

## Foreword

Random screening of comprehensive compound collections constitutes a major source of novel lead structures reflected by industry's ongoing commitment to invest in extensive compound libraries and screening technologies. During the last decade, High-Throughput Screening (HTS) has evolved to become an innovative multidisciplinary branch in biological chemistry combining aspects of medicinal chemistry, biology, and laboratory automation. While basic medicinal chemistry techniques and views are largely conserved throughout industry, HTS strategies differ to a great extent. Each strategy can be justified by scientific rationale. However, it is also the result of different scientific backgrounds, different therapeutic areas, different technical expertise within a group, and different ways HTS is integrated within the overall discovery process in a given organization. For most strategies, the close interrelation between HTS and the molecular target approach to drug discovery renders the validity of a disease link for a selected biomolecular target an essential prerequisite for success. As a consequence, a critical assessment of HTS has to incorporate also reflections on the discovery process from target selection to appropriate screening cascades. A different approach employing phenotypic readouts, e.g. cell proliferation, has a long tradition in screening, particularly for chemotherapeutic principles in cancer and anti-infectives research. Similarly, chemical genetics makes use of small molecule perturbation of specific cellular responses to unravel the underlying gene and pathways function. Within the later paradigm, High-Throughput Screening techniques have gained increasing relevance also in academic research.

The current book presents a collection of review-style papers written by experts in the field intended to provide insights into selected aspects of the experimental lead discovery process in High-Throughput Screening. It is by no means claimed to comprehensively cover the entire field. A number of aspects have been discussed in previous volumes within this series on "Methods and Principles in Medicinal Chemistry". It complements this book series by illustrating HTS as one of the technologies of great relevance to the medicinal chemist and molecular pharmacologist working in pharmaceutical or academic research.

I am personally thankful to the Series Editors not only for providing the opportunity to present High-Throughput Screening within a single dedicated

volume, but also for their patience during the preparation of this volume. In addition, the continuous support of my colleagues, Stefan Mundt, Nils Griebenow and Peter Nell, is gratefully acknowledged.

Wuppertal, July 2006  
Jörg Hüser