FASEB
Federation of American Societies for Experimental Biology

*FASEB IDeA/EPSCoR Webinar Series: Webinar #2*

# How IDeA Co-Funding Supports Early-Career Investigators

**August 20, 2024**

# 22 FASEB Member Societies: Representing over 110,000 Scientists
















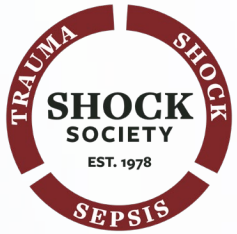








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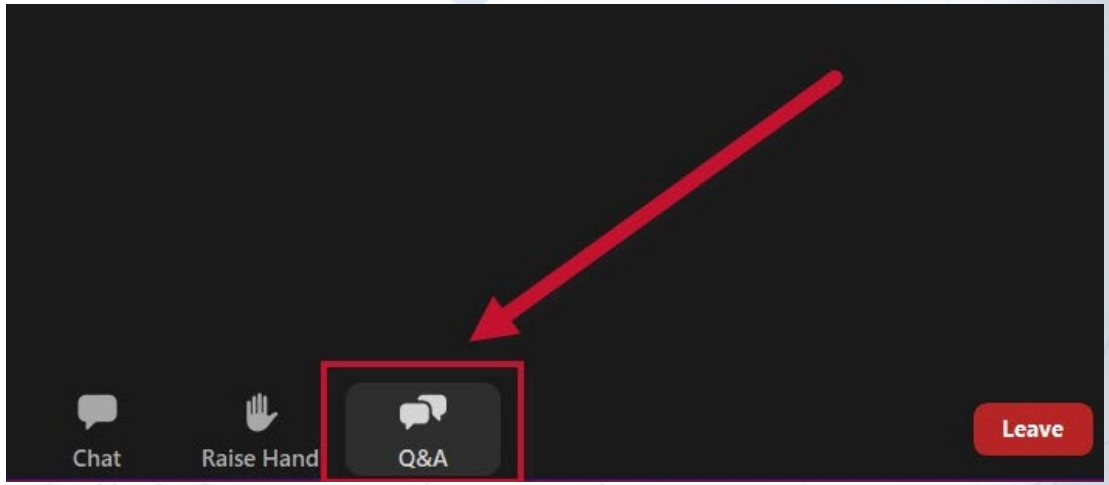
# Agenda

- **Overview of the NIH IDeA and NSF EPSCoR Programs**
  → Specific focus on co-funding mechanism
- **Speaker:** Dr. Eliseo Castillo, University of New Mexico
- **Q&A**

# Housekeeping

- Webinar format
- Chat and “Raise Hand” functions are disabled; please use the Q&A to type in your questions
- We will address as many questions as possible at the end
- Webinar is being recorded for on-demand viewing



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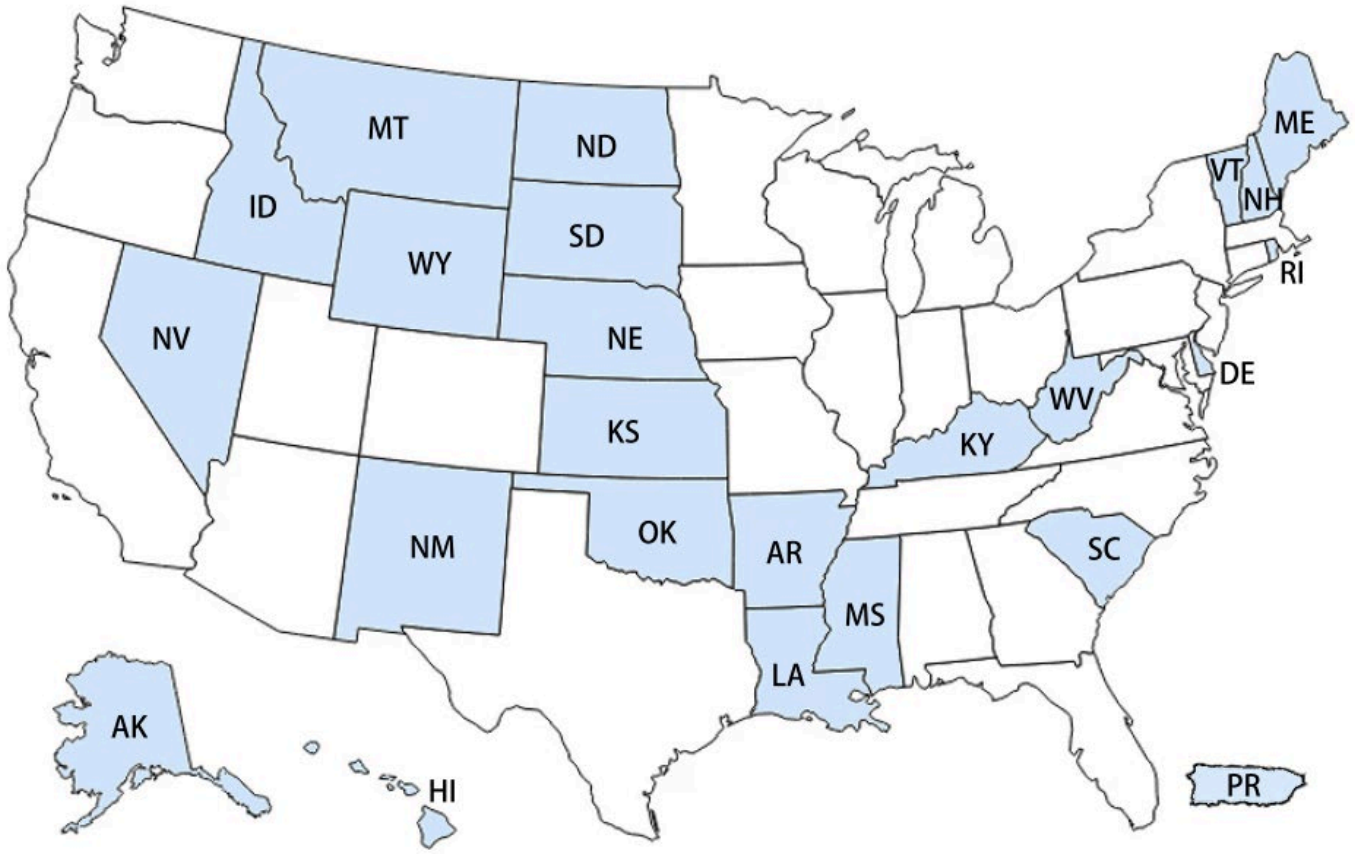
# Overview of NIH IDeA and NSF EPSCoR Programs

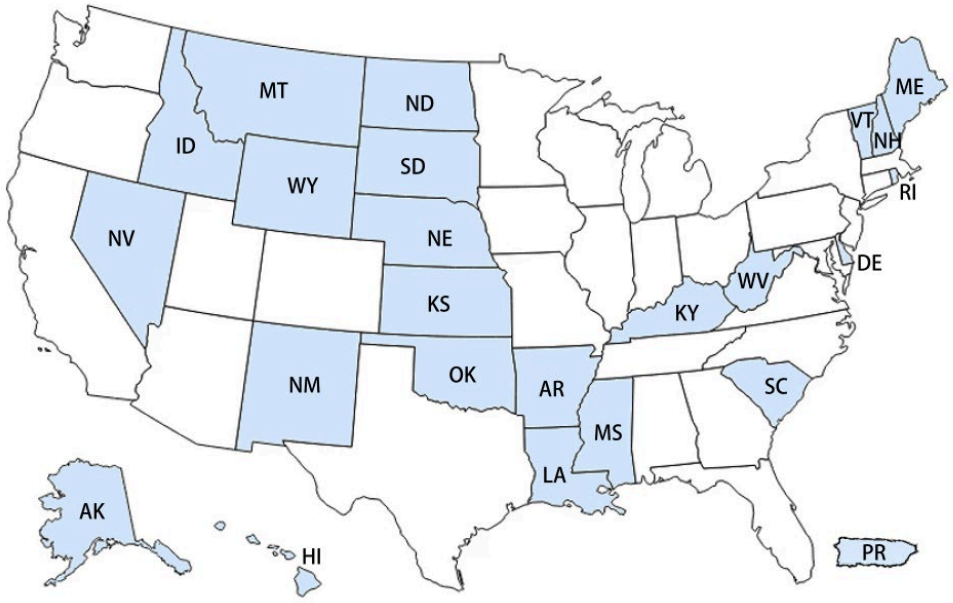
# NIH Institutional Development Award (IDeA) Program




