Commentary

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Advantages of the Use of Systems Biology Tools in Chemical Risk Assessment

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Description

Toxicological compound risk assessment has traditionally relied on animal testing. The study of chemical action at multiple scales of complexity, from the molecular to the system level, is made possible by omics technologies, particularly genomics and proteomics, which generate a large amount of data on genome-wide gene expression profiles, protein expression, and protein interaction with xenobiotics (particularly toxic ones).This permits point by point investigation of the systems of harmfulness. Despite the fact that all omics technologies have the potential to improve our comprehension of chemicals' toxicological effects, their use in chemical risk assessment has not yet been recommended for regulatory purposes. The combination of the modular framework of the adverse outcome pathway and the network organization within systems biology presents an opportunity to shift the paradigm of chemical risk assessment toward a better comprehension of chemical toxicology mechanisms with the recent development of the concept of the adverse outcome pathway. In this review, we discuss the benefits of using systems biology tools for chemical risk assessment as well as the challenges they pose, such as model over-parametrisation in quantitative modeling, managing data gaps in poorly studied substances, and a lack of expertise in bridging the gap between new approaches and regulatory levels.

Chemical and Their Metabolite Tissue Exposure Doses

To replace animal testing with more advanced technologies that can explain and extrapolate methods both in vitro and in silico is one of the main goals of safety assessment. Chemical risk assessment has traditionally relied on in vivo measurements of lower adverse effect levels and the no observed adverse effect level. Additionally, in risk assessments, physiologically based pharmacokinetic (PBPK) modeling is utilized as an addition to toxic chemical modes of action. Dose-response relationships have traditionally been used in human health risk assessments to quantify and characterize the potential adverse effects on human health. The availability of computers made it possible to use PBPK models as early as the 1970s. Since then, these models have been used and approved by authorities for chemical risk assessment. Pharmacokinetics, the study of how a chemical and its metabolites move over time in biological fluids and tissues, has been used to accomplish this. Chemical and their metabolite tissue exposure doses can be calculated using this kind of modeling for a variety of exposure conditions and species. Through the subdomain of systems toxicology, systems biology, which takes comprehensive approaches to understanding the properties of complex, dynamic, and nonlinear multilevel biological systems, has the potential to provide quantitative mechanistic models for addressing these issues.

New Method for Performing Chemical Risk Assessments That Is More Accurate

A new approach to chemical risk assessment is offered by systems toxicology, which makes use of a variety of levels of information obtained from integrating various data sources to provide a comprehensive mechanistic understanding of the underlying toxicological effects. New models that can assess chemical compounds by RAX can be developed using systems biology and systems toxicology. This provides a new method for performing chemical risk assessments that is more accurate, less expensive, and takes less time. Systems toxicology makes use of the data on exposure effects of pharmaceutical, industrial, and environmental compounds on various organisms as well as the pathways that are correlated with adverse outcomes to develop these models. These models will probably be even more accurate as omics technologies and big data are developed. In addition, the incorporation of systems biology into AOPs may make it possible to preserve the linearity of the biological pathway while simultaneously including the network and dynamic features that aid in the translation of one observation to the next. Although this linear representation of AOPs is useful and convenient, it is an abstraction of biology at the molecular level. The inclusion of feedback and feed forward loops in the mechanistic biology that underpins AOPs, which is discussed in greater depth in qAOPs, will broaden its application. This might make it easier to move away from using omics technologies in regulatory research.

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