Preface

The emergence of chemical biology represents the culmination of multifactorial forces in the fields of chemistry, biology, pharmacology, and medicine at the turn of the twenty-first century. Revolutions in genomic sequencing and robotic automation led to improved access to enabling technologies for academic researchers, and molecular biology methods for analyzing and manipulating intricate environmental cellular responses fostered new approaches to understanding biological systems. However, the sequencing of the human genome seemingly posed more questions than provided solutions to therapeutic hypotheses and strategies, and thus the genesis of chemical biology sought to employ the tools of chemistry to illuminate the complex underpinnings of cellular function.

To develop novel chemical tools, high-throughput screening (HTS) platforms and concepts traditionally utilized by the pharmaceutical and biotechnology industries for target-centric molecular discovery have been embraced for in vitro- and in vivo-based compound screening. In these chemical genetic systems, the fundamental ability of discrete chemicals to bind to and modulate the function of proteins leads to a phenotypic alteration. Most importantly, in contrast to biochemical HTS assays that screen for molecular binding to a protein with a therapeutic hypothesis, chemical genetic assays do not necessarily preselect for target identity, thus requiring the rate-limiting step of chemical biology: target identification.

With this compilation of methods in chemical biology, we seek to enable the discovery of novel chemical biology tools by providing readers with an array of techniques ranging from initial chemical genetic screening to target identification through the central theme of molecules. We have specifically organized the book into four parts to highlight essential components of the chemical biology tool discovery process. Part I details platforms for molecular discovery in in vitro cellular systems, and Part II provides in vivo chemical genetic screening protocols organized roughly in increasing order of organism complexity. These methods constitute a broad sampling of current state-of-the-art biological systems and phenotypic readouts for chemical genetic screening in chemical biology.

The unifying theme of chemicals in chemical biology necessitates the methods described in Part III, in which compounds are isolated, purified, selected, analyzed, and profiled to create their biological value. And the functional protein targets responsible for their phenotypes can be ascertained through methods described in Part IV for target identification. These four parts, taken together, describe processes for developing molecular tools to dissect biological function, and while no single prescription exists, our aim is to improve the success rate of this field through the dissemination of detailed, experiential knowledge.

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