**23 states & Puerto Rico** qualify for IDeA program benefits

- Congress established the IDeA program in 1993.
- **Purpose**: Broaden the geographic distribution of NIH funding, particularly for states that have historically received low levels of NIH support.
- Administered by the National Institute of General Medical Sciences (NIGMS)

# NIH Institutional Development Award (IDeA) Program




**23 states & Puerto Rico** qualify for IDeA program benefits

## Five Main Components

1. Centers of Biomedical Research Excellence (COBRE)
   *supporting development of multidisciplinary research centers*
2. IDeA Networks of Biomedical Research Excellence (INBRE)
   *support for faculty, postdocs, and graduate students*
3. Co-funding
   *support RPG application from investigators whose proposals received meritorious scores but fall just short of I/C payline*
4. Clinical and Translational Research Programs
   *develop competitive C&T research programs by supporting infrastructure and human resources*
5. IDeA Regional Entrepreneurship Development (I-RED)
   *supports small business opportunities to develop educational products*



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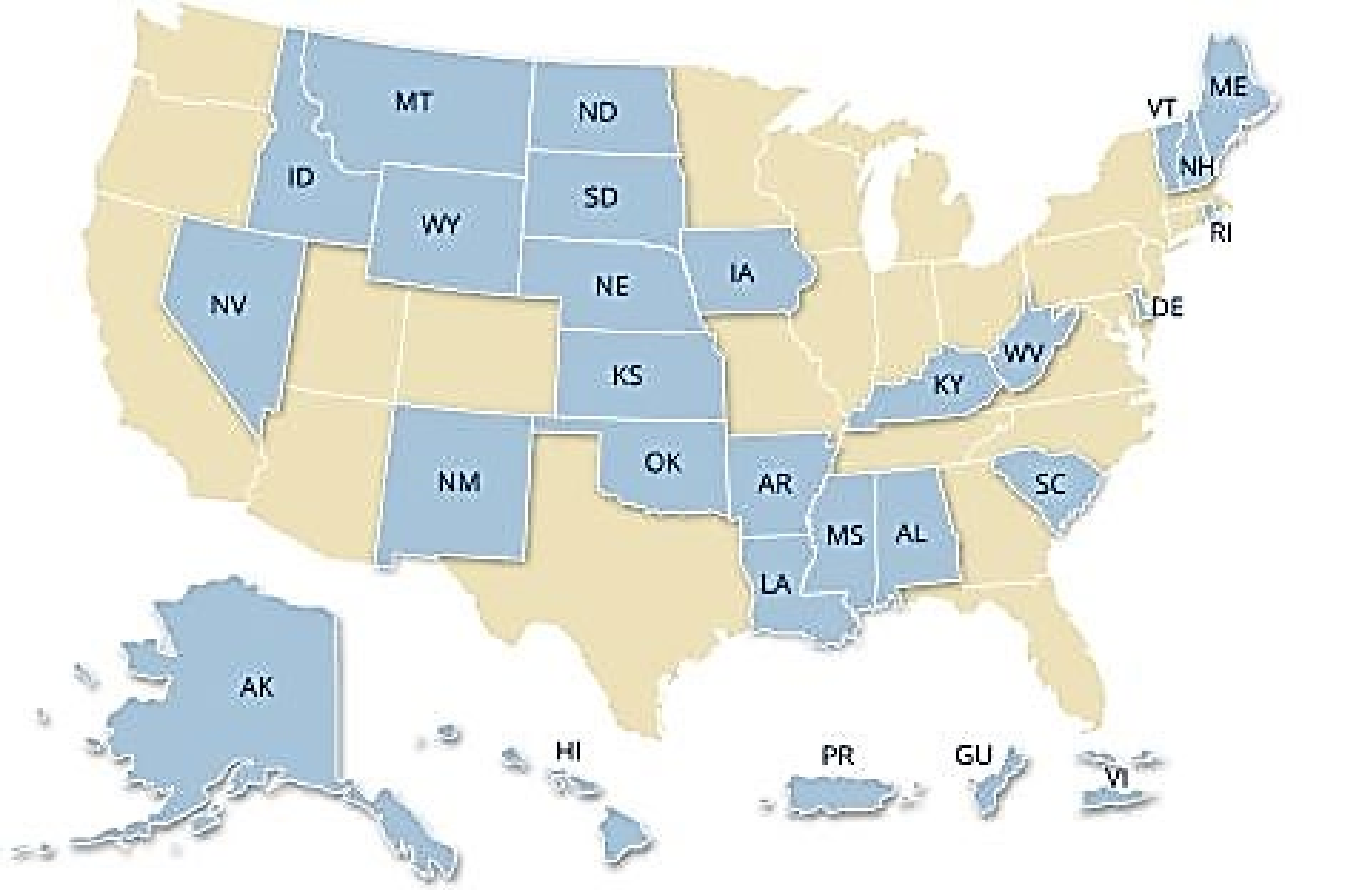
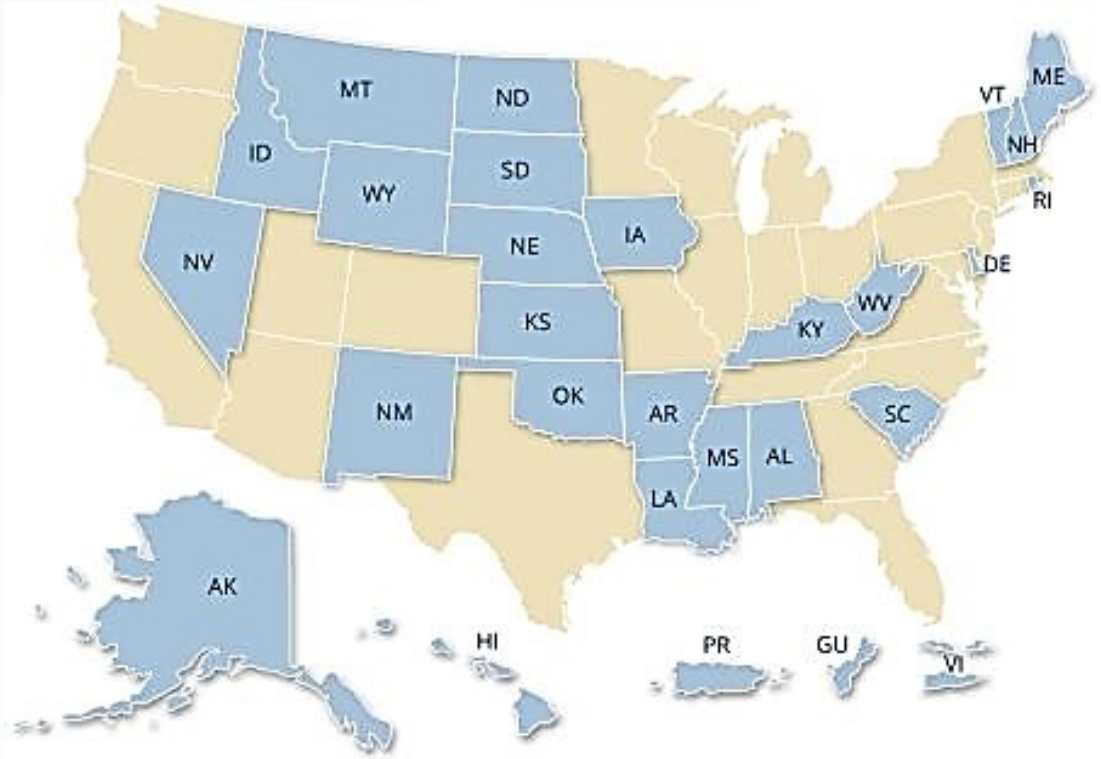
# NSF Established Program to Stimulate Competitive Research (EPSCoR) Program




