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Future of Toxicology

Toxicology is the study of poisons and poisoning and has an ancient and venerable history. There was rapid development of analytical methods in the late 19th century and then an acceleration of both method and scientific development in the latter half of the 20th century. Toxicology today are often subdivided into clinical toxicology, forensic toxicology, industrial or occupational toxicology, environmental toxicology, pharmaceutical toxicology, experimental toxicology, and workplace drug testing. Recent high-profile drug withdrawals increase the pressure on regulators and therefore the pharmaceutical industry to enhance preclinical safety testing. The vision is based on the notion that exposure to environmental agents leads to adverse health outcomes through the perturbation of toxicity pathways that are operative in humans. Implementation of the NRC vision will involve a fundamental change within the assessment of toxicity of environmental agents, moving faraway from adverse health outcomes observed in experimental animals to the identification of critical perturbations of toxicity pathways. Pathway perturbations are going to be identified using in vitro assays and quantified for dose response using methods in computational toxicology and other recent scientific advances in basic biology. Implementation of the NRC vision would require a serious attempt, not unlike that required to successfully map the human genome, extending over 10 to twenty years, involving the broad scientific community to map important toxicity pathways operative in humans. Although toxicological practice has been relatively stable for the past few decades, with the exception of the introduction of specialized tests for genetic and reproductive damage and some other special functional assessments, all indications are that the field is now poised for major change. A glance at the program of recent annual meetings of the Society of Toxicology, or at the ever-increasing schedule of toxico- or pharmacogenomics meetings, leaves little doubt that toxicologists in industry, academia, and government are intensively evaluating modern molecular technologies. Essentially, in vivo toxicological assessment of organ and tissue damage involves the assessment of three basic types of "biomarkers" that indicate adverse biological effects on the organism-markers of (1) function and homeostasis, (2) cell and tissue integrity, and (3) cell and tissue damage or damage-response. New technologies of molecular biology are being applied in several ways to assess the function and structure of the major organ and tissue systems. Much attention is currently focused on the potential of DNA microarrays to identify either inducible damage responses or shifts in genetic expression patterns that are characteristic of specific molecular insults to the cell. Nonetheless, despite several decades of research on mechanisms of drug-induced toxicity and the application of various new technologies to preclinical safety assessment, the overall impact on preclinical safety testing has been modest. Assessing the risk of exposing humans to new drug candidates still depends on preclinical testing in animals, which in many, but not all cases, predicts outcomes in humans accurately.

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