libraries for specific metalloprotease inhibitors. Stephen L. Gallion, ArQule (Medford, MA, USA), presented biased ligand arrays for voltage-gated ion channels; chemical libraries are characterized by 10,000–20,000 analogues of multiple chemotypes.

MIDAS™, a synthetically driven platform for rational identification of peptide ligands and their potential conversion to non-peptidic analogues, was described by Shubh Sharma, Palatin Technologies (Princeton, NJ, USA). Cys-containing peptides form chemically stable complexes, in which an X–Y–Cys sequence is conformationally restricted by complexation with an oxo-Re metal ion.

Nucleic acid inhibitors, especially aptamers, were discussed as tools for the validation of drug targets and for the development of small-molecule leads by Michael Famulok, University of Bonn (Germany), and Michael Blind (NascaCell GmbH, Tutzing, Germany). From libraries containing up to 10^{15} different sequences, functional oligomers are selected for their ability to bind to a certain protein. The process of selection and optimization of the nucleic acids has recently been automated.

The outcome

Although some contributions raised more questions than answers, the conference provided an excellent overview on current drug discovery technologies and especially on the enormous progress that has been made in recent years in target validation, as well as lead discovery, optimization and development. An exhibition with ~70 participating companies gave an overview on the available commercial solutions.

Bioinformatics – From Genomes to Drugs

Edited by Thomas Lengauer, Wiley-VCH, 2001, Price £170.00, 680 pp, ISBN 3-5272-9988-2

Bioinformatics is big business today for simple reasons of supply and demand. Consider the 'supply' to be the burgeoning corpus of data requiring our urgent attention, culminating in the sequencing of the human genome, but extending also to all manner of scaled-up platform technologies. The 'demand' then arises from the ultimate economic basis for the lion's share of this activity: human health, in particular the need to apply genomic knowledge to the discovery of new drugs. *Bioinformatics – From Genomes to Drugs* promises by its title to be the first book to comprehensively close the loop between genome-based bioinformatics and actual drug discovery. Such an expectation is reinforced by the fact that this publication represents Volume 14 in the Wiley-VCH series *Methods and Principles in Medicinal Chemistry*. So, how does it go about attempting this connection, and how well does it succeed?

The book is a compendium of review articles by 14 different sets of authors, and as in many such collections, the entries on each topic range from comprehensive reviews of the literature, to rather more didactic presentations of the subject matter, to even more detailed methodological disquisitions skewed towards the author's own work. In this book, the articles tend to be of a high quality; most make a useful reference for their individual topics. As well as the utility of the discrete articles within such an anthology, their selection and organization, and how this framework contributes to the overall theme, is also of interest. In structuring the collection the editor posits a basic distinction between 'intrinsic' approaches, centered on the fundamental problems in the field and the technologies adopted to address them, and 'extrinsic' approaches involving actual applications. The book is presented in two volumes to reflect this, with the first part, *Basic Technologies*, being approximately twice the length of the second, *Applications*.

Although bridging the gap between basic technologies and applications is a well-worn path in science, it proves to be dissimilar to connecting the undoubted riches of the genome to the promise of new drugs. The comparatively slim tome addressing extrinsic applications does not convincingly close this gap, and in fact the overall content leaves one with the impression that there is a more significant and persistent division in the field than that between the intrinsic and the extrinsic. Rather, the truly notable hiatus evident in this book is that between the bioinformatics of genes and genomes, and the computational structural biology and chemistry that actually deals with targets and drugs. Divided along these lines, the content is actually split more nearly down the middle.

The half of the book that deals with informatics of genes and genomes covers such topics as sequence analysis, gene identification, regulatory region analysis, support of sequencing projects, database technologies, and so on. These

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are firmly founded in the genome, and it is notable that these sections barely refer to drug discovery, either in principle or by example. However, where drugs really enter the picture is in the chapters relating to protein structure prediction, molecular modeling, docking, virtual screening of drug databases, and so on. These fields arguably antedate bioinformatics *per se,* and in any case are far from wholly dependent on the genome for their advancement. Although the boost expected to be given by the structural genomics movement to mainstream pharmaceutical discovery activities such as homology modeling is given much weight, these enhancements are based, after all, more in number than in kind.

It is largely left to the volume editor, Thomas Lengauer, to probe the connection of genome to drugs in his introductions and summaries. He does this, in essence, by discussing the traditional nexus of target validation. By and large, this encompasses functional assignment within a clear context of pathophysiology, which increasingly entails understanding disease pathways. However, relatively short shrift is given to such matters in the articles themselves. The two shortest chapters in the book are those relating to what might currently be the hottest topics in target validation: SNP-based genetic methods and array-based gene expression studies. Proteomics, which might be counted the third hot topic at the moment, is more thoroughly covered, but this only serves further to highlight the genome–drug gulf because, like structural genomics, proteomics is only marginally about the genome. The genome has greatly aided annotation in this field, but the chapter's content demonstrates that proteomics is still overwhelmingly about separation, instrumentation, and its own particular brand of analysis.

However, this is not to say that the genome is irrelevant to drug discovery; it is an indispensable backdrop to it, and bioinformatics itself is increasingly integral to pharmaceutical research in just the same way that it is interwoven in all biological discovery. But the truly systematic, methodological connection of genome to drug is still very much a work in progress, as illustrated by the present volumes.

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