**28 jurisdictions are eligible for EPSCoR funding**

- Congress established the EPSCoR program in 1979.
- **Purpose**: To bolster research competitiveness of designated jurisdictions by strengthening STEM capacity and enabling improvements in research and infrastructure.
- Administered by the NSF Office of Integrative Activities

# NSF Established Program to Stimulate Competitive Research (EPSCoR) Program




**28 jurisdictions are eligible for EPSCoR funding**

## Three Investment Strategies

1. Research Infrastructure Improvement (RII) Awards

   *infrastructure and workforce development through collaborations and team science*

2. Co-funding of Disciplinary and Multidisciplinary Research

   *co-funding proposals submitted to other NSF programs that are recommended for award but just short of budget means*

3. Workshops and Outreach

   *funding collaborative activities that explore opportunities in emerging areas of science*

# Today's Speaker

**Eliseo Castillo, PhD**
**University of New Mexico**
Associate Professor
Director of Gastroenterology Research
Division of Gastroenterology & Hepatology



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# IDeA/EPSCoR Series:
# Defining the Harmful Effects of Microplastics on Gastrointestinal Health

**Eliseo F. Castillo**

**Associate Professor**

ecastillo@salud.unm.edu

UNM SCHOOL of MEDICINE

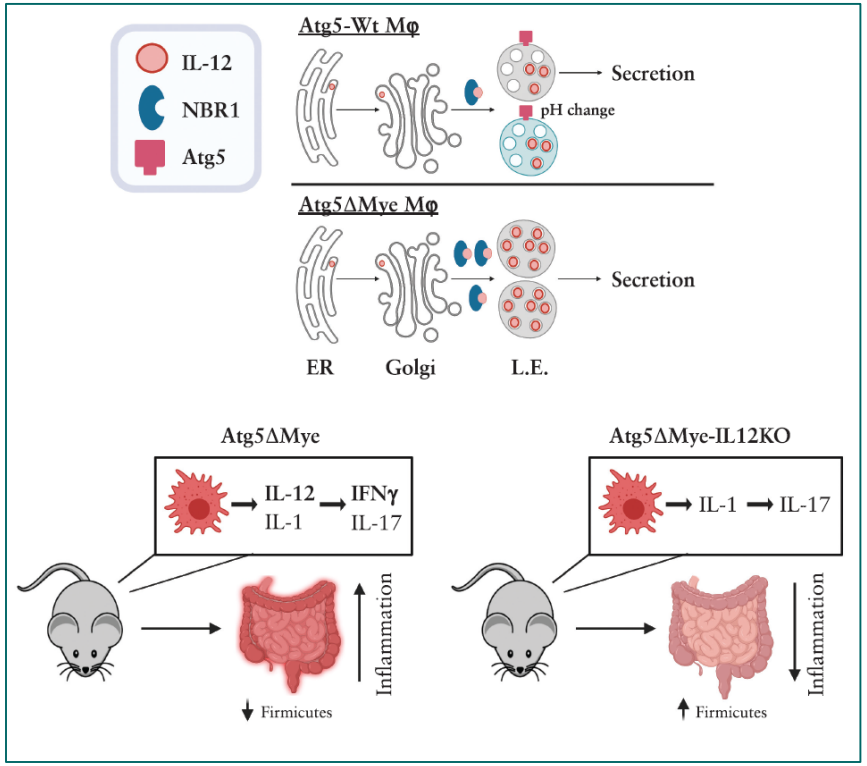
*Department of Internal Medicine*
*Division of Gastroenterology and Hepatology*

# Starting my own lab!

**2017: Assistant Professor/CTSC KL2 Scholar** - University of New Mexico Health Sciences Center (1 Technician)

**2023: Associate Professor** - University of New Mexico Health Sciences Center (1 Postdoc; 3 PhD students; 1 Sr. Scientist; 2 Undergraduates; and a team of close collaborator)

## Autophagy and macrophages




*Merkley et al., 2021 Journal of Crohn's and Colitis*

## Pilot Project: Microplastics and Gut health

Microplastics found in human stools for the first time

Study suggests the tiny particles may be widespread in the human food chain

Scientist looking through microscope in laboratory. Photograph: Alamy Stock Photo

Fiona Harvey *and* Jonathan Watts

Mon 22 Oct 2018 18.00 EDT

# First Submission of my Microplastics R01 → R56

Submitted my first R01 to NIEHS (Payline: 11th Percentile)

**Oct. 2019 "Defining the Harmful Effects of Microplastics on Gastrointestinal Health"**

- 38th Percentile
  - It was stated I had no papers on microplastics.
  - It was highly suggested I needed a toxicologist on the grant.
  - It was also highly suggested I needed a model to examine different doses.

Cell Biol Toxicol (2022) 38:31–41
https://doi.org/10.1007/s10565-021-09616-x

SHORT COMMUNICATION

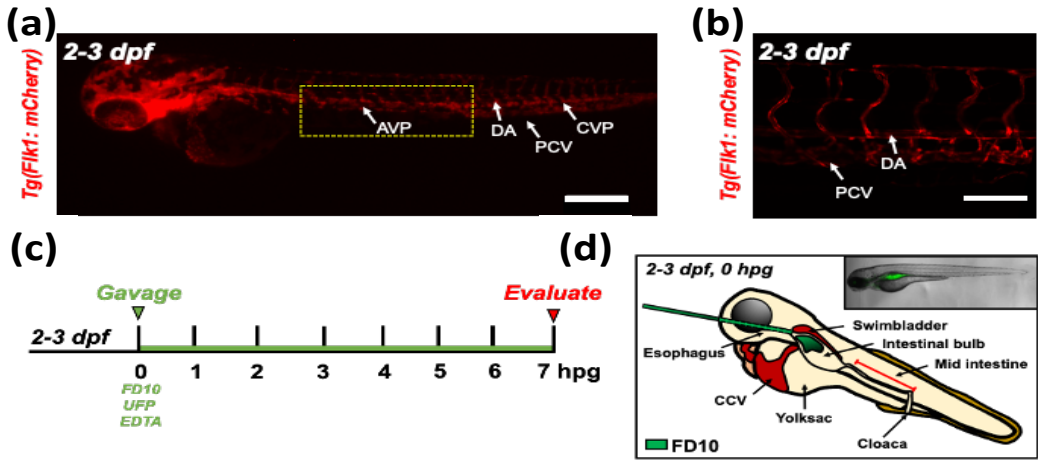
**Polystyrene microplastics induce an immunometabolic active state in macrophages**

Seth D. Merkley · Harrison C. Moss · Samuel M. Goodfellow · Christina L. Ling · Jewel L. Meyer-Hagen · John Weaver · Matthew J. Campen · Eliseo F. Castillo

Sent a brave email to the PO to discuss getting an **R56** on this new, untapped area of research:

- The application was nominated by NIEHS staff for a High Priority, Short-Term Project Award (R56) (9/2020)
- During this time we published a short communication article.
- Article included a toxicologist
- Met some new collaborators

