and red. Copper is shown as yellow-orange sphere. On panel (F) water molecules within ~2.4Å distance are shown as red spheres.



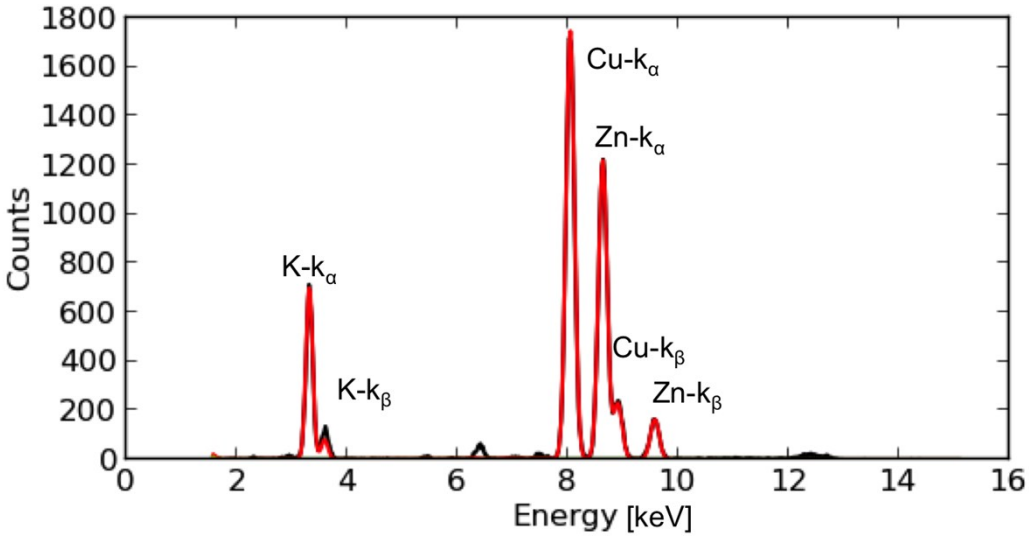
Supplementary Figure S2. Comparison of LS1-LS3 sites of rCp. (A) Superposition of LS1 and LS2 including surrounding. Residues are shown by sticks. Carbon, nitrogen and oxygen atoms are shown violet-blue, blue and red (LS1) or grey, dark blue and red (LS2). Residues in the LS2 and surrounding are labeled. Water molecules are shown by small red (LS2) and pink (LS1) spheres; copper ions are shown by gold (LS2) and brown-red (LS1) spheres. Metal bonds are shown by black lines; H-bonds are shown by grey dash lines. Copper binding in mononuclear site (T1) is shown by gold (domain VI) and dark red (domain IV) sphere. (B) LS3 site. Possible H-bonds of K512 with main chain of G478 or M519 are shown by dash lines. (C,D) Surface representation of rCP. Copper is shown by gold sphere in LS1 (C) and LS2 (D). (E,F) Surface representation of rCp near LS3. Surface of "gate" residues M500 and R461 are not shown for clarity, residues are represented by sticks. (F) Zoom of LS3 area.

Table S1. Comparison of LS3 ligands amino acid composition of different mammalian spices with rat ceruloplasmin (exept *Homo sapiens, Carlito syrichta, Pantholops hodgsonii, Ochotona princeps* and *Heterocephalus glaber)*. Upper line – region around amino acids aligned to 309-311, bottom line – region around amino acid aligned to 531. Identical amino acids of LS3 site are colored in red, different in green and similar in blue.

