Target Practice

Target Discovery and Validation: Reviews and Protocols. Volume 1: Emerging Strategies for Targets and Biomarker Discovery, and Volume 2: Emerging Molecular Targets and Treatment Options

Edited by *Mouldy Sioud*

Humana Press, Totowa 2007. xii + 354 pp., hardcover $ 125.00.—ISBN 978-1-58829-656-6 (vol. 1), xiv + 344 pp., hardcover $ 125.00.—ISBN 978-1-58829-890-4 (vol. 2)

These companion volumes are recent additions to the *Methods in Molecular Biology* series. The two volumes review current methods for drug target discovery and validation. The impact of recent improvements in understanding the molecular mechanisms of human pathology on drug target discovery is emphasized. The primary focus of the two volumes is on cancers and autoimmune disorders. The volumes contain a mixture of reviews and protocols making for a somewhat uneven, but nonetheless useful, compendium.

Volume 1 is focused on drug target and biomarker discovery. The topics covered in the 17 chapters range from a general overview of the approaches to target discovery and validation to a very specific, step-by-step protocol for an in vivo assay of human angiogenesis. Whether review or protocols, the chapters are generally well written and clear, and provide extensive references to the current literature. A wide range of bioinformatics, proteomic, and nucleic acid based approaches are described, along with cell and animal assays, and model systems.

Volume 2 contains another 17 chapters, again a mixture of reviews and detailed protocols. These chapters attempt to provide descriptions of the process required for the translation of new discoveries in proteomics into therapeutically applicable targets. Specific targets in cancers and autoimmunity are described and the potential of using siRNAs, antisense oligonucleotides, and RNA aptamers as therapeutic agents is reviewed. Again, the chapters are generally well written and clear, and provide extensive references to the current literature.

Overall, these two volumes provide useful overviews that would provide entry into this field. Novice and more experienced researchers alike would find useful information in both of these volumes.

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The Evolution from Protein Chemistry to Proteomics: Basic Science to Clinical Application

By *Roger L. Lundblad.*

CRC Press, Boca Raton 2006. 295 pp., hardcover £ 85.00.—ISBN 978-0-8493-9678-6

The spectacular development of proteomics in recent years has stimulated a fairly rich output of books on the subject, from general introductory texts to more specialized works on particular areas of proteomics, to hands-on laboratory guides. In such a fast-moving field, textbook obsolescence is practically inevitable so one is always on the lookout for new titles that enrich the literature of this very dynamic area of the life sciences.

Dr. Roger L. Lundblad, a recognized expert in protein chemistry, is well known for his contributions to the chemical modification of proteins, a field on which he has authored several books. In this new volume, he aims to emphasize the necessary, but not always recognized, connection between the classical methods of protein chemistry and the diverse concepts and techniques used in current proteomic research. With his extensive expertise in protein chemistry, Dr. Lundblad is in a privileged position to outline the evolution of the field, and to assess its current development and perspectives.

The book is divided into eight chapters dealing with different aspects of proteomics, with considerable focus—practically one half of the text—on the author's own area of expertise, as well as on other areas such as sample preparation and enrichment. The opening chapter provides a brief overview of the field, with some definitions and correlations to other "omics" technologies. Proteomics itself is classified into three main areas of activity: analytical, expression and biomarker identification. These activities are only succinctly outlined; a novice reader will need to look elsewhere for more informative presentations. The chapter ends with a substantial set of literature references to the different topics covered. Most references are simply listed, not discussed in the text of the chapter.

Chapters 2 and 3 constitute the *pièce de résistance* of the book. The first of the two is an authoritative review of the main methods of residue-specific modification of proteins. While original literature sources are extensively referenced for all the methods described, in my opinion the chapter would have been improved if, rather than the general discussion provided, some experimental procedures were recommended for the benefit of nonspecialists venturing into this field. This applies to other sections too, particularly sample preparation and prefractionation (Chapters 4–5, see below). Another aspect of this chapter, indeed of the entire book, that could have been improved is the representa-

tion of chemical structures, which appear to have been produced by a rather unskilled user of chemical software. Amino acid side chains and modification reagents more often than not are poorly drawn and, despite their fairly large size, illustrations are not always clear or informative enough about the relevance of the transformations under discussion.

In the subsequent chapter, the residue-specific transformations outlined in Chapter 2 are discussed in the light of current proteomic strategies, for example, stable isotope labeling for quantitative proteomics, modification at specific binding sites for activity-based proteomics, or protein labeling with fluorescent dyes prior to fractionation. This reviewer found this chapter to be probably the most useful one in the entire book, even if the above caveats about the quality and instructiveness of the chemical formulas remain.

