

CONCEPT CLEARANCE RECORD

FY 2016 RESEARCH INITIATIVE — NCATS

TITLE: Development of Stem Cell- or iPS Cell-Based Assays for Compound Toxicity Evaluation

INITIATIVE TYPE: Small Business Innovation Research (SBIR) contract proposal to be included in the U.S. Public Health Service 2016 Omnibus Contract Solicitation, to be released in October 2015

OBJECTIVE(S): The assays developed from these SBIR contract proposals can be used for testing toxicological related targets in a large compound collection of environmental chemicals and pharmaceutical compounds.

DESCRIPTION: There is a growing interest to test environmental chemicals using human stem cells or induced pluripotent stem (iPS)-derived cells because engineered, transformed and immortal cell lines lack xenobiotic metabolic capability and fail to represent normal physiology and pathophysiology.

- For the phase I contract, the goal is to develop toxicological related assays in homogenous format that can be used in human stem cells or iPS-derived cells with short-time compound treatment.
- For phase II contracts, the goal is to miniaturize the assays into 384-well and 1,536-well plate formats.

IMPORTANCE: Assays with various endpoints using iPS-derived cells in a 1,536-well plate format will greatly speed up the capacity of screening thousands of environmental chemicals. Also, using human stem cells and/or iPS-derived stem cells will make this screening approach even more relevant and the data more valuable in establishing predictive models of how these chemical compounds affect human tissues and pathways, ultimately making this technology the basis for future screening for the Toxicology in the 21st Century (Tox21) program and other quantitative high-throughput screening (qHTS) initiatives.

HISTORY: The current techniques for toxicological evaluation of environmental chemical compounds involve *in vitro* methods (immortalized/transformed cell lines with heterologous expression but lacks physiologically accurate regulation) and qHTS technologies to assess chemical toxicity. This initiative aims to address these limitations but also to greatly reduce the very high costs and inefficiency of animal testing. Progress in the field is currently limited by the relatively small number of pathways and cell types that have been developed into high-throughput screening-ready assays and the artificial nature of many of the assays that have been developed. Assays using iPS cells were performed only in 96-well plates and very seldom 384-well plates due to prolonged culture periods and constantly changing culture medium. Technology and methods for using iPS cells has significantly changed and will continue to change, making them the more relevant *in vitro* model system for the future.

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