The Thermodynamics of Thiol Sulfenylation

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Oxygen is one of the crucial building blocks of almost all living cells. However, reactive oxygen species (ROS), such as peroxides and oxygen radicals are formed as a natural byproduct of the metabolism of oxygen. These ROS can harm essential body proteins or damage DNA. To prevent such injuries, our body has anti-oxidant proteins such as human thioredoxin peroxidase B (Tpx-B) [1] which are specialized in ROS scavenging. To disarm ROS, human Tpx-B has an essential cysteine residue (Cys51) which is oxidized to sulfenic acid during ROS scavenging in a process called sulfenylation. Experimental work gives insight into the reaction rates of sufenylation, but not into the thermodynamic aspects. Therefore, we performed a quantum mechanics/molecular mechanics (QM/MM) study to elucidate how the protein environment of human Tpx-B drives sulfenylation. To this end, we recently developed a computational method to determine reduction potentials relatively compared to a reference system and based on reaction energies (REE) [2]. With this universally applicable computational protocol, we got a better understanding of the effects of several active site residues on the thiol/sulfenic acid oxidation potential of human Tpx-B. Especially a conserved arginine residue (Arg127) drives thiol sulfenylation, consistent with the observed Arg127--Cys51 interactions. This relates structure to reactivity.

References

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