METHODS IN MOLECULAR BIOLOGY™

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Chemical Genomics and Proteomics

Reviews and Protocols

Edited by

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Preface

The discipline of chemical genomics emerged from chemical biology around the year 2000, so it is now nearing its teenage years. An earlier version of this book was published in 2005; since then, technology has improved, and chemical genomics research has delivered new biological probes and drugs. Proteins have, of course, always been at the heart of the technology, but another change over recent years has been the more explicit use of the term "chemical proteomics," which is why the word "proteomics" is included in the title of this updated book. *Chemical Genomics and Proteomics: Reviews and Protocols* contains updated reviews of the chemistry of small molecules and their interaction with protein targets. The protocols cover different types of ligands, carbohydrates, lipids and the generation of their protein targets; methods for measuring their interactions are also covered.

The first review by Zanders provides a reminder of the relatively short history of chemical genomics (including genetics and proteomics) and gives some examples of problems of current biological interest, such as epigenetics, where chemical technologies are now playing a role. This is followed by an overview of chemical space by Yung-Sing Wong, in which he describes new chemical synthesis tools, such as the stereoselective multicomponent reactions that are being used to produce sophisticated drug-like molecules for screening. The importance of in silico design is not forgotten, as a review by Bernardo and Tong makes clear. There are several ways of measuring the interactions of small molecule ligands with proteins, and each has advantages and disadvantages. Surface plasmon resonance (SPR) is particularly interesting because it requires no modification of the ligand and also provides kinetic data. The throughput of SPR is improving all the time, which is why a review chapter has been devoted to this subject. Nico de Mol describes the recent introduction of array technology for SPR analysis as well as the integration with mass spectrometry to identify unknown ligands.

The protocols begin with methods for capturing ligands on affinity supports. El-Khoury and colleagues in Christopher Lowe's group, design new ligands for immunoglobulin purification using multicomponent reactions. Kanoh's group presents methods for covalently attaching small molecules to affinity supports using photoactivatable cross-linking. This can be achieved without prior modification of the small molecule and is independent of functional groups on the molecule. Specific types of molecular interaction are described in chapters on detecting lipoproteins (Hannoush) and finding ligands for non-ATP-binding sites on protein kinases (Simard and Rauh). Microarrays are central to genomics and proteomics of all types; chapters by Blackburn and colleagues on protein arrays, and by Cummings and colleagues on glycan arrays, provide up-to-date information on creating and using these tools. Nanotechnology is being exploited in various assay types. Nie and co-workers describe protocols for measuring low levels of small molecule analytes by binding aptamer molecules labeled with gold nanoparticles. Advances in protein expression and analysis are covered in chapters by Peleg and Unger (developments in expression systems

using *Escherichia coli* and insect cells) and Bernhard et al. (cell-free synthesis of membrane proteins). Finally, Webster and Oxley provide detailed protocols for identifying proteins using mass spectrometry.

We hope that this volume will provide inspiration to those who wish to use chemical genomics and proteomics in their work; equally, we hope that this young field develops into full maturity through the incorporation of the new biological and chemical technologies that are beginning to emerge here.

Cambridge, UK ***Edward D. Zanders***

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