The Role of Toxicogenomics in Drug Discovery & Development

Seokjoo Yoon, DVM, Ph. D

Toxicogenomics team, Korea Institute of Toxicology, Daejeon 305-343, Republic of Korea

Toxicogenomics is a new scientific field in which researchers study how the genome responds environmental stressors or toxicants. It contains researches of genetics, genome-scale mRNA expression (transcriptomics), protein expression(proteomics), metabolite profiling(metabonomics), and computational biology(bioinformatics) with classical toxicology(histopathology, blood chemistry etc.). Now we can measure the expression of hundreds to thousands of genes and proteins at a time, using DNA chips and proteins chips. These powerful tools are capable of big changes in toxicology field. Over the past several years there has been considerable investment by chemical and big pharmaceutical companies, government institutes, and biotechnology companies in the application of genomics(include toxicogenomics) in chemical and drug development. The value of genomic approaches to generate hypotheses is being realized for understanding toxicity and consequently contributing to an evaluation of drug and chemical safety both in predictive toxicology and in mechanism based risk assessment. The completion of the sequencing of the human genome, and those of other organisms, is expected to lead to many potential new drug targets in various diseases, and it is predicted that novel therapeutic agents will be developed against such targets. The estimated 35,000 genes in the human genome, as well as multiple splice variants of many mRNAs, mandates that these technologies must be higher in throughput than most current technologies, as it will be impossible to develop the traditional depth of knowledge about each target. Importantly, no single technology will be sufficient to generate all of the necessary information, and the integration of knowledge from several approaches is required to select the best new drug targets for drug development. It is essential, in order to minimize expensive drug failures due to toxicity being found in late development or even in clinical trials, to determine potential toxicity problems as early as possible. In view of the large libraries of compounds now being handled by combinatorial chemistry and high-throughput screening, identification of putative toxicity is advisable even before synthesis. Thus the use of predictive toxicology is called for. A number of *in silico* approaches to toxicity prediction are discussed. Since a typical drug takes 10–12 years, and costs up to $500 million, to reach the market, it is clearly important to discover potential toxicity as soon as possible. Modern pharmaceutical discovery is emerging as a new branch of science, thanks in large part to the technological advances that are allowing us to truly functionalize the genome. The investment made in sequencing the human (and other species') genome was made in reaction to the promise that this information would revolutionize medicine.