An Information Revolution

From the soon-to-be-completed Human Genome Project to combinatorial chemistry, scientific advances are poised to revolutionize drug discovery and even health care. This special issue takes a close look at how new chemical and biological approaches are changing the way in which therapeutic agents are discovered and developed.

In his historical account of drug discovery, Drews (p. 1960) traces back the roots of today's pharmaceutical industry to the turn of the 19th century and outlines the more recent impacts of molecular biology and genome sciences on the drug discovery process. A News story on page 1952 looks at the recent merger mania in the drug industry, driven by both increasing opportunities and escalating R&D costs.

The demand for large and diverse chemical libraries of potential drug compounds is providing new synthetic challenges for chemists. Schreiber (p. 1964) compares target-oriented synthesis and diversity-oriented chemistry. Retrosynthetic analysis is key to the successful synthesis of complex target molecules. Schreiber outlines possible routes toward a comparable methodology guiding diversity-oriented synthesis. In a TechView, Rademann and Jung (p. 1947) discuss strategies for extracting biologically relevant information from large chemical libraries.

Mechanism-based approaches to drug discovery aim to develop treatments targeting specific steps in biological pathways. Gibbs (p. 1969) uses breast cancer as an example to illustrate the promise of cancer treatments based on understanding of the genetic mishaps that propel a healthy cell toward cancer, and of the pathways and processes that keep tumors alive.

The low chemical variability of existing antibiotic treatments has allowed the escalation of drug resistance. Rosamond and Allsop (p. 1973) discuss how microbial genomics provide an opportunity to expand the range of potential drug targets and facilitate a shift away from direct antimicrobial screening programs toward rational, target-based strategies.

About one-third of the world's population lacks even the most basic medicines. Reich (p. 1979) discusses ways to improve access to pharmaceuticals in poor countries. A News story on page 1956 focuses on malaria. Despite emerging resistance to existing treatments and significant advances in understanding the malaria parasite's life cycle, drug companies are unwilling to invest big because of low commercial returns. Strategies for curbing the financial risks for companies include the Medicines for Malaria Venture, which funds collaborations between academia and industry.

Differences in drug regulatory procedures in different countries continue to be major roadblocks to delivering new drugs to patients worldwide (see the News story on p. 1958). A reform project involving the United States, Europe, and Japan may soon result in standardized and simplified drug regulations.

Fast-forward to a future in which whole cells can be simulated accurately on a computer and treatments are tailored to groups of people with specific genetic predispositions. On page 1977, Sander argues that genomics and bioinformatics will pave the way for an information revolution in biology and medicine, which may result in personalized health care. A key component of this information revolution is the availability of vast numbers of protein structures (see the News story on p. 1954), which hold the key to the rational design of drug molecules. Researchers are also now chemically modifying cell surfaces and carbohydrate linkages, with possible future therapeutic applications (see the Report by Saxon *et al.* on p. 2007).

Change is in the air for drug discovery. We hope that the articles in this issue capture some of the excitement of this interdisciplinary field at a time of transition.

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See also Tech.Sight on p. 1947 and Report on p. 2007.

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