



National Institute of Environmental Health Sciences  
*Your Environment. Your Health.*

# **NIEHS SBIR / STTR Program and Toxicity Screening, Testing, and Modeling**

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## SBIR/STTR Program Overview

3.2%

### SMALL BUSINESS INNOVATION RESEARCH (SBIR) PROGRAM

Set-aside program for small business concerns to engage in federal R&D -- with potential for commercialization

0.45%

### SMALL BUSINESS TECHNOLOGY TRANSFER (STTR) PROGRAM

Set-aside program to facilitate cooperative R&D between small business concerns and US research institutions -- with potential for commercialization

2019 Budget	SBIR	STTR
NIH	\$1B	\$141M
CDC	~\$12M	N/A
FDA	~\$1M	N/A
NIEHS	~\$16M	~\$2.6M

## SBIR/STTR Program Overview

- Stimulate technological innovation
- Use small business to meet federal R&D needs
- Foster and encourage participation by minorities and disadvantaged persons in technological innovation
- Increase private-sector commercialization innovations derived from federal R&D
- Stimulate and foster scientific and technological innovation through **cooperative research** and development carried out **between small business concerns** and **research institutions**
- Foster **technology transfer** between small business concerns and research institutions

*Small Business Innovation Development Act of 1982*

P.L. 114-328 Re-Authorizes program through FY2022

## NIEHS SBIR/STTR Programs

Emphasis on development of novel approaches using state-of-the-art technologies for environmental health sciences

Exposure Assessment Tools	Integrated systems or models combining sensor, biomonitoring technology, and existing databases
Nano Env. Health/Safety	Sensors, biomonitoring technology, and <i>in vitro</i> assays
Toxicity Screening, Testing, and Modeling	Improved or expanded methods with multiple endpoints and genetic diversity that reduce animal use
Biomarkers	Oxidative stress, inflammation, DNA damage, immune function, mitochondrial function, and epigenetic regulation
Education and Outreach	Tools that improve environmental health literacy, promote understanding of EHS, and support citizen science endeavors
Superfund Research Program	Detection and/or remediation technologies*

# Toxicity Screening, Testing, and Modeling to Reduce or Replace Animal Use

- ***In vitro* Approaches to Improve Predictivity in Toxicology Testing**

- Effectively model cellular functions and responses to chemical exposure reflective of responses in humans or animals
- Organotypic culture models (OCM) that more accurately predict *in vivo* function for characterizing toxicity and/or disease processes
- High throughput and/or Data-rich *in vitro* approaches
- *For various tissues* – e.g. liver, GI tract, kidney, neurological, mammary gland, lung, cardiac, and immune function).

- **Computational Approaches for Predictive Toxicology**

- New systems and tools for integrating toxicity data, extrapolating, modeling, and read across

- **Other Technologies for Enhanced Toxicology Testing**

- Alternative / Improved methods for tissue fixing, and novel techniques for extraction of contents

## Unsolicited SBIR/STTR Grants (FY18)

Grant Number	PI	Institution	Title	Technology Category
R44 ES029014	DERTINGER, STEPHEN D BEMIS, JEFFREY C	LITRON LABORATORIES, LTD.	Next generation testing strategies for assessment of genotoxicity	Cell-based Toxicity Assay
R44ES028163	DERTINGER, STEPHEN D BEMIS, JEFFREY C	LITRON LABORATORIES, LTD.	Validation of cross-species biomarkers of DNA damage	Cell-based Toxicity Assay
R43ES029024	KINEV, ALEXANDER	CREATIVE SCIENTIST, INC.	A new assay platform to screen for chemicals adversely affecting VEGFR signaling in endothelial cells	Cell-based Toxicity Assay
R43ES029406	CHOI, TED	PREDICTIVE BIOLOGY	Single cell aneugen assay in neural progenitor cells	Cell-based Toxicity Assay
R43ES029864	JIMENEZ-TORRES, JOSE ANTONIO	ONEXIO BIOSYSTEMS, LLC	Incorporating Phase I/II drug metabolism in HTS via micro scale co-culture	Cell-based Toxicological Assay; Alternative Animal Toxicological Model
R41ES028991	LI, QUANWEN; RAPPOLEE, DANIEL ALLEN	REPRODUCTIVE STRESS; MEASUREMENT, MECHANISMS AND MANAGEMENT, CORPORATION	Embryonic stem cell high throughput screen accurately reports toxic stress	Cell-based Toxicological Assay, Alternative Animal Toxicological Model
R42ES026908	SYKORA, PETER; GEORGE, JAY; ROSENTHAL, DEAN	AMELIA TECHNOLOGIES, LLC	Immuno-CometChip for human skin basal cell genotoxicity testing	3-D Tissue Model, Alternative Animal Toxicological Model
R44ES027374	YIN, LEI	REPROTOX BIOTECH, LLC	Three-dimensional testicular cell co-culture model for reproductive toxicity screening	3-D Tissue Model, Alternative Animal Toxicological Model
R44ES026909	MYATT, GLENN JOHN	LEADSCOPE, INC.	Rapid response toxicology prediction platform	Other (in silico assay/platform), Alternative Animal Toxicological Model
R43ES029901	HOWARD, BRIAN	SCIOME, LLC	Research and development of an open, extensible, web-based information extraction workbench for systematic review	Other (Computational)

