Bioorganic & Medicinal Chemistry 20 (2012) 1844–1845

Contents lists available at SciVerse ScienceDirect

Bioorganic & Medicinal Chemistry

journal homepage: www.elsevier.com/locate/bmc

Preface

The chemistry/biology interface

Novel bioactive compounds derived from microorganisms and plants are frequently used for the treatment of diseases as well as powerful tools to understand basic physiological phenomena. In recent decades, chemical biology has extended this research and attracted much attention serving as a bridge between chemistry and biology. Enormous technological developments and innovative ideas have contributed to significant progress in chemical biology. The specific links that have recently formed between chemistry and biology have yielded valuable tools for biomedical sciences. Indeed, these 'Chem/Bio interfaces' play an integral role in drug and biomarker discovery and development. Recent developments in this area have prompted us to introduce the topic of the Chem/Bio interfaces, which are already applied in many fields of chemical biology. For that purpose we have invited many experts to prepare either original papers or review articles related to the above mentioned advances. We are pleased with the resulting 18 papers from the chemical biology community, which span the following five categories.

1. Chemical approach to bioactive compounds

Use of synthetic compounds that modulate biological functions is a fundamental and powerful strategy of chemical biology. Carbohydrates are of crucial importance for a plethora of molecular recognition events. Awan and Werz review recent development in the synthesis of annulated carbohydrate derivatives enabling the production of specific chemical entities. Flavaglines are a family of plant natural products that show potent anticancer and neuroprotective activities. Ribeiro et al. describe recent achievements and biological properties of synthetic flavaglines, which may represent a new class of anticancer drugs. Chemical probes have contributed to the success in chemical biology research and have applicability to in vitro and in vivo studies. Tanaka et al. report on the modification of their method of the labeling of the intact cells with fluorescent bioprobes.

2. Screening of bioactive compounds

Discovery of novel bioactive compounds is a starting point and a key for fruitful research. Hang et al. describe a new high throughput screening system for small molecules modulating the Wnt pathway in the cell free system consisting of *Xenopus* egg extract as a source of biological activity. Filippakopoulos et al. describe structural requirements for a high affinity interaction of bromodomain and extra terminal proteins (BET), a family of transcriptional co-regulators that play a key role in cancer cell survival and proliferation, and benzodiazepine derivatives. HDAC inhibitors act via chromatin modification and can dramatically change epigenetic regulation of genes, and some of these have recently been approved for cancer treatment. Sasaki et al. describe current imaging techniques useful in the observation of histone acetylation in the living cells upon the treatment with HDAC inhibitors. For many years, researchers have obtained the compounds interacting with a pocket in the active site of the enzymes or the ligand binding site on a receptor. As a next strategy, Jeon et al. review current studies on small modulators controlling protein–protein interaction.

3. Target identification of bioactive compounds

Identification and validation of targets for bioactive small molecules is important to all of chemical biology and drug discovery. Currently, there is no universally applicable method and various new technologies have been applied to meet this task. Standing in their respective positions, the authors in five groups described current status of target identification for bioactive compounds. Titov and Liu describe the major technique for the target identification, and they showed the conceptual and technical steps used for the determination of the targets of DRB, Brefeldin A, and triptolide. Tashiro and Imoto describe comprehensively the current state-of-the-art technologies for the target identification. Cho and Kwon describe the importance of the combination of phenotypic screening and multi-omics-based target identification for the discovery of the new bioactive compounds. Azad and Wright describe various methods and approaches to study the mode of action of bioactive compounds. In addition to biochemical and chemical genetic approaches, they introduce recent advances including combination therapy, imaging, and RNAi methods. Protein tyrosine phosphates (PTPs) constitute a large and structurally diverse family of signal transduction enzymes. He et al. describe recent progress in the area of inhibitors of PTPs, indicating the importance of drug likeness.

4. Profiling of bioactive compounds

In the last few decades, we have been able to utilize a large amount of data through the development of suitable analytic equipment and by progress in omics research. Now we have started to apply these massive datasets to identification and validation of compound's target. One of the pioneering events was the introduction of a cancer cell line panel by the National Cancer Institute, USA (NCI60), which had a significant impact on the discovery and development of cancer drugs. A similar system was also introduced in Japan (JFCR39) and is presented in the paper by Kong and Yamori. Chemical-genomic platforms based on the yeast deletion mutant collection have been applied for the target identification and mode of action studies. The review by Andrusiak et al.

0968-0896/$ - see front matter
doi:10.1016/j.bmc.2012.02.053

described the chemical-genomics profiling of bioactive compounds. The identification of an additional target (off-target) of a compound often provides a clue to drug development. Profiling of cell responses might be a useful method for accelerating drug development. The paper by Ross-Macdonald et al. describes the prioritization of the validation in vivo assay using a large panel of kinase assay and transcriptional profiling of mRNA in a response to the exposure to a compound. The review by Bantscheff and Drewes describes the significant progress in current chemical proteomics research resulting from a wide application of newly developed technologies particularly in mass-spectrometry.

5. Novel approach to bioactive compounds

Finally, new technologies are continuously developed and applied in the field of chemical biology. Kemp et al. describe new approaches using unbiased binding assay that do not require *a priori* knowledge of protein structure or function. Affinity-based isolation methods of target identification are fundamental technologies in the research of chemical biology. Sakamoto et al. summarize recent progress on affinity chromatography system.

We hope the readers will find this collection of papers compiled for this special issue to be interesting. We thank our authors, the editors and the staff for their support.

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