



Ribosomal Protein S6 Phosphorylation in the Nervous System: From Regulation to Function

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Since the discovery of the phosphorylation of the 40S ribosomal protein S6 (rpS6) about four decades ago, much effort has been made to uncover the molecular mechanisms underlying the regulation of this post-translational modification. In the field of neuroscience, rpS6 phosphorylation is commonly used as a readout of the mammalian target of rapamycin complex 1 signaling activation or as a marker for neuronal activity. Nevertheless, its biological role in neurons still remains puzzling. Here we review the pharmacological and physiological stimuli regulating this modification in the nervous system as well as the pathways that transduce these signals into rpS6 phosphorylation. Altered rpS6 phosphorylation observed in various genetic and pathophysiological mouse models is also discussed. Finally, we examine the current state of knowledge on the physiological role of this post-translational modification and highlight the questions that remain to be addressed.

Keywords: rpS6 phosphorylation, mRNA translation, ribosome, mTOR, S6K, PP-1, brain, signaling cascades

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INTRODUCTION

The eukaryotic ribosome is composed of the small 40S and the large 60S subunits, comprising together 4 ribosomal RNA species and 79 ribosomal proteins (Kressler et al., 2010). In many organisms, ribosomal proteins undergo various post-translational modifications, including phosphorylation, acetylation, methylation, O-linked β -N-acetylglucosaminylation, and ubiquitylation (Xue and Barna, 2012). Historically, the phosphorylation of the 40S ribosomal protein S6 (rpS6) was the first post-translational modification described (Gressner and Wool, 1974). The presence of phospho-rpS6 (p-rpS6) at different levels in a 2D gel provided the first evidence that rpS6 phosphorylation could occur at several residues (Lastick et al., 1977). Ensuing studies identified five evolutionary conserved and clustered carboxy-terminal phospho-sites, which undergo phosphorylation in an ordered manner, beginning with Ser236 and followed sequentially by Ser235, Ser240, Ser244, and Ser247 (Martin-Pérez and Thomas, 1983; Wettenhall et al., 1992; Meyuhas, 2008, 2015). Intriguingly, the exact function of the post-translational modification of this indispensable ribosomal protein remains enigmatic. Despite the large debate regarding its physiological role, rpS6 phosphorylation is commonly used as a marker for neuronal activity and a readout of mammalian target of rapamycin complex 1 (mTORC1) activity (Meyuhas, 2008, 2015; Mahoney et al., 2009; Knight et al., 2012). This review summarizes our current knowledge regarding the molecular mechanisms as well as the variety of stimuli modulating rpS6 phosphorylation in the nervous system.

Protein Phosphorylation In The Nervous System

Paul Marangos



Protein Phosphorylation In The Nervous System:

Protein Phosphorylation in the Nervous System Eric J. Nestler, Paul Greengard, 1984-06-14 Considers the role of protein phosphorylation in neuron specific phenomena Comprehensively treats the enzymes and molecular biology of phosphorylation and dephosphorylation reactions examines evidence for the obligatory role of these reactions in neuronal function and extensively reviews the large number of phosphorylation pathways and their interactions Original schematic diagrams illustrate principles of the biochemical basis of cell regulation

The Cell Cycle in the Central Nervous System Damir Janigro, 2008-01-23 Cell Cycle in the Central Nervous System overviews the changes in cell cycle as they relate to prenatal and post natal brain development progression to neurological disease or tumor formation Topics covered range from the cell cycle during the prenatal development of the mammalian central nervous system to future directions in postnatal neurogenesis through gene transfer electrical stimulation and stem cell introduction Additional chapters examine the postnatal development of neurons and glia the regulation of cell cycle in glia and how that regulation may fail in pretumor conditions or following a nonneoplastic CNS response to injury Highlights include treatments of the effects of deep brain stimulation on brain development and repair the connection between the electrophysiological properties of neuroglia cell cycle and tumor progression and the varied immunological responses and their regulation by cell cycle

Protein Phosphorylation in the Nervous System Huiai Yang, 2000 **Receptors in the Nervous System** Abel Lajtha, 2013-06-29

A major advance in the biological sciences in the past decade has been the biochemical identification of cell membrane receptors The existence of receptor substances on the surface of cells that recognize and bind to extracellular molecules was proposed at the beginning of the century by the pharmacologist and immunologist Paul Ehrlich and the physiologist J N Langley Since then receptors have been found to play an important role in numerous physiological and pathological processes Over the years many attempts have been made to physically isolate and chemically characterize receptors but because of the receptors extremely low concentration and membrane localization these efforts have met with limited success Yet despite the failure to characterize receptor substances the concept of the presence of such molecules has had considerable heuristic value Using pharmacological physiological and immunologic approaches researchers have identified several specific receptors e g α and adrenergic nicotinic and muscarinic cholinergic and histaminergic With the characterization of various types of receptors on cell membranes many drugs were developed that proved to be experimentally and therapeutically useful It was only in the early 1970s that methods for the specific measurement chemical characterization and physical isolation of cell membrane receptors were developed These advances were made possible by the availability of ligands with high specific radioactivity that retained their biological activity and of experimental procedures that differentiated between specific and non specific binding of ligands

