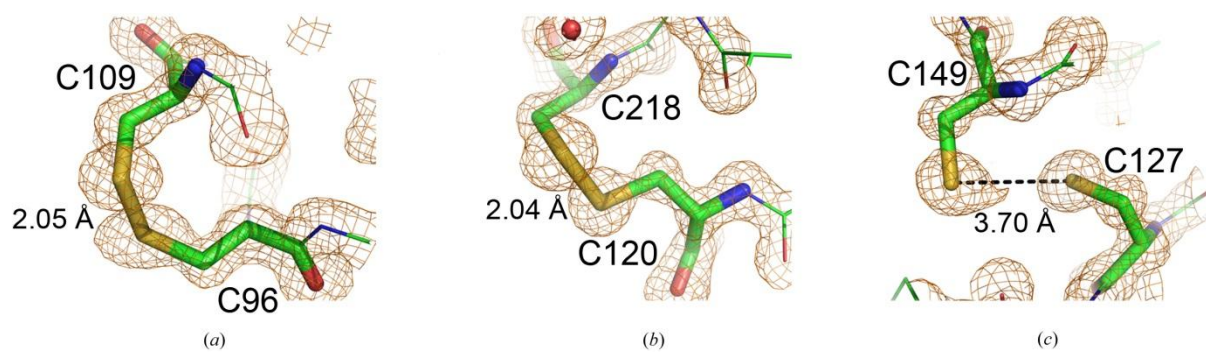
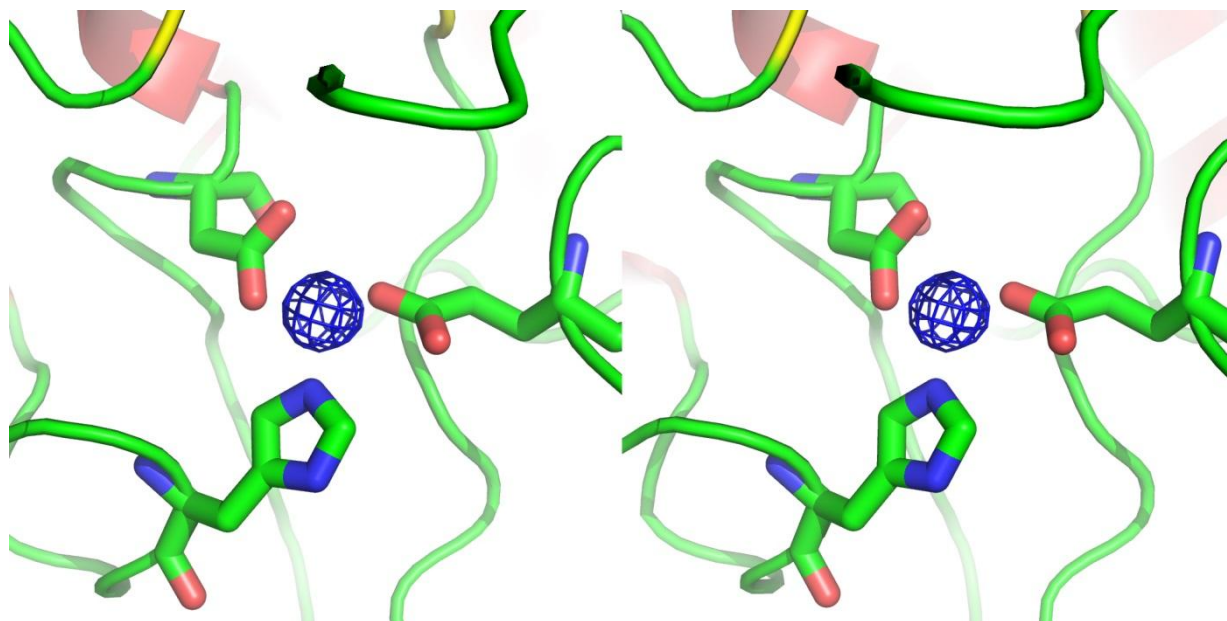


