Effect of copper on the carnitine transport mediated by the mitochondrial carnitine/acylcarnitine carrier. Structural basis and possible implications in pathophysiology.

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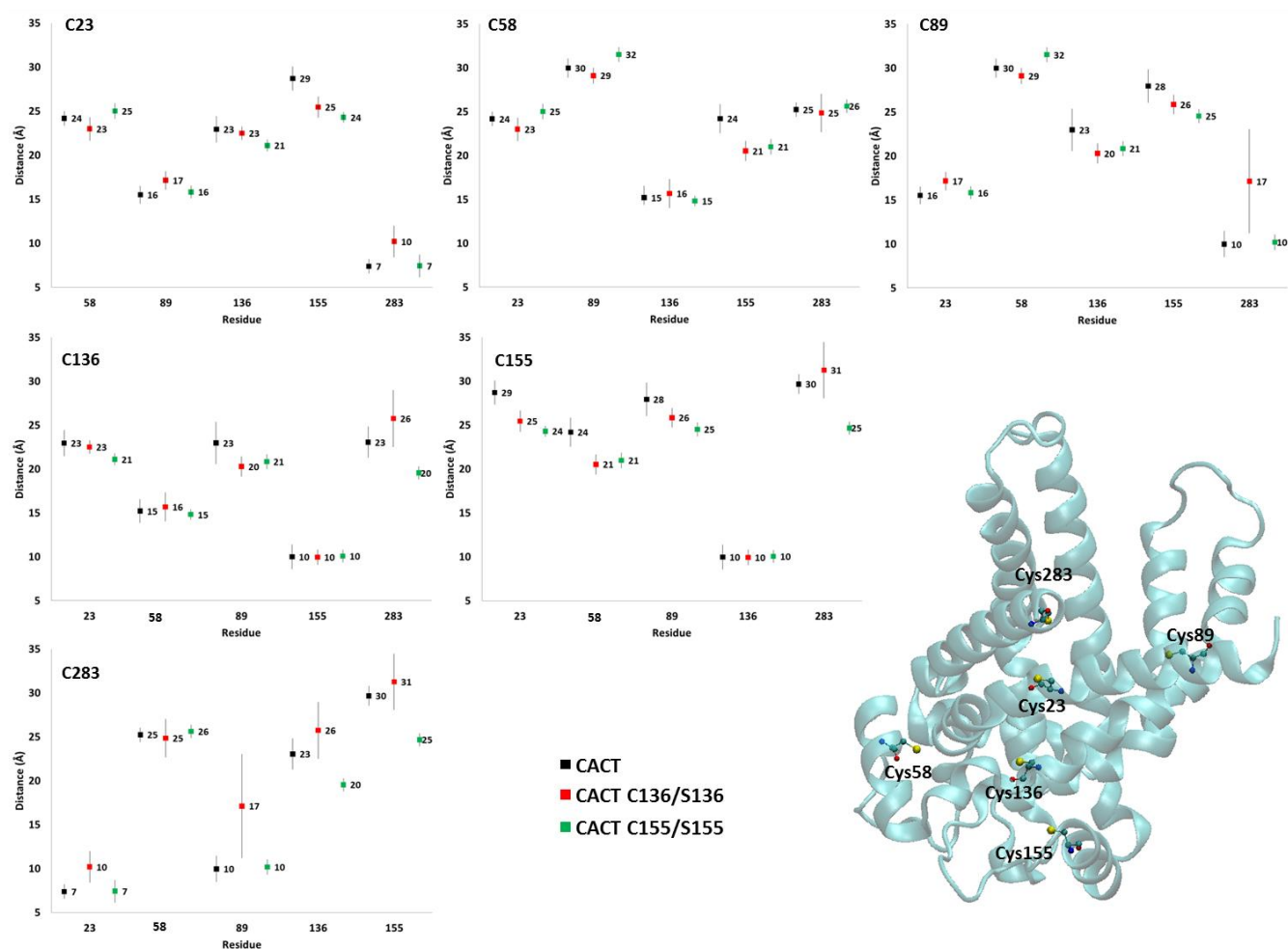***** Correspondence: E-mail: cesare.indiveri@unical.it; Tel:+39-0984-492939; (C.I.)

