NIH Tissue Chip Program: Updates

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The NIH Tissue Chip Program

GOAL: Develop an *in vitro* platform that uses human tissues to evaluate the efficacy, safety and toxicity of promising therapies.

**NIH**

Phase 1: Development

- 2012-13
- 2013-14
- 2014-15
- 2015-16

**DARPA**

Phase 2: Cell incorporation & organ integration

- 2012-13
- 2013-14
- 2014-15
- 2015-16

**FDA**

- DARPA: Organ integration
- **FDA provides insight and expertise throughout the program**

**Current Goals:**

- Integration
- Compound testing
- Validation
- Partnerships
- Adoptions of the tech to the community
New Tissue Chip Initiatives & Projects

- **Tissue Chip Testing Centers (2016-2018)**
  - Tech transfer and testing at 2 independent centers (Texas A&M and MIT)

- **Tissue Chips for Disease Modeling (2017–2022)**
  - Develop tissue chip models of human disease
    - Using human primary or induced pluripotent stem cell sources
  - Use to test effectiveness of candidate therapeutics
  - NCATS joined by NIEHS, NINDS, NIAMS, NIDDK, NICHD, ORWH, NIDCR, NIBIB, NHLBI

- **Tissue Chips in Space (2017–2021)**
  - Partnership with Center for the Advancement of Science in Space (CASIS)
  - Adapt, refine chips for on-flight experiments at the International Space Station U.S. National Laboratory
    - To understand diseases
    - Improve human health on Earth
Tissue Chips Testing Centers - Kidney MPS yielding first results at Texas A&M

Human Mechanism of Aristolochic Acid Nephropathy Elucidated by Coupled Liver-Kidney MPS (Himmelfarb, Wash U)
Functional coupling of four chips demonstrates physiological processing of the microbiome product trimethylamine (TMA).

- **Intestine MPS**: Microbiome Product TMA
- **Liver MPS**: Absorption of TMA
- **Kidney MPS**: Bioconversion TMA → TMAO
- **Blood Brain Barrier MPS**: TMAO crosses BBB

EVATAR
An ex vivo female reproductive tract

Steroid hormones affect liver metabolism
Liver proteins affect sex hormones function

Liver
Ovary
Ectocervix
Uterus
Fallopian Tube

Estrogen
Progesterone

Future Directions in Tissue-on-chips Technology

- **Human Fibroblasts**
- **Genetic reprogramming**
- **Differentiation/maturation into all major organs**

**iPSC’s**

- **Druggable Genome**
  - Gene Editing on isogenic background for physiological differences among diverse populations:
  - Genetic variation
  - Examine various demographics
  - Gender or age variation

- **Precision Medicine (you-on-chip)**
  - Drug response in individuals
  - Individualized medicine and therapeutics

- **Rare disease research and therapeutics**

**FY16** Tissue Chips Testing Centers

**FY17**

- **Disease Modeling**
  - Disease pathogenesis
  - Dissecting mutations in isogenic background

**FY17** Tissue Chips in Space

- **Human-on-a-Chip**

- **Microbiome**
- **Environmental Toxins**
- **Infectious disease**

- **Countermeasure Agents**

**NIH**

National Center for Advancing Translational Sciences

NCATS