Preface

DNA has been known to be the cellular target for many cytotoxic anticancer agents for several decades. The knowledge of its structure in atomic detail and the ease with which DNA fragments (both synthetic oligonucleotides and natural sequences) can be prepared and manipulated has aided the design of compounds that bind to it with improved selectivity. On the basis of this information, new generations of sequence reading compounds (including triplex forming oligonucleotides and minor groove binding ligands) have been prepared, which have the potential for targeting specific DNA sequences as anti-gene agents. Within the last 10 years, it has also become apparent that the familiar DNA duplex is not the only structure that can be targeted by DNA-binding ligands and there has been increased interest in triplex and quadruplex structures as drug targets, as well as protein-DNA complexes, such as those with nucleosomes or topoisomerases.

Each of these advances has required the availability and development of an arsenal of techniques for probing the interactions in both qualitative and quantitative terms. This volume of *Methods in Molecular Biology* brings together several techniques that are currently useful for examining these interactions. Some of these are updates on ones that were included in the earlier volume (*Methods in Molecular Biology* 90), published 12 years ago, while others are new. Molecular science is a multidisciplinary enterprise, and while individuals and laboratories may become experts in a few techniques, a detailed description of DNA-ligand interactions requires a combination of approaches. This volume should therefore be useful for established workers who wish to broaden their experimental repertoire, as well as for those who are new to the field and need expert advice and guidance.

The chapters have all been written by scientists who are experts in their own fields. They will obviously reflect their local preferences in experimental protocols, which can be modified to suit the requirements of the individual researcher. Each chapter begins with a short introduction, which outlines the background to the technique, the principles of its application, and the importance of the particular method. The most important part of each chapter is the methods section. These set out the experimental protocols in a step-by-step fashion and are accompanied by Notes sections which provide technical tips, based on experience, giving valuable information about potential problems and pitfalls and emphasizing the points at which special care is required. This volume should therefore be useful for post-graduates, post-doctoral workers, and established scientists, working in drug-DNA interactions.

The chapters in this volume combine a wide range of approaches, from the cellular to the structural. The first nine chapters describe various biophysical techniques for quantifying drug-DNA interactions and for describing these in molecular and atomic detail, while the later chapters describe molecular and cellular approaches. Together these provide methods for assessing the strength and mode of binding, the sequence selectivity, and their effect on biological systems.

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