Medicinal Chemistry into the Millenium. By M. M. Campbell, I. S. Blagborough. RSC: Cambridge, **2001**, £ 60.50, hardback; ISBN 0-85-404769-7, 390 pp.

Edinburgh, Scotland, was host to the XVth International Medicinal Chemistry Symposium in September, 1998. Proceedings from this symposium, a total of 30 papers, are contained within "Medicinal Chemistry into the Millenium". Drug discovery and development is amid a revolution of sorts with the continued development of new analytical tools, the information obtained from the human genome project, and a growing understanding of the design approaches that have been successful in delivering bioactive compounds. As expected, these methods and tools are related throughout the papers contained in this book.

This compilation begins with papers describing research that employs new technologies in drug discovery as a means to identify lead structures, optimize known leads, or to examine possible molecular targets for drug design. There are also sections dedicated to specific molecular targets including ion channels, 7TM receptors, and nitric oxide synthase, as well as sections on glycine antagonists, growth factors, and protease inhibitors. The remaining sections describe research in intracellular signaling, glycochemistry and glycobiology, plus a section on DMPK prediction as an important process now part of drug discovery rather than left to drug development.

Technological advances that have contributed significantly to recent drug discovery efforts include structure-based drug design, combinatorial chemistry, and high throughput screening. The proceedings contain many examples that employ these tools and several examples that incorporate them in novel fashion. For example, in the opening paper Bartlett, et al. describe the discovery of macrocyclic peptidase substrates by using trypsin to synthesize macrocycles from activated esters followed by a screening process to distinguish cyclized versus uncyclized products. Once identified, these substrates are potential precursors of peptidase inhibitors by incorporating a transition-state isostere.

Modern drug discovery has also invested heavily in the tools of genomics, proteomics, and bioinformatics, as it is expected that efforts in these areas can both deliver novel targets against disease in addition to yielding a better understanding of factors behind many disease states. These areas of research are represented in this book, although the examples are limited in comparison to the importance now placed on them.

Enzymes and receptors have long been part of traditional drug discovery targets. These targets are also appropriately represented in the papers from this meeting, though now in the form of enzymes such as the rhinovirus 3C protease, cathepsin K, or nitric oxide synthase as well as receptor subtypes like the 5-HT6 receptor. The receptor work describes in detail the pharmacological analysis of the system — another important and traditional component of drug discovery.

There are also reports of drug discovery against other novel targets such as the aforementioned growth factors, carbohydrates, and kinases that normally bind ATP. The kinase papers are interesting in the context of tradition medicinal chemistry since mimics of ubiquitous molecules like ATP were once considered too risky for drug discovery based on concerns over selectivity. An approach to developing inhibitors of protein-protein interactions, an important and highly sought goal, is also illustrated in one paper.

Traditional medicinal chemistry approaches such as single molecule-single synthesis research coupled with quantitative structure-activity relationships are present in several papers. The importance of natural product screening is nearly absent in these proceedings, with the exception of the didemnaketals discovered to inhibit HIV-1 protease as described in a paper by Rich, et al. These traditional approaches remain invaluable to drug discovery and it is proper that excitement over new techniques and approaches does not completely replace proven methods.

"Medicinal Chemistry into the Millenium" is neither a review of contemporary drug discovery nor does it cover all of the exciting developments that promise to impact this research in the near future. The compilation does, however, contain many fine examples of how drug discovery is accomplished by the creative combination of techniques, concepts, and tools discovered in recent years. In that light, this book provides a fascinating read for those with an interest and introductory background in medicinal chemistry.

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Synthesis 2002, No. 2, 01 02 2002. Article Identifier:
1437-210X,E;2002,0,02,0299,0299,ftx,en;B20202SS.pdf.

ISSN 0039-7881