**Utilization of Zebrafish** (Dr. Tzung Hsiai, UCLA)



# A1 Submission

**“Defining the Harmful Effects of Microplastics on Gastrointestinal Health”**

Resubmitted my R01 to NIEHS in March 2021 (**Payline:11th Percentile**)

- Responded to reviewer comments
- Added a New Aim using zebrafish to examine different sizes of microplastics (as requested by a reviewer)
- Added a toxicologist (as requested by the reviewers)
- Highlighted I published on microplastics (added the toxicologist as an author to show we were working together)
- **July 2021 received my summary statement: 12th Percentile (Impact Score: 28)**

- As soon as my summary statement came out, I emailed the PO and mentioned that UNMHSC was part of the NIH IDeA States (**find out if you live in an IDeA state**).
- Talked to Dr. Richard Larson, the Executive Vice Chancellor and Vice Chancellor for Research at the University of New Mexico, to discuss my options.
  - At that time Dr. Larson was also in charge of UNM HSC CTSA and CTSC KL2 Scholar Program.
  - There is a deadline – not advertised.
  - Find out who you need to talk to.
- **September 21, 2022 – I received my NOA.**

# A1 Submission – How much did it change?

**Original Submission**

Aim 1. Establish microplastics (MP) contribution to intestinal permeability (IP) through cellular metabolic changes in the epithelium and gut metabolome.

Aim 2: Determine the effects of MP on the GI tract of a susceptible host.

Aim 3: Delineate the mechanism of MP modulation of human macrophage metabolism and its impact on the intestinal barrier.

**A1 Submission**

Aim 1. Utilization of Zebrafish system as a high-throughput model to examine the effect of different sizes, types and concentrations of microplastics in inducing intestinal permeability.

Aim 2. Establish microplastics induces intestinal permeability through cellular metabolic changes in the epithelium and gut metabolome.

Aim 3. Demonstrate that gastrointestinal microplastic exposure promotes barrier dysfunction in a human intestinal organoid model.

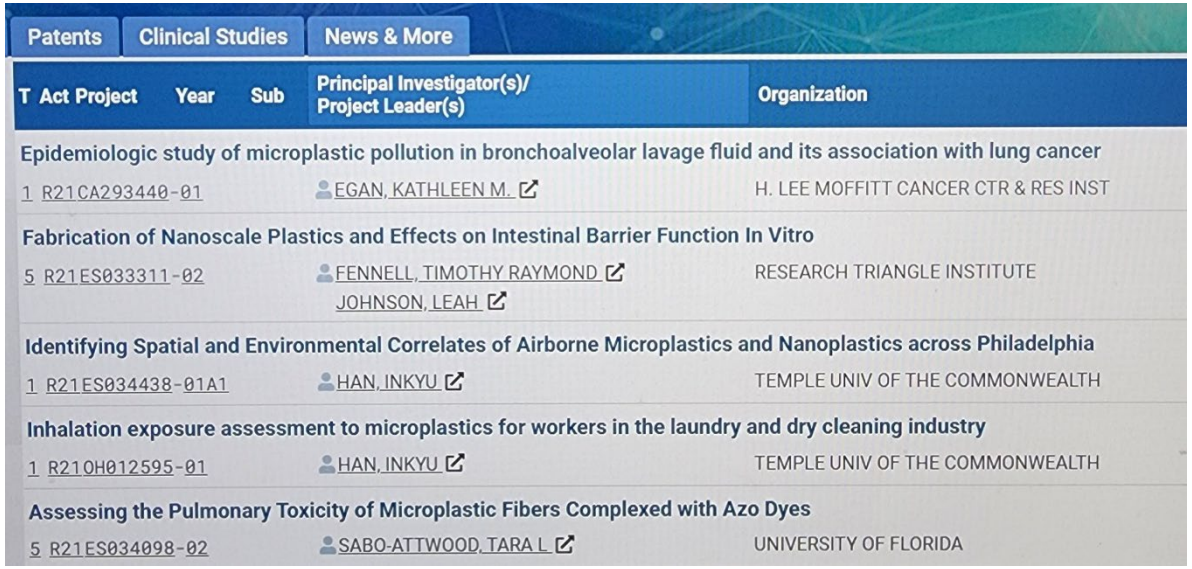
# First R01 on microplastics – this is the current funding situation

## R01

Patents | Clinical Studies | News & More

| T | Act | Project | Year | Sub | Principal Investigator(s)/ Project Leader(s) | Organization |
|---|---|---|---|---|---|---|
| * | | Diversity Supplement - Diego Ruiz | | | | |
| | 3 | R01ES032037-03S1 | | | CASTILLO, ELISEO F | UNIVERSITY OF NEW MEXICO HEALTH SCIS CTR |
| | | Defining the Harmful Effects of Microplastics on Gastrointestinal Health | | | | |
| | 5 | R01ES032037-03 | | | CASTILLO, ELISEO F | UNIVERSITY OF NEW MEXICO HEALTH SCIS CTR |
| | | Mechanisms for environmental microplastics-enhanced colorectal tumor progression | | | | |
| | 1 | R01ES035780-01A1 | | | XUE, XIANG | UNIVERSITY OF NEW MEXICO HEALTH SCIS CTR |

## R21



Patents | Clinical Studies | News & More

| T | Act | Project | Year | Sub | Principal Investigator(s)/ Project Leader(s) | Organization |
|---|---|---|---|---|---|---|
| | | Epidemiologic study of microplastic pollution in bronchoalveolar lavage fluid and its association with lung cancer | | | | |
| | 1 | R21CA293440-01 | | | EGAN, KATHLEEN M. | H. LEE MOFFITT CANCER CTR & RES INST |
| | | Fabrication of Nanoscale Plastics and Effects on Intestinal Barrier Function In Vitro | | | | |
| | 5 | R21ES033311-02 | | | FENNELL, TIMOTHY RAYMOND<br>JOHNSON, LEAH | RESEARCH TRIANGLE INSTITUTE |
| | | Identifying Spatial and Environmental Correlates of Airborne Microplastics and Nanoplastics across Philadelphia | | | | |
| | 1 | R21ES034438-01A1 | | | HAN, INKYU | TEMPLE UNIV OF THE COMMONWEALTH |
| | | Inhalation exposure assessment to microplastics for workers in the laundry and dry cleaning industry | | | | |
| | 1 | R21OH012595-01 | | | HAN, INKYU | TEMPLE UNIV OF THE COMMONWEALTH |
| | | Assessing the Pulmonary Toxicity of Microplastic Fibers Complexed with Azo Dyes | | | | |
| | 5 | R21ES034098-02 | | | SABO-ATTWOOD, TARA L | UNIVERSITY OF FLORIDA |

## Current Publications for this grant


1. Merkley SD, Moss HC, Goodfellow SM, et al. Polystyrene microplastics induce an immunometabolic active state in macrophages. ***Cell Biol Toxicol.*** 2022;38(1):31-41. doi:10.1007/s10565-021-09616-x

2. El Hayek E, Castillo E, In JG, et al. Photoaging of polystyrene microspheres causes oxidative alterations to surface physicochemistry and enhances airway epithelial toxicity. ***Toxicol Sci.*** 2023;193(1):90-102. doi:10.1093/toxsci/kfad023

3. Gonzalez-Ramos S, Wang J, Cho JM, et al. Integrating 4-D light-sheet fluorescence microscopy and genetic zebrafish system to investigate ambient pollutants-mediated toxicity. ***Sci Total Environ.*** 2023;902:165947. doi:10.1016/j.scitotenv.2023.165947

4. Garcia MA, Liu R, Nihart A, et al. Quantitation and identification of microplastics accumulation in human placental specimens using pyrolysis gas chromatography mass spectrometry. ***Toxicol Sci.*** 2024;199(1):81-88. doi:10.1093/toxsci/kfae021

