Mechanistic Read-Across of Chemical Toxicants Based on Big Data

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In 2016, the Frank R. Lautenberg Chemical Safety for the 21st Century Act became the first US legislation to advance chemical safety evaluations by utilizing novel testing approaches that reduce the testing of vertebrate animals. Central to this mission is the advancement of computational toxicology and artificial intelligence approaches to implementing innovative testing methods. In the current “big data” era, the volume (amount of data), velocity (growth of data), and variety (diversity of sources) are critical considerations when characterizing the currently available chemical, *in vitro*, and *in vivo* data for toxicity modeling purposes. Furthermore, as suggested by various scientists, the variability (internal consistency or lack thereof) of publicly available data pools, such as PubChem, also presents significant computational challenges. The development of novel artificial intelligence approaches based on massive public toxicity data is urgently needed to generate new predictive models for chemical toxicity evaluations and establish scientific confidence in the developed models as alternatives for evaluating untested compounds. In this procedure, traditional approaches (e.g., QSAR) purely based on chemical structures have been replaced by newly designed data-driven and mechanism-driven modeling. The resulting models realize the concept of adverse outcome pathway (AOP), which can not only directly evaluate toxicity potentials of new compounds but also illustrate relevant toxicity mechanisms. The recent advancements of computational toxicology in the big data era are paving the road to future toxicity testing and will have significant impacts on public health.