
Preface

Protein tyrosine phosphatases (PTPs) are major direct regulators of the phosphotyrosine cellular content and essential drivers of the tyrosine-phosphorylation status of key cell signaling proteins. Tyrosine phosphatases include proteins from the Cys-based PTP superfamily (containing a PTP catalytic domain and a CxxxxR signature catalytic motif) as well as enzymes from other gene families (Asp- and His-based phosphatases) that have converged to perform dephosphorylation of biological moieties by a two-step, nucleophile-based catalytic mechanism. Such convergence illustrates the adaptive relevance and the wide variety of the dephosphorylation functions mediated by these enzymes, whose manipulation could be important for specific therapeutic targeting in human disease, including cancer, neurodevelopmental, and metabolic diseases. Moreover, since mutations in many PTP genes are associated with hereditary diseases, several PTP family members are currently relevant in disease prevention and early molecular diagnosis. Tyrosine phosphatases are versatile enzymes in terms of substrate specificity and regulatory properties. Classical PTPs dephosphorylate specific phosphotyrosine residues from protein substrates, whereas dual-specificity PTPs dephosphorylate phosphotyrosine, phosphoserine, and phosphothreonine residues, as well as non-proteinaceous substrates, including phosphoinositides (the tumor suppressor PTEN being a hallmark) and carbohydrates, among others. In addition, several PTPs have impaired catalytic activity as a result of amino acid substitutions at their active sites but retain regulatory functions related to phosphotyrosine or phosphoinositide signaling. The substrate specificity and biological function of PTPs, as well as their regulation during cell homeostasis, is facilitated by a diverse array of protein-interaction and protein-targeting domains, and reversible oxidation of their active sites is a major physiological regulatory mechanism of the catalysis of many Tyr phosphatases.

This book is aimed to provide coverage, methodology, and laboratory protocols on the more essential aspects of PTP function and regulation, including the use of standardized in vitro functional assays, suitable cell systems, and animal and microorganism models. Chapters covering state-of-the-art technical approaches suitable to decipher the physiologic roles of PTPs, and their involvement in tissue-specific functions, are also included, which will be of utility for both newcomers and experienced researchers in the field of tyrosine- and phosphoinositide-phosphorylation/dephosphorylation. I wish to thank all authors for their valuable input and contribution to this issue of *Methods in Molecular Biology*. We think the book will be of interest to chemists, biochemists, molecular biologists, and cell biologists, as well as to clinicians focusing their attention on the role of protein kinases and phosphatases in human disease. It is our hope that the methods and protocols from the chapters of this book will help researchers to better define the common and individual features of the PTP family members, and how this knowledge can translate into PTP-based therapy for human disease.

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Protein Tyrosine Phosphatases

Methods and Protocols

Pulido, R. (Ed.)

2016, XII, 402 p. 79 illus., 51 illus. in color. With online files/update., Hardcover

ISBN: 978-1-4939-3744-8

A product of Humana Press