Integration of Technological Interference into the Interpretation of Curated High-throughput Screening (cHTS) Data

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Thousands of chemicals have been screened across a wide range of in vitro high-throughput screening (HTS) assays as part of the Tox21and ToxCast programs, generating millions of datapoints that can be difficult to review in detail. Many of these assays rely on luminescence, fluorescence, and colorimetric technological detection to generate readouts, which are susceptible to signal interference by certain chemical structures that can yield false positive outcomes. The InterPred (https://doi.org/10.1093/nar/gkaa378) resource provides quantitative structure-activity relationship model predictions of chemical interference for the Tox21 chemical inventory and can be leveraged to help identify potential false positive hit calls in HTS data. In this project, we are exploring how InterPred can be applied to integrate alerts for potential interference into the Integrated Chemical Environment's (ICE; ice.ntp.niehs.nih.gov/) curated HTS (cHTS) pipeline. We searched the assay technology annotation inventory in the U.S. Environmental Protection Agency's invitroDBv3.4 database and identified over 300 assays that use either luminescence, fluorescence, or colorimetric detection technology. Among those assays, we found positive hit calls for over 1,300 chemical-assay endpoint combinations, for which we then retrieved InterPred predictions to generate potential assay detection interference flags. The predicted interference flags will be integrated into the ICE cHTS pipeline to further curate the data and refine the accuracy in interpreting cHTS bioactivity calls. This project was funded with federal funds from NIEHS, NIH under Contract No. HHSN273201500010C.