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NIEHS SBIR/STTR Grants Supporting NICEATM

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NIEHS Division of Extramural Research and Training

NTP Board of Scientific Counselors

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Overview

- Background
- Current Grants
- Current solicitations
  - Phase IIB for Approaches to Reduce Animal Use in Toxicity Testing (U44)
  - Re-release of Novel Assays for Screening the Effects of Chemical Toxicants on Cell Differentiation (SBIR R44 – Phase II only)
  - Organotypic Culture Models developed from Experimental Animals for Chemical Toxicity Screening (R43/R44)

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SBIR = Small Business Innovation Research

- For Profit
- <500 employees
- US owned and operated
- 11 Federal Agencies w/ extramural budgets >$100M

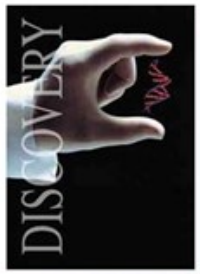
FY	SBIR Required Allocations	NIEHS Budget
2015	2.90%	~$12.6M
2016	3.00%	~$13.6M
2017	3.20%	~$15.1M
2018-2022	3.20%	

2017 - SRP ~$1.7M and WTP ~$740k

STTR = Small Business Technology Transfer

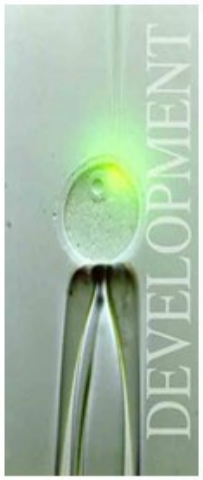
- Minimum - For Profit (40%) + Nonprofit (30%)
- <500 employees at For Profit
- US owned and operated
- 5 Federal Agencies w/ extramural budgets >$1B

FY	STTR Required Allocations	NIEHS Budget
2015	0.40%	~$2.1M
2016	0.45%	~$2.4M
2017	0.45%	~$2.4M
2018-2022	0.45%	



PHASE I Feasibility Study (SBIR R43, STTR R41)

- Budget Guide: Up to $150K Total Costs
- Project Period: 6 months (SBIR); 1 year (STTR)

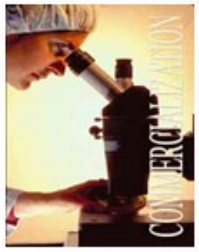


PHASE II Full Research/R&D (SBIR R44, STTR R42)

- Up to $1M Total Costs over 2 years

PHASE IIB Competing Renewal/R&D

- Clinical R&D; Complex Instrumentation/Tools to FDA
- Many, but not all, ICs participate
- Varies ~$1M/year for 3 years



PHASE III Commercialization Stage

- NIH, generally, not the "customer"
- Consider partnering and exit strategy early

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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 *in vitro* assays
Toxicity Screening, Testing, and Modeling	Improved or expanded methods with multiple endpoints, incorporation of genetic diversity, and reduction of 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

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Unsolicited SBIR/STTR Grants

Grant Number	PI	Institution	Title	Technology Category
R43 ES027711-01	Clewell, Rebecca	Scitovation, LLC	Development of high sensitivity in vitro assay to detect DNA double strand breaks	Cell-based Toxicity Assay
R43 ES027375-01	Mcclelland, Randall	Scikon Innovation, Inc.	Microfluidic Biotool to Accurately Model Corrosive Chemical Exposures for Human	Cell-based Toxicity Assay
R43 ES027703-01	Herron, Todd	Cartox, LLC	Functionally Mature Human Stem Cell Derived Cardiac Monolayers for Cardiotoxicity Testing	Cell-based Toxicity Assay
R43 ES028654-01	Choi, Ted	Predictive Biology	Novel Single Cell Assay to Identify Genes Underlying Developmental Neurotoxicity	Cell-based Toxicity Assay
R43 ES025501-01	Lebrun, Stewart	Lebrun Labs, LLC	Non-Animal Test Method To Determine The Ocular Safety Of Consumer Products and Chemicals	Cell-based Toxicity Assay
R44 ES024052-02	DeGeorge, George	MB Research Laboratories	Integrated In Vitro and Alternative Ocular (IIVAO) Irritation Testing Strategy	Cell-based Toxicity Assay
R44 ES024644--02	Souza, Glauco	Nano3DBiosciences, Inc	Development of high-throughput cardiotoxicity and hepatotoxicity assays with magnetic 3D bioprinting	Organotypic model for Tox Testing
R43 ES027374-01	Yin, Lei	Reprotox Biotech	Innovative three-dimensional testicular Co-culture (Mini-Testis) model for reproductive toxicity testing: a pathway based High throughput (HT) and High Content Analysis (HCA)	Organotypic model for Tox Testing

