Abstract 128 — Poster Presentation: Session II-13 "Endocrine Disruption"

Performance of the BG1Luc and ER β-Lactamase Estrogen Receptor Transactivation Assays in Tox21 Compound Screening

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Abstract

The BG1Luc and ER-β-Lactamase (ER-Bla) estrogen receptor transactivation (ER TA) assays were adapted for use in the U.S. Tox21 program. Each assay was used to screen ~10,000 chemicals for ER agonist and antagonist activity. Concentration–response data (N=15) were analyzed to evaluate assay performance. Data quality was high for both assays as indicated by acceptable signal to background ratio (2.5 to 8), coefficient of variation (<10.5%), reproducibility (outcome mismatches across triplicate runs ≤0.5%), and Z' factor (≥0.4). Results for both assays were compared to the ICCVAM ER TA performance standards (42 agonist, 25 antagonist compounds) (1). Agonist assay accuracy, sensitivity, and specificity were 97%, 96%, and 100% for BG1Luc assay and 90%, 87%, 100% for ER-Bla assay. Antagonist accuracy, sensitivity, and specificity were 100% for both assays. EC50 reference standard values for estradiol were 30 pM (BG1Luc) and 275 pM (ER-Bla), and IC50 reference standard values for hydroxytamoxifen were 71 nM (BG1Luc) and 6 nM (ER-Bla). Understanding the differences in performance of these assays is critical to their acceptance and utilization by both regulators and industry.
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References

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