
Preface

It seems fashionable today to simply place the word “molecular” in front of a traditional field and consider it reinvented. This, without a clear consensus on what the “molecular” actually means. Certainly chemists working in the field of toxicology have always considered that they worked at the “molecular” level. It has not been so clear on the biological side, however, where there has been a history of ongoing discovery and characterization of toxic mechanisms. In other biological fields, “molecular” really implies using the tools of “molecular” biology, i.e., recombinant DNA. Just as the adoption of molecular biological techniques first invaded, then transformed such biological fields as genetics, physiology, and developmental biology, so too have these new methods begun to transform toxicology.

Molecular Toxicology Protocols is a book about science on the interface, and a science that is about to explode upon the clinical and popular horizon. Toxicology, a subdiscipline of pharmacology, is actually the interface of chemistry and biology. As most practice it, this field also extends into nonchemical “agents” of deleterious biological effects, especially radiation, the purview of the radiobiologist and health physicist. With the huge increase in computational power made available over the last ten years it has become possible to model and predict the potential toxicity of as yet unmade chemicals. Perhaps the greatest change in the practice of toxicology has been application of the tools of the trade directly to the human population, in what are known clinically as “translational” studies, opening the new frontier of epidemiology through the more conventional portal of biostatistics. These studies expand the traditional public health aspect of toxicology, screening of synthetic agents for toxicological potential prior to their introduction into the environment, attempting to define “normal” or “background,” perhaps unavoidable, exposures as mechanisms of human disease, and to design methods of preclinical intervention (“chemo-prevention”).

Thus, for our purposes, we will define “molecular” toxicology as either any study of toxicological mechanism, or any translation of toxicological practice into the human population.

Today, such “molecular” toxicology is mostly genetic toxicology, where the genetic material itself, the DNA, is the target molecule. Of course DNA is found throughout the human body, such that all of the traditional modulators of toxicological effect, uptake, distribution, metabolism, and so on, must be taken into account. Although genetic damage can have many outcomes, the one outcome most clearly linking exposure and disease is cancer.

During the past several years, important progress has been made in the understanding of the molecular biology of the cell, the responses of cells to genotoxic agents, and the molecular biology of human cancer. This progress has been achieved thanks to the ongoing development of new state-of-the-art techniques, as well as

improvements made upon existing methods to study changes not only in cellular morphology, but also in the cellular genetic material, the DNA, the cellular transcript, the mRNA, and the translated product, proteins. These molecular methods are now opening up many areas to potential clinical applications. Several books are currently available on the applications of molecular methods to various types of technology. However, to our knowledge, there is no book emphasizing the application of molecular methods to genetic toxicology.

Therefore, the aim of *Molecular Toxicology Protocols* is to bring together a series of articles, each describing commonly used methods to elucidate specific molecular aspects of toxicology. With such content, this book addresses not only molecular biologists and molecular toxicologists, but also all individuals interested in applying molecular methods to clinical populations, including geneticists, pathologists, biochemists, and epidemiologists. The volume is divided into seven parts, roughly corresponding to the spectrum of biomarkers intermediate between exposure and disease outcome as proposed in molecular epidemiological models. Thus, Part I includes chapters describing methods of detecting premutagenic lesions in the genetic material, while Part II contains chapters describing the applications of methods to assess gross or macroscopic genetic damage. Parts III and IV focus on detection and characterization of viable mutations, in surrogate markers and cancer-related genes, respectively. The chapters of Part V describe methods for the analysis of the various pathways of DNA repair, an important modulator of genotoxicity. Part VI addresses the application of the new array technologies to genetic toxicology, including methods for the analysis of individual variation in biotransformation and the effects of genotoxic exposure on gene expression. Finally, Part VII describes methods for analysis of cytotoxicity caused by the induction of apoptosis, because cell death can either protect the organism from a transforming cell or cause distinct health effects itself.

We have no doubt that as time goes by “molecular” approaches will play an expanding role in all types of toxicology, not just genetic toxicology. Moreover, genetic toxicology will undoubtedly be found to play a role in many more diseases of aging than cancer alone; it is probably a fundamental mechanism of aging itself. Therefore, while the current focus of *Molecular Toxicology Protocols* is genetic toxicology, and more specifically the genetic toxicology of cancer, we believe this represents just the tip of the iceberg with respect to how the field of molecular toxicology will eventually be understood.

**Phouthone Keohavong
Stephen G. Grant**



<http://www.springer.com/978-1-58829-084-7>

Molecular Toxicology Protocols

Keohavong, P.; Grant, S.G. (Eds.)

2005, XIV, 489 p., Hardcover

ISBN: 978-1-58829-084-7

A product of Humana Press