A computational approach to mechanistic and predictive toxicology of pesticides

Emerging challenges of managing and interpreting large amounts of complex biological data have given rise to the growing field of computational biology. We investigated the applicability of an integrated systems toxicology approach on five selected pesticides to get an overview of their modes of action in humans, to group them according to their modes of action, and to hypothesize on their potential effects on human health. We extracted human proteins associated to prochloraz, tebuconazole, epoxiconazole, procymidone, and mancozeb and enriched each protein set by using a high confidence human protein interactome. Then, we explored modes of action of the chemicals, by integrating protein-disease information to the resulting protein networks. The dominating human adverse effects affected were reproductive disorders followed by adrenal diseases. Our results indicated that prochloraz, tebuconazole, and procymidone exerted their effects mainly via interference with steroidogenesis and nuclear receptors. Prochloraz was associated to a large number of human diseases, and together with tebuconazole showed several significant associations to Testicular Dysgenesis Syndrome. Mancozeb showed a differential mode of action, involving inflammatory processes. This method provides an efficient way of overviewing data and grouping chemicals according to their mode of action and potential human adverse effects. Such information is valuable when dealing with predictions of mixture effects of chemicals and may contribute to the development of adverse outcome pathways.