ACS Green Chemistry abstract in Session "Chemical Design: Minimizing Adverse Impact and Assessing Alternatives"

Title: Too many chemicals, too little time: Rapid *in silico* methods to characterize and predict ADME properties for chemical toxicity and exposure prioritization

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Evaluating proposed alternative chemical structures to support the design of safer chemicals and products is an important component of EPA's Green Chemistry and Design for the Environment (DfE) Programs. As such, science-based alternatives assessment is essential to support EPA's efforts to promote a sustainable approach to chemical risk assessment. Alternative testing strategies, such as those that rely on computational chemistry, can be leveraged to efficiently assess the toxicity of chemicals and minimize their impacts to human health, ecosystems and the environment and provide a sound basis for the vision outlined in the National Research Council's *Toxicity Testing in the 21st Century* (NRC 2007) and *Exposure Science in the 21st Century* (NRC 2012) reports. Current computational tools and models are being employed for screening of adverse impacts (*i.e.*, toxicity, persistence, bioaccumulation and transformation potential) as well as prioritizing limited resources for the evaluation of new and existing chemicals. Computational chemistry (*e.g.*, target-based pharmacophore models and force-field docking methods) and chemoinformatic (*e.g.*, data-mining workflows) tools historically used in drug discovery settings are well poised to detect activity enrichment and guide discovery and development of local models within areas of chemical space that share common reactivity and interaction properties and/or exhibit similar bio profiles or biological activities. Elucidation of key molecular features and their relationship to chemical structure is critical towards these efforts especially at the biomolecular interface of protein targets and ligands (*i.e.*, molecular initiating events). The ability to incorporate and leverage high throughput biological *in vitro* and *in vivo* data along with current chemical databases within existing or new models and current informatics approaches will be discussed. Current computational research efforts to characterize and predict relevant pharmacokinetic parameters (ADME) will be highlighted with specific case studies for human exposures to consumer product and environmental chemicals.

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