## Toxicology: Cell-based Assay, Alternative Toxicity Testing Model

### Non-Animal Test Method to Determine the Ocular Safety of Consumer Products and Chemicals

R44ES025501- awarded in 2019

STEWART LEBRUN, LEBRUN LABS



- Validation of a non-animal based test for ocular toxicity based on damage to corneal stroma, keratin, and pH measures of non-irritants, irritants, and corrosive agents.
- VMT from NICEATM and ICCVAM and ECVAM members to test chemicals across EPA and GHS hazard categories

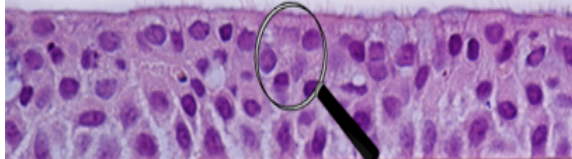
# Cell-based Assay, Alternative Toxicity Testing Models – (Phase IIB Grants)

## 1. Validation of an *In Vitro* Human Airway Model for Regulatory Toxicity Testing

Patrick Hayden, MatTek Corporation - U44ES012312

- Development and validation of an *In vitro* human bronchial tissue model for inhalational toxicity testing of chemicals - The EpiAirway Respiratory Toxicity test
- Conduct formal ring trial studies and submit to regulatory agencies in support of adoption as a non-animal model for use in regulatory inhalation toxicity testing.

Occupational Safety & Health Administration (OSHA) Globally Harmonized System (GHS)					
Category 1	Category 2	Category 3	Category 3 Respiratory System	Category 4	Category 5
					No pictogram
Danger	Danger	Danger	Danger	Warning	Warning
330 Fatal if inhaled	330 Fatal if inhaled	331 Toxic if inhaled	335 May cause respiratory irritation	332 Harmful if inhaled	333 May be harmful if inhaled



## 2. CometChip: Development of a high throughput DNA damage assay in hepatocytes

Recio, Leslie (Intergrated Laboratory Systems, Inc.) and Engelward, Bevin (MIT) - U44ES024698

- The development of Comet assay platform using metabolically competent HepaRG that maintains active, inducible spectrum of CYP450s and Phase II enzyme.
- Test chemicals, perform interlaboratory validation, and pursue efforts for adoption as an *in vitro* alternative to the *in vivo* Comet assay for genotoxicity assessment in liver.



## Organotypic Culture Models Developed from Experimental Animals for Chemical Toxicity Screening (SBIR R43/R44)

- Develop *in vitro* organotypic models for toxicity screening that are derived from animal species that are typically used for toxicology testing
- Liver, lung, heart, brain, and kidney OCMs (but also organs/tissues)
- Allows for direct comparison between animal OCM and existing *in vivo* results
- Can also compare animal OCM to human cell-derived *in vitro* models
- Goal – increase confidence in the relevance of the *in vitro* systems for pre-clinical and chemical testing

### **RFA-ES-17-008**

Applications received: January 12, 2018

Review: May 30, 2018 -(Dr. Leroy Worth)

