Book Reviews

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Genetic Instabilities and Hereditary Neurological Diseases. Edited by R. D. Wells and S. T. Warren. San Diego: Academic Press, 1997. Pp. 829. $159.95.

Only 7 years have passed since the discovery of trinucleotide-repeat expansions, yet, somehow, it seems that we have waited a long time for a comprehensive text on the subject. This delay is understandable. The triplet-repeat field moves so rapidly that reviews written just a few years ago are laughably out of date. Given that it takes ~2 years to get a book to publication, a text devoted to trinucleotide repeats runs the risk of being behind the times, even before its time. Now, at last, we have the first major text devoted to repeat-expansion diseases, *Genetic Instabilities and Hereditary Neurological Diseases*. The editors have set out to create a comprehensive, up-to-date review of what is an increasingly broad field. They succeed admirably in their task. R. D. Wells and S. T. Warren have enlisted recognized experts in the field, to contribute discussions about the various diseases and their underlying mechanisms, with the end result being chapters that are usually highly informative and that nearly always present the latest findings. This text, like most, is not meant to be read from cover to cover; the amount of detail is exhaustive, and nearly every one of its >800 pages is packed with facts. Instead, *Genetic Instabilities* is an extremely useful reference book that geneticists, researchers, and clinicians will want on their shelves.

Although the book touches briefly on other genetic instabilities, it focuses on trinucleotide repeats. The first half of the book is dedicated to the individual triplet-repeat diseases, beginning with an excellent overview chapter by G. R. Wilmot and S. T. Warren. The diseases are presented in their order of discovery, more or less, beginning with the two diseases discovered virtually simultaneously in 1991, fragile X and spinal and bulbar muscular atrophy (SBMA), and ending with Friedreich ataxia. For many of the diseases, separate chapters describe the clinical features, molecular mechanisms, and animal models. Chapters on the molecular basis of fragile X, SBMA, and spinocerebellar ataxia type 1 (SCA1); P. Harper's review of the clinical and genetic features of myotonic dystrophy, which includes a nice description of the history of anticipation; and all three chapters on Huntington disease are outstanding. This section is followed by a brief discussion about neuropsychiatric disorders that *may* show anticipation and, thus, *may* be candidate triplet-repeat diseases, followed by several chapters that describe commonly used techniques of identification of expanded triplet–repeat disease genes and proteins. Some of these technique chapters read like lab protocols, but researchers just entering the field may find them useful. The next 13 chapters—very nearly the last half of the book—represent a remarkably detailed discussion of the molecular basis of genetic instabilities. Included here are numerous chapters on the biophysical properties of DNA-repeat sequences, the basic mechanics of DNA replication and repair, and model systems for the analysis of repeat instability. For many clinicians and some geneticists, these chapters will be difficult reading. Several chapters, however, are quite enjoyable and at the same time are detailed (e.g., the chapters on genetic instabilities in yeast and on duplex triplet-repeat structures). The book's final section contains two superb reviews of the general mechanism of polyglutamine toxicity and single chapters on the dodecanucleotide repeat disease, progressive myoclonic epilepsy, and microsatellite instabilities in cancer. The book concludes with a (too brief) chapter that highlights the things we don't know about triplet repeats, the areas that still demand research.

Genetic Instabilities is not without its faults. Many chapters repeat the same points about general mechanisms; a few strategically placed overview chapters would be better. For the second edition (and surely there will be one), the editors should strive to eliminate this redundancy. Some diseases also receive a disproportionate amount of attention, whereas others are neglected. For example, if an extremely rare dentatorubral pallidoluysian atrophy variant, Haw River syndrome, deserves its own chapter, then surely so does SCA6, a relatively common form of hereditary ataxia. Likewise, there is little discussion about the clinical and pathological features of Machado-Joseph disease, also known as SCA3, which may be the most common dominant ataxia worldwide. Harper's otherwise excellent description of myotonic dystrophy is missing its last nine references. Last, it would have made more sense to group the diseases by category. For example, chapters on the eight glutamine-repeat diseases and polyglutamine toxicity would make a logical subgrouping. These are minor flaws, however, that do not mar an otherwise excellent text. There is no doubt that *Genetic Instabilities* will be a much-sought-after reference text in many laboratories—it certainly already is in ours.

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