

PREFACE

This is a book about medical genomics, a new field that is attempting to combine knowledge generated from the Human Genome Project (HGP) and analytic methods from bioinformatics with the practice of medicine. From my perspective as a research molecular biologist, genomics has emerged as a result of automated high-throughput technologies entering the molecular biology laboratory and of bioinformatics being used to process the data. However, from the perspective of the medical doctor, medical genomics can be understood as an expanded form of medical genetics that deals with lots of genes at once, rather than just one gene at a time. This book is relevant to all medical professionals because *all* disease has a genetic component when hereditary factors are taken into account, such as susceptibility and resistance, severity of symptoms, and reaction to drugs. The National Institutes of Health (NIH) defines medical genetics to include molecular medicine (genetic testing and gene therapy), inherited disorders, and the ethical legal and social implications of the use of genetics technologies in medicine.

The ultimate goal of genetic medicine is to learn how to prevent disease or to treat it with gene therapy or a drug developed specifically for the underlying defect. Other applications include pharmacogenomics and patient counseling about individual health risks, which

will be facilitated by new DNA chip technology. Concerns include how to integrate genetic technology into clinical practice and how to prevent genetic-based discrimination.

Collins, 1999

Before a coherent discussion of genomics is possible, it is necessary to define what is meant by a genome. A genome is the total set of genetic information present in an organism. Generally, every cell in an organism has a complete and identical copy of the genome, but there are many exceptions to this rule. Genomes come in different shapes and sizes for different types of organisms, although there is not always a simple and obvious connection between the size and complexity of an organism and its genome.

An operational definition of genomics might be: The application of high-throughput automated technologies to molecular biology. For the purposes of this book, genomics is defined broadly to include a variety of technologies, such as genome sequencing, DNA diagnostic testing, measurements of genetic variation and polymorphism, microarray gene expression, proteomics (measurements of all protein ins present in a cell or tissues), pharmacogenomics (genetic predictions of drug reactions), gene therapy, and other forms of DNA drugs. A philosophical definition of genomics might be: A holistic or systems approach to information flow within the cell.

Biology is complex. In fact, complexity is the hallmark of biological systems from cells to organisms to ecosystems. Rules have exceptions. Information tends to flow in branching feedback loops rather than in neat chains of cause and effect. Biological systems are not organized according to design principles that necessarily make sense to humans. Redundancy and seemingly unnecessary levels of interlocking dynamic regulation are common. Molecular biology is a profoundly reductionist discipline—complex biological systems are dissected by forcing them into a framework so that a single experimental variable is

isolated. Genomics must embrace biological complexity and resist the human tendency to look for simple solutions and clear rules. Genomic medicine will not find a single gene for every disease. To successfully modify a complex dynamic system that has become unbalanced in a disease state will require a much greater subtlety of understanding than is typical in modern medicine.

The HGP was funded by the United States and other national governments for the express purpose of improving medicine. Now that the initial goals of the project have largely been met, the burden has shifted from DNA sequencing technologists to biomedical researchers and clinicians who can use this wealth of information to bring improved medicine to the patients—medical genomics. The initial results produced by these genome-enabled researchers give every indication that the promises made by those who initially proposed the genome project will be kept.

The initial sequencing of the 3.2 billion base pairs of the human genome is now essentially complete. A lot of fancy phrases have been used to tout the enormous significance of this achievement. Francis Collins, director of the National Human Genome Research Institute called it “a bold research program to characterize in ultimate detail the complete set of genetic instructions of the human being.” President Clinton declared it “a milestone for humanity.”

This book goes light on the hyperbole and the offering of rosy long-term predictions. Instead, it focuses on the most likely short-term changes that will be experienced in the practice of medicine. The time horizon here is 5 years into the future for technologies that are currently under intensive development and 10 years for those that I consider extremely likely to be implemented on a broad scale. In 5 years’ time, you will need to throw this book away and get a new one to remain abreast of the new technologies coming over the horizon.

This book is an outgrowth of a medical genomics course that I developed in 2000 and 2001 as an elective course for medical students at the New York University School of Medicine. Based on this experience, I can predict with confidence that medical genomics will become an essential and required part of the medical school curriculum in 5 years or less. I also learned that medical students (and physicians in general) need to learn to integrate an immense amount of information, so they tend to focus on the essentials and they ask to be taught “only what I really need to know.”

It is difficult to boil down medical genomics to a few hours' worth of bullet points on *PowerPoint* slides. There is a *lot* of background material that the student must keep in mind to understand the new developments fully. Medical genomics relies heavily on biochemistry, molecular biology, probability and statistics, and most of all on classical genetics.

My specialty is in the relatively new field of bioinformatics, which has recently come in from the extreme reaches of theoretical biology to suddenly play a key role in the interpretation of the human genome sequence for biomedical research. Bioinformatics is the use of computers to analyze biological information—primarily DNA and protein sequences. This is a useful perspective from which to observe and discuss the emerging field of medical genomics, which is based on the analysis and interpretation of biological information derived from DNA sequences. Two chapters were written by colleagues who are deep in the trenches of the battle to integrate genome technologies into the day-to-day practice of medicine in a busy hospital. Harry Ostrer is the director of the Human Genetics Program at the New York University Medical Center, where he oversees hundreds of weekly genetic tests of newborns, fetuses, and prospective parents. John Hay is co-director of the molecular biology core lab for the New York University General Clinical Research Center and the principle

investigator of numerous projects to develop and test gene therapy methods.

Stuart M. Brown

REFERENCE

Collins F., *Geriatrics* 1999; 54: 41–47