TIER-1 SCREENING CLASSIFICATION SYSTEM FOR ESTROGENIC EDCs USING THE LUMI-CELL® ER BIOASSAY

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There is a growing need for a reliable tier-1 screening classification system for estrogenic endocrine disruptor chemicals (EDCs). The concern for EDCs arises from the detrimental effects on human and wildlife populations resulting from its bioaccumulation in the food chain. A classification system would help researchers and regulators determine which compounds pose the greatest potential threat to human and wildlife populations. Here we report a possible method for classification of xenoestrogenic EDCs based on dose response criteria using the LUMI-CELL® ER bioassay. Fifty compounds, which were on ICCVAM's priority list to validate an estrogen receptor transcriptional activation (ER TA) assay, were analyzed using the LUMI-CELL® ER bioassay. We evaluated gene induction data for all compounds to establish a classification scheme based on dose dependent response and induction efficacy. The resulting data allowed estrogenic chemicals to be divided into 4 classes: Class IV (greater than 10^{-5}M); Class III (10^{-5}M to 10^{-7}M); Class II (10^{-7}M to 10^{-9}M); and Class I (less than 10^{-9}M). Compounds were further classified by the efficacy of their agonist ER TA response. Group D includes compounds with a maximal response of less than or equal to background. Group C includes compounds with a maximal response of greater than background, but less than 50% of the relative light unit (RLU) response for 17β-estradiol (E2). Group B includes compounds with a maximal response of greater than 50% of the E2 response but less than 100% of the E2 response. Group A compounds include responses greater than 100% of the response of E2. This system of *in vitro* classification should help prioritize compounds for subsequent analysis in animal and cell systems and will help minimize animal use.used, and help determine initial doses for further studies. Supported by NIEHS SBIR ES10533-03 and Superfund Basic Research Grant ES04699.