Micro- and Nanoplastic Exposure During Pregnancy

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Air Pollution and Particulate Matter (PM) - Epidemiological Studies

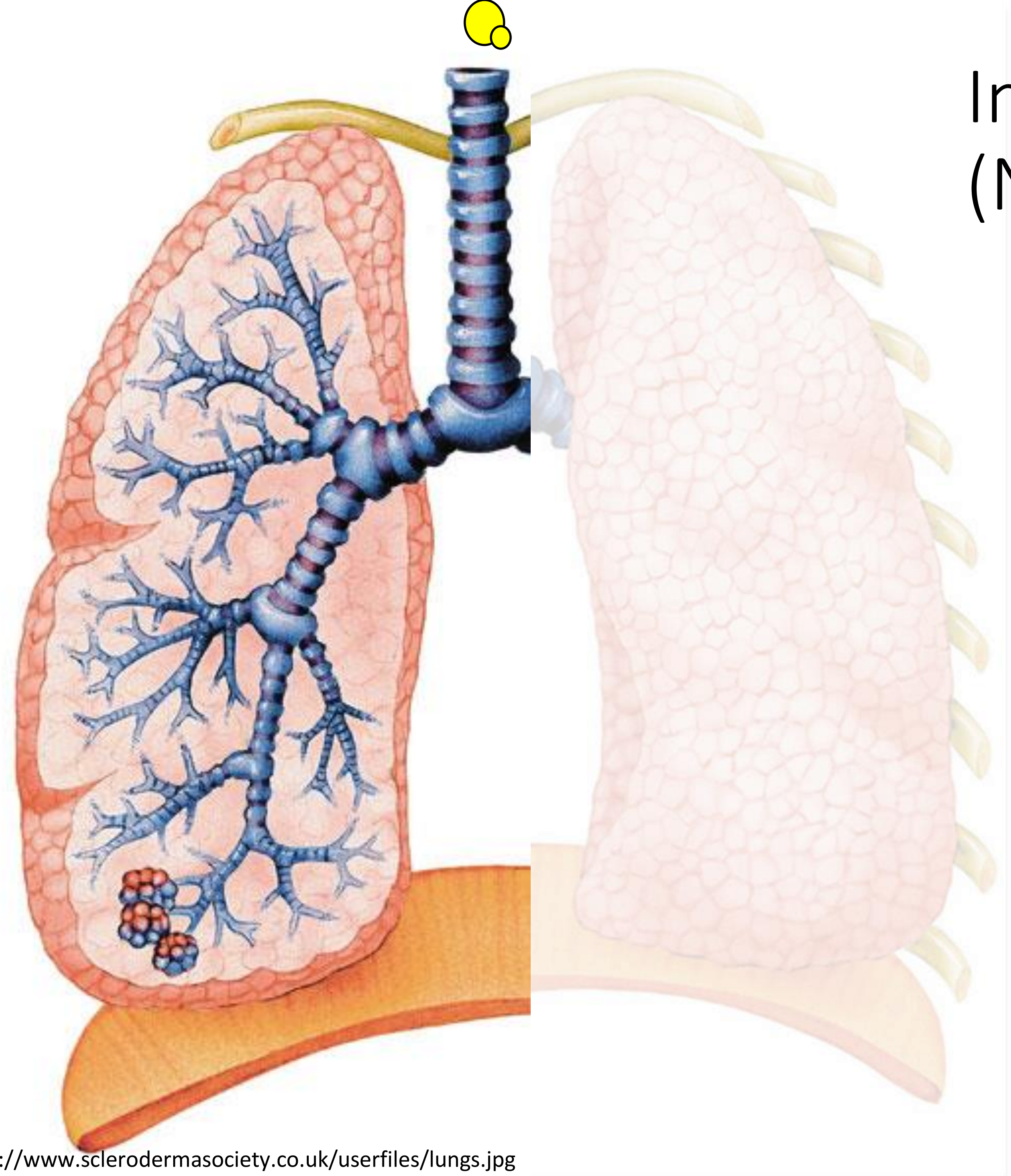
- Epidemiologic evidence of cardiovascular (not pulmonary) effects after air pollution exposure.[1]
- Increased incidence of heart attacks within 24 hours of exposure.[2]
- Increased risk of fetal growth restriction (FGR) from air pollution exposure during pregnancy.[3,4]
- **Overall, exposure to air pollution has adverse effects on cardiopulmonary health.**[5,6]

San Francisco, Camp Fire wildfires, 2018

[1.] Dockery, 2001; [2.] Peters, 2001;

[3.] Nobles, 2019; [4.] Liu, 2007

[5.] Pope, 2015; [6.] Van Eeden, 2002



http://www.sclerodermasociety.co.uk/userfiles/lungs.jpg

Inhalation of Fine vs. Ultrafine (Nanosized) Particles

- Smaller particles (100 nm) have a greater retention in the lung than larger (<2.5 μm) particles.[1]
- Greater inflammation within the lung, and blood plasma, following exposure to ultrafine (nanosized) particles[2]
- Evidence of neural activation[3]
- Ultrafine particle translocation from the lungs to systemic organs[4]

- **Overall, ultrafine (nano) particles have a greater toxicity than fine (sub micron) particles of the same chemical composition.**

Animation – Dr. Cody Nichols

[1]Husain, 2013

[2]Baisch, 2014

[3]Knuckles, 2012; Stapleton, 2015

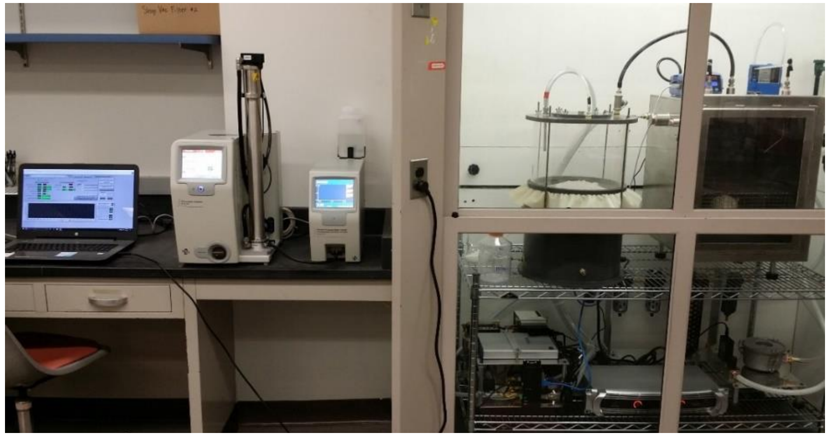
[4]Elder, 2006; Stapleton, 2012

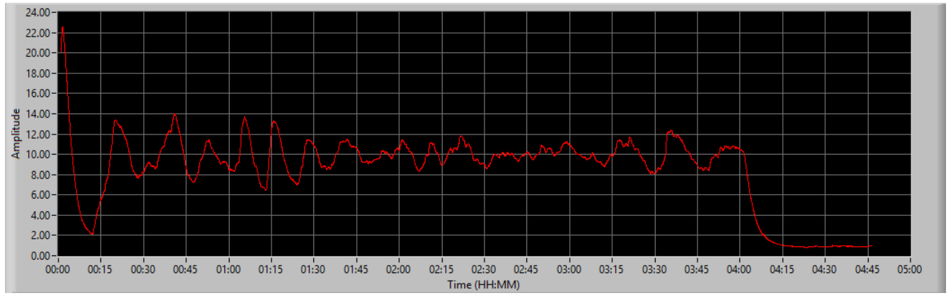
Maternal-Fetal Model

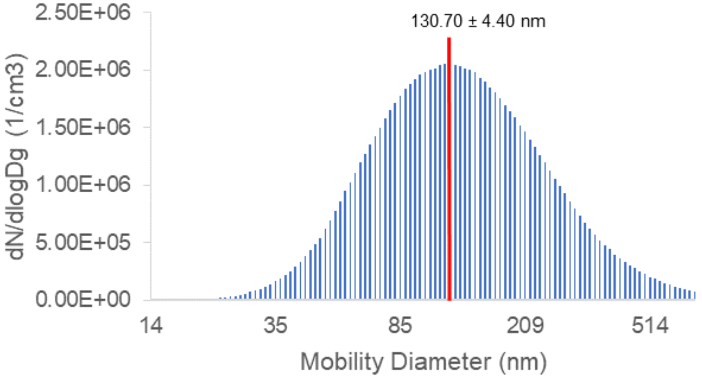
- Complex and widely understudied model
  - *Rapid and precise tissue development*
  - *Hormonal variation*
  - *Physiological disparities (normal)*
    - *Increased Blood Volume*
    - *Increased Heart Size*
    - *Increased Tidal Volume*
  - *Fetal growth restriction increases risk of*
    - *fetal/offspring morbidity/mortality*
    - *cardiovascular, metabolic, neurological disease*

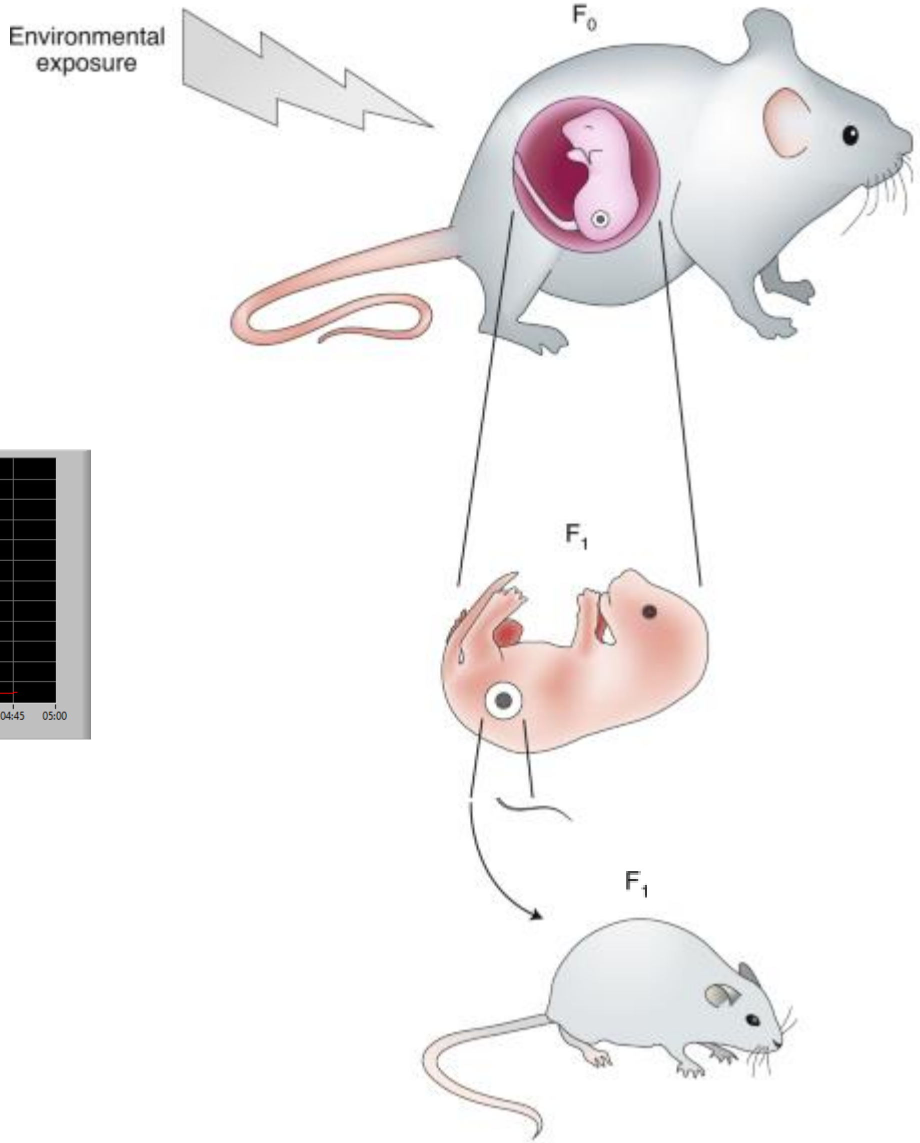
<u>Research Question</u>: How something a mother inhales during pregnancy affects her health, fetal health, and surviving offspring.

