

# Crystal Structure of *Escherichia coli* Thiol Peroxidase in the Oxidized State

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Thioredoxin-dependent thiol peroxidase (Tpx) from *Escherichia coli* represents a group of antioxidant enzymes that are widely distributed in pathogenic bacterial species and which belong to the peroxiredoxin (Prx) family. Bacterial Tpxs are unique in that the location of the resolving cysteine (C<sub>R</sub>) is different from those of other Prxs. *E. coli* Tpx (*EcTpx*) shows substrate specificity toward alkyl hydroperoxides over H<sub>2</sub>O<sub>2</sub> and is the most potent reductant of alkyl hydroperoxides surpassing AhpC and BCP, the other *E. coli* Prx members. Here, we present the crystal structure of *EcTpx* in the oxidized state determined at 2.2-Å resolution. The structure revealed that Tpxs are the second type of atypical 2-Cys Prxs with an intramolecular disulfide bond formed between the peroxidatic (C<sub>P</sub>, Cys<sup>61</sup>) and resolving (Cys<sup>95</sup>) cysteine residues. The extraordinarily long N-terminal chain of *EcTpx* folds into a β-hairpin making the overall structure very compact. Modeling suggests that, in atypical 2-Cys Prxs, the C<sub>R</sub> loop as well as the C<sub>P</sub> loop may alternately assume the ‘fully folded’ or ‘locally unfolded’ conformation depending on redox states, as does the C<sub>P</sub> loop in typical 2-Cys Prxs.