NIEHS SBIR/STTR Solicitations

- **RFA-ES-15-016**: NIEHS SBIR Phase IIB Awards for Validation and Commercialization of Approaches to Reduce Animal Use in Toxicology Testing (U44)
- **RFA-ES-17-007:** Novel Assays for Screening the Effects of Chemical Toxicants on Cell Differentiation (SBIR R44)
- **RFA-ES-17-008**: Organotypic Culture Models developed from Experimental Animals for Chemical Toxicity Screening

NIEHS SBIR Phase IIB Awards: Validation and Commercialization of Approaches to Reduce Animal Use in Toxicology Testing (U44)

- Supports efforts to accelerate acceptance & commercialization of alternative methods & approaches
- Grantees work through SC and ICCVAM/NICEATM to address validation needed for acceptance by U.S. federal agencies

RFA-ES-15-016
Applications due: Nov 13, 2017
Review: March 2018
(Dr. Leroy Worth)

- **Approaches:** In vitro assays, QSAR, and computational methods to predict toxicity
- **Priority areas:** Ocular toxicity, developmental toxicity, carcinogenicity, and acute toxicity testing
- **Example:** Validation of an In Vitro Human Airway Model for Regulatory Toxicity Testing (2U44ES014312-04 – Patrick Hayden, MatTek Corp.)

MatTek CORPORATION

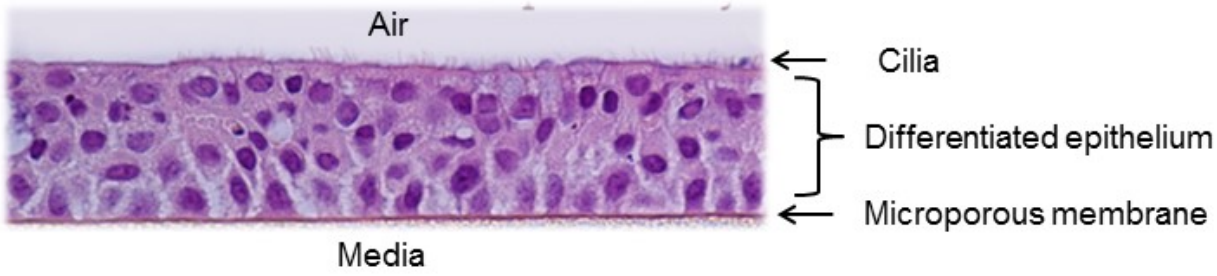
Validation of an In Vitro Human Airway Model for Regulatory Toxicity Testing

- Formal validation of the EpiAirway™ in vitro human bronchial tissue model for predicting toxicity of inhaled chemicals
- Expanded number of test chemicals to verify the accuracy and relevance of the final prediction model
- Multi-laboratory GLP ring trial to establish the transferability, reproducibility, accuracy and relevance of the tissue model
- Final report and submission of test data to US federal regulatory agencies and OECD

The EpiAirway Model

EpiAirway is an *in vitro* 3D organotypic model of human tracheal/bronchial tissue.

- Constructed from primary cells
- Highly reproducible
- Differentiated epithelium at the air-liquid interface
  - Beating cilia
  - Mucus secretion
  - Barrier function
- Physiologically relevant & predictive of the human outcome



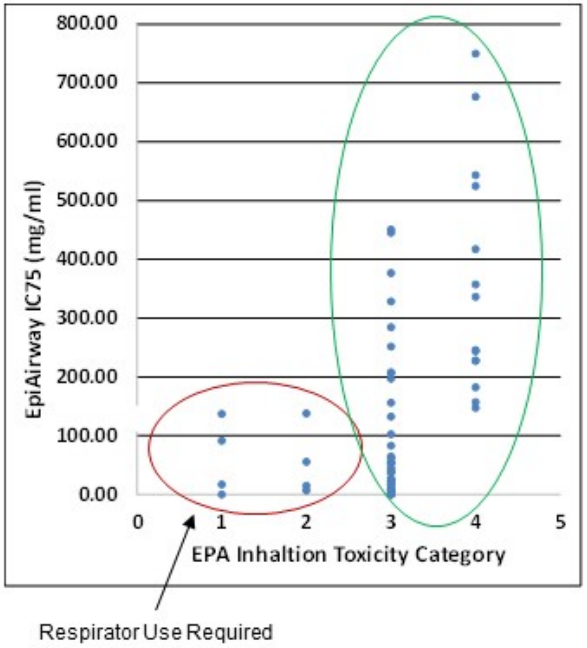
Regulatory systems for classifying the acute inhalation toxicity of chemicals

