Cancer Proteomics: From Bench to Bedside

Edited by *Sayed S. Daoud.*

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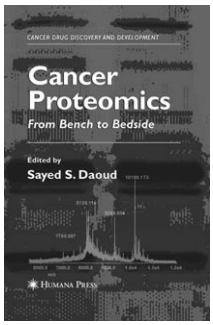

According to the Preface, this book is intended to provide the reader "broad perspectives and breadth of knowledge on current topics related to the use of proteomic strategies in cancer therapy as well as anticipated challenges that may arise from its application in daily practice". The book is divided into four parts. The first part promises to cover current technologies (specifically mass spectrometry-based protein characterization and protein microarrays) used in proteomics that allow for protein profiling and for the identification of druggable targets in human samples. The second part is devoted to the use of proteomics in cell signaling in the context of understanding protein–protein interaction and post-translational modifications for the purpose of developing potentially useful small-molecule inhibitors of many pathways important to cancer that have yet to be taken to clinical trials. The third part of the book is intended to demonstrate the actual move from the proteomic interrogation of cancer-related signaling to actual clinical applications with the promise of case studies discussing many tumor types to show the feasibility of generating the critical information needed to individualization of therapy in cancer patients. The fourth part of the book is meant to provide in-depth information on the effort to annotate the human proteome and the role of the Food and Drug Administration (FDA) in regulating the use of proteomics in cancer therapy.

Unfortunately, the book does not deliver on most of the promises outlined in the Preface. Part one consists of a single chapter entitled "Current and Emerging Mass Spectrometry Instrumentation Methods for Proteomic Analyses". Essentially, it is a narrative assessment of recently developed instruments, new(er) ion fragmentation methods and contemporary mass spectrometry-based techniques for protein analysis. The authors apparently intended the chapter to update readers already familiar with instrumentation and methodology enabling proteomics. However, experts will discover several inaccuracies that diminish its value to them. The layman summary of Fourier-transform ion cyclotron resonance (FTICR) is a typical example, and reference to the dated theory on the nonergodic nature of electron capture dissociation (ECD) is another such mistake. On the other hand, the subsection about mass spectrometry-based quantitative proteomics is a well-written and informative summary containing numerous practical hints usually not discussed in the primary literature. Contrary to the promise in the Preface, part one of the book did not cover protein microarray technologies at all.

Part two entitled "Cell Signaling Proteomics" consists of two chapters. The first one (Chapter 2) aspires to highlight the significance of an integrated genomics and proteomics approach to decipher the intricate signaling network associated with p53, a well-known protein involved in cancer. While the review of p53-focused genomics appears adequate, the outcome of the authors' attempt to demonstrate the potential value of proteomics through presenting their own experiments is truly disappointing. Apart from taking a "minimalist" approach, which hardly represents the state-of-the-art in methodology, the poor quality of the previously unpublished data would actually argue against the claim that the presented approach might provide "robust measures of the p53 signaling pathway". The consistent misspelling of Mascot (the software used for the protein identification from the mass spectrum presented) as MOSCOT (sic) also undermines the authors' credibility regarding their views about the current status of proteomics in the field of cancer research. The second contribution (Chapter 3) in part two of the book focuses on interfacing knowledge on protein tyrosine kinases (PTKs) with proteomic profiling for the purpose of screening for potential surrogate markers to predict response to therapeutic intervention and disease relapse. The thorough introduction to PTKs as versatile targets for human cancer and coverage of their genomic and structural features is followed by a fairly brief review on the subject that, in my opinion, did not meet its stated goal "to introduce the reader to the potential of these techniques and elucidate their role in studying tyrosine kinase circuitry". Presenting the methods through typical experimental examples would have been helpful.

Part three of the book opens with Chapter 4 that aspires to describe "the role of proteomics in developing personal management of cancer". The coverage of the subject is sketchy at best. For example, at the end of the first paragraph in the introduction the author refers to Figure 1, which is supposed to summarize the role of proteomics in the development of individualized therapy for cancer, apparently leaving the interpretation of the presented flowchart entirely to the reader. The following paragraph declares that the chapter will describe the use of the technique for its stated purpose, yet states that proteomics technologies have been described elsewhere and references the author's self-published book on the subject. Overall, sections about the role of proteomics in the discovery of cancer biomarkers, application of proteomics in oncology, in clinical trials of personalized anticancer drugs, and in management of various cancers, are superficial and poorly referenced.

On the other hand, the second contribution of part three (Chapter 5) is a well-written summary on the use of serum and tissue proteomics to understand and detect solid tumors. The methodologies are presented concisely by describing principles and pointing to critical issues to address upon their application. Chapters 6 and 7 review the pathological background of renal cell carcinoma and lung tumors, respectively, followed by a mostly retrospective summary discussing a limited number of proteomic studies related to the malignancies covered. Although these reviews were well written, they do not deliver on the editor's promise to "demonstrate the actual move from the proteomic interrogation of

cancer-related signaling to actual clinical applications", especially in the context of therapeutic individualization. Chapter 8 is another review covering acute myeloid leukemia in a similar fashion as the preceding two contributions did; however, it is an almost verbatim reprint (with slight changes in the section and subsection titles, deleting of a useful scheme, and omission of two co-authors) of a publication that appeared in 2006 in *Current Pharmaceutical Biotechnology*.[1] This paper has been made available online by its publisher, which begs the question why is it included in this book? On the other hand, the closing Chapter 9 of part three is an excellent contribution describing key elements in tumor biomarker development toward clinical use. This goal is accomplished by the authors through summarizing checklist-style practical considerations on pre-analytical, analytical and post-analytical aspects of biomarker assessment, followed by discussions on biomarker modalities (early detection, prognostic, predictive and therapy-monitoring markers). Similar summaries and discussions are hard to find in the scientific literature.

Chapter 10 in the final part of the book provides a summary of the efforts towards the annotation of the human proteome. This contribution does its best to put into perspective the potential outcome of such a daunting task still in the very early stages, which would enable actual tools for identifying new targets for cancer diagnostics, prognosis and therapeutics to be developed by proteomics rather than providing merely a "parts list". Finally, Chapter 11 reviews issues and requirements in proteomic biomarker development and validation for targeted cancer therapeutics. Again, a similar overview is hard to find in the scientific literature. Therefore, researchers engaged even in early-phase biomarker discovery would benefit from this contribution by putting their work into perspective regarding the requirements for regulatory (FDA) approval without having to delve into detailed agency guidelines.

In summary, I found that contributions with disappointingly poor quality outnumbered chapters that did a good job in covering their chosen subject for the intended audience in this scantily edited book. Therefore, it fell short of delivering the ambitious goals of providing broad perspectives and knowledge about cancer proteomics, especially concerning the move of the technique from bench to bedside.

Prof. Laszlo Prokai
University of North Texas Health Science Center at Fort Worth (US)
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[1] G. Sjøholt, S. L. Bedringaas, A. P. Døskeland and B. T. Gjertsen, *Curr. Pharm. Biotechnol.* **2006**, *7*, 159 – 170.