## SUPPORTING INFORMATION



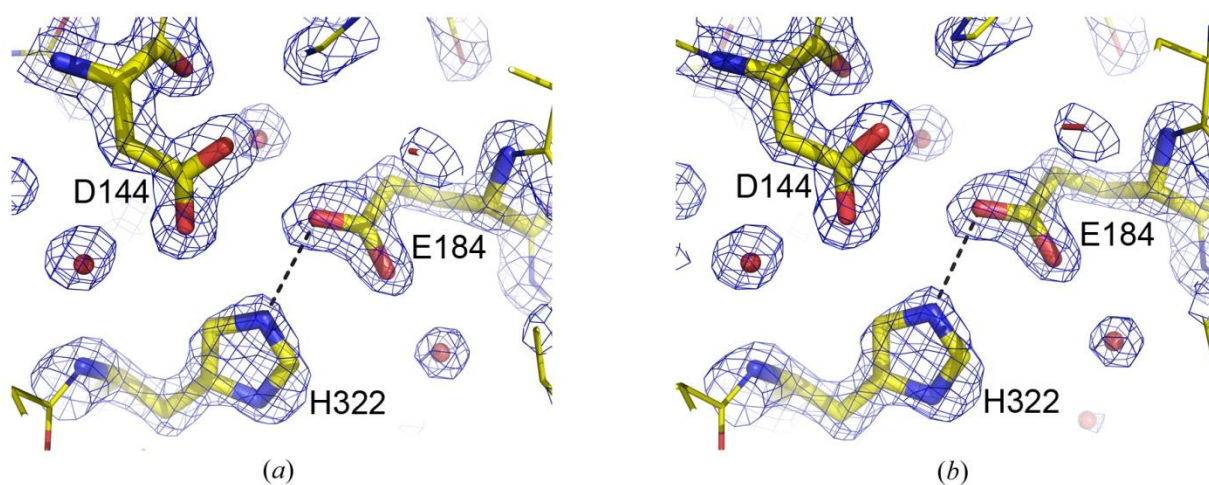
### Figure S1

The disulfide bridges in *Is*-QC. The final refined models around (a) C<sup>96</sup>-C<sup>109</sup>, (b) C<sup>120</sup>-C<sup>218</sup>, and (c) C<sup>127</sup>-C<sup>149</sup> are overlaid with the  $2F_o - F_c$  electron-density maps contoured at  $2.5\sigma$  level. The distances between the sulfur atoms are indicated.



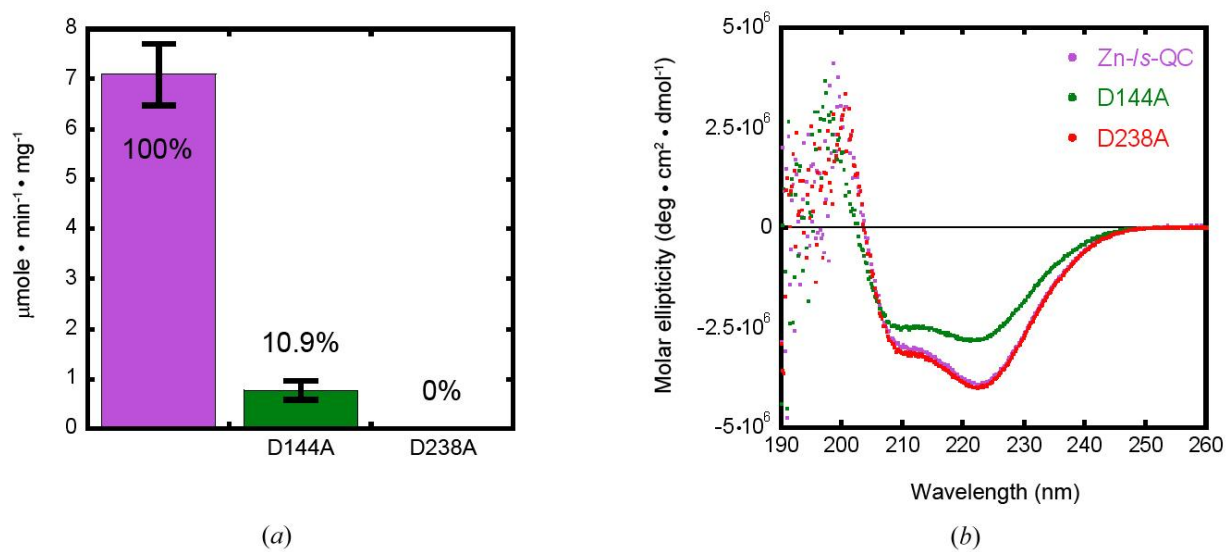
**Figure S2**

A stereo view of the anomalous difference map for Zn-*Is*-QC structure calculated by using an X-ray data collected at a zinc-absorption wavelength. The density map of zinc, colored in blue, is contoured at  $20\sigma$  level.