5. Garcia MM, Romero AS, Merkley SD, et al. *In Vivo* Tissue Distribution of Polystyrene or Mixed Polymer Microspheres and Metabolomic Analysis after Oral Exposure in Mice. ***Environ Health Perspect.*** 2024;132(4):47005. doi:10.1289/EHP13435

6. Campen M, Nihart A, Garcia M, et al. Bioaccumulation of Microplastics in Decedent Human Brains Assessed by Pyrolysis Gas Chromatography-Mass Spectrometry. Preprint. *Res Sq*. 2024;rs.3.rs-4345687. Published 2024 May 6. doi:10.21203/rs.3.rs-4345687/v1

# Internal Pilot funding that resulted in a R01!

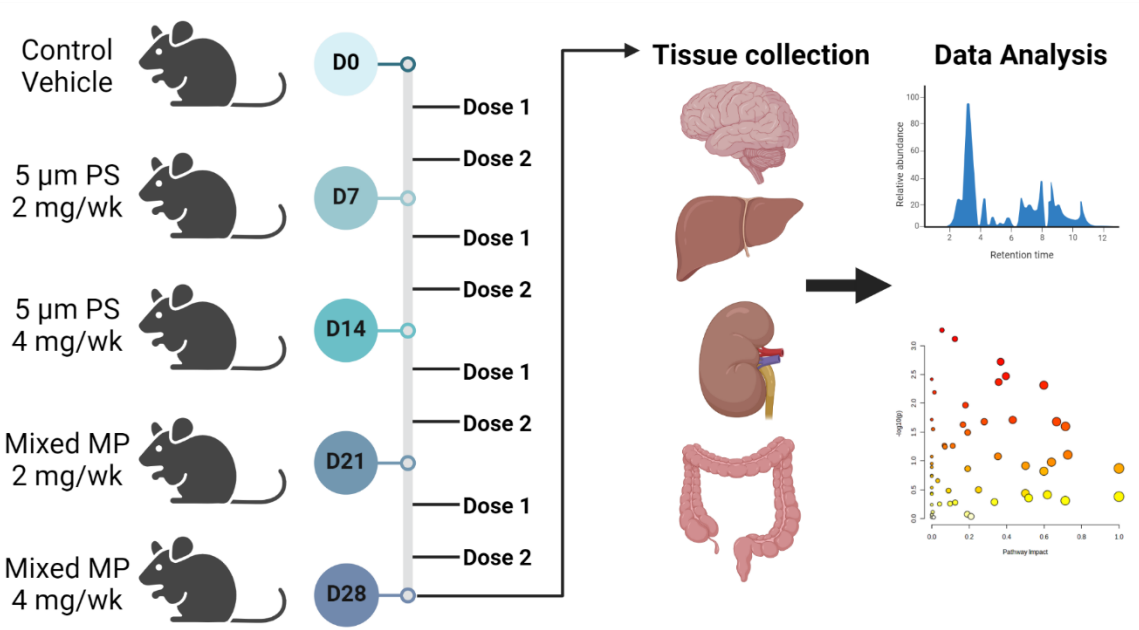

- MPs found in the gut after consumption of food and water (Deng Y. *et al*., 2017; Jin Y. *et al*., 2019)
- Drinking and eating have been classified as the most common exposure type (WHO, 2022)
- It is estimated that humans consume 5 grams of MP per week
- Discuss our recent findings published in Environmental Health Perspectives.
- Show some unpublished work and future plans.

# Garcia *et al*., Environmental Health Perspectives (2024)

## Major Findings of the Paper

- Detected polystyrene microspheres in distant tissues including the brain, liver, and kidney after oral exposure.
- Found metabolic differences in the colon, liver, and brain.
- Differential responses that were dependent on concentration and type of microsphere exposure

## Study Design for Microplastic Exposure

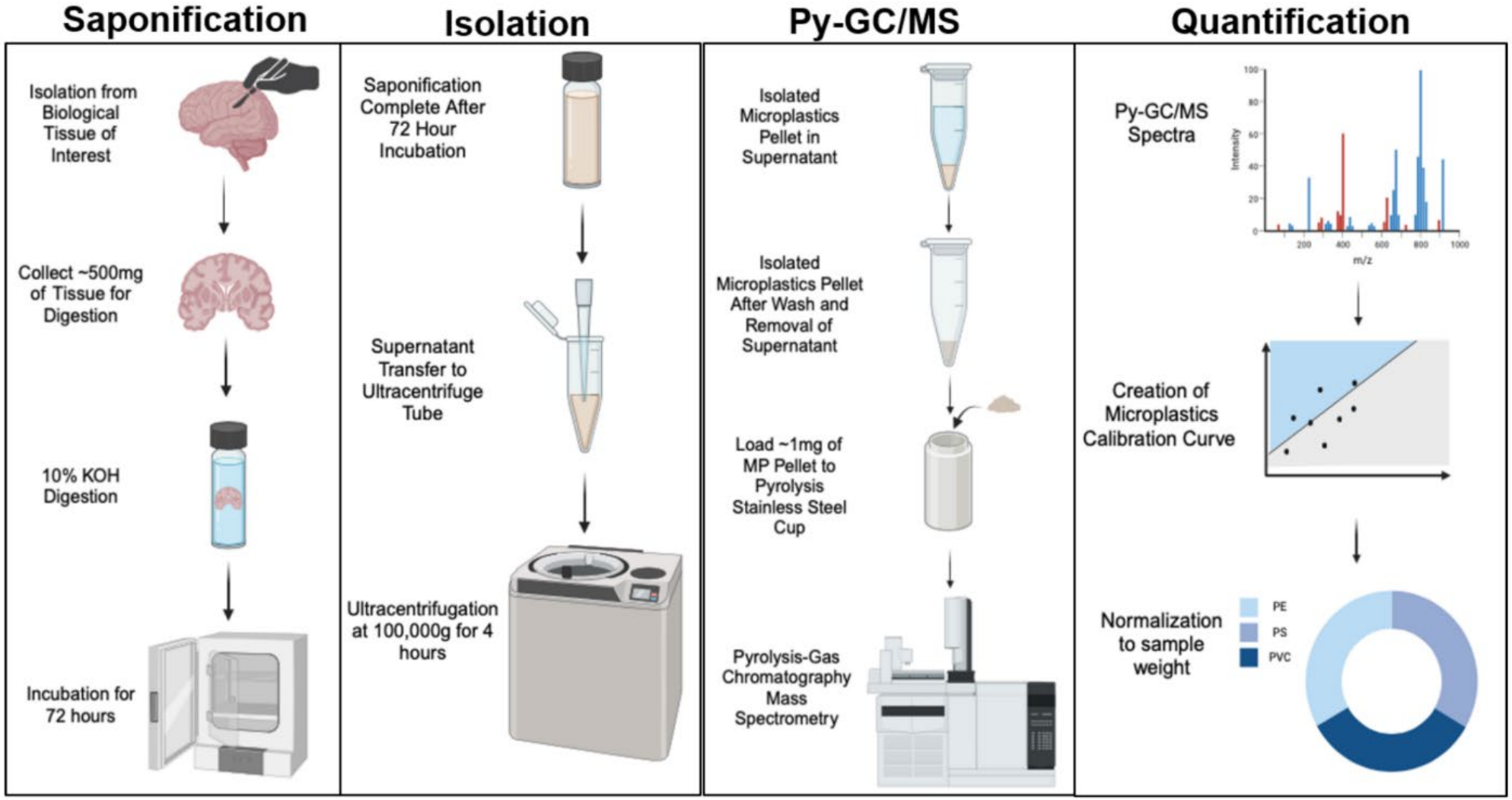



**Microplastics**

- 5 µm Polystyrene
- Mixed Microplastics: 1-4 µm Polyethylene, 5 µm Polystyrene, 5 µm poly(lactic-co-glycolic acid) (PLGA)

