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Cyclic nucleotide phosphodiesterases (PDEs) are promising targets for pharmacological intervention. Multiple PDE genes, isoform diversity, selective expression and compartmentation of the isoforms, and an array of conformations of PDE proteins are properties that challenge development of drugs that selectively target this class of enzymes.

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Phosphodiesterases as Targets for Intermittent ...
PDEs as drug targets As selected PDE family members are critical regulators of cyclic AMP signaling, they make terrific targets for designing new medicines. For example, PDE4 inhibitors such as Otezla ® (apremilast) and Daxas ® (roflumilast) exert their effects by reducing cyclic AMP breakdown and enhancing the cyclic AMP signal.

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Because of the heterogeneous group of disorders, the therapeutic approach and response often depends on the underlying disease. In many of these conditions, there is evidence that cyclic nucleotide signaling and specifically phosphodiesterases (PDEs) are disrupted. PDE inhibitors represent an emerging class of pulmonary vasodilators in adults.

Phosphodiesterases: Emerging therapeutic targets for ...
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Abstract Cyclic nucleotide phosphodiesterases (PDEs) are promising targets for pharmacologicalintervention.Thepresence ofmultiplePDEgenes,diversityofthe isoforms produced from each gene, selective...

Cyclic nucleotide phosphodiesterases (PDEs) are promising targets for pharmacological intervention. Multiple PDE genes, isoform diversity, selective expression and compartmentation of the isoforms, and an array of conformations of PDE proteins are properties that challenge development of drugs that selectively target this class of enzymes. Novel characteristics of PDEs are viewed as unique opportunities to increase specificity and selectivity when designing novel compounds for certain therapeutic indications. This chapter provides a summary of the major concepts related to the design and use of PDE inhibitors.

Cyclic nucleotide phosphodiesterases (PDEs) are promising targets for pharmacological intervention. Multiple PDE genes, isoform diversity, selective expression and compartmentation of the isoforms, and an array of conformations of PDE proteins are properties that challenge development of drugs that selectively target this class of enzymes. Novel characteristics of PDEs are viewed as unique opportunities to increase specificity and selectivity when designing novel compounds for certain therapeutic indications. This chapter provides a summary of the major concepts related to the design and use of PDE inhibitors.

Written by the pioneers of Viagra, the first blockbuster PDE inhibitor drug. Beginning with a review of the first wave of phosphodiesterase (PDE) inhibitors, this book focuses on new and emerging PDE targets and their inhibitors. Drug development options for all major human PDE families are discussed and cover diverse therapeutic fields, such as neurological/psychiatric, cardiovascular/metabolic, pain, and allergy/respiratory diseases. Finally, emerging chemotherapeutic applications of PDE inhibitors against malaria and other tropical diseases are discussed.

This volume of Pharmaceutical Biocatalysis starts with a discussion on the importance of biocatalytic synthesis approaches for a sustainable and environmentally friendly production of pharmaceuticals and active pharmaceutical ingredients. Among the enzymes discussed in detail with respect to their pharmaceutical relevance are cyclic nucleotide phosphodiesterases playing an important role in modulating signal transduction in various cell types; human DOPA decarboxylase, related to Parkinson's disease and aromatic amino acid decarboxylase deficiency; and phospholipase D enzymes as drug targets. Isocitrate dehydrogenase 1 and 2 mutations are novel therapeutic targets in acute myeloid leukemia. An additional chapter is devoted to the use of enzymes for prodrug activation in cancer therapy. The other topics include small-molecule inhibitors targeting receptor tyrosine kinases in cancer, β-lactams and related compounds as antibacterials, non-vitamin K oral anticoagulants for the treatment of thromboembolic diseases, and the molecular mechanisms for statin pleiotropy and its clinical relevance in cardiovascular diseases. The last chapter is a review of lysosomal storage disorders with an overview of approved drugs for treating these disorders by enzyme replacement therapy.

Disease-relevant intracellular protein-protein interactions occurring at defined cellular sites possess great potential as drug targets. They permit highly specific pharmacological interference with defined cellular functions. Drugs targeting such interactions are likely to act with fewer side effects than conventional medication influencing whole cell functions. This book discusses therapeutically relevant protein-protein interactions with a major focus on scaffolding proteins tethering signal transduction processes to defined cellular compartments by direct protein-protein interactions. Recent advances in the development of pharmacological agents interfering with protein-protein interactions are highlighted.

