THE SHAPE OF MEDICINES TO COME:
PHARMACEUTICALS IN THE 21ST CENTURY

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Abstract. The pharmaceutical sciences are advancing rapidly in the post-genomic era of the 21st century with the completion of the human genome, as well as those of many other organisms including bacteria and parasites, and the rapid advances in proteomics. Genomics and proteomics, with advances in combinatorial chemistry and high throughput screening, are yielding enormous amounts of data that are linked and integrated through bioinformatics to provide actual information on new targets, new delivery systems, gene and gene repair therapies, and personalized medicine. However, these promised, but thus far incompletely realized, advances will be challenged by the economics of health care delivery in both the rich and the poor worlds, where poverty and environmental degradation continue to grow in this era of globalization. Demands for medicines to treat existing, reemerging and new diseases will escalate and intellectual property rights and patent protection will be increasingly challenged. The rich world's reluctance to deal with these issues in an honest and equitable manner provides naught for our comfort.

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Introduction

The technological progress of the 19th and early 20th centuries is typically associated with the discoveries of physics—from steam engines to atomic fission—and their exploitation by engineers. Indeed, it was the renowned British physicist Ernest Rutherford who so famously observed that, "In science, there is only physics: all the rest is stamp collecting". It was also the British astrophysicist Sir Martin Rees who argued that the conditions for life on this planet depend on six physical constants being what they are (1). These constants have given us our living world—a three-dimensional and carbon-based world familiar to organic chemists. Rutherford was however, actually awarded the 1908 Nobel Prize in Chemistry, and appropriately enough the latter half of the 20th century and the 21st century are increasingly dominated by exploitation of the chemistry of this world as it has shaped the basic themes of biology—diversity, replication, self-organization, and evolution—viewed under the overall theme of "listening to nature", since nature remains our most creative chemist. The application of these themes to the pharmaceutical sciences provides a powerful example as drug discovery transitions to an increasingly genomic-based paradigm.

Drug Discovery: Making the Molecules

"The achievements of chemical synthesis are firmly bound in our attempts to break the shackles of disease and poverty"

Roald Hoffmann, 1993.

The traditional pathway of drug discovery, essentially a “one-molecule-at-a-time” individualized assembly line, has been significantly changed through the enabling technologies of functional genomics, combinatorial chemistry and high throughput screening, technologies that are linked through the informational glue of bioinformatics. The issue is not, as sometimes popularly advanced, whether one will shop for “Designer Genes” or “Designer Jeans” at some 21st Century Therapy Mall, but rather the impact of genomics on all facets of the drug discovery process—from target discovery and validation to personalized medicine. This process of transformation to the realization of Paul Ehrlich’s “magic bullet”—seen in 21st century terms as a “self-synthesizing, self-evolving, self-organizing and self-targeting” molecule—is far from complete and, indeed, there is much concern about the current costs of drug development and the lack of productivity in the pharmaceutical industry (2,3). Few doubt, however, that this goal will be ultimately realized, although the social implications of the delivery of this achievement to a world that is increasingly unequal are profound indeed (4,5).