Laboratory Model and Experimental Design









Maternal Outcomes

Fetal

Offspring Health

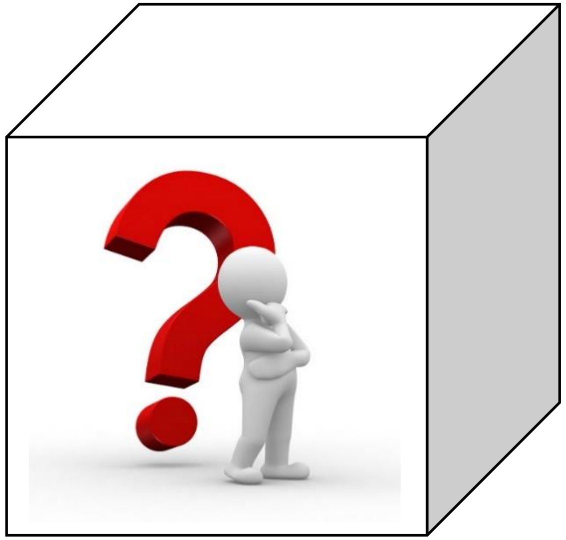
Knowns

(Based on our work in maternal-fetal nanotoxicology)

Maternal

- Uterine blood vessels do not dilate well after nanoparticle exposure. *(Stapleton, 2013; Stapleton, 2018; Fournier, 2019; Cary, 2024)*
- Culminate in an inability to meet fetal blood flow demands. *(Stapleton, 2013; D'Errico, 2019b)*
- Develop an FGR phenotype. *(Stapleton, 2013; Fournier, 2019)*
- May impair conception and postpartum coronary recovery. *(Stapleton, 2018; Cary, 2024; Adams, in preparation)*

Placental



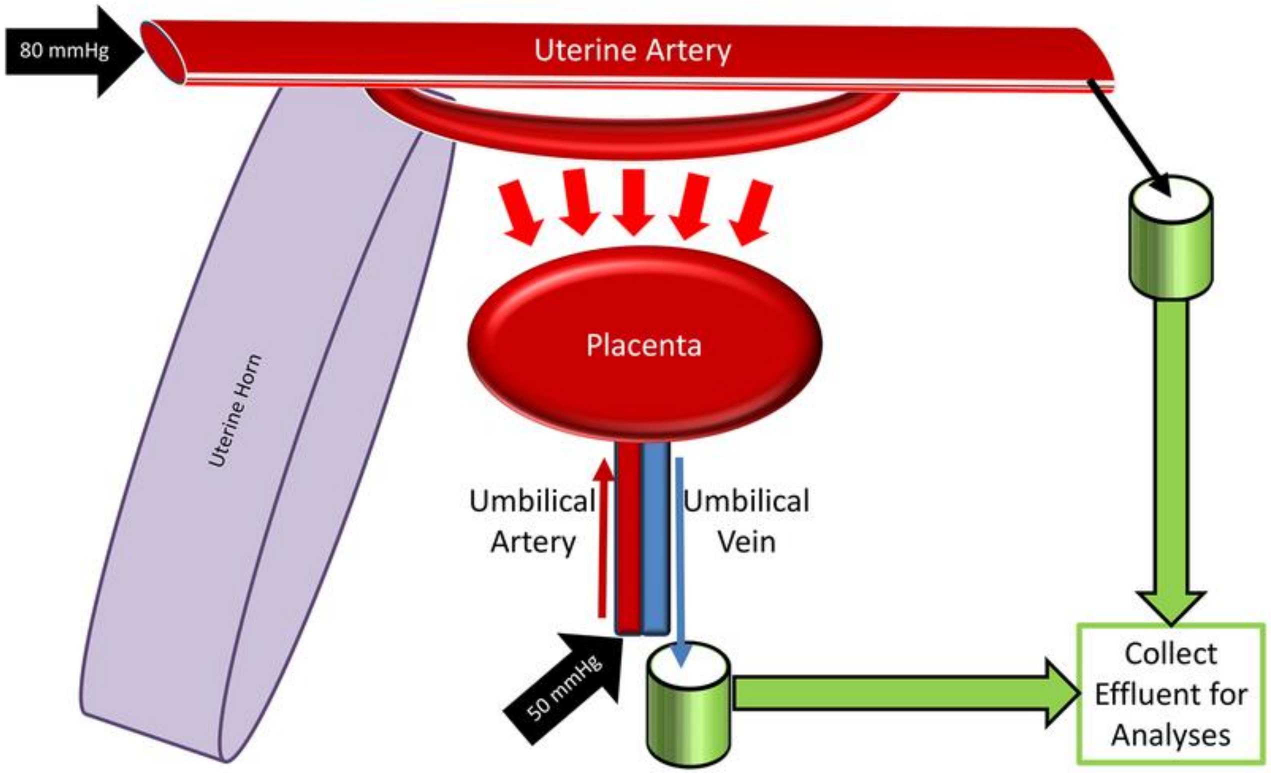
Maternal and fetal outcomes associated with particle translocation or secondary effects due to exposure?

Does the placenta act as a biological barrier or can nano-sized particles translocate across the placenta?

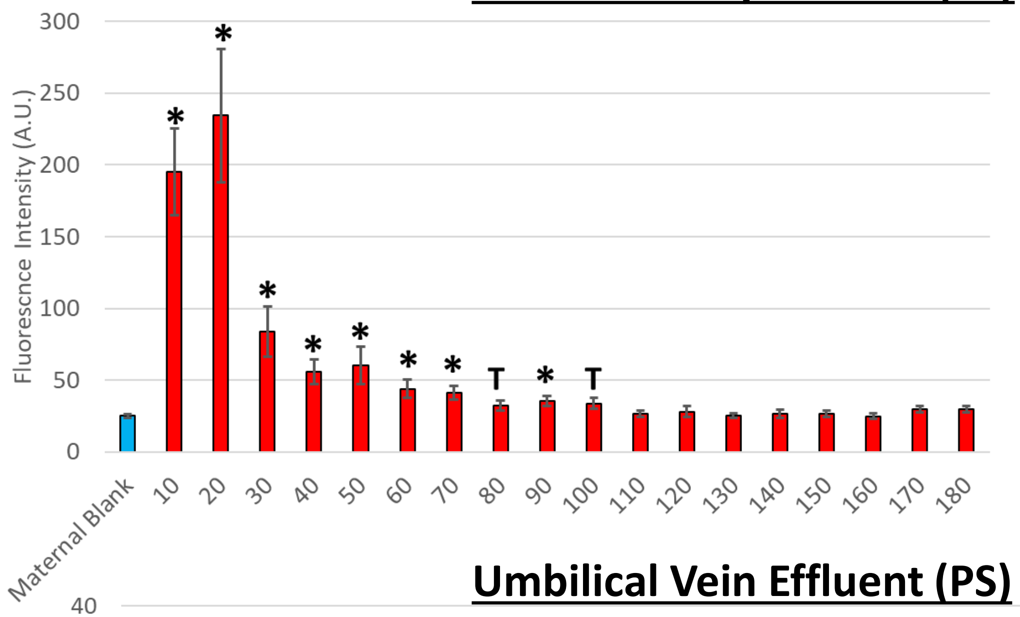
Fetal/Offspring

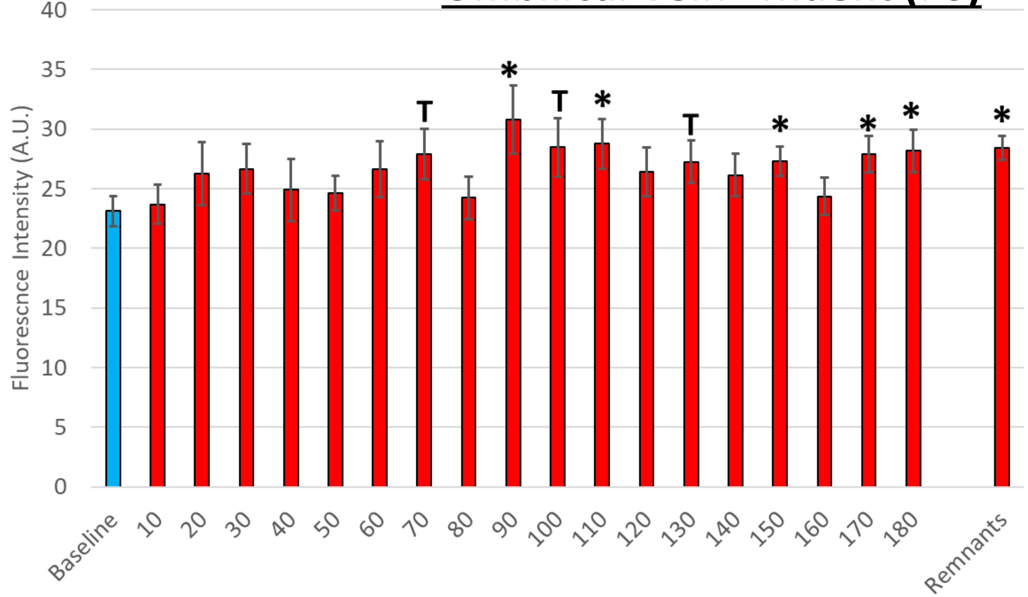
- Development of FGR phenotype *(Stapleton, 2013; Fournier, 2019)*
- Impaired *fetal* cardiovascular health
  - Vascular dysfunction *(Stapleton, 2013)*
  - Cardiac/coronary dysfunction *(Hathaway, 2017)*
  - Reduced coronary bioenergetics *(Hathaway, 2017)*
  - Epigenetic alterations *(Stapleton, 2018)*
- Impaired *adult* cardiovascular health *(Stapleton, 2015; Fournier, 2021)*

