Supporting Information to the manuscript

Identification of Cisplatin-Binding Sites on the Large Cytoplasmic Loop of the Na^+/K^+-ATPase

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1) MALDI-TOF mass spectrometry results

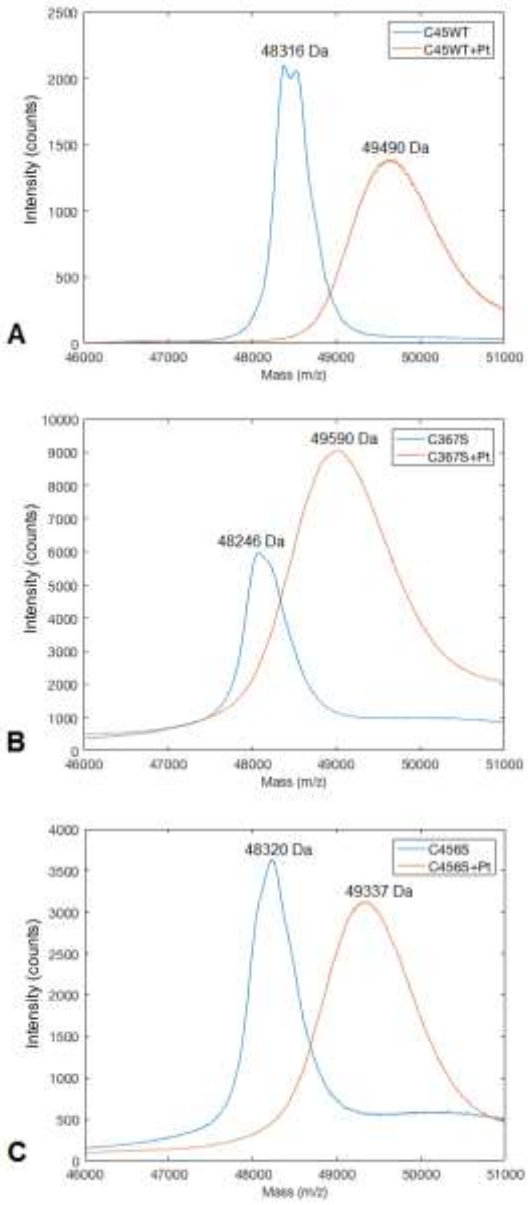

Figure S1: Intact masses of C45 WT (A), C452S (B), and C549S (C) for the untreated (in blue) and cisplatin-treated (in red) proteins measured by MALDI-TOF mass spectrometry. Each indicated mass value is the calculated mean from ten replicates.

2) Molecular dynamics

The molecular dynamics simulations were performed in duplicates and denoted as WT1 and WT2. Radial Distribution Function, g(r), describes the ratio between the number of water molecules in a sphere with radius r centred at a selected cysteine, and the number of water molecules in the bulk solvent in a sphere of the same radius. There are no clear peaks, but the shape of the function differs depending on water accessibility. In the case of buried residues, the value of g(r) remains under 0.2 until distances over 1 nm, whereas in water accesible residues the g(r) value rises above 0.2 at about 0.5 nm. In the case of a helix unwinding in WT2, the g(r) value rises even more rapidly.

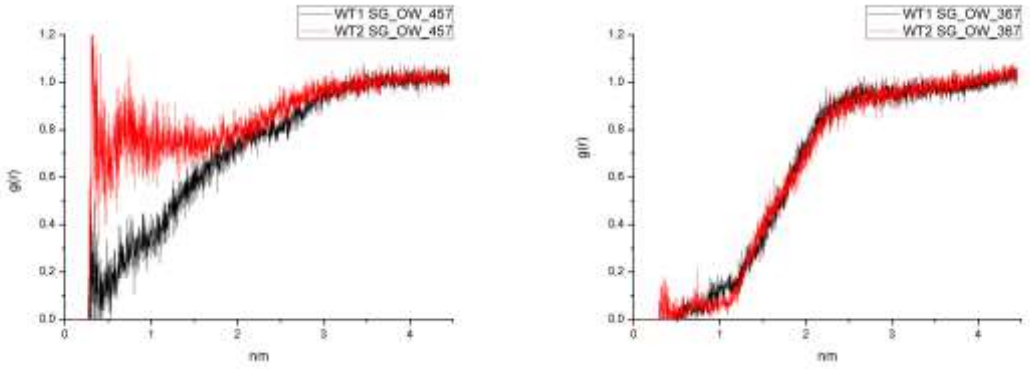

Figure S2: Examples of radial distribution function between the cysteine sulphur and water oxygen for C457 (left) and C367 (right). The radial distribution function for C457 in the first simulation (black) exhibits a typical pattern for the residue on the protein surface. A partial helix unwinding in the second MD simulation (red) causes better water accessibility of C457 and higher radial distribution function value even for small radius. In contrast, C367 is buried under the protein surface, and a substantial number of water molecules is observed only at distances over 1 nm.