(antimonials, pentamidine, amphotericin B, and miltefosine) and laboratory (and in some cases field) derived resistance to these agents. The introductory chapter (*Leishmaniasis: Epidemiological Trends and Diagnosis* by Jhingaran et al.) gives a good discussion of the manifestations of the disease and its geographical distribution, although the inclusion of maps and tables would have been helpful. *Regulation of Gene Expression in* Leishmania *Throughout a Complex Digenetic Lifestyle* by Papadopoulou et al. summarizes insights into gene expression in the parasite gained from the genome project, such as the characteristics of transcription and life stage-specific expression of mRNAs. For those interested in animal models of visceral and cutaneous leishmaniasis, *Host Responses to Infections with* Leishmania by Tacchini-Cottier and Launois provides a brief but useful summary before describing in detail the host immunological responses to *Leishmania* infection. Other reviews discuss topics such as the *Leishmania* genome structure and content, the *Leishmania* proteome, *Leishmania* differentiation, *Leishmania* surface proteins, interactions between the parasite and the Sandfly host, interactions between the parasite and the host macrophage, and the influence of the genome on vaccine development.

This book provides a comprehensive, up-to-date snapshot of the biology of this parasite and is an essential resource for those interested in *Leishmania*, chemist and nonchemist alike. However, does the book succeed in communicating the impact of the availability of *Leishmania* genomic information on the discovery of new antileishmanial drugs? No chapters are included on the identification of new drug candidates based on genomic data, so perhaps the book gives an answer to this question through its silence. The chapter by Myler dealing with the structure and content of the *Leishmania* genome points out that a known function can be assigned to only about 35% of the genes predicted to code for proteins in the *L. major* genome, and a better knowledge of the function of the other genes may help to identify critical drug targets. However, agents that affect multiple targets or nonprotein targets could be equally effective and may be less likely to engender the rapid development of resistance. A balanced approach between genome-driven drug discovery and chemistry-driven strategies aimed at identifying agents with selective activity against live organisms is likely to bear more fruit in the search for novel chemotherapeutics against this parasite, compared with a strategy based solely on genomic approaches.

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Glycogen Synthase Kinase 3 (GSK-3) and Its Inhibitors

Edited by *Ana Martinez*, *Ana Castro* and *Miguel Medina*.

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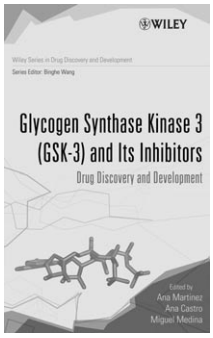

The appreciation of GSK-3's multifold roles in developmental signaling, cellular pathway regulation, and etiology of disease has undergone a renaissance since its discovery some 25 years ago. No longer thought of simply as a mediator of insulin signaling, activating glycogen synthase and increasing glycogen deposition; GSK-3 research has revealed a complex tapestry of signaling regulation in which GSK-3 plays numerous roles depending on the developmental stage of an organism, the metabolic state of tissues and cells, and the differential regulation in specific tissues or cell types. GSK-3 regulation occurs through a wide variety of cellular regulatory molecules, such as insulin, Wnt proteins, growth factors, estrogen, acetyl choline among others, and a plethora of substrates. Unraveling the key roles for GSK-3 in developmental processes like stem cell maturation and differentiation, and in disease states such as diabetes, Alzheimer's, neurodegeneration, and cancer is a daunting task whether a seasoned veteran researcher trying to keep informed amidst the hundreds of new GSK-3 papers being published yearly, or someone new to the field who may be interested in a specific therapeutic area. Speaking to audiences ranging from advanced undergraduates and graduate students to pharmaceutical researchers, therapeutic area experts and cellular signaling specialists, this book will provide insight into current GSK-3 research, and understanding through a series of well-written, referenced and indexed review monographs. Well respected expert GSK-3 authors examine the biology, regulation, signaling pathways, physiology, role in human diseases, potential for therapeutic application, and some current small-molecule drug discovery research programs, giving the reader a breadth of knowledge and viewpoint.

The foreword of the book is an introduction to the discovery of GSK-3, and a personal account of the trials and triumphs that led to the isolation and identification of this unique kinase written by Professor Sir Philip Cohen. This intriguing retrospective gives insight into the evolution of GSK-3 research touching on the pivotal innovations and breakthroughs, which exposed GSK-3's multifaceted regulation, even within the insulin pathway, and many of the significant collaborators and researchers who were integrally involved through the quarter century of GSK-3 investigation. One of the original investigators and expert in GSK-3 biology, Professor James R. Woodgett, provides a comprehensive introductory overview to the regulation, structure, biochemical function, selectivity and involvement in glucose metabolism and neuronal biology of GSK-3. This chapter gives a firm grounding in the basics of GSK-3 biology and function, which lays the ground work for more specific and detailed chapters. Topics covered in the subsequent chapters branch out to include embryonic and neuronal development, neuronal cell biology, and the important modulation of Tau phosphorylation at an expert level including primary

research into the roles of GSK-3, PKA, CDC2 and CDK5 on Tau regulation in rat hippocampus.

Of high utility to pharmaceutical researchers are the chapters on the crystal structure, small-molecule inhibitors, and roles in therapeutic areas of GSK-3. The review of the X-ray crystal structures includes details on the molecular interactions of the kinase with substrates, ATP and small-molecule inhibitors. While the book does not cover all small molecule programs or disease targets, like ischemia, bone healing, adipogenesis, biological clock function, inflammation and sepsis among others, each author brings an expertise and focus on their own specialty. The role of GSK-3 in Alzheimer's disease, bipolar disorder, neurodegeneration and stem cell differentiation are thoroughly reviewed with insightful comments and current references, many from the author's own research. The five chapters on small molecules, while not comprehensive, gives a strong account of several important classes of GSK-3 inhibitors. The original and shaping inhibitor, lithium, is described from its origins as a treatment for manic depression in 1949 to modern uses. This long history gives a wealth of information about GSK-3 function and regulation in humans, and can be overlaid with the myriad of biological inquiry done with lithium *in vitro*. Major contributions in the design and optimization of pharmaceutical small molecules are covered with sections devoted to AR-A014418 (AstraZeneca), thiadiazolidines (NeuroPharma), 3-amino-pyrazoles (GlaxoSmithKline), and a chapter on mining marine sources for new potent and selective GSK-3 inhibitors. These chapters contain concentrated discourses on the discovery, characterization and optimization of small molecule programs, including in vivo results.

Overall, this book is a wonderful resource for anyone interested in GSK-3-mediated signaling pathways, regulation and physiology. There are high level overviews for the newly initiated and detailed thorough reviews of specialties for experts. This book is recommended for any researcher with an interest in neuronal development, neuroprotection, mood disorders, diabetes, certain cancers, and stem cell research. While most of the book is dedicated to GSK-3 biology, nearly a third is focused on structure-based design and optimization of small-molecule inhibitors. GSK-3 research has vastly expanded form its origins as a regulator of glycogen storage to areas not expected 25 years ago, such as stem cell development and circadin rhythms. Research into the potential therapeutic applications of this unique kinase remains dynamic, and shows great promise as a target for future drug development.

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