

Concepts and Case Studies in Chemical Biology

Concepts and Case Studies in

Chemical Biology, edited by Herbert

Waldmann and Petra Janning, provides

a discerning selection of 27 current case

studies contributed by established as well as

young research group leaders working throughout the field of chemical biology. The case studies cover a wide range of material, characteristic of literature falling under the umbrella term “chemical biology”. Following the principle structure from the previous book *Chemical Biology—Learning through Case Studies*, published in 2009 by the same editors, a problem-based approach is consistently used to present the material, with each case study loosely following an organizational template that first describes the biological problem, followed by the chemical approach, and the chemical biological research/evaluation, along with other customized subdivisions. The organized presentation has the subtle, though important effect of uniting the material while maintaining the variation in tone, focus, and specific expertise of the diversity of contributors. With over a decade of experience writing, teaching and researching chemical biology, Waldmann and Janning demonstrate outstanding selection, editing and organization of material, providing a sophisticated though accessible learning tool and an up-to-date report for researchers throughout the field.

One of the challenges of giving an overview of the field of chemical biology is that the biological context is often required to understand the disparate targets. Waldmann and Janning group the case studies by common biological themes, which compacts background reading and encourages analysis and comparison without underplaying the depth of information involved in experimental design. Furthermore, the chapters are supplemented with side-boxes with introductions to specific techniques and instrumentation described, providing background material without slowing the pace of the text.

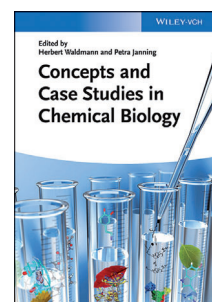
This organization is demonstrated in the first four case studies, which focus on different aspects of the general kinase/phosphatase specificity problem. Despite the common theme, the methods and approaches are otherwise very different in each of these chapters. Peterson and Imperiali of MIT describe the rational synthesis of peptide-substrate, kinase-activity sensors to allow continuous and real-time fluorescent monitoring of enzyme activity, followed by a case study by Rauh and Simard, who describe structure-based development of FLiK and FLiP protein constructs (modified kinases and phosphatases) that enable functional assays for screening specific inhibitors of an enzyme. The next

two studies feature different research projects within the Köhn group at EMBL; overviews of methodological and theoretical development of bivalent inhibitors and rationally designed Ser/Thr phosphatase activators are described, respectively.

Case studies touch on a wide range of themes, including site-specific chemical protein modifications to study autophagy in a chapter by Wu and Zhao, activity-based probes to profile proteasome and glucosidase activity, which are described in two subsequent contributions from Overkleeft and other researchers from the University of Leiden, as well as inhibitor and assay development using both high-throughput screening and rational design. Concerning the latter, Gersch and Sieber from the Technical University of Munich describe rational synthetic improvements made to a set of natural products that showed antibiotic activity but poor pharmacological efficacy, resulting in elucidation of a novel class of potent antibiotics. The researchers also describe the use of activity-based profiling in the identification of antivirulents, or molecules that inhibit pathogenicity without killing the bacteria, to stagger the development of resistance, supporting a shift in focus toward antivirulence and away from antibiotics entirely.

Cheung and Cong from Novartis give a nice overview of the design and considerations involved in a chemical genetics high-throughput screen for Wnt/ β -catenin pathway inhibitors, including compound identification and hit selection, and the chemical proteomic strategy used to successfully identify the target of the small-molecule inhibitor. In contrast, Grossmann and Verdine of Harvard University describe a design-based strategy for developing cell-permeable inhibitors of the Wnt/ β -catenin pathway through the use of stapled peptides, or peptides locked into an active α -helical conformation at specific positions by a hydrocarbon staple. Stapled peptides offer pharmacological benefits and importantly provide a diversification method for peptide screening. Methods to increase diversity in compound libraries are approached in multiple ways. The importance and major principles of diversity-oriented synthesis is well-described by members of the Spring lab at the University of Cambridge, who successfully applied scaffold-oriented branching strategies to the identification of modulators of mitosis. This case study is followed by a close look at the synthetic considerations involved in generating scaffold diversity by Kamal Kumar.