Awards made in FY 2018



## Organotypic Culture Models Developed from Experimental Animals for Chemical Toxicity Screening (SBIR R43/R44)

Grant Number	PI	Institution	Title	Description
R43ES029879	Jeffrey Barnes	Probetex, Inc.	3D Biomimetic platforms to model kidney cell biology for <i>In Vitro</i> toxicity screening	<b>Mouse, Kidney Model, 3D Organotypic</b> - For testing adverse effects of drugs and toxins on kidney medullary development and disease
R43ES029883	Kelvin Brockbank	Tissue Testing Technologies, LLC	Construction and testing of a rabbit cornea-equivalent for evaluation of chemical injury <i>in vitro</i>	<b>Rabbit, Corneal, Organoid</b> - Develop, test and compare with endpoints from <i>in vivo</i> rabbit studies of ocular irritants.
R43ES029897	Connie Lebakken	Stem Pharm, Inc.	Mouse neural organoids for <i>in vitro</i> toxicity screening	<b>Mouse, Neuronal, 3D Organoid</b> - Develop and test small set of compounds, compare to <i>in vivo</i> data to demonstrate feasibility for neurotoxicity screening
R43ES029886	Anup Sharma	Axosim, Inc.	Development of 3D rat nerve-on-a-chip model for chemical toxicity screening	<b>Rat, Peripheral Nerve, Chip</b> - Develop and test using on-chip microelectrodes to detect the nerve conduction as a measure of chemical toxicity <i>in vitro</i>
R43ES029891	Balabhaskar Prahakar Pandian	CFD Research	Rodents derived synthetic blood brain barrier models for chemical toxicity screening	<b>Rat, BBB using endothelial, astrocytes, pericytes and neurons, 3D Organotypic</b> - Develop, test with toxic metals for transport, calcium imaging, and inflammatory markers and compare to rat data
R44 ES029892-01	Michael Shuler	Hesperos, LLC	Development of an integrated 4-organ animal model (liver, cardiac, skeletal muscle, and neuronal)	<b>Rat, 4 Organs, Body on a Chip</b> - Construct , compare to human OCM model to understand species differences in response to exposure to drugs or chemicals

## Novel Approaches for Characterizing Exposure and Response to Engineered Nanomaterials (R43)

- Develop and/or adapt novel technologies to enable assessment of exposures to ENMs (environmental and biomonitoring)
- Assays for biological responses to ENM exposures (e.g., uptake, inflammation, oxidative stress in skin, GI tract, lung)
- Verify the identity (size, shape, physico-chem properties) of test ENMs

### **RFA-ES-18-008**

Applications received: Sept. 11, 2018

Review: Dec 4, 2018 - (Dr. Leroy Worth)

Awards were made in FY 2019



## Novel Approaches for Characterizing Exposure and Response to Engineered Nanomaterials (R43)

Grant Number	PI	Institution	Title	Description
R43 ES030648-01	Seyoum Ayeahunie	MatTek, Corp.	Novel Approach for Characterizing Exposure and Response to Engineered Nanomaterials in the Gut	<b>Intestinal tissue model</b> to screen for effects of ENMs on cell viability, inflammation, oxidative stress and genotoxicity
R43 ES030650-01	William Cary Hill	NanoSafe, Inc	NanoSafe Tested™ Third Party Verification Process for Characterizing Exposures to Products Containing Engineered Nanomaterials	Exposure assessment using <b>clean room testing for ENMs released from consumer products</b> (EM, mass spec, Raman spectroscopy)
R43 ES030649-01	Arantzazu EigurenFernandez	Aerosol Dynamics, Inc	Characterization of Toxicity of Airborne ENMs using Direct In Vitro Exposure (DIVE)	Cell-based system (ALI) <b>for in situ analysis of airborne ENM particles</b>
R43 ES030652--01	Deborah Ramsey	CFD Research, Corp.	Microfluidic Nasal Epithelial ALI Model to Evaluate Inhalation Toxicity Caused by Engineered Nanomaterials	Microfluidics platform using <b>nasal epithelial cells screen</b> aerosolized ENMs for toxicity

## Summary

- NIEHS SBIR/STTR program continues to promote the development of alternative *in vitro* testing methods, *in silico* approaches and other methods to reduce or replace animal in toxicology screening
- Work closely with NTP/NICEATM in updating the SBIR/STTR omnibus research topic areas and developing ideas for targeted funding announcements related to toxicology testing
- Involve ICCVAM members as steering committee members of NIEHS SBIR U44 grants and utilize their expertise and guidance for advancing the grantees projects
- NIEHS SBIR/STTR program details -  
<https://www.niehs.nih.gov/funding/grants/mechanisms/sbir/index.cfm>

Thank you !!!