



Computational Toxicology: Chapter 7. Computational Translation of Nonmammalian Species Data to Mammalian Species to Meet REACH and Next Generation Risk Assessment Needs

Edward J. Perkins, Natàlia Garcia-Reyero

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New concepts in toxicology facilitate the use of nonmammalian vertebrate species (e.g., fish) and nonanimal models (nonvertebrates, early embryo vertebrates, or cell-based) as surrogates for mammals. We present a strategy to translate nonmammalian species data to estimate potential impact of chemicals on mammalian species based on highly conserved proteins and biological pathways linked to a defined adverse effect. Protein “targets” and pathway-level information can be mapped across species through identification of orthologs in mammals. Nonmammalian pathway data can be used to identify potential modes of action across species, establish toxicological dose-response relationships, and be used to estimate possible hazard levels of chemicals. Systems-level approaches are identified that offer unique opportunities to incorporate dynamic events such as homeostasis, effects over time, and species-specific parameters relevant to mammals. Ultimately, a pathway-centric focus enables use of alternative models to support protection of mammalian species.

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