Placenta Does Not Act as a Barrier to Nanoparticles



20 nm Rhodamine Polystyrene

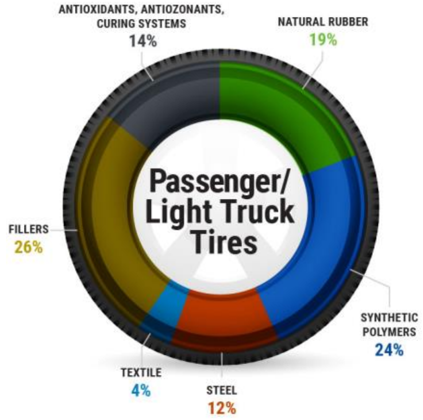


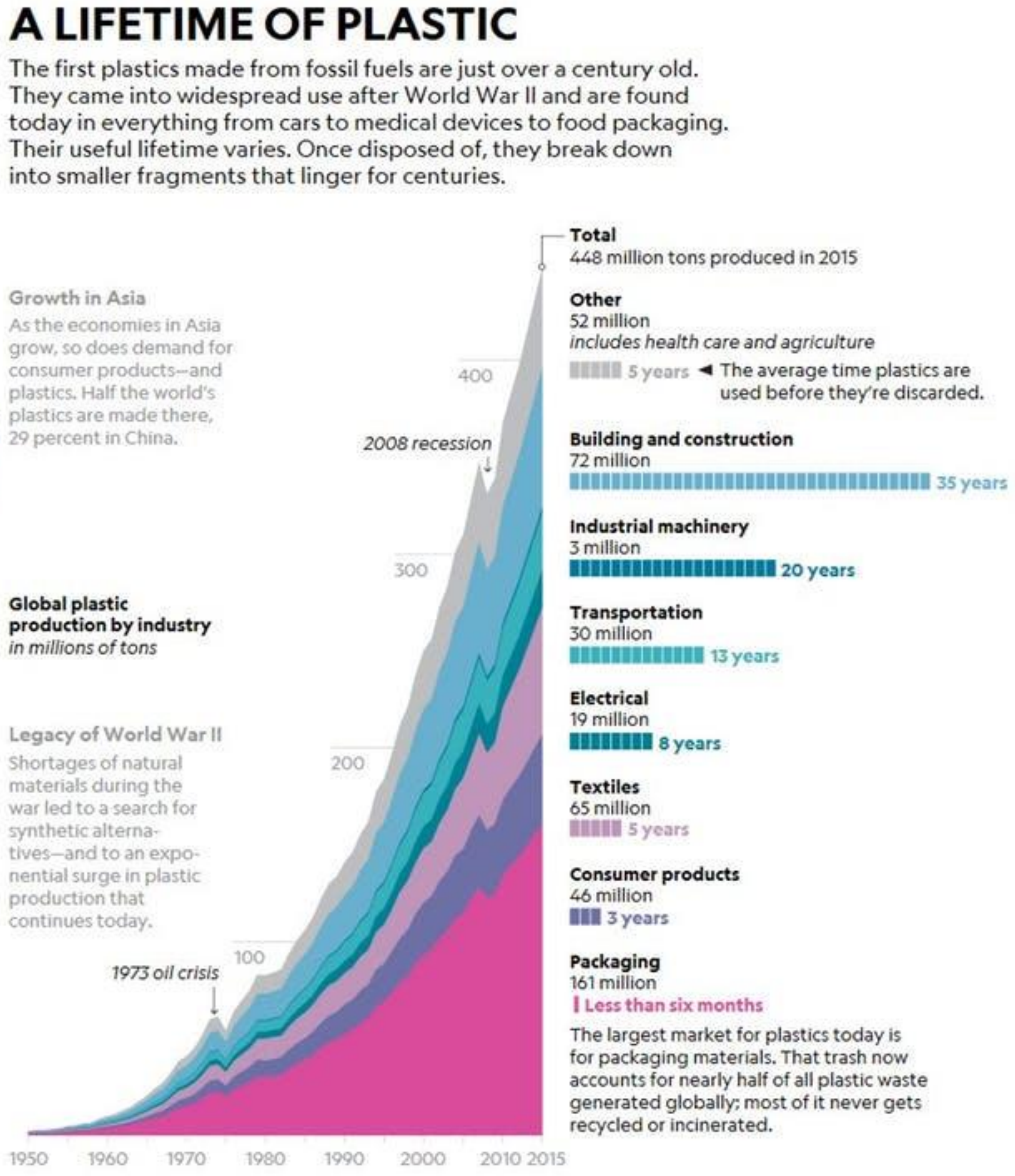


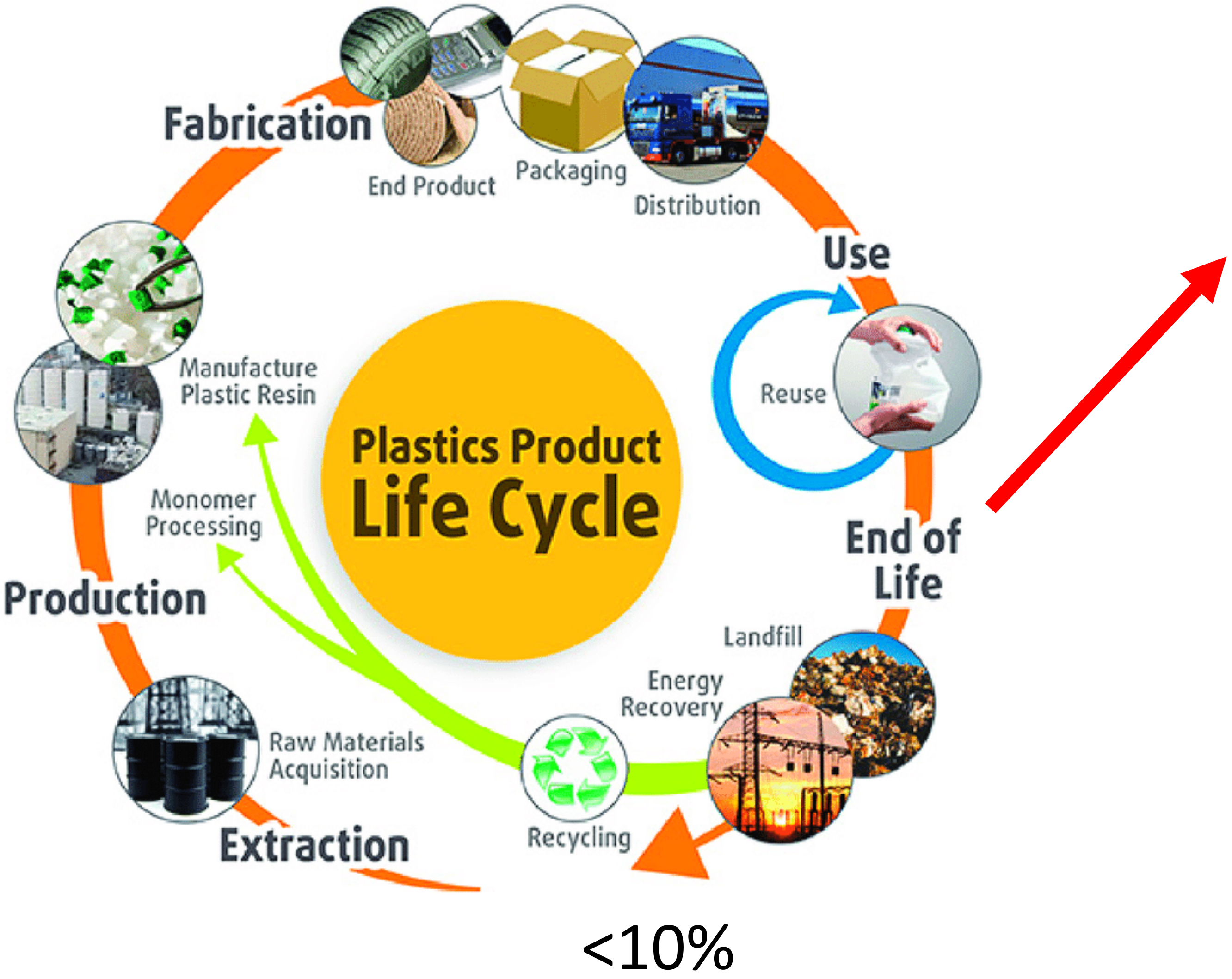
Placenta does not act as a barrier to nanosized particles.

D'Errico, 2019; Fournier, 2020

We are surrounded by plastics.







Plastics are made through the chemical-linkage of monomers to polymers.

Breakdown of plastics ranges from 10 – 1000 years often through thermal, UV, and mechanical degradation.

The average estimate for plastic bag degradation is 20 years, while a plastic bottle to breakdown is 450 years.

This concept of decomposition is unclear.

- Not always referring to chemical degradation.
- May refer to particle size.

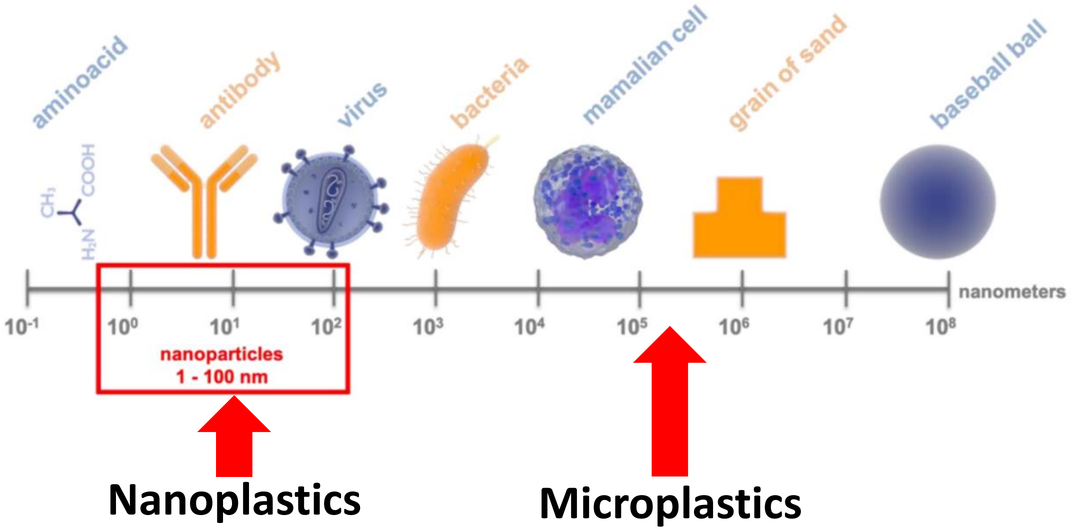
Just because something is invisible, doesn’t mean that it isn’t there…

Micro- and Nanosized Plastics

Microplastics are not a specific kind of plastic, but a plastic fragment that is less than **5 mm** in length.