# Detection of Microplastics in tissue

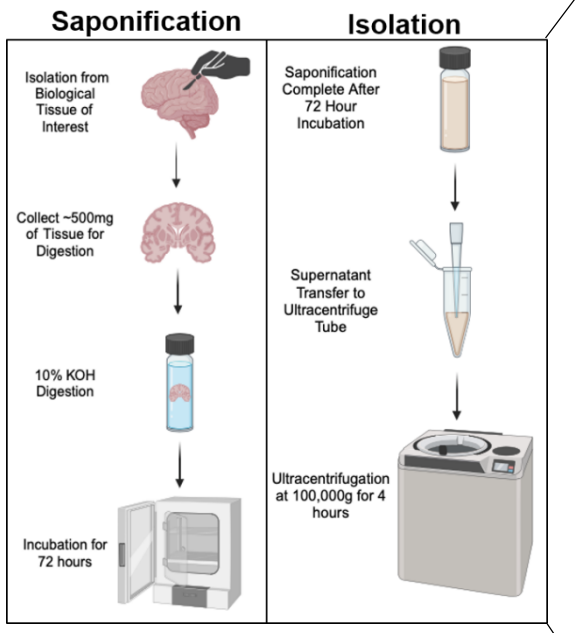
## Methodology to detect microplastics

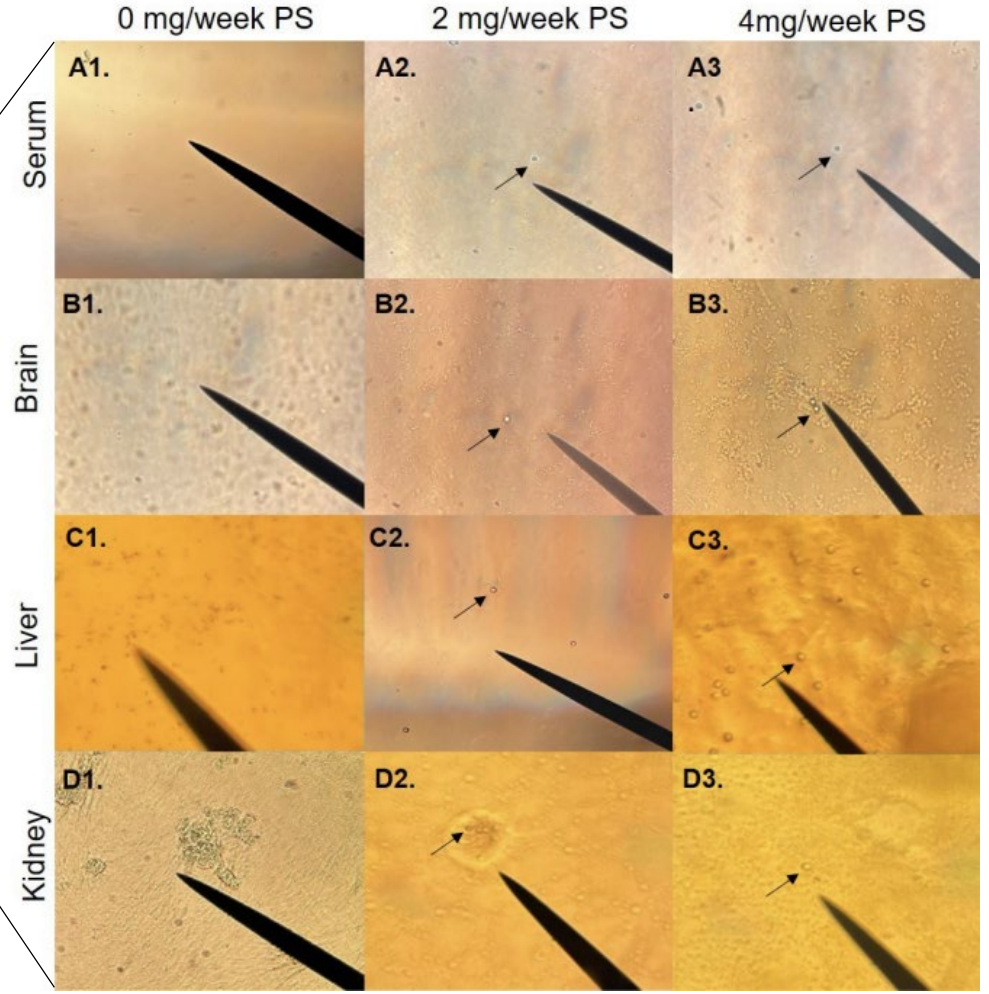



*Garcia et al., Toxicological Sciences 2024 PMID: 38366932*

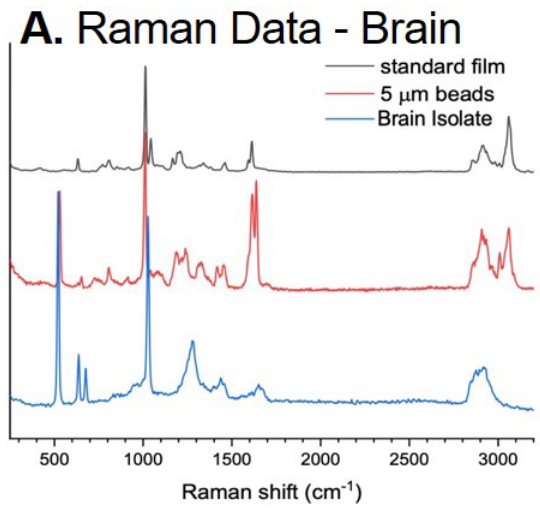
# Microplastics are distributed to multiple organs following oral gavage in mice

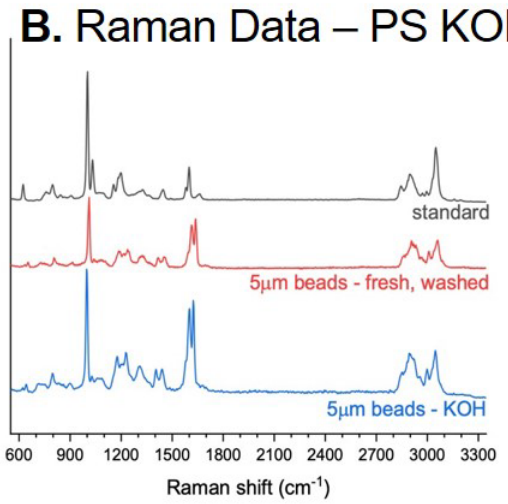
## Microplastic Detection in Various Tissues




