ACS Medicinal Chemistry Letters

Editorial

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New Frontiers in Kinases: Special Issue

Human protein kinases (PKs) represent the third largest enzyme class and are responsible for modifying an estimated one-third of the human proteome.[1] These enzymes catalyze the transfer of the gamma phosphate group from ATP to specific serine, threonine, or tyrosine hydroxyl groups on a target protein substrate, involved in a number of cell signaling pathways. It has been firmly demonstrated that kinase alterations (especially hyperactivation, hyperproduction, or mutations), leading to the disruption of cell signaling cascades, play important roles in several diseases, including cancer, inflammation, neurological disorders, and diabetes, thus making PKs one of the most attractive targets for pharmaceutical industry.[2] Discovery of kinase inhibitors has been successful, with about 150 kinase-targeted drugs in clinical development and more than 20 drugs approved by the Food and Drug Administration (FDA) for treatment of tumors. Many of these drugs are multitargeted inhibitors since they inhibit more than one kinase, and this activity is important in many malignancies, where several cell pathways are deregulated. Despite the increasing number of FDA-approved kinase drugs, the identification of selective molecules continued to be a great challenge.[3] Indeed, almost all kinase inhibitors studied so far bind the ATP binding pocket, and the research of compounds with allosteric mechanisms of inhibition is at an early stage.[4] Although oncology will be still for a long time the main focus of kinase drug discovery, the development of kinase inhibitors to treat diseases other than cancer is increasing. Many human pathologies including chronic inflammatory and autoimmune diseases, diabetes, infectious diseases, cardiovascular disorders, neurodegenerative diseases, and even AIDS are the therapeutic areas on which the kinase drug discovery programs are focusing.

Identifying novel kinases, obtaining target selectivity, developing allosteric inhibitors, applying kinase inhibitors to nononcology therapeutic areas, overcoming drug resistance and undesired side effects, finding efficient screening and profiling technologies, and exploring novel applications for existing inhibitors are only some of the most important challenges to be faced by researchers over the next 10 years.[5]

Because of the continued increasing interest in the kinase drug discovery, the collection of the major advancements in the field has become one of the main objectives of *ACS Medicinal Chemistry Letters*, *Journal of Medicinal Chemistry*, *ACS Chemical Biology*, and *Biochemistry*, which will collaborate to publish a thematic collection on kinases in January 2015. We hope that these Special Issues will stimulate the discussion on the most important recent findings and will favor the progress in this area. We encourage you to submit your manuscripts at https://acs.manuscriptcentral.com/acs by September 1, 2014.

Accepted articles for the thematic issues can be published immediately as JAMS and/or ASAPs but will be published together in the January 2015 Special Issue. In addition, articles will appear on a special online landing page dedicated to kinases drug discovery.

Maurizio Botta, Editor

AUTHOR INFORMATION

Notes

Views expressed in this editorial are those of the author and not necessarily the views of the ACS.

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