

# Advances in Computational Toxicology

Toxicology has up to now not been a primary focus of molecular informatics. The reasons for this are manifold. A traditional toxicologist who accomplished her/his education five or more years ago will most probably not have received any training on computational approaches in toxicology. If the toxicologist's primary professional task is risk assessment, main focus will be on (animal) in vivo toxicity data. Given this background and the fact that predicting in vivo toxicity is still in its infancy, it is understandable that a toxicologist has usually no genuine affinity for computational toxicology. In addition, available predictive tools may be suitable to identify toxicological hazards. However, they have yet to mature into a state where exposure information can be adequately included for a meaningful use in risk assessment.

The situation is slightly different for specific sub-disciplines of toxicology, such as ecotoxicology or genetic toxicology, where predictive systems have found regulatory entry and are meanwhile also tools quoted in international guidelines.<sup>[1,2]</sup> The majority of currently available predictive systems are pure chemistry-based tools. This is a meaningful approach particularly for those toxicities which are driven by the physicochemical properties (e.g. phospholipidosis) or the chemical reactivity of a specific compound. Even though such systems still experience significant improvements through the application of more sophisticated descriptors or the modeling of new, previously unavailable data sets, a consensus seems to evolve that modeling approaches solely on the basis of a compound's structure will seldom suffice to predict the complex mechanisms of in vivo toxicity. This perception is a consequence of various in silico toxicology initiatives, which were launched predominantly for reducing animal studies ("3R"; replace, refine, reduce) in the area of chemical assessment (OECD QSAR Toolbox, OpenTox<sup>[3]</sup>), cosmetics (COSMOS<sup>[4]</sup>) and preclinical toxicology (eTOX<sup>[5]</sup>). In vivo toxicities are influenced or caused by a number of factors such as off-target pharmacology, metabolism or drug transporter involvement influencing exposure levels, to name just a view. The decisive factors leading to in vivo toxicity have to be identified by thorough mechanistic analyses before they can be integrated into future predictive systems in a modular way.

Given all the recent developments in this still fragmented field, we considered it timely to compile some of the above addressed facets in a special issue on *Computational Toxi-*

*cology*. It may still take some time until the full picture emerges, but the cornerstones and the frame of the puzzle are already getting visible.



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## References

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