(Sesame Seed)

(Toothbrush Bristles)

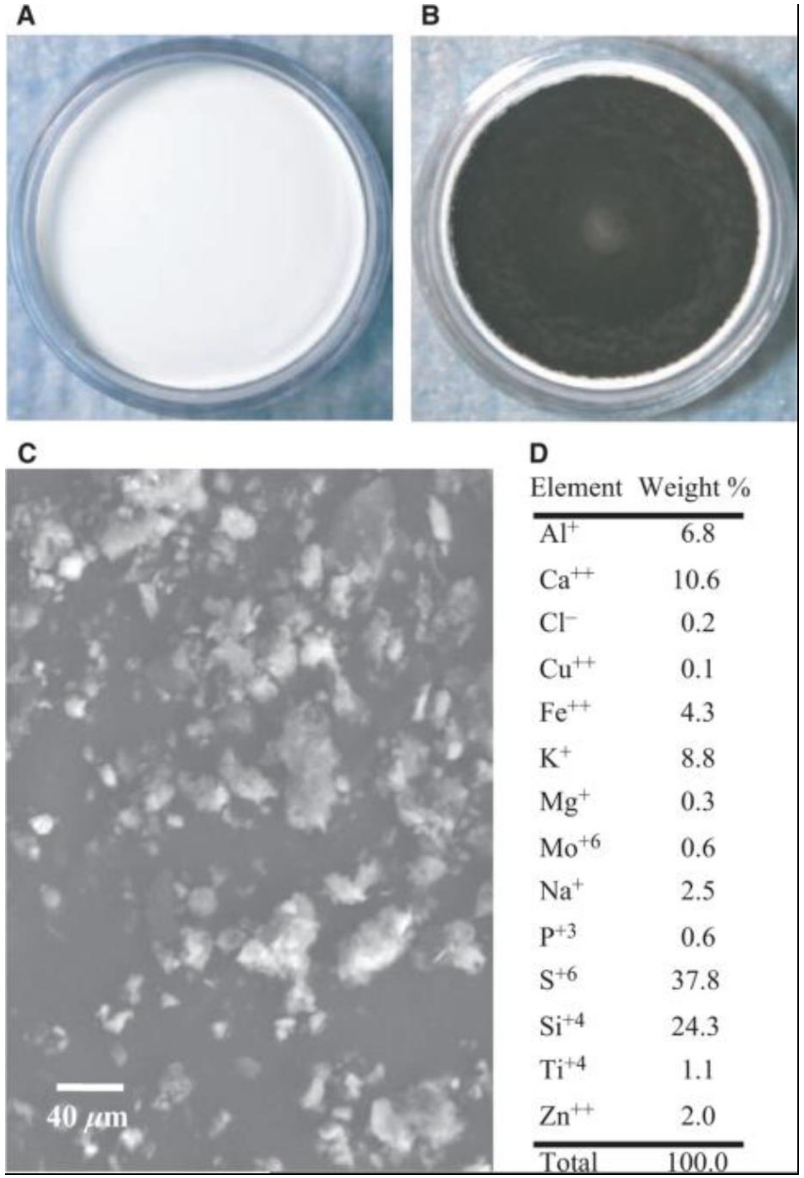


Nanoplastics are defined as less than **1000 nm in environmental studies and 100 nm in laboratory studies**[1].

(Surface Area)

NOAA, Ocean Facts, March 30, 2020
Image: Washington Post
[1]Stapleton, 2019, AIMS Environmental Science

Microplastics In the Environment



Element	Weight %
Al^{+}	6.8
Ca^{++}	10.6
Cl^{-}	0.2
Cu^{++}	0.1
Fe^{++}	4.3
K^{+}	8.8
Mg^{+}	0.3
Mo^{+6}	0.6
Na^{+}	2.5
P^{+3}	0.6
S^{+6}	37.8
Si^{+4}	24.3
Ti^{+4}	1.1
Zn^{++}	2.0
Total	100.0

National park or wilderness	State	Size (km^2)	Mean plastic deposition rate (plastics m^{-2} day^{-1})	Metric tons of plastic per year (visual counts)	Metric tons of plastic per year (FTIR proportions)
Grand Canyon	AZ	4926	112 ± 6	10.7–11.9	11.0–21.3
Wind River Range	WY	7252	68 ± 6	9.3–11.1	10.9–22.3
Craters of the Moon	ID	2893	139 ± 10	7.7–8.8	11.5–19.3
Rocky Mountain	CO	1047	435 ± 8	9.4–9.8	4.2–9.0
Joshua Tree	CA	3200	54 ± 2	3.4–3.7	3.7–9.8
Uinta High Wilderness	UT	1849	120 ± 6	4.3–4.8	1.6–2.8
Canyonlands	UT	1366	48 ± 7	1.2–1.5	3.0–6.1
Indian Peaks	CO	311	148 ± 5	0.9–1.0	0.4–1.3
East River	CO	300	140 ± 9	0.8–0.9	0.4–0.9
Great Basin	NV	312	107 ± 5	0.65–0.72	0.4–1.3
Bryce Canyon	UT	145	80 ± 6	0.22–0.26	0.4–0.8
All western protected areas	**USA**	**496,350**	**132 ± 6**	**1012–2419**	**1185–3773**

Figure 1, Knuckles, 2013; Table 3, Brahney, 2020 (4μm-3mm); Mason, 2013

Microplastic Exposures

INGESTION:

Bottled Water (Kosuth, 2018)
Beer (Kosuth, 2018)
Wine (Prata, 2020)
Tea (bags; Hernandez, 2019)
Rice (Dessi, 2021)
Sugar and Honey (Liebezeit, 2013)
Feces (Schwabl, 2019)

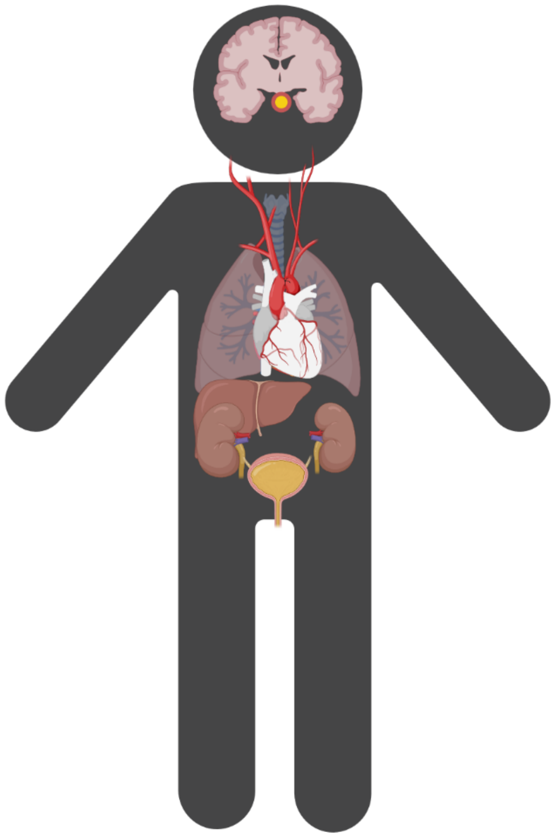
INHALATION:

Indoor Air (Kaprzak, 2022)
Outdoor Air [Rural and Urban] (Perera, 2022)
Human Lung Samples (Jenner, 2022)

Especially concerning as humans spend 70-90% of the time indoors (Alzona, 1979)

Microplastics in Human Tissues

- Human Lung (patient and cadaver; Jenner, 2022; Amato-Lourenco, 2021)
- Carotid Artery plaque (Marfella, 2024)
- Olfactory Bulb, a group nerve cells at the bottom side of the brain (Amato-Lourenco, 2024)
- Heart (Yang, 2023)
- Liver (Horvatits, 2022)
- Kidney (Massardo, 2024)
- Urine (Massardo, 2024)
- Penile tissue (Codrington, 2024)
- Testes (Hu, 2024)
- Breastmilk (Ragusa, 2022)
- *Placenta (Ragusa, 2021; Braun, 2021; Garcia, 2024)
- *Meconium (Braun, 2021)



Made with BioRender

Nanoplastics in Bottled Water

PNAS RESEARCH ARTICLE | CHEMISTRY ENVIRONMENTAL SCIENCES

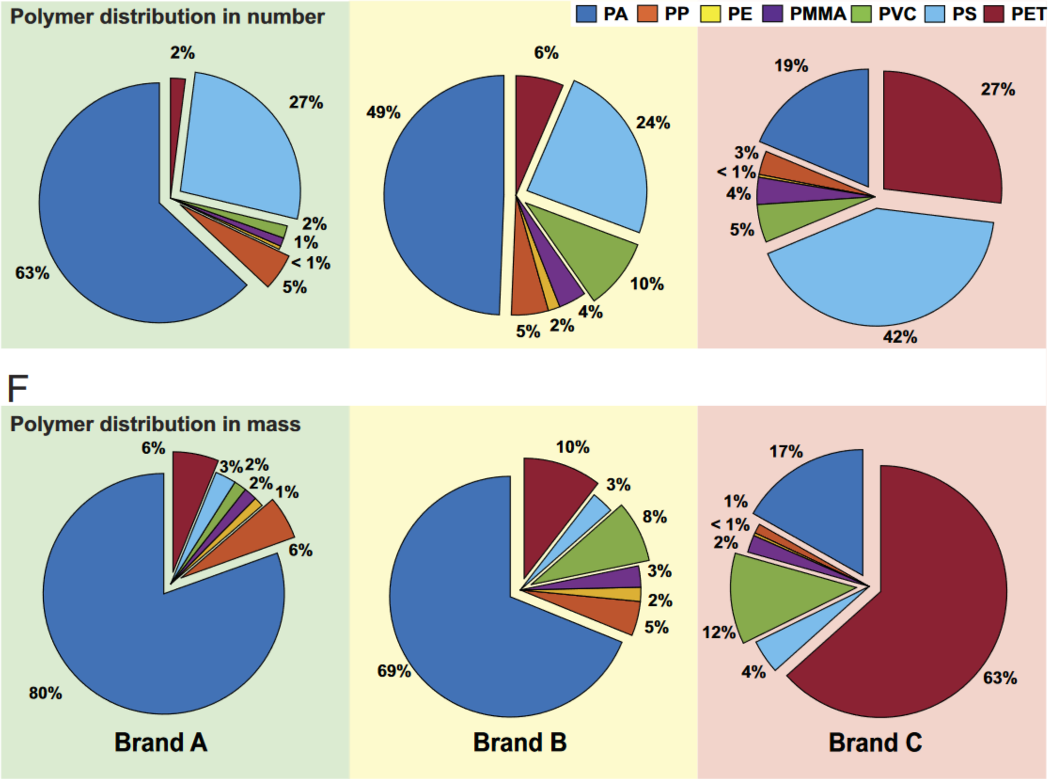
OPEN ACCESS

Check for updates

Rapid single-particle chemical imaging of nanoplastics by SRS microscopy

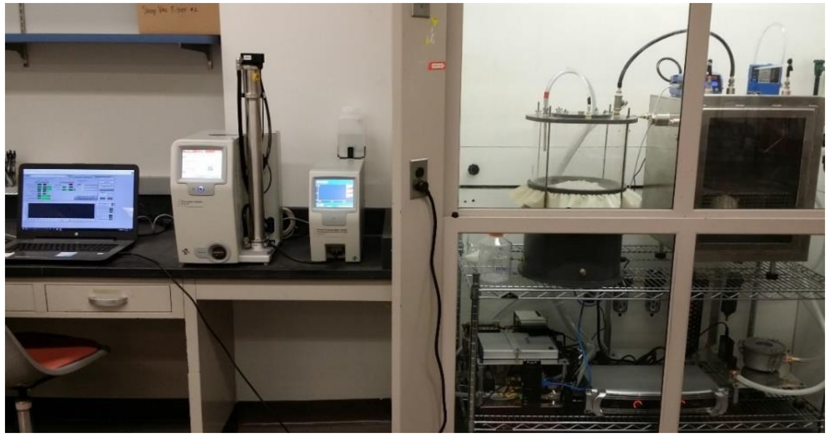
Naixin Qian[a], Xin Gao[a], Xiaoqi Lang[a], Huiping Deng[b], Teodora Maria Bratu[b], Qixuan Chen[c], Phoebe Stapleton[d], Beizhan Yan[b,1], and Wei Min[a,e,1]