Basic Neurochemistry R. Wayne Albers, Donald L. Price, 2005-11-11 Basic Neurochemistry Molecular Cellular and Medical Aspects a comprehensive text on

neurochemistry is now updated and revised in its Seventh Edition This well established text has been recognized worldwide as a resource for postgraduate trainees and teachers in neurology psychiatry and basic neuroscience as well as for graduate and postgraduate students and instructors in the neurosciences It is an excellent source of information on basic biochemical processes in brain function and disease for qualifying examinations and continuing medical education Completely updated with 60% new authors and material and entirely new chapters Over 400 fully revised figures in splendid color

Glycobiology of the Nervous System Robert K. Yu, Cara-Lynne Schengrund, 2014-08-23 A thorough introduction is provided to the variety and complexity of the roles that glycoconjugates play in the cells of the nervous system Basic information as well as the latest developments in neural glycobiology are discussed Topics covered range from the structure and metabolism of the saccharide chains and current approaches used in their study to changes glycoconjugates undergo during development and aging of the nervous system and the roles they have in neurological disease The breadth and depth of topics covered make it an essential reference for those new to the field as well more seasoned investigators *Basic Neurochemistry* Scott T. Brady, PhD, George J. Siegel, MD, R. Wayne Albers, Donald L. Price, 2012 Includes bibliographical references and index The Crustacean Nervous System Konrad Wiese, 2013-04-17 Crustacean preparations have been successfully used for more than 50 years to investigate the principles which enable nerve cells and neural circuitry to perform in a wide variety of functions The proud record of information of general significance obtained from crayfish and lobster nervous systems testifies that the use of an experimental system precisely matching theoretical and experimental requirements of a measurement is an essential part of the success In some respects the secondarily diversified vertebrate and mammalian nervous systems pose severe obstacles to experimentation and measurement whereas the crustacean nervous system recommends itself by being composed of individual neurons of unique morphology and physiology which can be used repeatedly in several preparations Moreover a restricted number of invariantly displayed behaviors enable the experimenter to correlate neuron activity with parts of the behavior easier Experts use these advantages to focus on a well defined neuron and mechanism and to take a convincing measurement within a minimum amount of time In this book distinguished neurobiologists the leading experts in the field have joined efforts to present research using crustacean experimental systems Thus they have contributed comprehensive information regarding a nervous system other than that of vertebrates and mammals that of crustaceans The accumulated knowledge on the crustacean nervous system shows that it is clearly divergent in evolution but functions in a similar way to neuronal circuitry found in the vertebrate system and can be used to interpret it Nucleotides and their Receptors in the Nervous System P. Illes, H. Zimmermann, 1999-08-31 The study of purinergic mechanisms has for long been focused on the actions of the nucleoside adenosine whereby the contribution of nucleotides to the signaling systems has been underestimated Based on the proceedings of a IUPHAR Satellite Conference held in Leipzig Germany this book offers a comprehensive update and overview of nucleotide release the structure and

function of nucleotide receptors nucleotide metabolizing ecto enzymes as well as the physiological functions of nucleotides in the nervous system The physiology and molecular biology of receptors for ATP and other nucleotides are examined as are the physiology and molecular biology of enzymes that hydrolyze extracellular nucleotides At present a pharmacology of the nucleotide signaling system is being developed Of particular interest is the production of receptor subtype specific antagonists and of drugs that selectively affect the extracellular lifetime of the nucleotide An excellent source of reference for institutes of pharmacology biochemistry neurology zoology and physiology and for the pharmaceutical industry

Neuronal and Glial Proteins Paul Marangos, 2012-12-02 Neuronal and Glial Proteins Structure Function and Clinical Application focuses on the basic and clinical information relating to a number of proteins that are either enriched in or unique to nervous tissue This book discusses the structural and functional characteristics of cell specific proteins which provide a better understanding of the molecular mechanisms involved in processes that are specific to glia or neurons Organized into three sections encompassing 15 chapters this book starts with an overview of the fundamental principles and strategies involved in studying the anatomical structural functional and immunological aspects of brain protein This text then discusses the techniques including the preparation of brain tissues as well as the preparation of neural and glial cells in purified form Other chapters review the two dimensional gel electrophoresis which is recognized as a significant technique for discovering brain molecules The final chapter deals with the membrane associated nervous system proteins Neurochemists and clinical researchers will find this book useful

Reviewing **Protein Phosphorylation In The Nervous System**: Unlocking the Spellbinding Force of Linguistics

In a fast-paced world fueled by information and interconnectivity, the spellbinding force of linguistics has acquired newfound prominence. Its capacity to evoke emotions, stimulate contemplation, and stimulate metamorphosis is truly astonishing. Within the pages of "**Protein Phosphorylation In The Nervous System**," an enthralling opus penned by a very acclaimed wordsmith, readers attempt an immersive expedition to unravel the intricate significance of language and its indelible imprint on our lives. Throughout this assessment, we shall delve to the book is central motifs, appraise its distinctive narrative style, and gauge its overarching influence on the minds of its readers.

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Protein Phosphorylation In The Nervous System Introduction

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