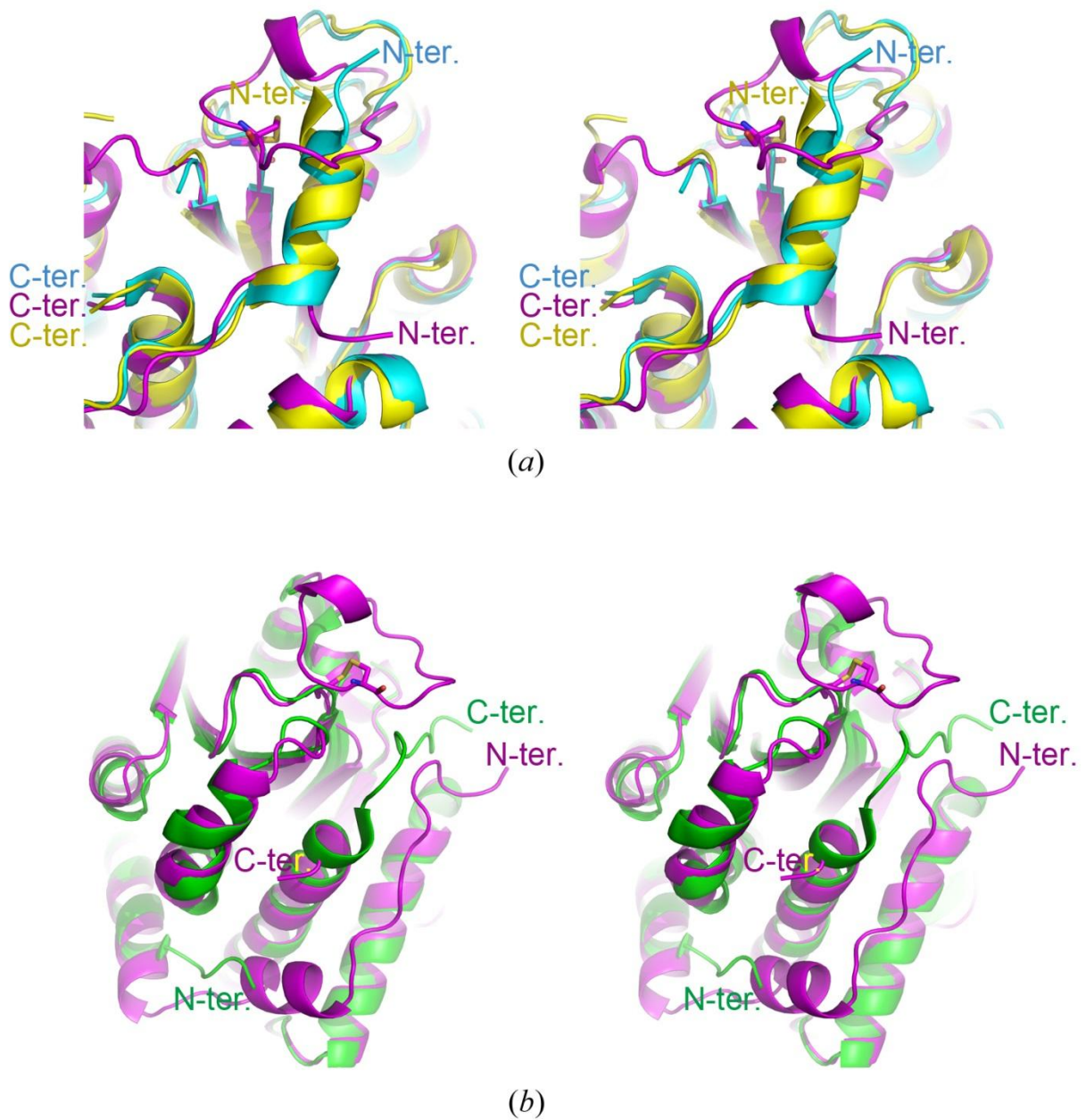
### Figure S3

Removal of zinc ion by EDTA. (a) Zn-Is-QC was co-crystallized with 1 mM EDTA and the crystal structure was determined and refined to 1.75-Å resolution. The final refined structure, shown as stick model, is overlaid with the  $2F_o - F_c$  electron-density map contoured at  $2.0\sigma$  level. (b) The Zn-Is-QC crystals were soaked in the mother liquor added with 1 mM EDTA and the crystal structure was determined and refined to 1.75-Å resolution. The final refined structure is also overlaid with the  $2F_o - F_c$  electron-density map contoured at  $2.0\sigma$  level.



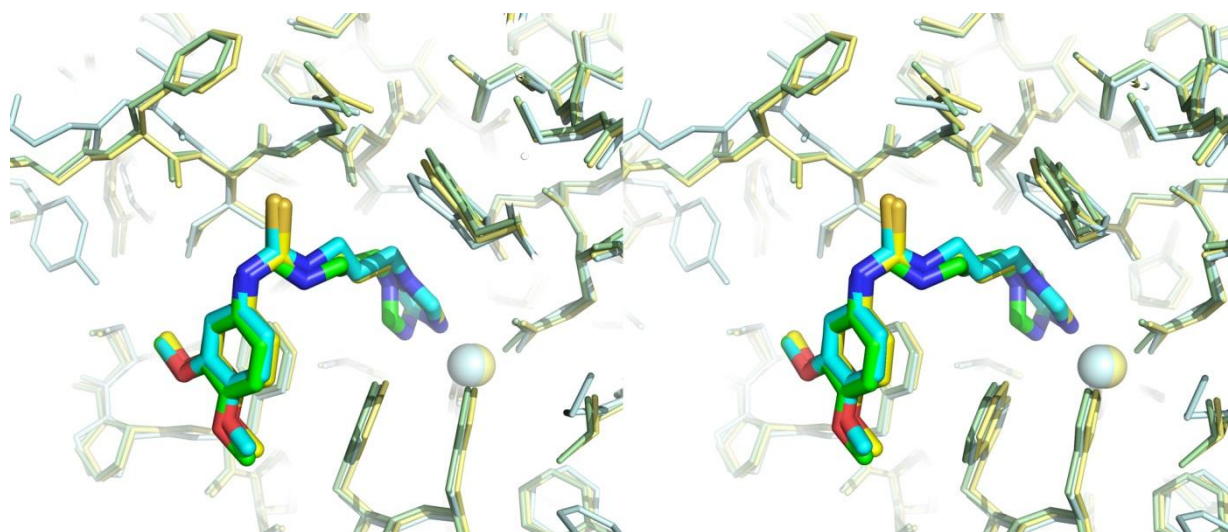
### Figure S4

Site-directed mutagenesis. (a) Enzymatic activities of the *Is*-QC mutants D144A and D238A and comparison with the activity of wild-type Zn-*Is*-QC. The results in activities  $\pm$  SD were calculated from three independent experiments. (b) Circular dichroism spectroscopy analysis of D144A, D238A, and Zn-*Is*-QC.



**Figure S5**

Comparison of the N-terminal and C-terminal structures of *Is*-QC and the human, mouse, and *Drosophila* sQCs. (a) A stereo view of *Is*-QC structure (magenta) superimposed with the structures of human (cyan) and mouse (yellow) sQCs. (b) A stereo view of *Is*-QC structure (magenta) superimposed with the structure of *Drosophila* sQC (green). The N-terminus and C-terminus of these QC structures are further indicated.



**Figure S6**

Superimposition in stereo view of the PBD150-bound structures of Zn-*Is*-QC, apo *Is*-QC, and the human secreted QC. The bound PBD150 molecules in Zn-*Is*-QC, apo *Is*-QC, and human secreted QC are drawn with stick model and colored in yellow, green, and cyan, respectively.