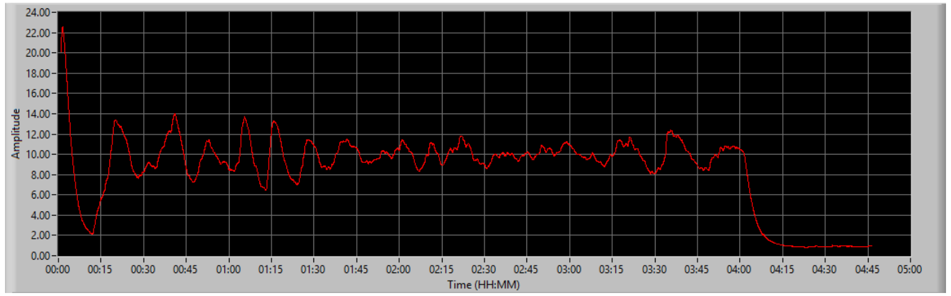
240,000 – 400,000 nanoplastic particles per **Liter** of bottled water

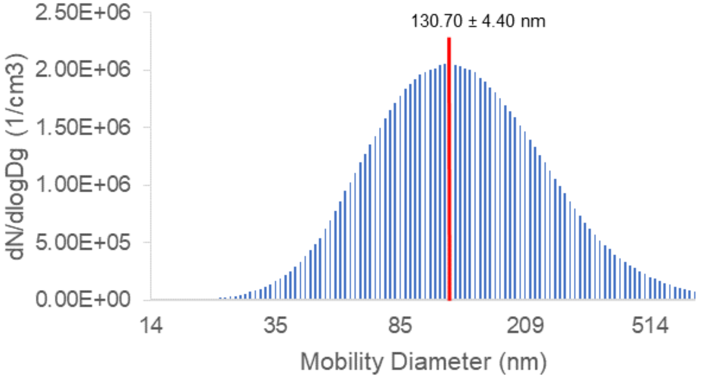


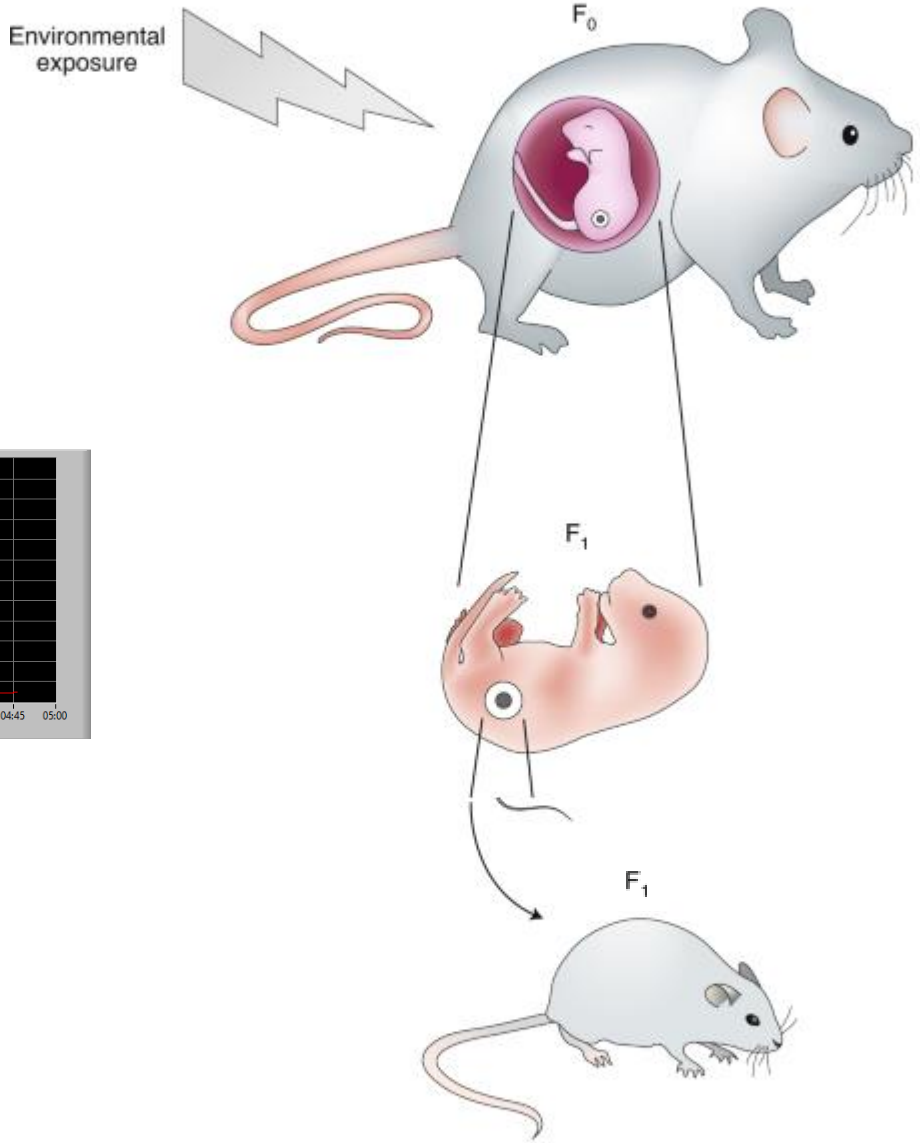
Qian, 2024

Laboratory Model and Experimental Design







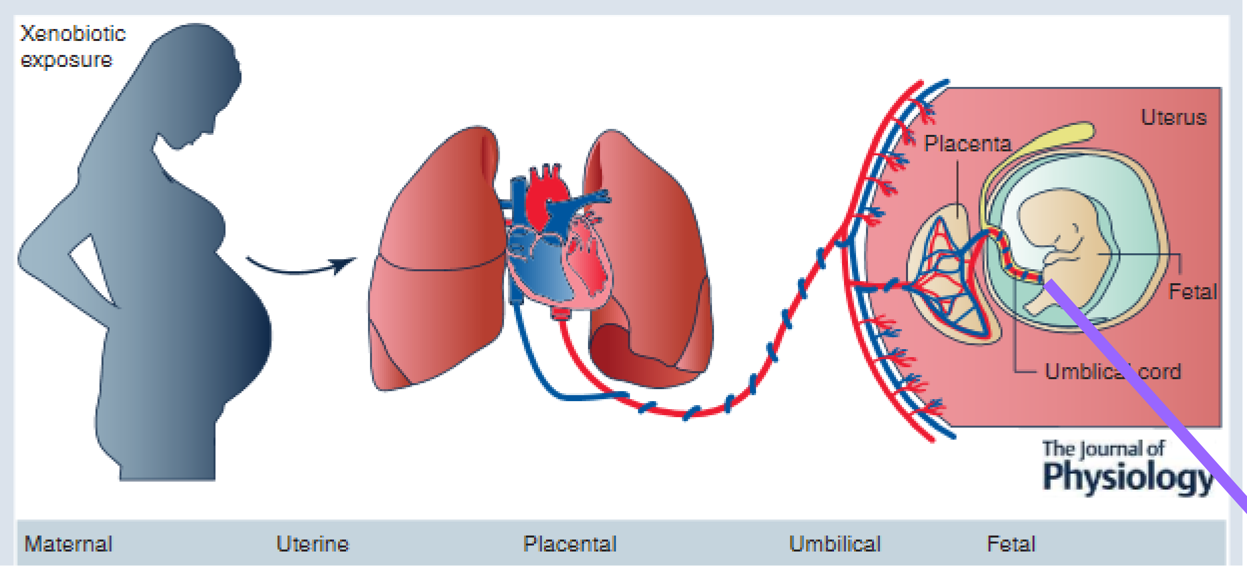


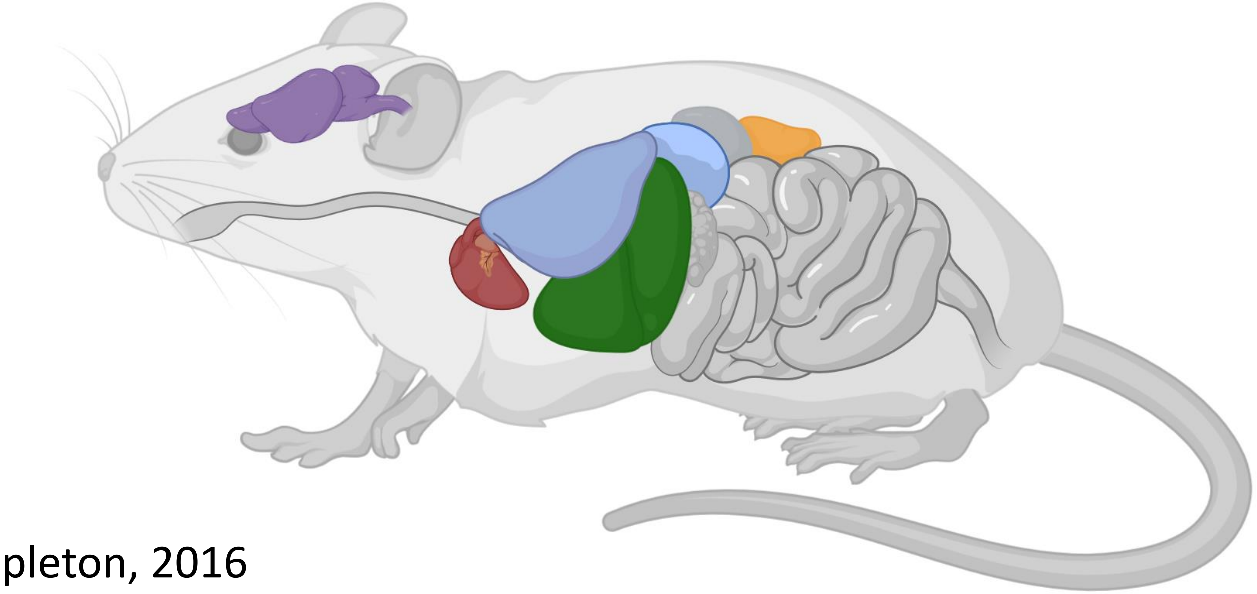
Maternal Outcomes

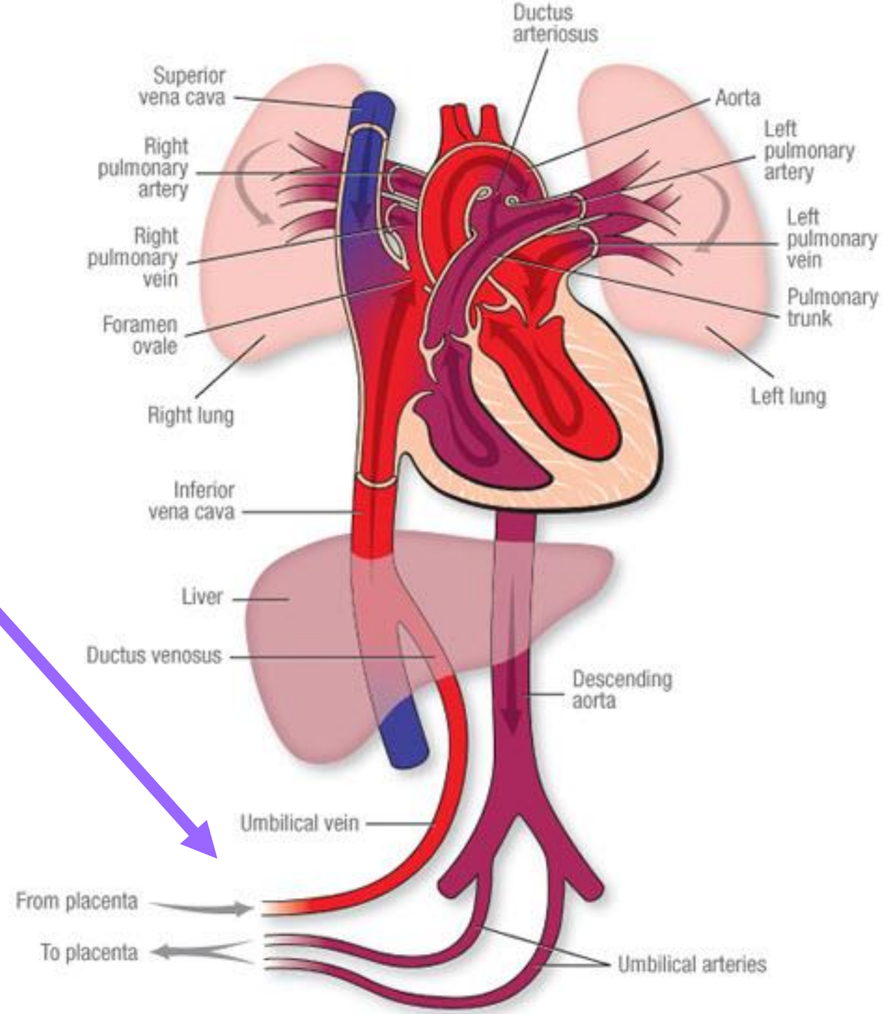
Fetal

Offspring Health

MNP Exposure and Translocation 24h after exposure





