YACs for the Uninitiated

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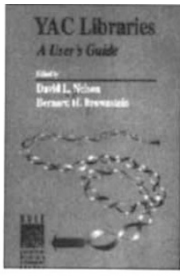
The isolation of all the functional elements of the chromosomes of the yeast *Saccharomyces cerevisae*—centromeres, telomeres, and potential replication origins (ARS elements)—has meant that artificial yeast chromosomes may be constructed *in vitro*. The use of such yeast artificial chromosomes (YACs) as cloning vectors to isolate large contiguous segments of nonyeast DNA was pioneered by Maynard Olson and his colleagues. This technique has proven invaluable to the analysis of large genomes (such as those from humans, higher plants, and the nematode worm, *Caenorhabditis elegans*), since the cloning of YACs far exceeds that of bacteriophage or cosmid vectors. Indeed, yeast cells seem to be able to grow and divide while containing a YAC molecule whose size exceeds that of any of its natural chromosomes, provided that the insert DNA does not have too extreme a base composition. The use of YAC vectors often involves new investigators in two technologies with which they may be unfamiliar—yeast molecular genetics and the handling of very large DNA molecules. It is for such people that this book is primarily intended.

YAC Libraries: A User's Guide is quite a short one (just over 200 pages) but is an edited work and suffers from all of the problems to which multiauthor compilations are prone. There is no uniformity of treatment or, indeed, nomenclature. Some authors provide detailed experimental protocols, somewhat in the style of the much-respected Cold Spring Harbor Manuals, while other convey their techniques in the more narrative format found in the methods section of most journal articles. Indeed, chapter 10 (Den Dunnen et al.) is written as a journal paper, with all the usual sections; this is an inappropriate, and even confusing, format in the present context. The nomenclature variations are a minor irritation except for those referring to yeast genetics, where it is often difficult to distinguish genotype and phenotype. Another problem is one of redundancy—a number of central techniques (such as yeast transformation, growth media, and the preparation of high molecular weight DNA) are described more than once.

The multiauthor format does have one significant advantage however. All of the authors write from a deep personal knowledge of the techniques that they describe and most chapters contain all sorts of wise tips and warnings that will be invaluable to the novice. This is particularly true of chapter 4 (Mendez et al.), which gives a very clear-headed review of the approaches that may be used to isolate YAC clones from genomic libraries; it includes excellent experimental protocols. One of the major problems in constructing such libraries, that of chimera formation, is first dealt with in chapter 5 (Zoghbi and Chinault), which discusses the generation of YAC contigs by "walking." However, this chapter deals with the chimera problem only in the context of the analysis of the human genome. Thus, the formation of chromosome-plastid DNA chimeras, which has dogged the analysis of plant genomes, is not discussed. Moreover, the recommended method for detecting chimeras is *Alu* PCR amplification—a technique that may only be applied to the human genome, to which the *Alu* repetitive elements are peculiar.

The whole book deals with YACs only in the context of human genome analysis. The exclusion of other systems does a disservice, not only to the excellent work that has been done with *C. elegans* and the higher plants, but also to the ubiquity of the YAC technology itself. Nevertheless, chapter 7 (Joslyn et al.) on the use of YACs in the positional cloning of APC (a human disease gene) provides an excellent illustration of the problems and strategies involved in isolating a large and complex locus. Curiously, this chapter never explains what PAC is, and one is left to sift the references to discover that is stands for adenomatous polyposis. The use of cDNA is, of course, central to the analysis of such genes and chapter 6 (Marchuk and Collins) provides a rigorous account of the use of YACs to identify expressed sequences by screening cDNA libraries. It contains excellent descriptions of essential controls that often exploit particularly neat pieces of technology. It is only the final chapter (Den Dunnen et al.) that we learn something of the yeast life cycle, and how it may be exploited to reconstitute large loci. It is also here that we find, for the first time, some reference to cloning systems (such as P1, BACs, and EBV), which rival YACs in their cloning capacity and which may provide alternative, or complementary, approaches.

The editors of multiauthor works have an unenviable task these days. Even getting authors to submit their chapters in the right year is an achievement; most chapters in this book review the literature up to 1991 or 1992. However, had Nelson and Brownstein been tougher on their authors (or been prepared to extensively rewrite some chapters), they might have changed what is a good and useful book into an excellent and indispensable one. ///



YAC Libraries: A User's Guide, *David L. Nelson and Bernard H. Brownstein, editors, Oxford University Press, New York, 1994, $39.95.*

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