The following two chapters (4–5) deal with sample preparation and prefractionation, respectively; two aspects usually crucial for the success of any proteomic experiment. As it is, they receive a disparate treatment in the text. The former is discussed at reasonable length, again with chemical modification as a frequent but justified recurring theme. Issues such as cell and tissue extraction, sample stability, or proteolytic inhibition receive adequate coverage with abundant reference to both classical and current literature. In contrast, prefractionation is dealt with in a slighter way. For instance, prefractionation strategies based on affinity capture (e.g. pull-down or depletion experiments), often the bedrock of any proteomics workflow, are only succinctly discussed, arguably because in these approaches the role of chemical modification is less conspicuous.

The last three chapters are dedicated to analytical technologies (Chapter 6), clinical proteomics (Chapter 7), and validation issues (Chapter 8). Chapter 6 covers most current aspects of protein analytical methodology, including mass spectrometry, though again not in substantial detail. Given its superficial treatment of most issues, the chapter will not be particularly helpful to readers not already versed in the matter. Chapter 7 offers a limited but insightful review of some selected topics in the fast-expanding field of clinical proteomics, and concludes with a pessimistic and controversial assessment of the promise of these technologies to deliver clinically relevant results any faster than more traditional biochemical or immunochemical approaches. The last chapter of the book offers a prospect into issues such as assay variability and validation, and their bearing on the long-term goal of proteomics-based personalized medicine.

In summary, this may be a useful book for readers already familiar with the essential aspects of proteomics. In stressing the connection, both historical and current, between classical protein chemical modification and modern proteomics methodologies, Dr. Lundblad is undoubtedly on target, and this is clearly the strongest point of the book.

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Entry Inhibitors in HIV Therapy

Edited by *Jacqueline D. Reeves* and *Cynthia A. Derdeyn*.

Birkhäuser, Basel 2007. x + 200 pp., hardcover € 119.00.—ISBN 978-3-7643-7782-3

Human immunodeficiency virus (HIV) infection affects around 40 million people worldwide, and represent the fourth leading cause of mortality. The discovery of a safe and effective HIV vaccine is still a hope, and the focus on this disease treatment remains on anti-HIV agents. The presently available antiretroviral therapy (ART) is able to delay the destruction of the host immune system, to reduce severity and frequency of opportunistic infections, and so, to delay the progression of acquired immune deficiency syndrome (AIDS). Highly active antiretroviral therapy (HAART) is a combination of nucleoside/nucleotide reverse transcriptase inhibitors (N(t)RTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs) and/or aspartic protease inhibitors (PIs), which were eventually combined with fusion inhibitors (FIs); the introduction of HAART has made it possible to reduce the viral load in plasma, resulting in improved patient health and life span. However this kind of therapy only suppresses, and not eradicates, the virus and multiple-drug therapies like HAART can lead to increased adverse effects and toxicity due to long-term use and drug–drug interactions. Furthermore, the massive viral replication (with more than 10^9 virions produced daily), and the high error rate of the reverse transcriptase, has led to the emergence of drug and multidrug-resistant viral strains and the stringent need of new therapeutic strategies. Ultimately several new approaches have been explored. The emergence of the worldwide AIDS epidemic has fostered much research and great progress in this area of antiviral drugs, and presently more than 32 antiviral drugs are available, possessing a variety of mechanisms of action; most of these drugs are used for the management of HIV infection and AIDS, but are also used for the treatment of other viral diseases such as hepatitis B, influenza, herpes simplex, varicella-zoster and cytomegalovirus infections.

HIV entry and fusion are two steps in the viral life cycle that were shown to be targeted by several classes of antiviral drugs. The discovery of chemokines focused the attention on cellular coreceptors used by the virus for entering cells, and to the various steps of such processes, which are subject to interactions with small molecules. Intense research led to a wide range of effective compounds that are able to inhibit these initial steps of viral replication. All steps in the process of HIV entry into the cell may be targeted by specific compounds, classified in three main classes: (i) attachment inhibitors, (ii) coreceptor-binding inhibitors, and (iii) fusion inhibitors that may be (or have already been) developed as novel types of antiretroviral drugs.

The book edited by Reeves and Derdeyn represents a collection of valuable articles describing in some detail these processes, the various strategies used to target HIV entry into the cells, the compounds in clinical development at the time the chapters were written (presum-