Figure S1. Interatomic average distances, calculated along 200 ns of MDs for the three different systems, between residues deputed to bind the copper ions. The reported standard deviation bar were evaluated according to the equation $\sigma = \sqrt{\dfrac{\sum_{i=1}^{N}(d_i - \bar{d})^2}{N-1}}$.
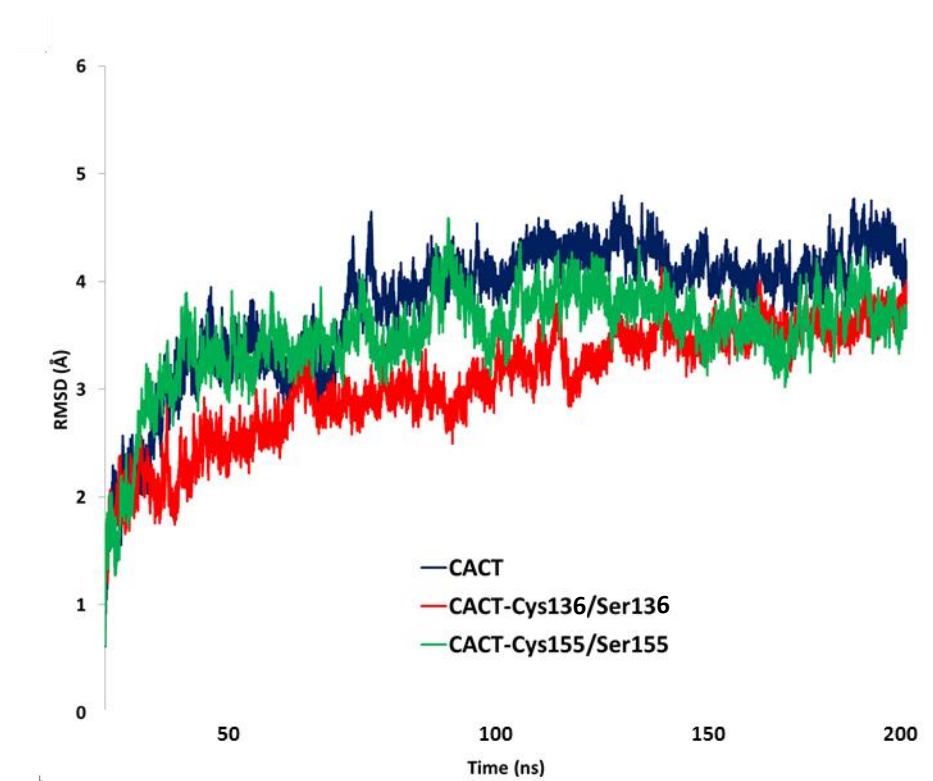
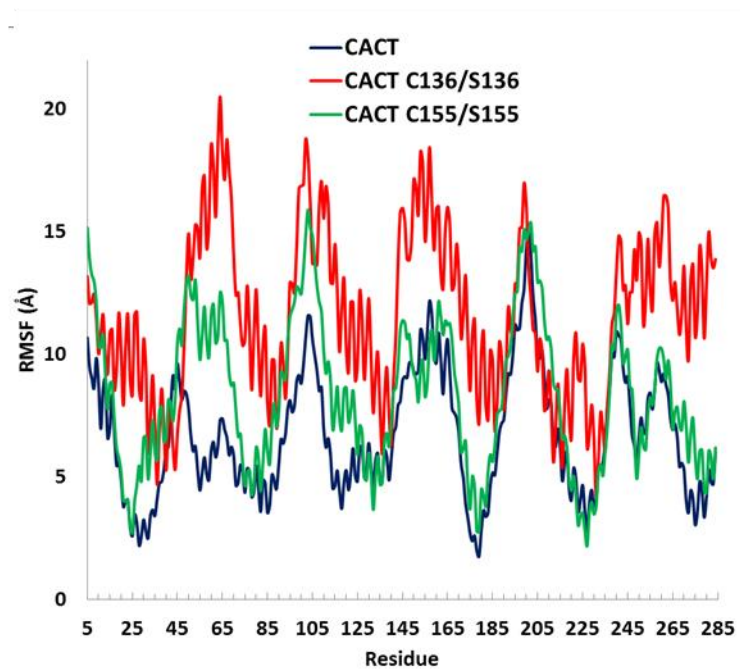**Figure S2.** Root Mean Square Deviation (RMSD) calculated along 200 ns of MDs for the three different systems.