## Microplastic Validation

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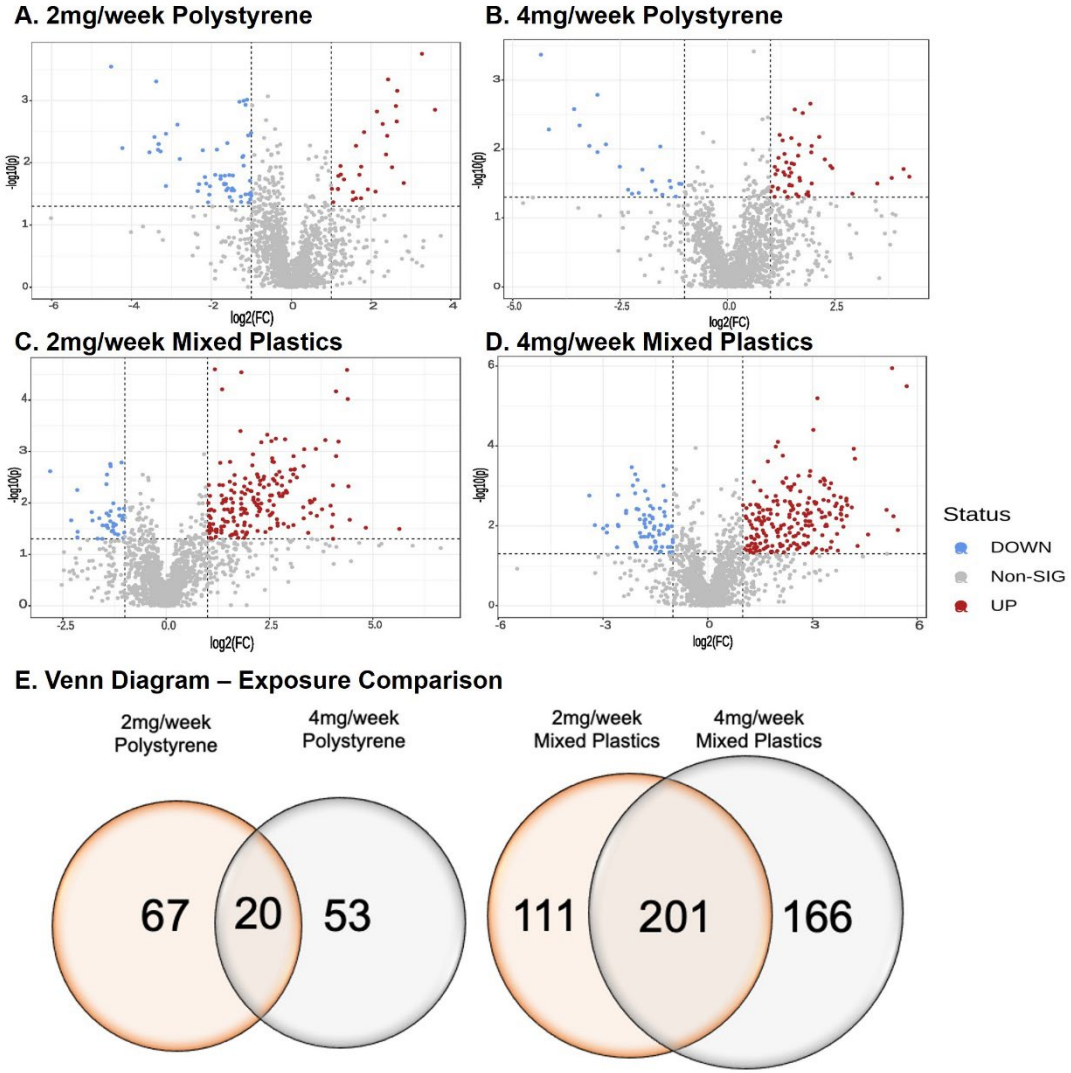
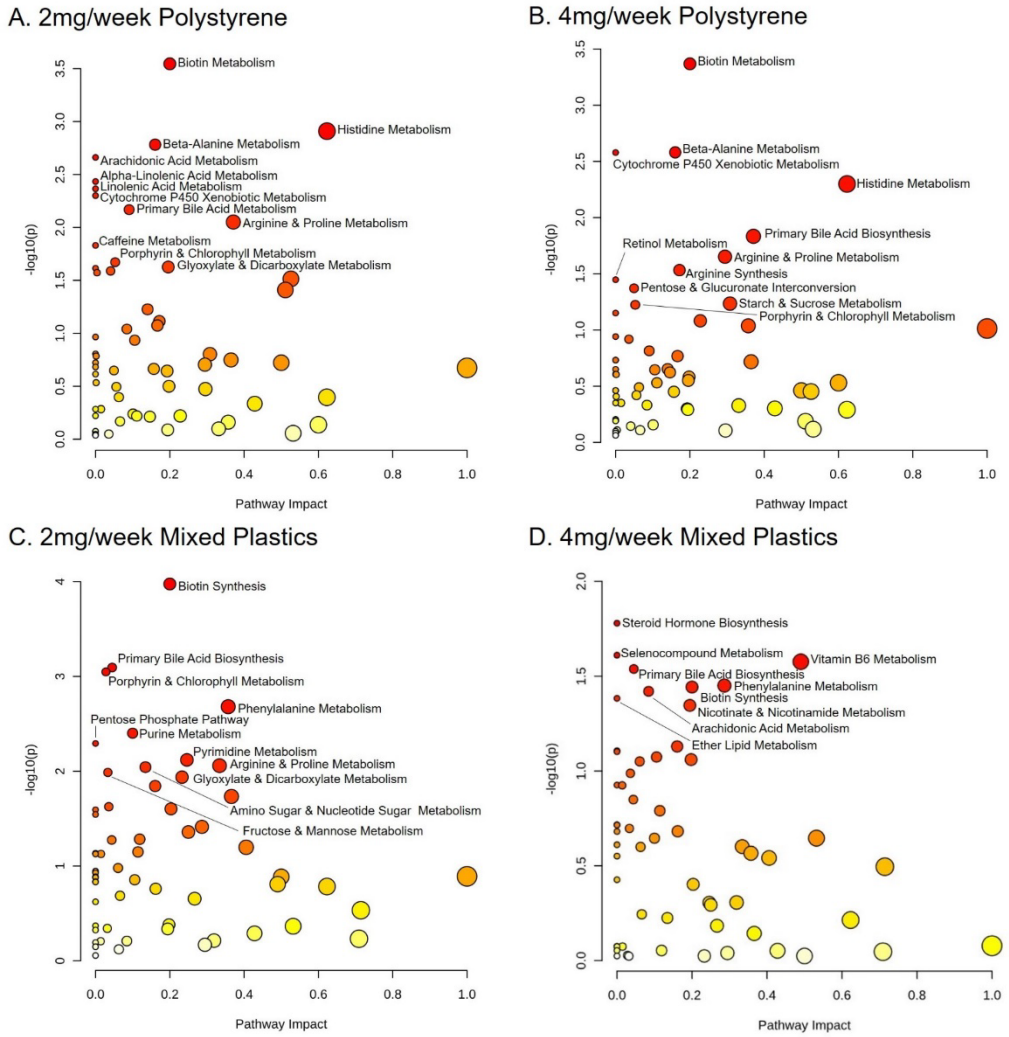
*Garcia et al., Environ Health Perspect.2024 PMID: 38366932*

