Preface

Small Molecule Microarrays (SMMs): Methods and Protocols showcase a cornucopia of ways in which SMM technology may be deployed for multiplexed screening and profiling. SMMs were introduced just a decade ago in 1999 and, within a short space of time, have already established themselves as a vibrant, next generation platform for high-throughput screening. Significant developments, over the last decade, have equipped practitioners with an array of synthetic options, immobilization chemistries, assay modalities, and data processing schemes, thereby propelling the SMM platform to exciting new heights. Many of the scientists personally responsible for the success of these research endeavors have contributed chapters to this volume. As a result, the richness and diversity of this collection offers unique learning opportunities, both in fueling the development of new ideas and applications, as well as in tailoring proven solutions for different sets of libraries and microarray formats. Proven approaches, however, rarely work at the first attempt. Moreover, microarrays are notorious for the technical challenges they pose. It is to address these shortcomings that we have put together this volume, to supplement the open literature with practical tips for improved experimental design and the avoidance of potential pitfalls. The case studies in each chapter explain the key considerations and principles in getting things done right.

What challenges do working with SMMs pose? First and foremost is the complexity of the library synthesis and array fabrication steps. These processes lie at the core of SMM technology, for they govern how the molecules will be oriented and whether they will be accessible to the samples (such as proteins or proteomes) being screened. Quick and efficient means to construct pure and high-yielding libraries for SMMs is another major bottleneck; alternative approaches of array creation through in situ synthesis face similar challenges in ensuring the quality of the resulting arrays. The next major hurdle is in designing the methods for detecting positive readouts on the arrays and in using labels that minimally affect the interactions being probed. Finally, discerning between true interactions and false positives and improving signal to noise are among the challenges in enhancing readout quality and hit identification. These challenges are not without resolve. With careful preparation and informed decisions, these hurdles can be met and overcome using proven designs and strategies. Each chapter is designed to equip and inform the readers on these intricacies of SMM, as well as to provide the relevant guidance and means to harness and apply this technology.

The book is organized by the categories of small molecules presented on the microarrays. The molecules described herein include chemical libraries, peptide libraries, and carbohydrates. Each section covers a number of strategies for molecular immobilization, customized to the intended application. Chapter 1 provides an overview of SMM. Chapters 2–8 describe SMMs constructed from chemical libraries. A variety of covalent (Chaps. 2–3), noncovalent (Chaps. 4–5), and droplet-based techniques (Chaps. 6–7) are adopted for applications spanning enzyme profiling, inhibitor discovery, and in lysate protein screening (Chaps. 2–8). Chapters 9–15 describe peptide microarrays, including their fabrication using in situ synthesis (Chap. 9) and characterization with mass spectrometry (Chap. 10).
for applications in antibody detection (Chaps. 11–13) and kinase profiling (Chaps. 14–15). Chapters 16–17 describe ways in which carbohydrate microarrays may be fabricated (Chap. 16) and applied to glycobiology (Chaps. 16–17).

In reality, words alone are insufficient to learn the tricks of the microarray trade. The essential skills can only be learnt through hands-on experience and feedback at the bench. Each contributor has faced problems that have been solved with creativity and imagination. The chapters have been crafted to inspire a future generation of microarray practitioners to take the technology forward. In time, these individuals will create novel solutions of their own, which may possibly appear in future editions of the *Methods in Molecular Biology* series.

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