Environmental Protection Agency (EPA)			
Category I	**Category II**	**Category III**	**Category IV**
	No Pictogram	No Pictogram	No Pictogram
Danger - Poison	Warning	Caution	Caution (Optional)
Fatal if inhaled	May be fatal if inhaled	Harmful if inhaled	

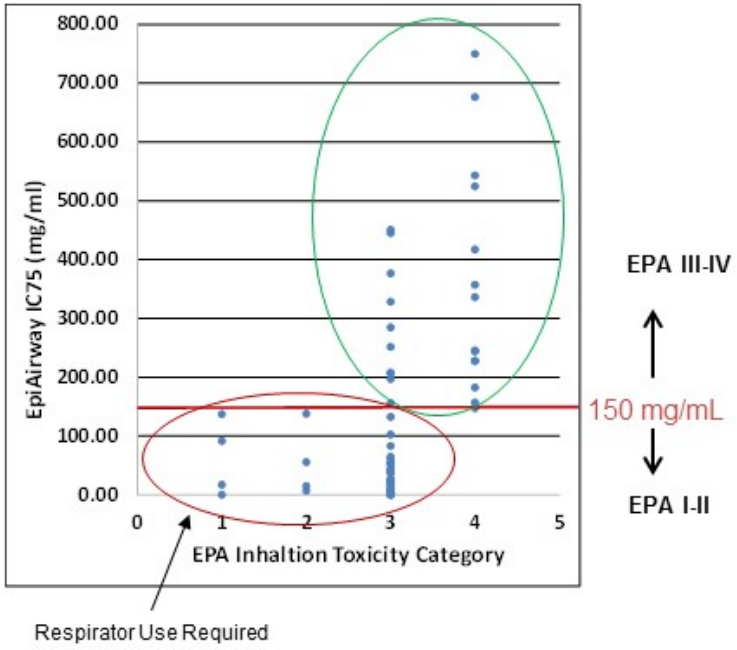
Occupational Safety & Health Administration (OSHA) Globally Harmonized System (GHS)					
Category 1	**Category 2**	**Category 3**	**Category 3** Respiratory System	**Category 4**	**Category 5**
					No pictogram
Danger	Danger	Danger	Danger	Warning	Warning
330 Fatal if inhaled	**330** Fatal if inhaled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

Classification of EPA categories: *In vivo* rat vs. the EpiAirway test

Based on rat *in vivo*



Based on EpiAirway *in vitro*



Novel Assays for Screening the Effects of Chemical Toxicants on Cell Differentiation (SBIR R44 – Phase II only)

Approaches can include:

- Assays evaluating alteration of ES/iPS cell differentiation
- Human iPS or mouse ES/iPS to incorporate genetic variation into toxicity screening
- Engineered stem cell lines to simulate common genetic variants in human disease (Parkinson's Disease, autism, breast cancer, etc.)
- High-content screening or 'omics-based assays for toxicant-induced effects using differentiated cell types derived from pluripotent or multi-potent cells

RFA-ES-17-007
Applications due:
Oct 4, 2017
Review: Dec 2017
(Dr. Leroy Worth)

Organotypic Culture Models developed from Experimental Animals for Chemical Toxicity Screening (R43/R44)

- Develop 3D or organotypic models using cells derived from experimental animals typically used in toxicology testing
- Derived from ES or pluripotent cells, or single of multiple cell types to replicate target organ function with respect to toxicity

RFA-ES-17-008
Applications due:
Jan. 12, 2018
Review: June 2018
(Dr. Leroy Worth)

- Allows comparisons between in vivo and in vitro test results
- Concordance between in vivo and in vitro test results will improve confidence in the utility of the in vitro models (both animal and human)
- In vitro models will help to reduce the need for animals in tox testing

Questions?