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## Preface

The Bacterial Artificial Chromosome (BAC) system was developed in the early 1990s—at about the same time the Human Genome Project (HGP) was officially launched—as a vector for cloning high molecular weight genomic DNA. BAC clones were large enough for recovering full-length genes that included exons, introns, and distal regulatory elements. Moreover their low-copy replication conferred stability to complex human DNA, including repetitive sequences that would ordinarily rearrange in most plasmids. These qualities quickly made BACs indispensable for sequencing the human and other genomes.

At the same time these very features acted like double-edged swords—their large size and low-copy nature made it challenging to work with BACs for functional studies. Routine plasmid techniques such as DNA isolation and transfer into *E. coli* and mammalian cells became extremely tricky when attempted with BACs because of their low yield and degradation issues. And since restriction enzyme-based modifications were limited when applied to large DNA, mutagenesis of BAC clones became laborious. However, with time new protocols were developed that overcame these obstacles, gaining BACs widespread use in many new applications, including for deciphering gene structures and function, understanding disease phenotypes, and developing treatment approaches in cell and animal models.

*Bacterial Artificial Chromosomes* (2nd edition) presents a blend of some of the most important methods developed for working with BACs. It begins with fundamental techniques used for BAC construction and characterization (Chapters 1–3) and follows up with more advanced procedures for introducing modifications (Chapters 4–6) and for achieving gene expression from these vectors (Chapters 7–10). The book ends with chapters describing applications of BACs in model organisms (Chapters 11 and 12) and in medical genetics and drug discovery (Chapters 13–18).

These chapters follow the proven format of the *Methods in Molecular Biology Series*: a brief introduction that provides an overview of the method, a materials section, followed by a series of detailed protocols divided into clear sections and subsections that are supported with timely Notes to guide the reader. The Notes section is the hallmark of the Series, supplying the reader with valuable tips and tricks that aim to help them execute the method successfully. This section may include information that are traditionally not found in the methods section of research papers and therefore not widely known. Or they may detail specific modifications that are developed and applied by an expert lab or experienced researcher with extensive familiarity with the technique.

This book would not have been possible without the support of many people. I am indebted to John Walker for inviting me to this project and for all his advice and help with the overall editing of the chapters. My deep gratitude goes to all the authors who graciously contributed their time and effort to this project and for following through their original drafts with many rounds of editing to bring their chapters to the final form that

appears in the pages of this book. At Humana Press, Patrick Marton and David Casey have been a great source of help with editing and for bringing the book to print. Finally, I would like to thank my wife Stella Salleh for selflessly letting me spend many hours in solitude working on my writing. Her patience, understanding, and support inspired me to finish this book.

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<http://www.springer.com/978-1-4939-1651-1>

Bacterial Artificial Chromosomes

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2015, XI, 348 p. 48 illus., 36 illus. in color., Hardcover

ISBN: 978-1-4939-1651-1

A product of Humana Press