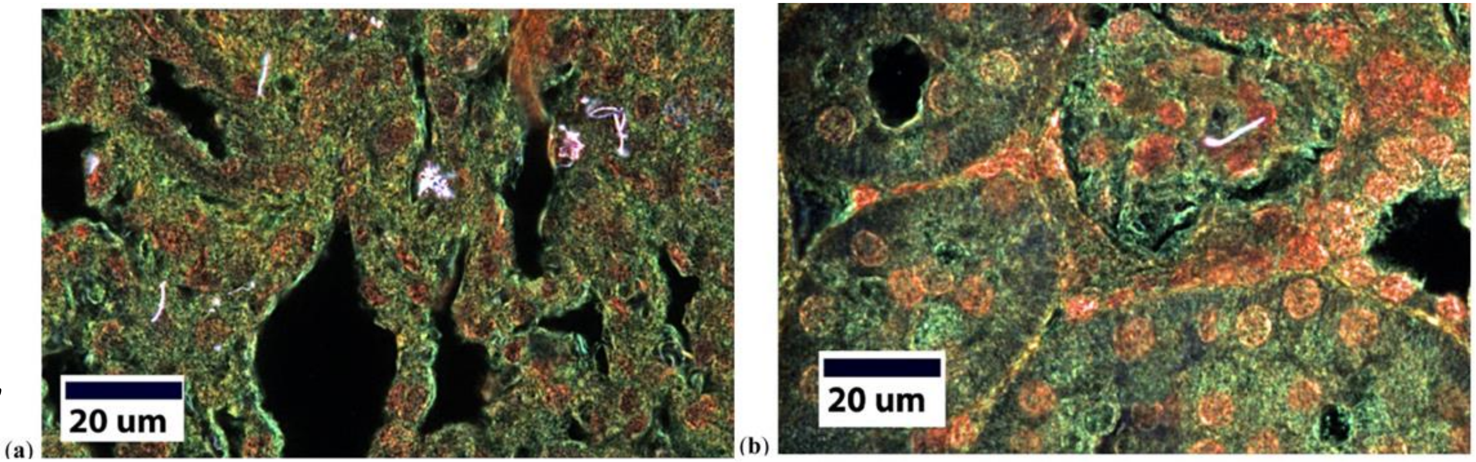


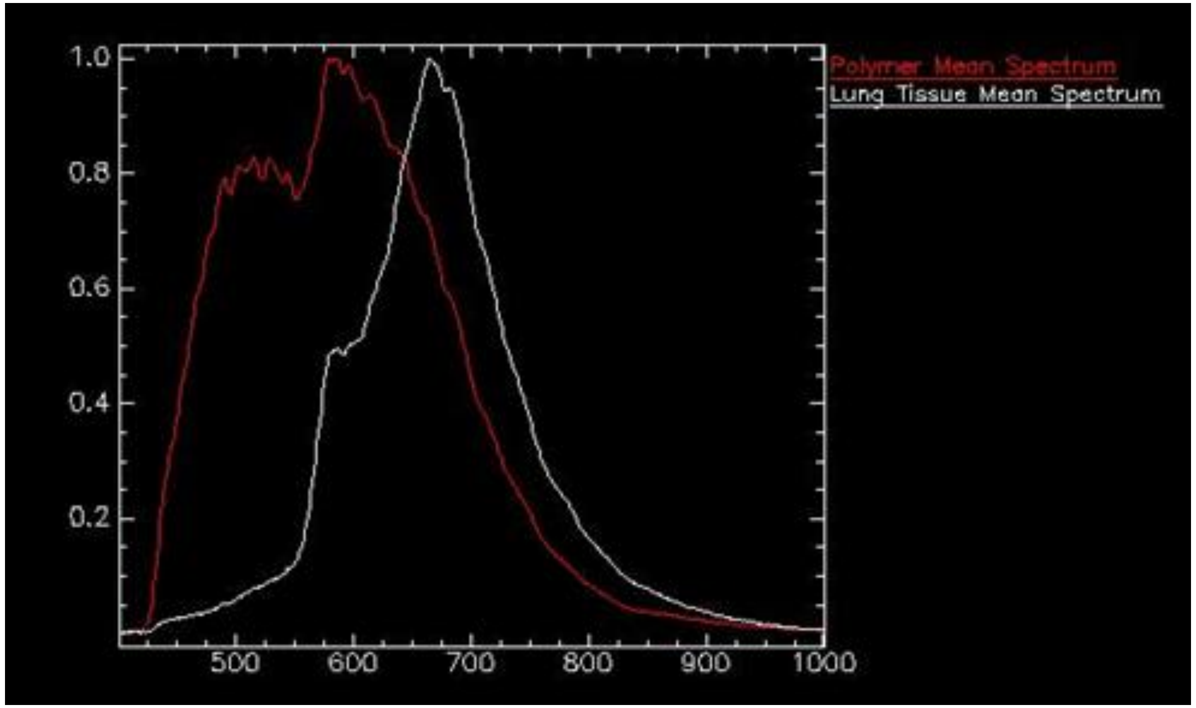
Stapleton, 2016

Nanoplastic Identification - Laboratory

- **Hyperspectral Dark-Field Microscopy**
  - ***Light Refraction***

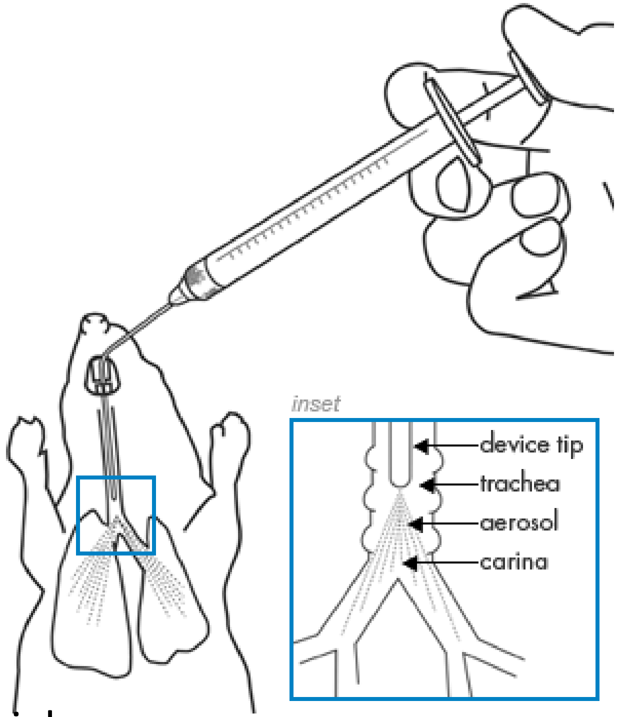
- ***Challenge – difficult for mixtures, not ideal for real world evaluations***





Stapleton, 2012

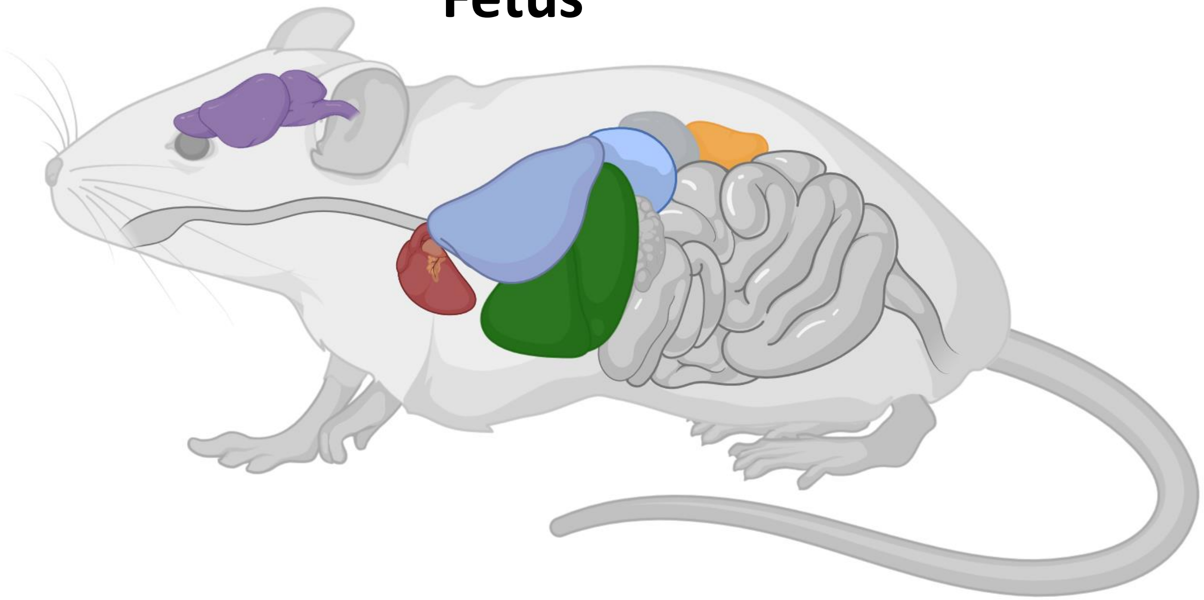
MNP Exposure and Translocation 24h after exposure