Spice	LS3 sequence	Spice	LS3 sequence
Rattus norvegicus	TSKNYHTDIINLF PVCLSKMYYSG	***Rattus norvegicus***	TSKNYHTDIINLF PVCLSKMYYSG
Microcebus murinus	TNKNYRIDTINLF PVCLSKMYYSA	*Aotus nancymaae*	TNKNYRIDTVNLF PVCLAKMYYSA
Leptonychotes weddellii	TNKNYRIDTVNLF PVCLSKMYYSA	*Propithecus coquereli*	TNKNYRIDTINLF PVCLSKMYYSA
Pan paniscus	TNKNYRIDTINLF PVCLAKMYYSA	*Mandrillus leucophaeus*	TNKNYRIDTINLF PVCLAKMYYSA
Elephantulus edwardii	THKKSRTDTINLF PVCISKMYYSA	*Cercocebus atys*	TNKNYRIDTINLF PVCLAKMYYSA
Mus musculus strain C57BL/6J	TSRNYQTDIINLF PVCLSKMYYSG	*Colobus angolensis palliates*	TNKNYRIDTINLF PVCLAKMYYSA
Echinops telfairi	TNQNYRVDTINLF PVCLSRMYYSA	*Macaca nemestrina*	TNKNYRIDTINLF PVCLAKMYYSA
Nannospalax galili	TNKNYRTDAINLF PVCLSRMYYSA	*Pteropus vampyrus*	TNKNYRIDTINLF PVCLSKMYYSA
Chinchilla lanigera	TNKNYRIDTINLI PVCLSRMYYSA	*Felis catus*	TNKGYRIDTVNLF PVCLSKMYYSA
Mesocricetus auratus	TSKNYRTDTINLF SNCVTRIYHSH	*Camelus dromedarius*	TNKNFRIDTVNLF PVCLAKMYYSA
Marmota marmota	TNKNYRVDTIHLF PVCLSRMYYSA	*Bison bison*	TSKNYRVDTINLF PVCLAKMYYSA
Otolemur garnettii	TNKNYRIDTVNLF PVCLARMYYSA	*Ursus maritimus*	TNKNYRIDTVNLF PVCLSKMYYSA
Ictidomys tridecemlineatus	TNKNYRVDTIHLF PVCLSRMYYSA	*Galeopterus variegatus*	TNKNYRIDTINLF PVCLSKMYYSA
Microtus ochrogaster	TSKNYRTDTINLF PVCLSRMYYSG	*Equus przewalskii*	TNKNYRIDTINLF PVCLSKMYYSA
Cavia porcellus	INKNYRIDTINLF PVCLPGMYYSA	*Eptesicus fuscus*	TNKNYRIDTINLF PVCLAKMYYSA
Cavia porcellus	INKNYRIDTINLF PVCLPGMYYSA	*Orycteropus afer*	TNKNYRVDTINLF PVCLSKMYYSS
Octodon degus	TNKNYRIDAVNLF PSCLPGMYYSA	*Chlorocebus sabaeus*	TNKNYRIDTINLF PVCLAKMYYSA
Fukomys damarensis	TNKNYRVDTINLF PVCLSGMYYSA	*Erinaceus europaeus*	TNKNYRVDTVNLF PVCLAKMYYSA
Rhinopithecus roxellana	TNKNYRIDTINLF PICLTWFYYSS	*Lipotes vexillifer*	TNKNYRVDTINLF PVCLAKMYYSA
Acinonyx jubatus	TNKGYRIDTVNLF PVCLSKMYYSA	*Balaenoptera acutorostrata scam.*	TSKNYRVDTINLF PVCLAKMYYSA
Macaca mulatta	TNKNYRIDTINLF PVCLAKMYYSA	*Physeter catodon*	TNKNYRVDTINLF PVCLAKMYYSA
Ovis aries	TSKNYRVDTINLF PVCLAKMYYSA	*Panthera tigris altaica*	TNKDYRIDTVNLF PVCLSKMYYSA
Equus asinus	TNKNYRIDTINLF PVCLSKMYYSA	*Pteropus alecto*	TNKNYRIDTINLF PVCLSKMYYSA

Table S1. (continuation)

Spice	LS3 sequence	Spice	LS3 sequence
Rattus norvegicus	TSKNYHTDIINLF PVCLSKMYYSG	***Rattus norvegicus***	TSKNYHTDIINLF PVCLSKMYYSG
Camelus ferus	TNKNFRIDTVNLF PVCLAKMYYSA	*Canis lupus familiaris*	TNKNYRVDTVNLF PVCLSKMYYSA
Vicugna pacos	TSKNFRIDTVNLF PVCLAKMYYSA	*Sus scrofa*	TNKNYRIDTINLF PVCLTKMYYSA
Tupaia chinensis	TNKNYRIDTVNLF PVCLAKMYYSA	*Loxodonta africana*	TSKNYRIDTINLF PVCLCKMYYSA
Myotis lucifugus	TNKNYRVDTINLF PVCLAKMYYSA	*Pan troglodytes*	TNKNYRIDTINLF PVCLAKMYYSA
Bubalus bubalis	TSKNYRVDTINLF PVCLAKMYYSA	*Oryctolagus cuniculus*	TNKNYRIDTINLF PVCLSKMYYSA
Bos mutus	TSKNYRVDTINLF PVCLAKMYYSA	*Bos taurus*	TSKNYRVDTINLF PVCLAKMYYSA
Myotis brandtii	TNKNYRVDTINLF PVCLAKMYYSA	*Pongo abelii*	TNKNYRIDTINLF PVCLAKMYYSA
Macaca fascicularis	TNKNYRIDTINLF PVCLAKMYYSA	*Equus caballus*	TNKNYRIDTINLF PVCLSKMYYSA
Condylura cristata	TNKNYRVETINLF PACLSKMYYSA	*Monodelphis domestica*	TNKNHRVDTINLF PNCLTKMYYSA
Odobenus rosmarus divergens	TNKNYRIDTVNLF PVCLSKMYYSA	*Sarcophilus harrisii*	TNQHHRVDTINLF PNCLTKMYYSG
Trichechus manatus latirostris	TNKNYRIDTINLF PVCLCKMYYSA	*Saimiri boliviensis*	TNKNYRIDTINLF PVCLAKMYYSA
Tursiops truncatus	TNKNYRVDTINLF PVCLAKMYYSA	*Nomascus leucogenys*	TNKNYRIDTINLF PVCLAKMYYSA
Orcinus orca	TNKNYRVDTINLF PVCLAKMYYSA		



Supplementary Figure S3. Fluorescence spectrum of rCp crystal. K-emission lines of copper, zinc and potassium (0.2 M in crystallization solution) are labeled. Incident beam energy was set to 12.7 keV.