

Identifying Reference Chemicals for Androgen Receptor Activity

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Mandated testing of thousands of chemicals to identify those that may act as androgen receptor (AR) agonists or antagonists will cost millions of dollars, use thousands of animals, and take decades to complete using current validated methods. High-throughput methods such as those used in ToxCast and Tox21 can rapidly and inexpensively identify potential androgen-active chemicals, but development and evaluation of such tests require high-quality in vivo and in vitro reference data. A list of 121 androgen-active or inactive chemicals for which ToxCast results were available was compiled from previous AR test method validations. We conducted semi-automated literature searches for in vitro AR activity data on these chemicals using PubMatrix and Scopus. High-quality binding and transactivation data were extracted from identified references using a standardized ontology, compiled into a single database, and analyzed for consistency. Antagonist data were only considered if they included concurrent cytotoxicity evaluations. Based on quantitative data such as relative binding affinity and transactivation activity concentrations, chemicals with reproducible results were assigned potency ranges. Resulting reference chemical lists and documentation will be made publicly available and submitted to the OECD Validation Management Group-Non Animal to facilitate international harmonization of test method evaluations. *This work does not reflect EPA policy. This project was funded in whole or in part with Federal funds from the NIEHS, NIH under Contract No. HHSN273201500010C.*

Keywords:

1. Endocrine Disruptor Screening Program
2. Global harmonization
3. ToxCast/Tox21