Resuscitation and Evolution of a Classic

Recombinant DNA: Genes and Genomes—A Short Course
Authors: James D. Watson, Jan A. Witkowski, Richard M. Myers, and Amy A. Caudy
W.H. Freeman (2007)
474 pp., $106.25 paperback.

Regular readers of the *American Journal of Human Genetics* probably can point to one or two experiences that crystallized their decision to focus on not just science but genetics for their professional lives. For some, a summer laboratory project stimulated interest; for others, an inspiring teacher conveyed enthusiasm for variation in fruit flies. For me, and probably many others of my generation, a major stimulus was a book, specifically the first edition of James Watson's *Molecular Biology of the Gene*. After three editions of that book, in 1982 Watson and colleagues published the first edition of *Recombinant DNA*, and a new generation was exposed to not only the basics of molecular biology but also the emerging techniques of manipulating genes within and between organisms. With little competition, the book became the basis for numerous undergraduate and graduate courses. Fifteen years after the last edition, we have a revision, entitled *Recombinant DNA: Genes and Genomes—A Short Course*. Is this version likely to have the same impact as its predecessors?

Watson and his three coauthors faced a major task of updating, given the enormous progress during the recent past, and chose a pragmatic approach. In the first section, the early chapters that review molecular biology remain little changed but fundamentally sound. The major additions to this "toolkit" part of the book address homologous recombination, mobile elements, epigenetic modifications, and RNA interference. As in the rest of the book, concepts are presented through the original experiments and excellent color illustrations, often with mention of the principal investigators. The second half of the book is divided into three sections that address various aspects of genomics. Here, the title of the book fails to convey the extensive scope of the subject material because the term "recombinant DNA" can have a somewhat narrow meaning, especially for those of us of a certain age. The material is organized logically and presented succinctly. Successive sections deal with sequencing and analyzing whole genomes, the latter including a discussion of proteomics. The three chapters that comprise the final section, "Human Genomics," focus on "Finding Human Disease Genes," "Understanding the Genetic Basis of Cancer," and "DNA Fingerprinting and Forensics." The authors readily admit that the selection of these three topics was highly arbitrary, and they were guided, in part, by a desire to excite not only students of genetics but also students in other fields of science, medical students, and even patent attorneys and journalists. So did they achieve their aims, and will this edition serve as a stimulus for a new generation of undifferentiated students to become geneticists?

There is certainly a lot more competition, with recent editions of numerous texts and handbooks that cover genetic and genomic topics in exhaustive detail. Watson and colleagues do not intend to compete at all levels and encourage readers to delve into specific subjects in other sources. By using *Recombinant DNA* as a primary text, a course director could construct a comprehensive and exciting syllabus for undergraduate science majors and even first-year graduate students. The addition of a CD-ROM or website to provide, among other potential embellishments, access to the illustrations for instructional purposes would be helpful. In the health sciences, advanced medical students and postdoctoral fellows beginning forays into bench research would be well served by spending a few weeks studying this book.

Not unexpectedly, there are a few annoyances, such as the statement, "Mutations are almost invariably deleterious." Although this might hold for mutations that alter the phenotype in a detectable way, the vast majority of spontaneous genetic changes are neutral. Mitosis and meiosis are covered in one figure, and meiotic recombination in another, thereby emphasizing that this text is not for the student naive to genetics. The authors emphasize at several junctures how studying human genetics will lead to new and improved treatments for disease but never note the importance of first understanding pathogenesis to develop effective therapies. The genetics of complex traits, including association studies and linkage disequilibrium, is discussed very superficially. Examination of haplotype structure, such as by Haploview, is not illustrated. The discussion of the risk-benefit analysis for retroviral-mediated gene therapy in a fatal disease, X linked severe combined immunodeficiency, which is accompanied by a substantial risk of developing T cell leukemia, is based on false logic; whereas "leukemia in children is treatable," this particular variety is not so amenable to standard methods, and considerable morbidity and mortality occurs from therapy and recurrent disease. Nearly 200 scientists are mentioned in the text in association with key discoveries and referenced in the index; unfortunately only 16 of them are women. Some gender skewing results from the

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preponderance of male scientists in the early 20th century, but in descriptions of recent experiments, more women could have been highlighted. Finally, the text is now more than a year old, and references include those only up to mid-2006.

These issues notwithstanding, this new edition of *Recombinant DNA* will provide ample stimulus and education for those predisposed to believe its first sentence: "There is no substance so important as DNA."

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