INVESTIGATIONS INTO THE CHEMISTRY OF PROTEIN TYROSINE PHOSPHATASE REDOX REGULATION

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ABSTRACT

Transmission of complex intracellular signals, such as those for glucose uptake or proliferation, is often accomplished through the reversible phosphorylation of specific protein tyrosine residues. This reversible phosphorylation serves as a biochemical "rheostat" that alters a protein's functional properties and leads to propagation of the signal. The phosphorylation status of these tyrosine residues, thus transmission of the cellular signal itself, is tightly controlled by the opposing actions of protein tyrosine kinases that catalyze the addition of phosphoryl groups and protein tyrosine phosphatases (PTPs) are cysteine based enzymes that catalyze their removal. Abstraction of these phosphoryl groups, in many cases, serves as an "off switch" to terminate the cellular responses to the extracellular stimulus. PTPs, therefore, play a central role in the regulation of diverse cellular processes including glucose metabolism, cell cycle control and immune responses. Accordingly, small molecules capable of inactivating PTPs through reversible oxidation of their active site cysteine thiolate may find use as therapeutic agents and/or tools for the study of diverse signal transduction pathways. In the body of work presented here we report the chemical properties of a novel PTP redox regulator and develop new methodologies for studying PTP redox regulation.