Metabolomics-2013
OMICS Group Conferences
Accelerating Scientific Discovery
2nd International Conference and Exhibition on
Metabolomics & Systems Biology
April 8-10, 2013 Hilton Chicago/Northbrook, USA

The use of metabolomics with human pluripotent stem cells (hPSCs) to predict developmental toxicity

Paul R. West
Stemina Biomarker Discovery, USA

Abstract

The application of predictive developmental toxicity screens can increase pharmaceutical and chemical safety and ultimately reduce birth defects by limiting exposure to teratogens. Human pluripotent stem cells (hPSCs, i.e. hES, iPS), combined with metabolomics, provides an innovative *in vitro* model system of early human development that can predict the potential teratogenicity of a substance. We profiled functional metabolic changes in hPSCs metabolism following exposure to test agents, to identify a metabolic signature that can classify the teratogenicity of known human teratogens and non-teratogens. The resulting metabolic signature was refined and reduced to several key metabolites, and a threshold indicative of developmental toxicity was identified. From this signature, we have developed a targeted, rapid, and predictive assay based on a few specific biomarker metabolites and have combined it with independent measurements of cellular viability across a 9-point dose curve. The cell viability data is used to identify the maximum tolerated exposure prior to cytotoxicity, and the metabolic signature identifies the exposure level that exceeds the metabolic teratogenicity threshold. The assay differentiates between cytotoxicity-related teratogenicity and metabolic changes at non-cytotoxic levels of the test agent which may be related to developmental toxicity prior to cell death. This differentiation is a key strength of the assay and distinguishes it from existing *in vitro* screens. The assay requires small quantities of test agent and can be applied to a variety of compounds including agrichemicals and pharmaceuticals at early stages of compound discovery and development to help reduce costs, animal testing and time.

Biography

West is the Director of Bioanalytical Chemistry at Stemina since 2007. His responsibilities include directing mass spectrometric experimental design, method development and data interpretation. He is the Principal Investigator for two SBIR grants. Paul has over 20 years of experience in LC-MS, MS-MS and HRMS of small molecules. He was previously employed at Abbott Laboratories as an Associate Research Investigator where he implemented and performed a variety of MS analyses for the Global Pharmaceutical Research Division. He earned a BS in Chemistry from Cameron University in 1988 and a PhD in Analytical Chemistry from Oklahoma State University in 1994.