

Tentative Outline

Special Issue for Current Topics in Medicinal Chemistry

Modulation of Kinases by Small Molecules for Therapeutic Management of Various Diseases

Guest Editors: Dr. Sandip B. Bharate

Aims & Scope:

After the discovery of kinase-mediated signaling pathways, it was obvious that designing small molecule inhibitors of kinases (or activators of phosphatases) would be an ideal way to target many dysregulated pathways, particularly in cancer progression and metastasis. However, this premise was met with significant scepticism in the scientific community due to the perceived difficulty of selectively targeting a specific kinase without affecting several other kinases (overall, 519 kinases are encoded in the human genome), due to the conservation of the ATP binding pocket of most kinases. However, in 1994 Parke-Davis scientists reported the first generation of very potent kinase inhibitors with manifold selectivity against other kinases. This discovery spurred the development of projects throughout the pharmaceutical industry; 18 kinase inhibitors have now been approved by FDA for various diseases, and more than 500 candidates are in active clinical development. In addition, an entirely new type of biological therapeutics (monoclonal antibodies) was created to successfully target many such kinase receptors and enzymes. However, despite these remarkable success stories, target selectivity remains a formidable challenge in drug development because almost all approved kinase inhibitor drugs works by competing with ATP for the ATP binding site of the enzyme. Hence, there is a great need for next-generation kinase inhibitors that work through alternative mechanisms such as allosteric inhibition, or by targeting inactive conformations of kinases. Thus, kinases are one of the important class of therapeutic targets for cancer as well as for many other important diseases including diabetes, neurodegenerative diseases, protozoal diseases.

This special issue will gather all important preclinical and clinical literature on this novel class of therapeutic target at one place, and it will be useful to medicinal chemists and clinicians.

Keywords: Protein kinases, lipid kinases, cyclin-dependent kinases, cancer, Alzheimer's disease, malaria

Subtopics:

The subtopics to be covered within this issue are listed below:

The objective of this thematic issue is to critically review the role of various kinases in the pathology of various diseases, and most importantly the drug discovery paradigms such as computational approaches, medicinal chemistry research, preclinical studies and clinical trials on small molecule kinase inhibitors. The topics covered in this special review are listed below:

- Three-dimensional structures of kinases
- Computational approaches for discovery of kinase inhibitors
- Approaches for discovering allosteric inhibitors of kinases
- Medicinal chemistry of kinase inhibitors
- Kinase inhibitors for therapeutic management of cancers
- Targeting kinases for therapeutic management of infectious diseases
- Modulation of Tau pathology in Alzheimer's disease via inhibition of kinases
- Kinases and stroke
- Clinical studies on kinase inhibitors
- Monoclonal antibodies as kinase inhibitors

Schedule:

Manuscript Submission Deadline: June 30, 2018
Peer Review Due: July 30, 2018
Revision due Date: August 30, 2018
Announcement of Acceptance by Guest Editor: September 15, 2018
Final Manuscripts Due: July 30, 2019

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