

PREFACE

The goal of this volume of *Methods in Enzymology* is to describe diverse applications of high-density sequencing to research in microbial molecular genetics. Microorganisms are well suited for multiscale approaches ranging from single molecules to communities of cells. The protocols described here give an overview of how applications in high-density sequencing have been adapted to studies with prokaryotic and eukaryotic microorganisms. Many of the chapters include a brief introduction, suggestions about pitfalls to avoid, a discussion about interpretation of results, and recommendations for follow-up work to validate conclusions. For some applications, a protocol can be used without modification. For other applications, a protocol can be a roadmap to adapt the method to a different microorganism or to a different experimental condition.

Advances permitting sequence depths of tens of millions of reads per library have opened the way to a diversity of comprehensive genome-wide studies including mapping, processing, and stability of transcripts; measurement of protein synthesis rates; determination of the specificity of RNA- and DNA-binding proteins; and analysis of chromosome structure and integrity. In addition to genome-wide studies, high-density sequencing is applicable to any protocol whose output is a library of sequences. As examples, this volume of *Methods in Enzymology* includes chapters on the functional characterization of toxin-antitoxin systems and the characterization of sequence elements that determine levels of transcription.

It is my hope that the chapters in this volume of *Methods in Enzymology* will stimulate imaginative approaches for the application of high-density sequencing to integrative research with microorganisms. As high-density sequencing becomes widespread and relatively inexpensive, genome-wide analyses are rapidly becoming standard practice. This methodology is part of the foundation of synthetic and systems biology.

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