Figure S3. Root Mean Square Fluctuation (RMSF) calculated along 200 ns of MDs for all the amino acid residues of the three systems.
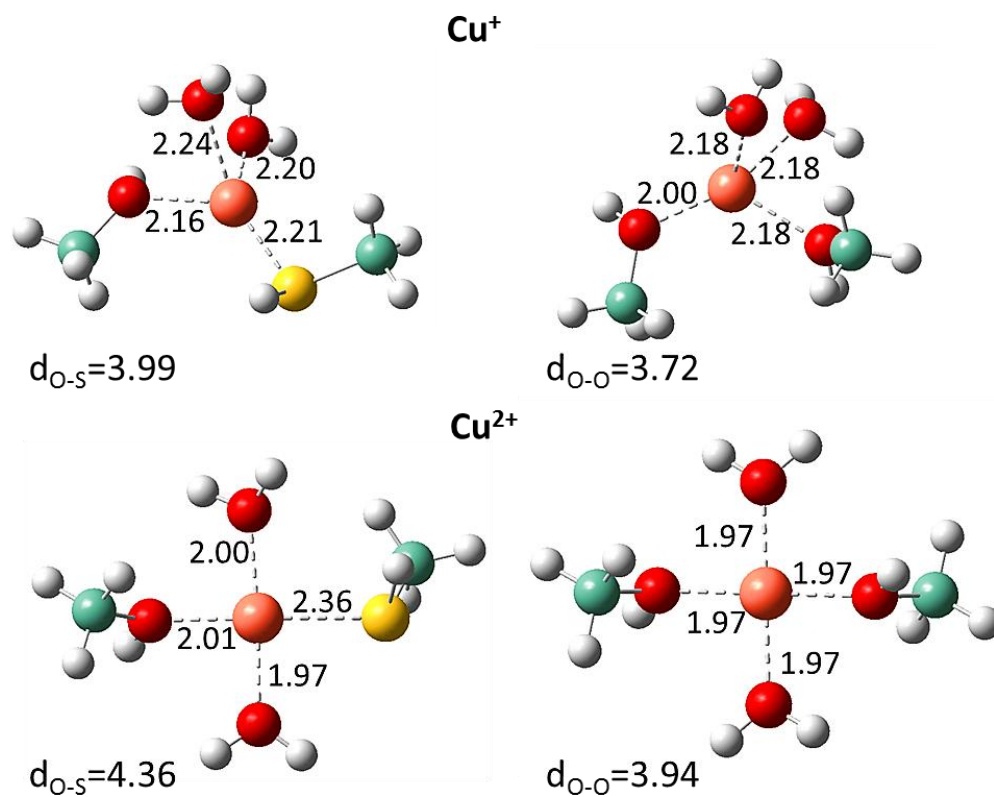
Cu⁺

$d_{O-S}=3.99$ $d_{O-O}=3.72$

Cu²⁺

$d_{O-S}=4.36$ $d_{O-O}=3.94$

Figure S4. B3LYP-D3/6-31+G(d,p) optimized structures of [Cu⁺(CH₃SH)(CH₃OH)(H₂O)₂], [Cu⁺(CH₃OH)₂(H₂O)₂], [Cu⁺⁺(CH₃SH)(CH₃OH)(H₂O)₂], and [Cu⁺⁺ (CH₃OH)₂(H₂O)₂]. Main geometrical parameters are reported in (Å).
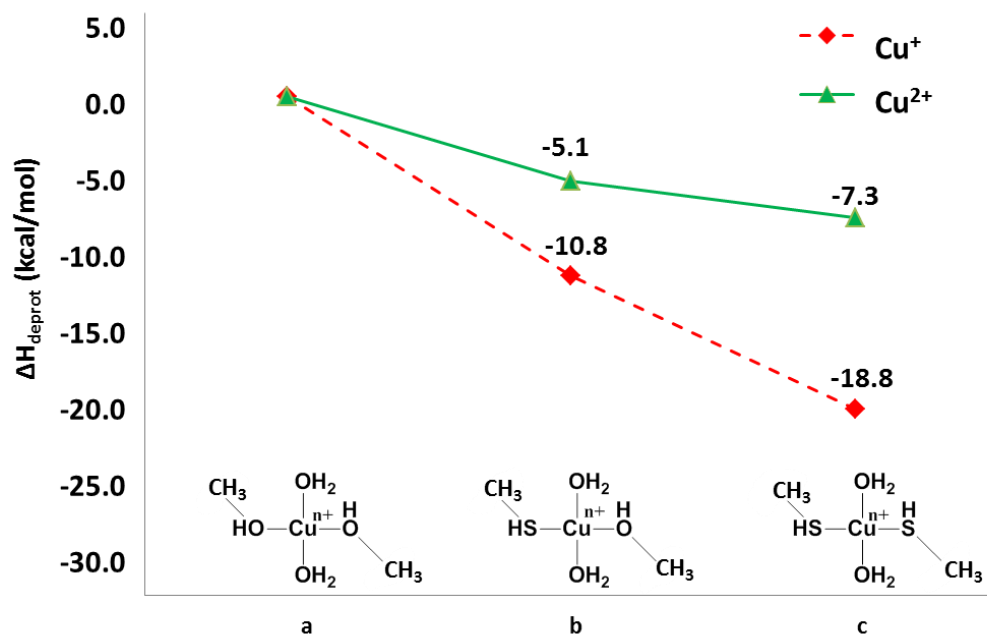
Figure S5. Calculated $\Delta H_{deprotonation}$ according to the following reactions:

a) $[Cu^{n+}(CH_3SH)_2(H_2O)_2] \rightarrow [Cu^{n+}(CH_3S)_2(H_2O)_2]^{n-2} + 2H^+$

b) $[Cu^{n+}(CH_3SH)(CH_3OH)(H_2O)_2] \rightarrow [Cu^+(CH_3S)(CH_3O)(H_2O)_2]^{n-2} + 2H^+$

c) $[Cu^{n+}(CH_3OH)_2(H_2O)_2] \rightarrow [Cu^{n+}(CH_3O)_2(H_2O)_2]^{n-2} + 2H^+$