Systems Approaches to Drug Safety

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The recent explosion of data linking drugs, proteins, and pathways with safety events has promoted the development of integrative systems approaches to large-scale predictive drug safety. The added value of such approaches is that, beyond the traditional identification of potentially labile chemical fragments for selected toxicity endpoints, they have the potential to provide mechanistic insights for a much larger and diverse number of safety events in a statistically-sound non-supervised manner, based on the similarity to drug classes, the interaction with secondary targets and the interference with biological pathways. The combined identification of chemical and biological hazards enhances our ability to assess the safety risk of bioactive small molecules with higher confidence than using structural alerts only. We are still a very long way from reliably predicting drug safety but advances towards gaining a better understanding of the mechanisms leading to adverse outcomes represent a step forward in this direction.

[1] Garcia-Serna R, Vidal D, Remez N, Mestres J. Large-Scale Predictive Drug Safety: from Structural Alerts to Biological Mechanisms. Chem. Res. Toxicol. 2015;28(10):1875-87.
[2] Remez N, Garcia-Serna R, Vidal D, Mestres J. The In Vitro Pharmacological Profile of Drugs as a Proxy Indicator of Potential In Vivo Organ Toxicities. Chem. Res. Toxicol. 2016;29(4):637-48.