Kumar and Ziegler, both from the Max Planck Institute of Molecular Physiology, also co-write a separate case study describing natural-product-inspired compound synthesis for screening mitotic inhibitors and subsequent target identification and validation. Indeed, strategies for improving all aspects of screening—including library synthesis,



Concepts and Case Studies in Chemical Biology
Edited by Herbert Waldmann and Petra Janning. Wiley-VCH, Weinheim, 2014.
464 pp., softcover,
€ 69.00.—ISBN 978-3527336111

screening assays, hit validation and optimization, and target identification—receive significant attention throughout the book. The identification of drug targets through affinity purification and the synthesis of small-molecule affinity resins are described by Sato and Uesugi of Kyoto University, along with the benefits of early target discovery.

This review offers only a small sample of the wide range and depth of material compacted into a relatively short read. This book is highly recom-

mended to chemical biologists of all stages and other scientists wishing to gain an up-to-date, adeptly communicated overview of the field.

Marcie B. Jaffee, Christian P. R. Hackenberger
Leibniz-Institut für Molekulare Pharmakologie und
Department Chemie, Humboldt-Universität zu Berlin
(Germany)

DOI: 10.1002/anie.201500293

Computational Molecular Science

The ultimate resource on all aspects of computer applications in chemistry, biology and materials science

The successor of the highly acclaimed *Encyclopedia of Computational Chemistry*, this new multi-volume reference captures the interdisciplinary flavour of the field, addressing key topics and presenting different levels of understanding in this important and rapidly growing area.

Computational Molecular Science features all content published in the review journal *WIREs Computational Molecular Science* between January 2011 and December 2013.

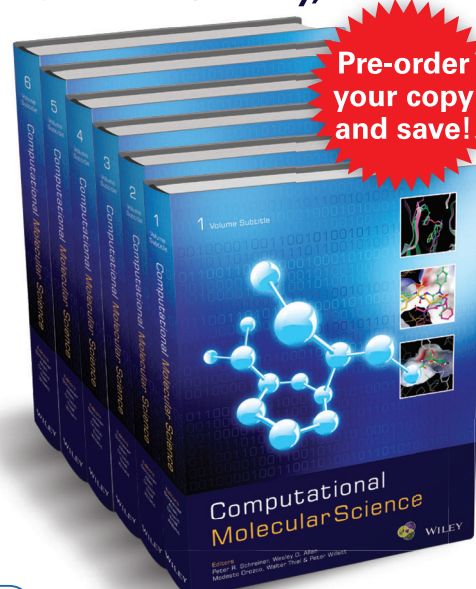
EDITORS:

Peter R. Schreiner
Professor, Institute of Organic
Chemistry, Justus-Liebig
University, Giessen, Germany
Wesley D. Allen Associate
Professor, Department of
Chemistry, University of
Georgia, Athens, USA

Walter Thiel
Director of Institute for
Theoretical Chemistry,
Max-Planck-Institut für
Kohlenforschung, Germany

Modesto Orozco Professor
and Group Leader of the
Institute of Molecular
Modelling and Bioinformatics,
Institute for Research in
Biomedicine, Barcelona, Spain

Peter Willett Professor of
Information Science, University
of Sheffield, UK



WIREs

COMPUTATIONAL MOLECULAR SCIENCE

The logical online successor of the highly acclaimed *Encyclopedia of Computational Chemistry*, the review journal *WIREs Computational Molecular Science* combines the best possible features of major online reference works (high visibility, fast searches, and electronic accessibility) with the completeness, rigor, and overall high quality of review journals.

For further information and to recommend *WIREs* to your librarian visit
www.wires.wiley.com/compmolsci

6 Volume Print Edition • February 2014

ISBN: 978-0-470-72307-4

Introductory Price valid until 31st May 2014:

£1050.00 / €1350.00 / \$1695.00

Prices will revert back to
£1250.00 / €1610.00 / \$1995.00 thereafter

**Find out more and
download sample content at
www.wiley.com/go/cms**

WILEY