Open-source Workflows for In Vitro to In Vivo Extrapolation

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Introduction

- In vitro to in vivo extrapolation (IVIVE) links in vitro assay results to in vivo effects. IVIVE tools currently available in the public domain (e.g., ADMET Predictor) make use of physiologically based pharmacokinetic (PBPK) models to extrapolate from concentration in blood to concentrations in target tissues.
- The P-PK model is used to derive the "effective tissue concentration" in target tissues, which is translated into a response via a toxicity response function that accounts for target tissue mass.

Examples Using the KNIME Workflow

- IVIVE analysis for P-A and A-P workflow: P-A and A-P workflows were run on 32 chemicals to assess their toxicity in the mouse embryo cancer (MEC) assay.
- The model used in this workflow is a one-compartment rat PK model that is used to simulate chemical exposure in the blood. The EAD values are then compared to in vivo LELs to assess the accuracy of the IVIVE workflow.

References

- Kirman et al. 2015. Applied In Vitro Toxicology 1(2):140-146.

Discussion and Conclusion

- Our open-source workflow provides a transparent and user-friendly approach for IVIVE analysis.
- The modularity and graphic interface of the KNIME platform facilitates integration with other cheminformatics workflows.
- The open-source workflow can be modified to suit the needs of individual labs and can be easily integrated into existing workflows.

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