Developing proteomics approaches for identifying new, redox-regulated proteins

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For many years it was thought that hydrogen peroxide was only a toxic substance to cells. However, recent work has revealed that hydrogen peroxide can be utilized by organisms as a cellular signaling molecule. Hydrogen peroxide has the ability to react with proteins involved in signal transduction causing the activity of these proteins to be turned on or off. One such example is protein tyrosine phosphatase 1B (PTP1B) whose enzymatic activity is turned off by reacting with hydrogen peroxide. A cysteine residue in the active site of PTP1B is oxidized by hydrogen peroxide to form a sulfenic acid which then reacts with a neighboring amide nitrogen in the protein backbone to form a cyclic sulfenamide. The formation of this heterocycle causes PTP1B to lose its activity. In order to discover new proteins that are oxidatively regulated by hydrogen peroxide, chemical tools for selective detection of cyclic sulfenamide residues in cellular probing need to be developed. We describe results obtained using simple chemical models to identify reagents that have the ability to selectively tag protein derived sulfenamide residues.