



Original Research Article

INTEGRATING TOXICOGENOMICS AND EPIGENETICS FOR NEXT-GENERATION TOXICITY RISK ASSESSMENT

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Abstract:

Modern toxicology is currently in process of fundamental change from observational toxicity testing to molecular-level evaluations of the effects of a chemical. Toxicogenomics and epigenetics have individually built on our knowledge of how toxicants alter biological systems via gene expression modifications and heritable regulatory pathways. Despite these advances, current risk assessment frameworks remain limited in their ability to interpret complex molecular responses, particularly associated with low-dose exposure or chemical mixtures, and the presence of long-term or latent health effects. Absence of an integrated molecular approach constrains the accurate prediction of toxicity to human health. We reviewed the prospect of synergistic benefit of integration of the toxicogenomic and epigenetic knowledge in the next-generation toxicity risk evaluation through mechanistic knowledge of chemical-induced biological perturbations. Existing experimental and computational reports were systematically reviewed, specifically transcriptome analysis, epigenetic alterations including DNA methylation and non-coding RNA regulation and their inclusion in systems toxicology and adverse outcome pathway analysis. There is evidence that integrated molecular signatures can enhance early recognition of toxic effects, clarify modes of action, and sensitivity to chronic and transgenerational toxicity risks. These designs also facilitate animal testing alternatives and enhance regulatory considerations. The fusion of toxicogenomics and epigenetics has presented a strong mechanism-driven basis for the future analysis of toxicity risk, leading the way to a more predictive, ethical, and human-appropriate chemical safety evaluation in the future.

Keywords:

Toxicogenomics, Epigenetic regulation, Mechanism-based toxicity, Next-generation risk assessment, Systems toxicology