

METHODS IN MOLECULAR BIOLOGY

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High Throughput Screening


Methods and Protocols

Third Edition

Edited by

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Preface

Everything changes and nothing stands still—Heraclitus of Ephesus

This quote from Heraclitus was written almost 2500 years ago but could not fit the modern world more clearly. It has definitely proven true of the field of High Throughput Screening (HTS). When I began to work in HTS in 1989 it was virtually unheard of outside of a few industrial research laboratories. As an illustration, there are nine citations in PubMed from that year that contain “HTS” or “High Throughput Screening” in the title or key words. In 2013 there were over 2000. HTS has become integrated with large segments of research and across many fields. It has evolved from a highly specialized and secretive activity to a function that is made available to researchers through academic core labs.

But, “the more things change the more they stay the same” (Jean-Baptiste Alphonse Karr). This quote is also true of HTS. The basic processes underlying HTS have not changed in the last 25 years. Test a large number of potential effectors of a biological system as rapidly as possible while maintaining sufficient rigor to allow conclusions to be drawn from the data that is generated. The size, quality, and complexity of the chemical libraries used in HTS have changed, growing into the millions of compounds with rapid QC of compound composition. HTS assays have expanded to include complex cellular systems, mass spectrometer techniques, microfluidics and, in the most telling change of all, many of these have become widely available as kits. Systems that are capable of capturing, calculating, and visualizing millions of data points have become competitive sets of commercial software rather than custom-built systems that often relied on spreadsheet calculators. And last, but certainly not least, the recognition that quality is paramount in all of these factors has become an accepted tenet of not only HTS, but drug discovery in general.

So, in short, HTS has become mainstream. It is an important part of the drug discovery process, but is integrated with many other tools and techniques. The road that HTS has traveled in this period is paralleled by the three editions of this book. The first edition was designed to introduce the reader to basic HTS techniques and the chapters were designed to cover broad applications while the second added more detail and included key chapters providing detailed protocols. In recognition of this evolution, I have tried to move this edition more towards the traditional format of Method in Molecular Biology and have asked the authors to present detailed protocols for the techniques that they describe. The introductory chapter (Chapter 1) still provides an overview of important assay development techniques, but the following chapters provide what is needed in HTS today: details on how to develop and execute screens at whatever throughput the user needs.

I hope you enjoy this volume and find it useful.

Cambridge, MA, USA

William P. Janzen

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