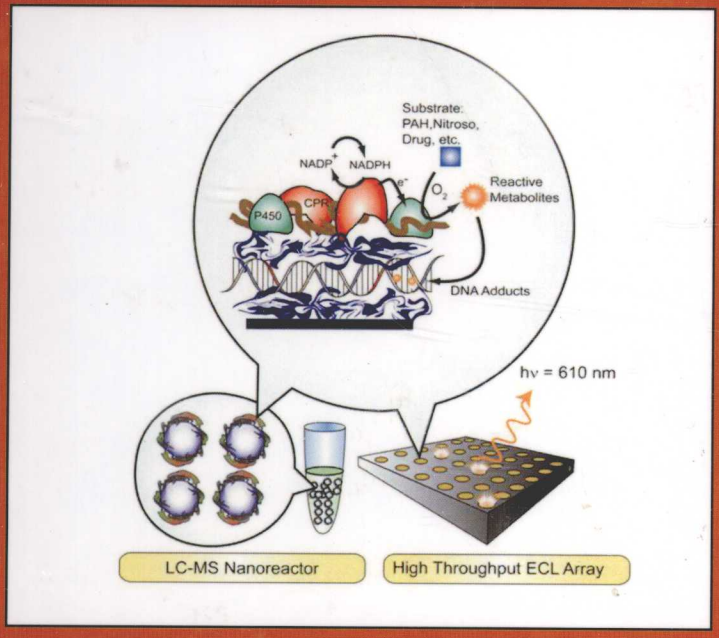
High-Throughput Screening Methods in Toxicity Testing



EDITED BY

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HIGH-THROUGHPUT SCREENING METHODS IN TOXICITY TESTING

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HIGH-THROUGHPUT SCREENING METHODS IN TOXICITY TESTING

PREFACE

Conventional approaches to toxicity testing of chemicals and drugs are often decades old, costly, do not allow high-throughput testing, and are of questionable value when wanting to estimate human risk. The publication of the document entitled "Toxicity Testing in the 21st Century: A Vision and Strategy" by the US National Research Council and the implementation of the European legislation on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) have led to a paradigm shift regarding the strategy to be pursued when evaluating the toxic potential of chemicals and drugs. Namely, toxicity evaluation should be preponderantly performed by using high-throughput *in vitro* methods and toxicity testing methods in animals should play, if at all, a minimal role.

The book gives an overview on a variety of high-throughput screening methods being used in toxicity testing nowadays and should be of help to all scientists working in the field of toxicity evaluation and risk assessment of chemicals and drugs in chemico-pharmaceutical as well as biotechnology companies, contract laboratories, academia as well as regulatory agencies. The book chapters are written in such a way that they lend support to those wanting to establish these methods in their laboratories as well as those having to evaluate the data generated. Each chapter describes the principle of the method and includes detailed information on data generation, data analysis, and the use/application(s) in risk assessment. Moreover, the chapters not only list the advantages of the high-throughput method over the "conventional" methods used up to now in safety evaluation of chemicals and drugs but also point out limitations and pitfalls.

The book is divided into five parts. Part I includes the strategies pursued nowadays to predict the toxicity potential of chemicals and drugs through high-throughput bioactivity profiling, the incorporation of human dosimetry and exposure data into

high-throughput *in vitro* toxicity screening, and the use of human embryonic stem cells in high-throughput toxicity assays. Part II presents a variety of high-throughput assays to assess different cytotoxicity endpoints; Part III describes high-throughput assays to assess DNA damage and carcinogenesis; Part IV includes high-throughput assays to assess reproductive toxicity, cardiotoxicity, and hematotoxicity; and Part V presents high-throughput assays to assess drug metabolism and receptor-related toxicity. By including all these above-mentioned aspects, the book should be of great value to toxicologists, pharmacologists, analytical chemists, and pharmaceutical scientists working in academic institutions, industry, and regulatory agencies that are involved in safety evaluation and risk assessment of chemicals and drugs and an excellent complement to the current literature on toxicology in general and safety evaluation/risk assessment in particular. Because of the test systems and the toxicity endpoints described, this book could also be extremely interesting for all scientists working in the fields of biochemistry, cell biology, molecular biology, systems biology, and computational toxicology.

I hereby would like to thank all authors for their excellent contributions. Only because of them it was possible to conceive a book including such a broad spectrum of toxicity testing methods. The development of high-throughput methods to screen the toxic potential of drugs and chemicals is a rapidly evolving field. If the one or the other method was missed, then this omission was not on purpose and an incentive to actualize this version of the book in the future.

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PART I

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