

Principles of Toxicogenomics: Implications for Preclinical Drug Development

Jürgen Borlak

*Fraunhofer Institute of Toxicology and Experimental Medicine (ITEM),
Hannover, Germany*

1. INTRODUCTION

Modulation of gene expression is of paramount importance in the mechanisms of drug-induced toxicity, and major efforts are being made to determine the relevance of gene expression in response to drug exposure. DNA arrays offer the unique opportunity to explore the simultaneous gene expression of literally thousands of genes, up to entire genomes. Based on global gene expression profiles, and in conjunction with other molecular endpoints, reliable predictions of drug safety may now become feasible at early stages in drug development.

2. TRANSCRIPT PROFILING

Because of the completion of the human genome sequencing program, an assignment of all human genes to their chromosomal locations has been achieved. An important finding was an identification of a significant number of nucleotide polymorphisms, although not all nucleotide polymorphisms are of functional importance. At present, the difficulty lies in the dissection of functional and silent nucleotide polymorphisms that can be linked to a