New and emerging directions in pharmaceutical research to better treat schizophrenia Although the dopamine hypothesis has been the cornerstone of schizophrenia therapeutics, it is clear that dopamine-based approaches do not treat all aspects of the disease. Moreover, many schizophrenia patients fail to respond to current antipsychotics. Integrating chemistry, biology, and pharmacology, this book explores emerging directions in pharmaceutical research for drug targeting and discovery in order to find more effective treatments for schizophrenia, one of the most serious and widespread psychiatric diseases. Targets and Emerging Therapies for Schizophrenia presents the basics of schizophrenia, drug targets for the disease, and potential new drugs and therapeutics. It begins with a discussion of prevalence and etiology. Then, it describes therapies such as dopamine agonists and phosphodiesterase (PDE) inhibitors as well as growing research aimed at addressing untreated symptoms. Next, the authors discuss receptor modulators, inhibitors, and targeting strategies for drug discovery. Both the neurobiological and chemical aspects of all major pharmacological targets are examined. With contributions from an international team of pioneering pharmaceutical researchers, this book compiles the current knowledge in the field, setting the stage for new breakthroughs in the treatment of schizophrenia. Targets and Emerging Therapies for Schizophrenia: Provides a comprehensive resource for neuro-drug discovery and the development of molecular targets for schizophrenia treatment Draws from chemistry, biology, and pharmacology for more effective drug targeting and discovery Explores a wide range of receptors and molecular targets, including dopamine, PDEs, and neuropeptides With Targets and Emerging Therapies for Schizophrenia as their guide, drug discovery and development scientists have the information they need to advance their own research so that new, more effective treatments for schizophrenia will soon be a reality.

This book reviews advances in understanding phosphodiesteraseswithin the central nervous system and their therapeuticapplications. A range of expert authors from both academia andindustry describe these, then focus on the areas of greateststscientific and medical interest to provide more detailed coverage.Therapeutic and drug discovery applications are covered fordiseases including Alzheimer's, Parkinson's, schizophrenia,erectile dysfunction, and spinal cord injuries. There is also achapter on drug discovery tools such as in vitro assays and X-raystructures for medicinal chemistry studies.

A comprehensive look at current drug discovery and development methods—and the roadmap for the future Providing both understanding and guidance in characterizing potential drugs and their production and synthesis, Development of Therapeutic Agents Handbook gives professionals a basic tool to facilitate research and development within this challenging process. This comprehensive text brings together, in one resource, a compendium of concepts, approaches, methodologies, and limitations that need to be considered in the formulation of therapeutic agents across a range of therapeutic fields. Both a reference and a call to action for the pharmaceutical industry, Development of Therapeutic Agents Handbook examines recent innovations taking shape in the various medical disciplines involved in drug discovery, and shows why these advances need to be embraced universally among researchers to improve their solution strategies. Additional subject matter includes: Extensive coverage and in-depth look into novel treatments and therapeutics Discussion of hot topics like new drugs and nutraceuticals, the discovery and development of vaccines, cancer therapeutics, and market overviews Coverage of therapeutic drug development for specific disease areas, such as cardiology, oncology, breast cancer, and kidney diseases As research in biology, chemistry, medicine, and technology rapidly progresses, it is becoming increasingly important for medical researchers to maintain an up-to-date knowledge base of emerging trends directing promising new therapies. Development of Therapeutic Agents Handbook serves this purpose, acting as both a one-stop reference rich in valid science, and a tool to carve out new pathways in the pursuit of bringing safer and more effective drugs to the marketplace.

Handbook of Basal Ganglia Structure and Function, Second Edition, offers an integrated overview of the structural and functional aspects of the basal ganglia, highlighting clinical relevance. The basal ganglia, a group of forebrain nuclei interconnected with the cerebral cortex, thalamus, and brainstem, are involved in numerous brain functions, such as motor control and learning, sensorimotor integration, reward, and cognition. Those nuclei are essential for normal brain function and behavior, and their importance is further emphasized by the numerous and diverse disorders associated with basal ganglia dysfunction, including Parkinson ' s disease, Tourette ' s syndrome, Huntington ' s disease, obsessive-compulsive disorder, dystonia, and psychostimulant addiction. This updated edition has been thoroughly revised to provide the most up-to-date account of this critical brain structure. Edited and authored by internationally acclaimed basal ganglia researchers, the new edition contains ten entirely new chapters that offer expanded coverage of anatomy and physiology, detailed accounts of recent advances in cellular/molecular mechanisms and cellular/physiological mechanisms, and critical, deeper insights into the behavioral and clinical aspects of basal ganglia function and dysfunction. Synthesizes widely dispersed information on the behavioral neurobiology of the basal ganglia, including advances in the understanding of anatomy, cellular/molecular and cellular/physiological mechanisms, and behavioral and clinical aspects of function and dysfunction Written by international authors who are preeminent researchers in the field Explores, in full, the clinically relevant impact of the basal ganglia on various psychiatric and neurological diseases

A drug is typically manufactured through chemical synthesis, which means that it is made by combining specific chemical ingredients in an ordered process. Biologics are medicines made from living cells through highly complex manufacturing processes and must be handled and administered under carefully monitored conditions. Biologics are used to prevent, treat, diagnose, or cure a variety of diseases including cancer, chronic kidney disease, autoimmune disorders, and infectious diseases. A biosimilar is a biologic that is similar to another biologic drug already that has already been approved. This book is a complete guide to the use of biologics and biosimilars in the treatment of dermatologic disorders. Beginning with an overview of the history and classification of biologics and the concept of biosimilars, the following chapters explain their therapeutic use for different skin conditions. The final sections cover related topics such as cost effectiveness and quality of life with biologic therapy, and the book concludes with discussion on future developments and the use of small molecule treatment. Key points Complete guide to use of biologics and biosimilars in treatment of dermatologic disorders Covers many different skin diseases and conditions Discusses related topics such as cost effectiveness and quality of life Covers future development of small molecule therapy