devTOX^{qP} quickPREDICT

Human Stem Cell *in vitro* Developmental Toxicity Assay

Low Cost | **Minimal Compound** | **Rapid Turnaround** | **Multiple Exposures**

devTOX^{qP} is a biomarker-based human ***in vitro*** assay for prediction of developmental toxicity that utilizes key biomarkers identified using our metabolomics platform.

COMPARING *IN VITRO* MODELS

Assay	Model	Endpoints	Accuracy*
devTOX^{qP} quickPREDICT	Human pluripotent stem cells	Quantitative, metabolic biomarkers	89%
ZET	Non-mammalian endpoints	Subjective, embryo morphology	75%
mEST	Non-human embryonic stem cells	Subjective, cardiomyocyte differentiation	74%
rWEC	Non-human embryos	Subjective, embryo morphology	73%

ZET: Zebrafish Embryotoxicity Test; mEST: Mouse Embryonic Stem Cell Test; rWEC: Rat Whole Post-Implantation Embryo Culture Assay

* Palmer JA, Smith AM, Egnash LA, Conard KR, West PR, Burrier RE, Donley EL, Kirchner FR. Establishment and assessment of a new human embryonic stem cell-based biomarker assay for developmental toxicity screening. Birth Defects Res B Dev Reprod Toxicol. 2013; 98(4): 343-363.

devTOX^{qP} provides

- Accurate, sensitive, and specific results
- Data for multiple exposure levels
- Positive and negative controls
- Human test system
- Rapid turnaround

Flexibility Choice of human embryonic stem (hES) cells or induced pluripotent stem (iPS) cells.

Sensitivity The assay is performed using human pluripotent stem cells exposed to eight different concentrations of each test compound to yield a broad look at developmental toxicity potential.

UPLC/HRMS Ultra performance liquid chromatography, coupled with high-resolution mass spectrometry, results in selective and reproducible biomarker measurement.

Data Analysis & Reporting

- SOP-driven analysis
- LIMS-controlled data analysis pipeline
- Identification of critical exposure where cellular metabolism is altered
- Uniform reporting for rapid turnaround
- Custom reporting available

Assay validation Our assay has been internally validated with more than 80 compounds with published human/*in vivo* developmental toxicity data.

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How it works

- The assay can be performed using just 15 mg of compound.
- The biomarker ratio (ornithine/cystine) for eight exposure levels is fitted with a dose-response model.
- A test compound shows developmental toxicity potential where the curve drops below the threshold.
- Metabolic response is more sensitive than cell viability.

Predictive Power

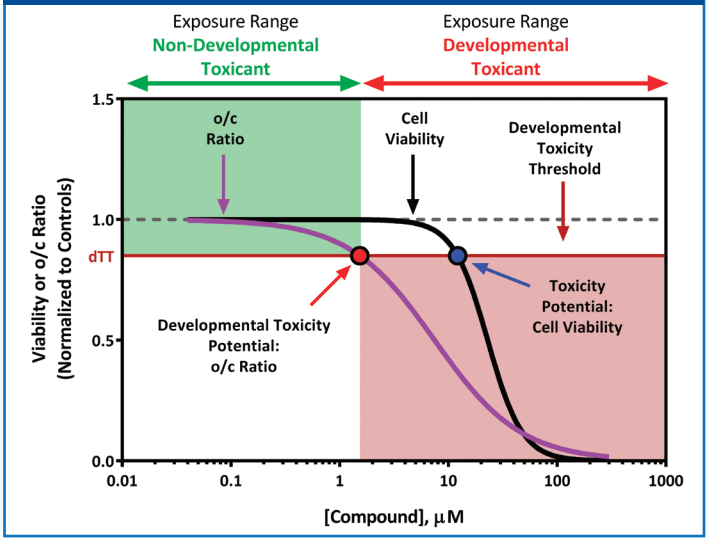
	N	Accuracy	Sensitivity	Specificity
hESC	79	85%	81%	89%
iPSC	80	85%	82%	89%

COMPARISON TO PUBLISHED *IN VIVO* RESULTS

Compound	devTOX quickPREDICT	*In vivo*		
		Human	Rodent	Rabbit
Diphenhydramine	NON	NON	NON	NON
Doxylamine	NON	NON	NON	NON
All-*trans* Retinoic Acid	DT	DT	DT	DT
Hydroxyurea	DT	DT	DT	DT
Methotrexate	DT	DT	DT	DT
Thalidomide	DT	DT	NON	DT
Warfarin	DT	DT	DT	NON

DT = Developmental Toxicant

ASSAY OUTPUT



Commitment to Quality

From start to finish, Stemina has a well-defined, quality program to ensure data integrity. Compounds in our test set and controls show excellent reproducibility over time.

Experience Counts

Our team has extensive experience in screening a wide variety of proprietary compounds including pharmaceuticals, agri-chemicals, tobacco products, consumer products, and cosmetic ingredients. Stemina was founded in 2006; its state-of-the-art facilities are located in the United States.

Extending Our Global Reach

CiToxLAB

Stemina has partnered with CiToxLAB, which has facilities in Canada, France, Denmark, and Hungary, to provide worldwide service.

EPA ToxCast™ Contractor

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