Comparing and Interpreting Tox21 Data Analysis Approaches

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In vitro testing platforms for rapid high-throughput, high-content screening, and multiplexed assays have propelled the field of toxicology into the realm of big data. High-throughput screening (HTS) approaches used in toxicology are designed to generate concentration-response data to characterize chemical effects on biochemical pathways and biological systems. Inherently this means that modeling the concentration-response curve is just as important as understanding the magnitude of effects to ultimately determine reliable and robust activity calls and potencies. Because millions of data points can be generated by HTS approaches, a (semi-) automated approach is needed for the calculation of potency and efficacy to summarize chemical-mediated effects. The Tox21 HTS program is a collaborative effort among U.S. federal agencies, and several partners have developed their own approaches to data processing and analysis methods leading to potential differences in data interpretation. We conducted a comparison of four Tox21 analysis methods (3Stage, CurveClass, CurvepwAUC, and TCPL) including development and implementation, data interpretation, and ultimately activity calls. Overall concordance among the approaches was quite high, with over 98% of activity calls having consensus across three of four methods. The parameters contributing most to differences between approaches were identified. When applying these data, e.g. in building predictive models, it helps to provide a single call that leverages the collective strengths of all approaches. Accordingly, we discuss establishing such a consensus call that incorporates the knowledge gained from all approaches. This project was funded with federal funds from the NIEHS, NIH under Contract No. HHSN273201500010C. This abstract does not necessarily reflect EPA policy.