Using Bioactivity Based Read-Across (BaBRA) to Characterize the ToxCast Library

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The large chemical library and diverse assay space included in the ToxCast program present a unique opportunity to characterize environmental chemicals based on their *in vitro* bioactivity patterns across hundreds of critical targets and in comparison to reference chemicals with known toxicological effects. We used an unsupervised random forest approach to create a proximity matrix that clusters chemicals based on their bioactivity patterns across all the ToxCast assays within the context of the entire chemical library. Using the resulting clusters, we implemented a bioactivity based read-across (BaBRA) approach to examine the 1047 ToxCast Phase I and II chemicals. This analysis identified a large cluster of inactive chemicals, including food additives such as sucrose, as well as two clusters comprised predominantly of active pesticide ingredients. A cluster of highly cytotoxic chemicals (n=14) included mercuric chloride, phenylmercuric acetate, organotins, and multiple donated pharmaceuticals. Several confirmatory patterns were observed in the proximity matrix, such as steroid hormones and other clusters of chemicals with similar use cases (e.g., surfactants, anti-inflammatory drugs) clustering together. Clusters containing known human toxicants, such as diethylstilbestrol and azathioprine, were examined via BaBRA to identify untested environmental chemicals with similar bioactivity patterns. The presentation will discuss *in vitro* assay patterns across the ToxCast Phase I and Phase II libraries and identify *in vitro* targets and bioactivity trends that may be driving unique clusters. BaBRA predictions will be compared to toxicity and exposure data from the literature to identify potential patterns relating to use case and/or environmental persistence. *This project was funded in whole or in part with Federal funds from the NIEHS, NIH under Contract No.HHSN27320140003C.*