Analyzing High-Throughput Assay Data to Advance the Rapid Screening of Environmental Chemicals for Reproductive Toxicity

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Fig 1. Dose-response for Bisphenol-A (BPA)

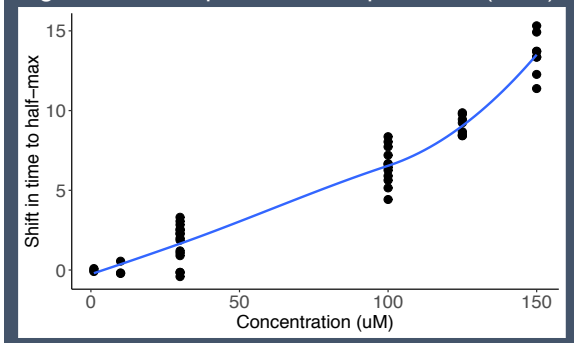


Fig 2. Yeast assay data ranked by potency based on BMD10

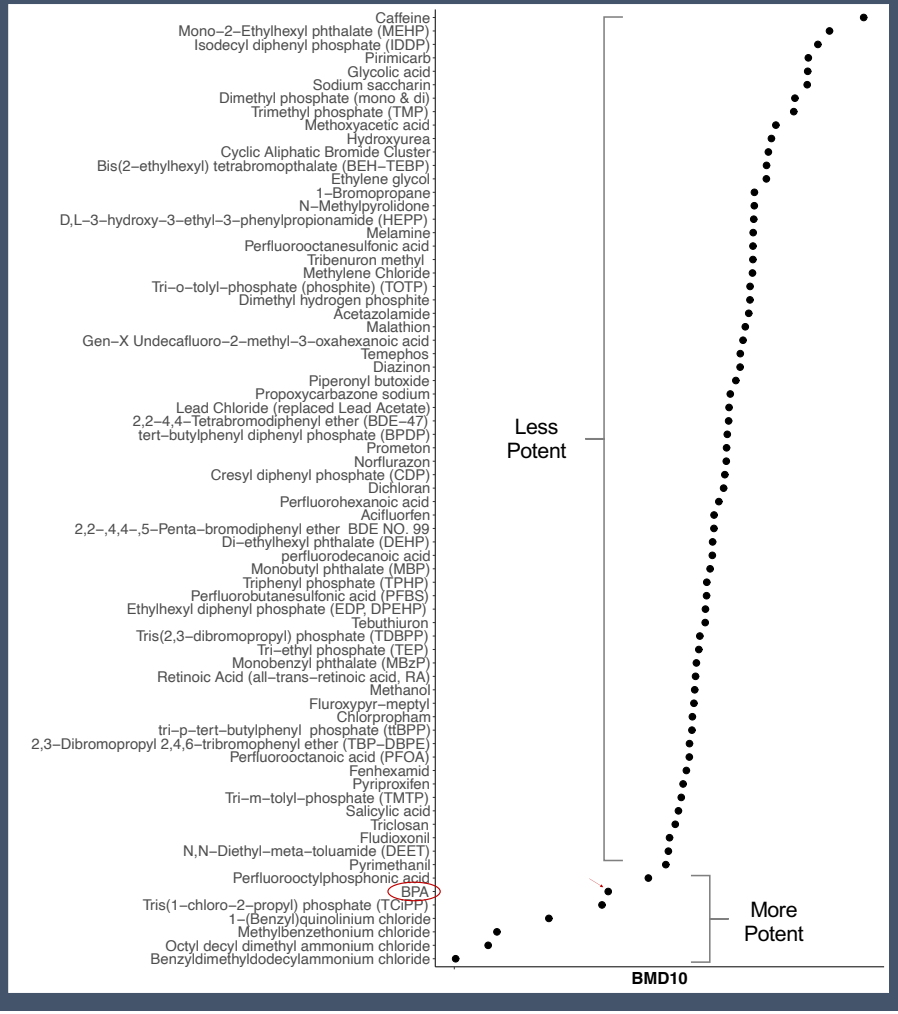
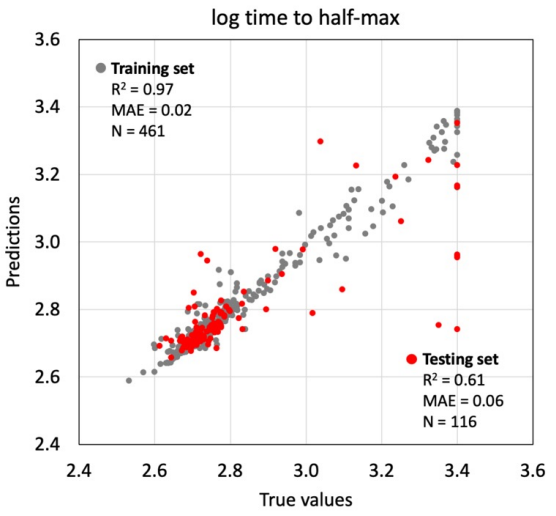


Fig 3. Machine learning prediction model



BACKGROUND

- Rapid screening of environmental chemicals for reproductive toxicity would advance predictive toxicology and chemical assessment.
- High-throughput (HTP) assays have been used as platforms for rapid assessment of reproductive toxicants; however, additional germline assays and method validation would improve knowledge for fertility and reproductive health.

METHODS

- We assessed a yeast (S. cerevisiae) HTP assay related to germline function and other reproductive health endpoints by screening toxicity of 134 environmental chemicals and modeling each data set using a streamlined, semi-automated benchmark dose software (BMDS) approach.
- We then extracted and modeled mammalian *in vivo* data from the Toxicological Reference Database (ToxRefDB, Version 2.0) and potency-ranked the data from each evidence stream by BMD.
- Finally, we constructed a prediction model using machine learning to incorporate model descriptors (including data on QSAR, chemical properties, etc.) and tested model performance in predicting time to half-max (yeast assay).
- Agreement of the coefficient of determination (R2) and mean absolute error (MAE) were compared between training and testing sets (80/20 split) to evaluate the model's predictive power.

RESULTS AND CONCLUSIONS

- We found great promise in predicting toxicological outcomes with reasonable accuracy (Training R2: 0.97, testing R2: 0.61).
- Agreement between the training set and the testing set showed the algorithm has a great potential of making accurate predictions outside its calibration domain and could play a significant role in predicting reproductive toxicity of environmental chemicals.

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