# Microplastics alter the colonic metabolome of mice

## Colon: Untargeted Metabolomics




## Colon: Altered Metabolic Pathways

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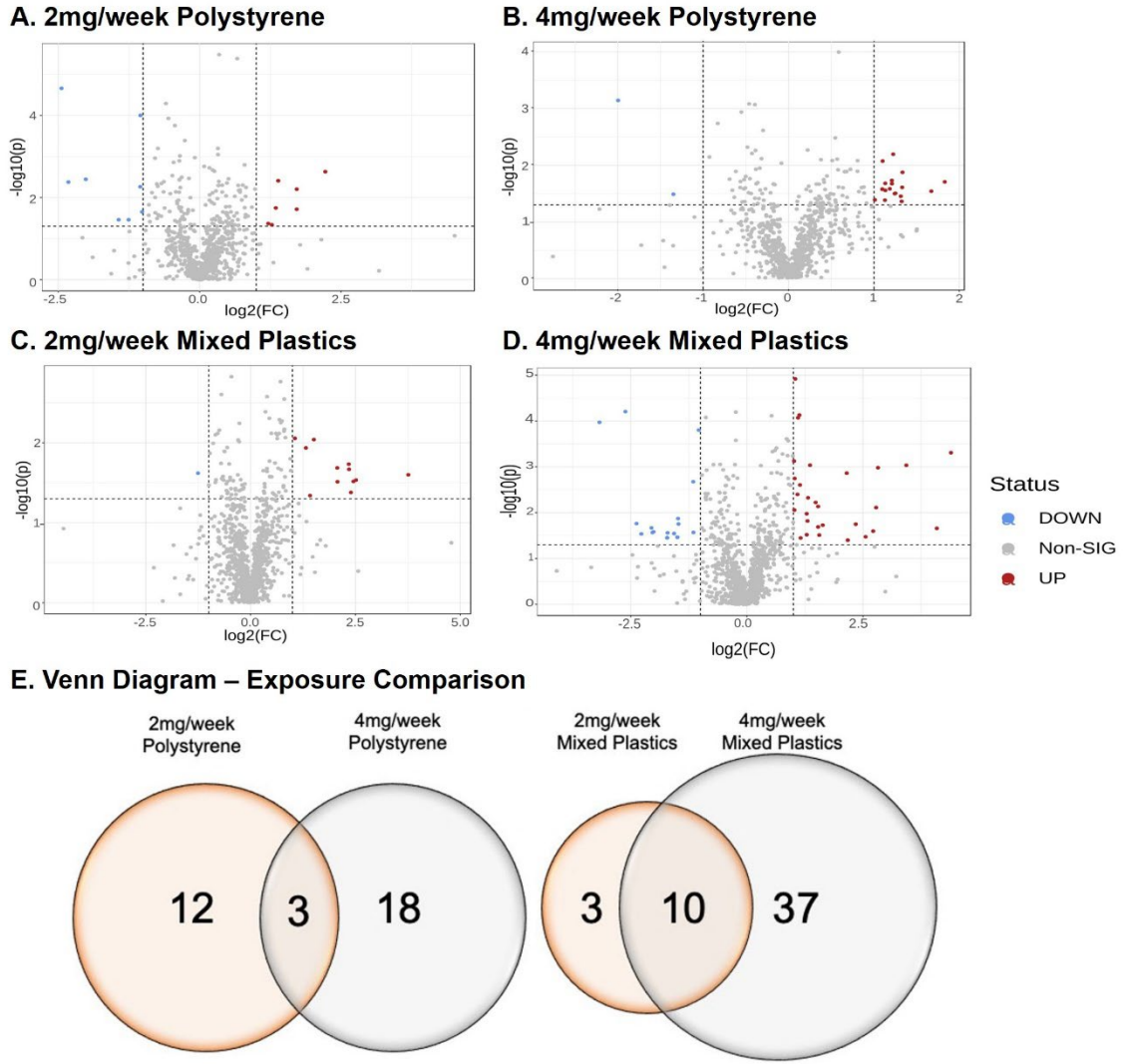
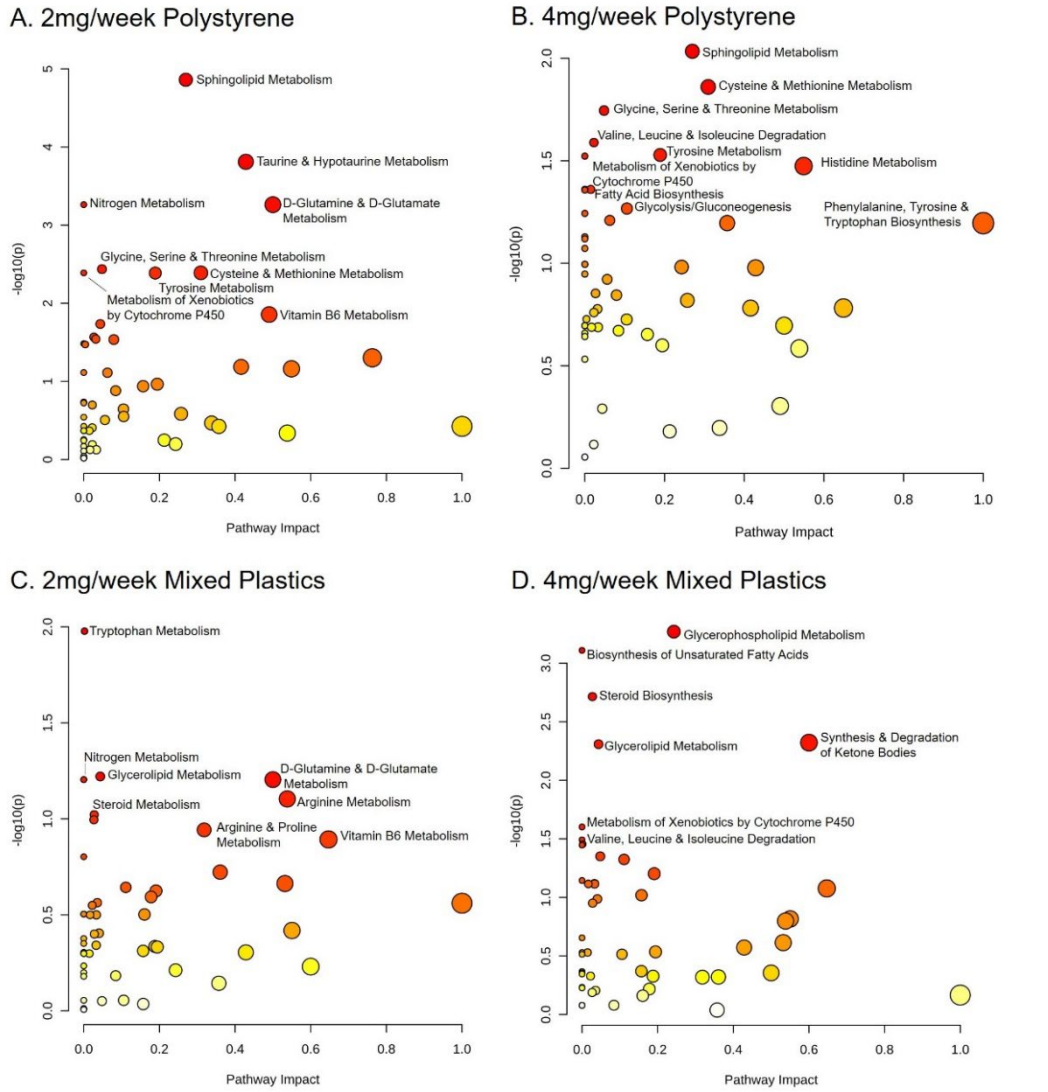
*Garcia et al., Environ Health Perspect.2024 PMID: 38366932*

# Microplastics alter the brain metabolome of mice

## Brain: Untargeted Metabolomics




## Brain: Altered Metabolic Pathways

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*Garcia et al., Environ Health Perspect.2024 PMID: 38366932*

# Conclusion for EHP story and Standing Questions

- We were able to detect polystyrene microspheres in the brain, liver, and kidney after oral exposure.
- Found metabolic differences in the colon, liver, and brain.
- Differential responses that were dependent on concentration and type of microsphere exposure.

**Standing QUESTIONS**

- Do MP cause inflammatory bowel disease? Neurological diseases?
- Did the plastic cause metabolomics changes in the brain or was it due to a change in the microbiota?
- Where is at in the Brain? Were MP in the tissue or brain vasculature?
- Does diet influence the amount of MP being dispersed in the body?
- The list goes on and on……

# UNM Comprehensive Cancer Center

**The Recruitment of Early Career Scientists and Clinicians. Particularly individuals who have a major focus in starting a research program in cancer biology.**

**<u>Rising Star Lectureship</u>**
**Invitation of K99 (or other K) awardee's to present their work at UNMCCC.**

**<u>UNM HSC CTSC K12 Program</u>**
**Potential to recruit through the CTSC K12 Program.**

# Acknowledgments


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**Seul Ki Park, PhD (UCLA)**
Matt Campen, PhD
Marcus Garcia, PharmD
Sumira Phatak, PhD

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Jewel Meyer-Hagen, MD
Chris Moss
Xavier Cardona
Eduardo Peralta-Herrera

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P20GM121176 – NIH NIGMS

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