Nanopolystyrene Intratracheal Instillation

Pregnant Dam

Fetus



Material:

20 nm FL labeled polystyrene bead

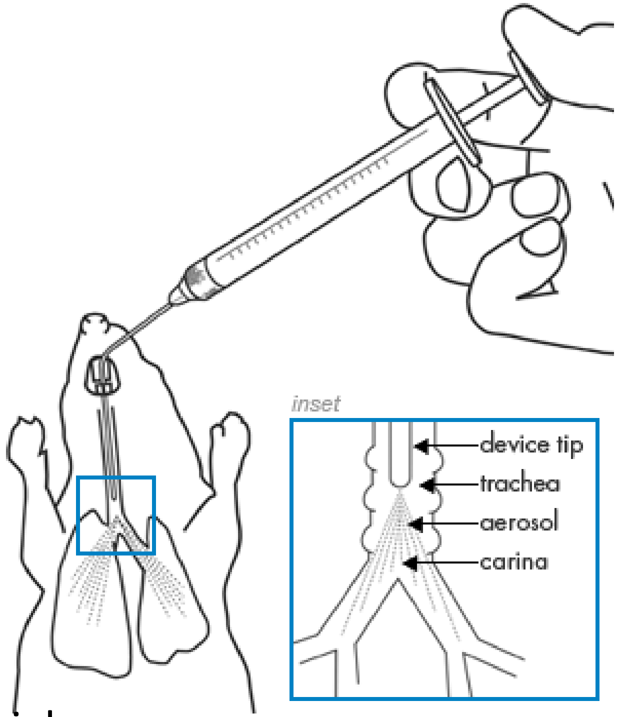
$(IT)\ 2.64\ x\ 10^{14}$ PS particles

Our experimental dosage of $\mathbf{2.64\ x\ 10^{14}}$ **nanoplastic particles** is lower than the calculated environmental exposure dose.

Fournier, 2020

Penncentury.com

MNP Exposure and Translocation 24h after exposure



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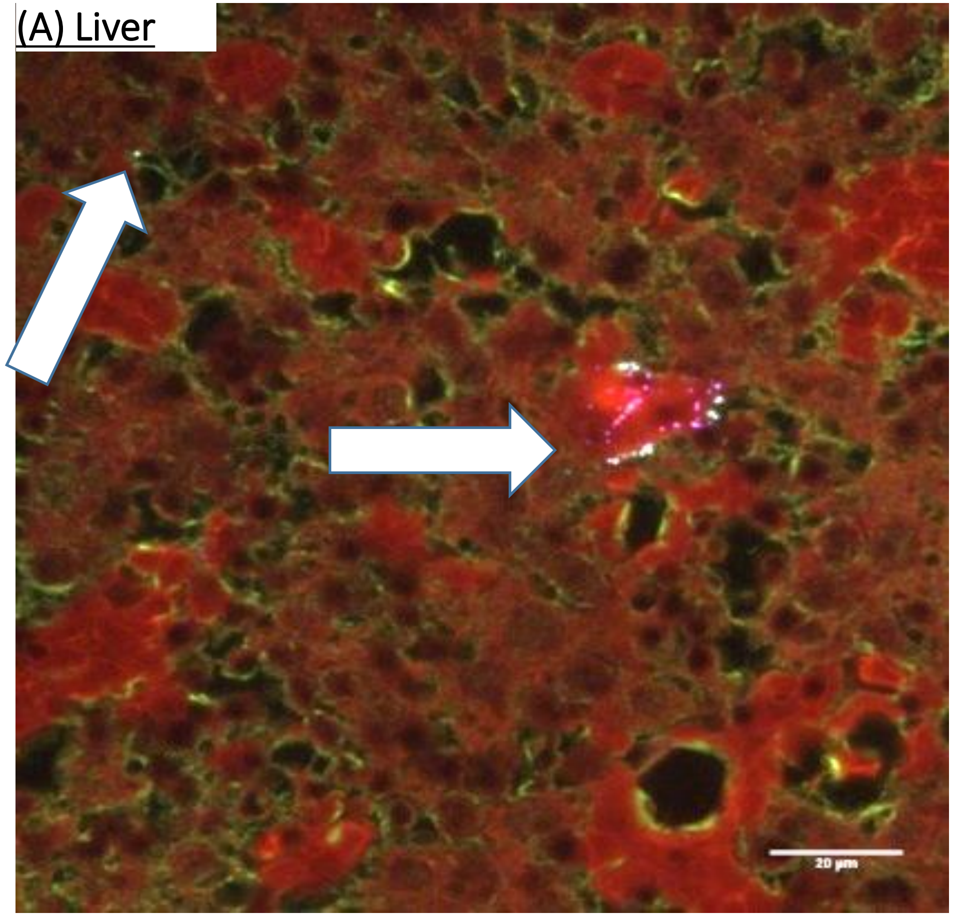
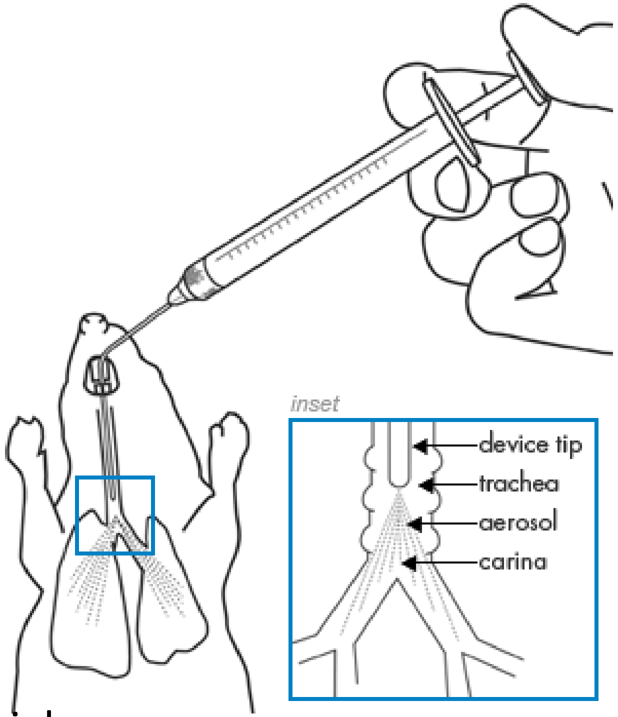
Fournier, 2020
Penncentury.com

Nanopolystyrene Intratracheal Instillation

(A) Liver



MNP Exposure and Translocation 24h after exposure



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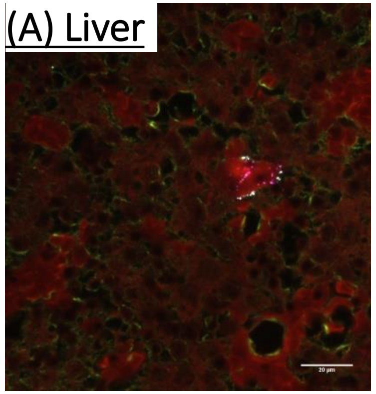

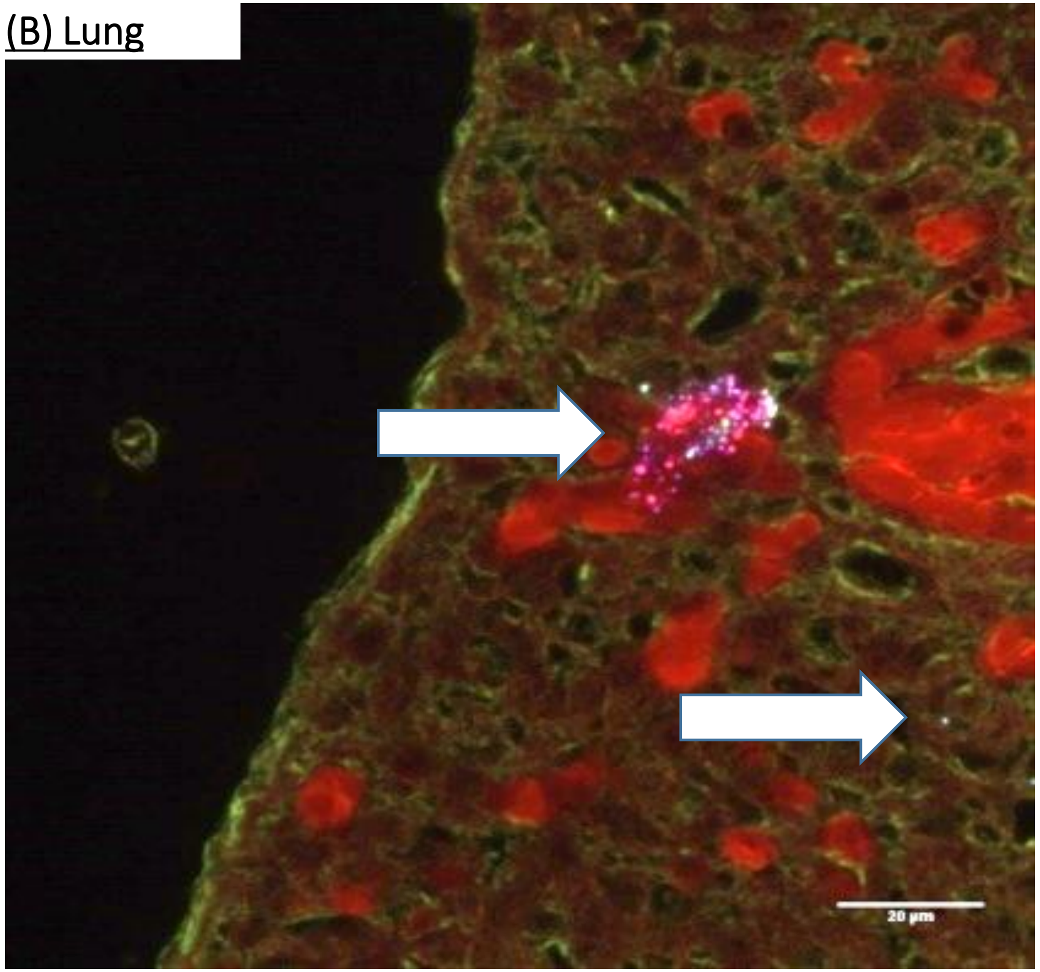

Fournier, 2020

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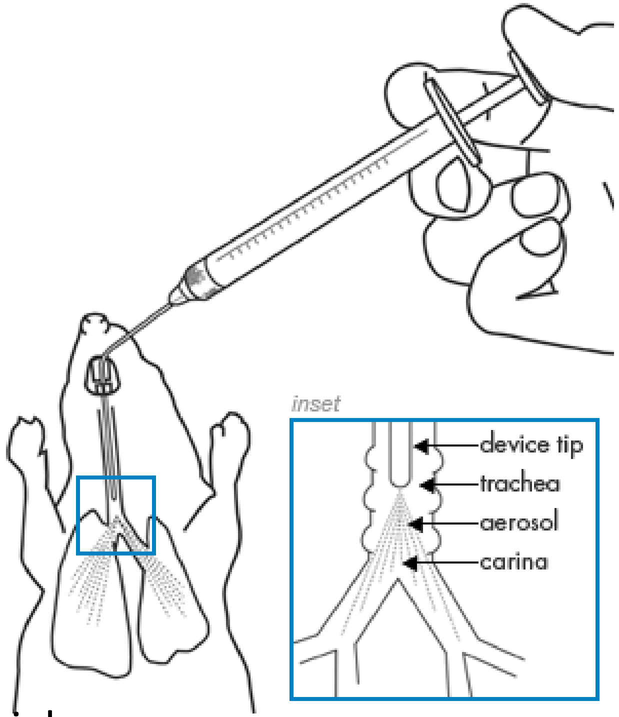

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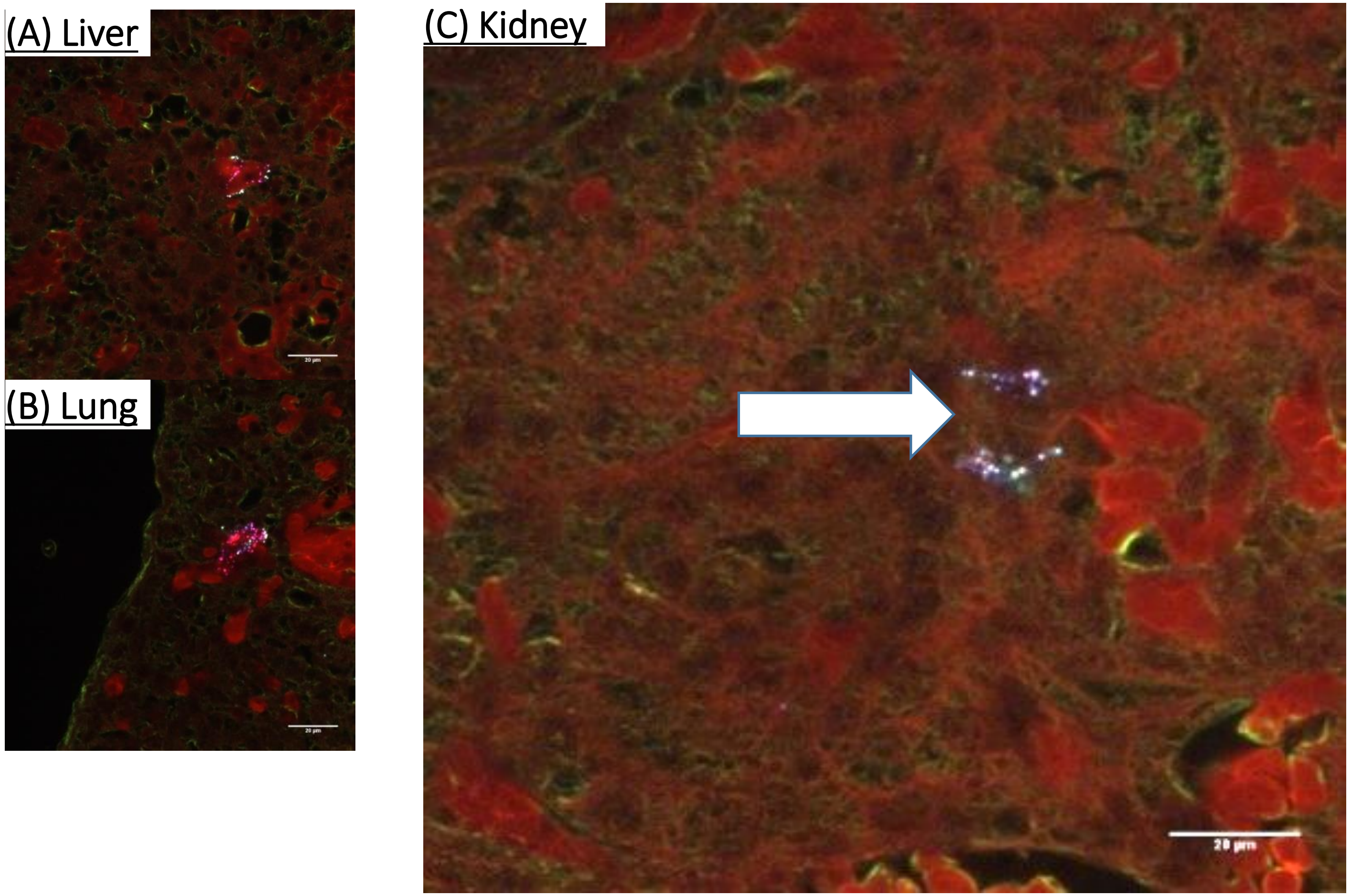

Fournier, 2020

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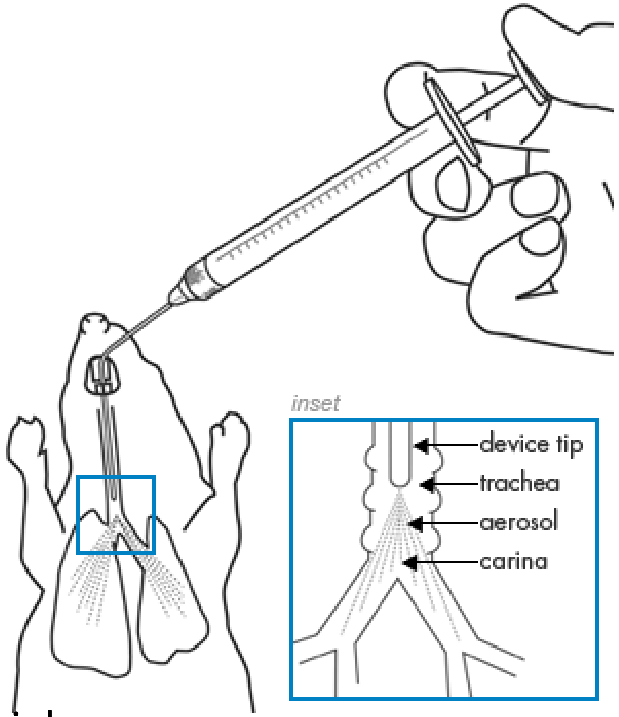

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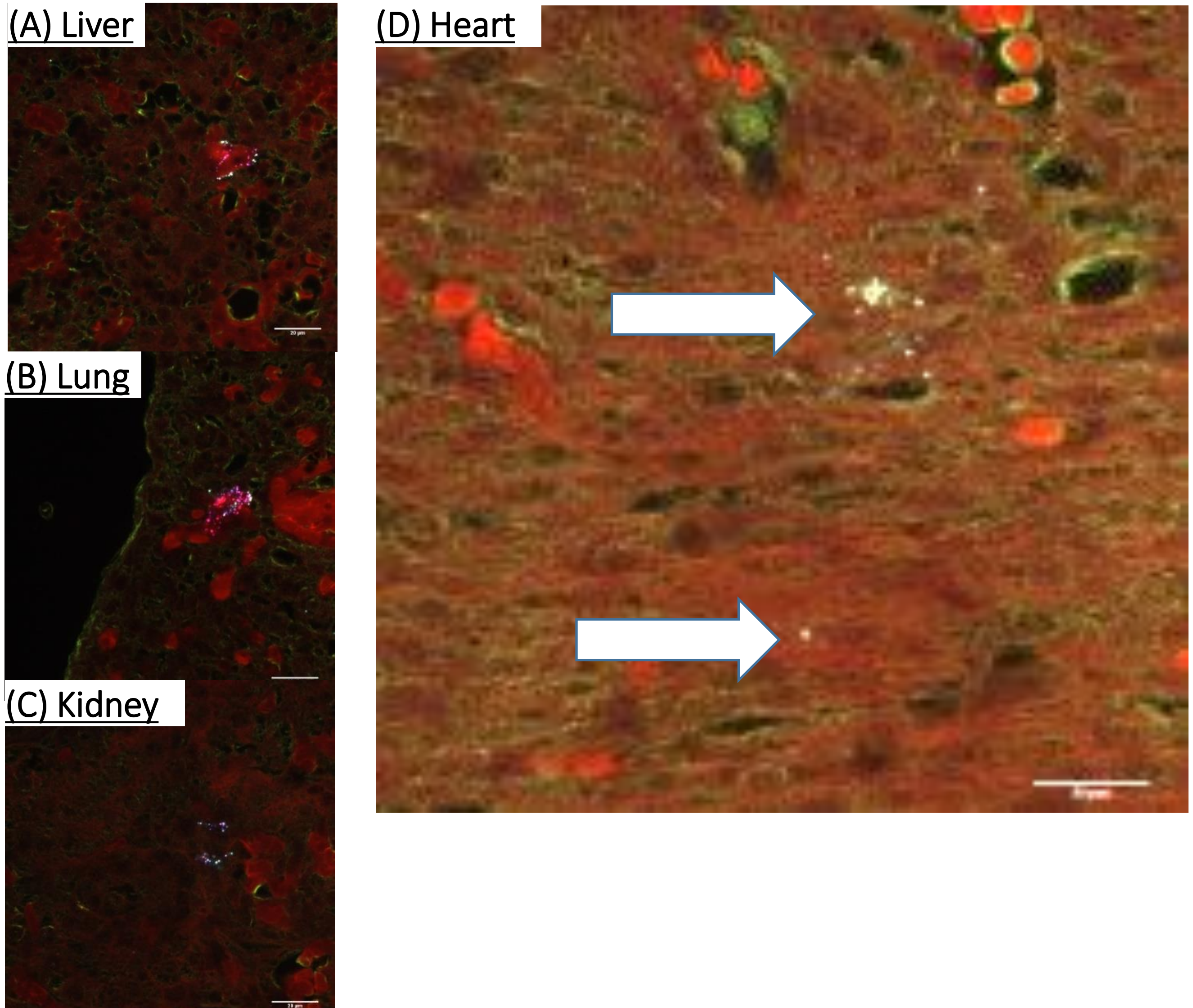

Fournier, 2020

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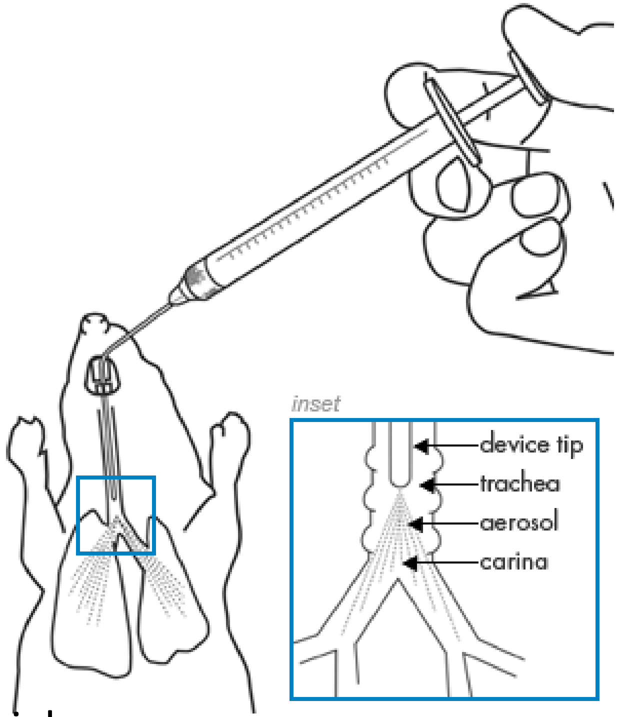

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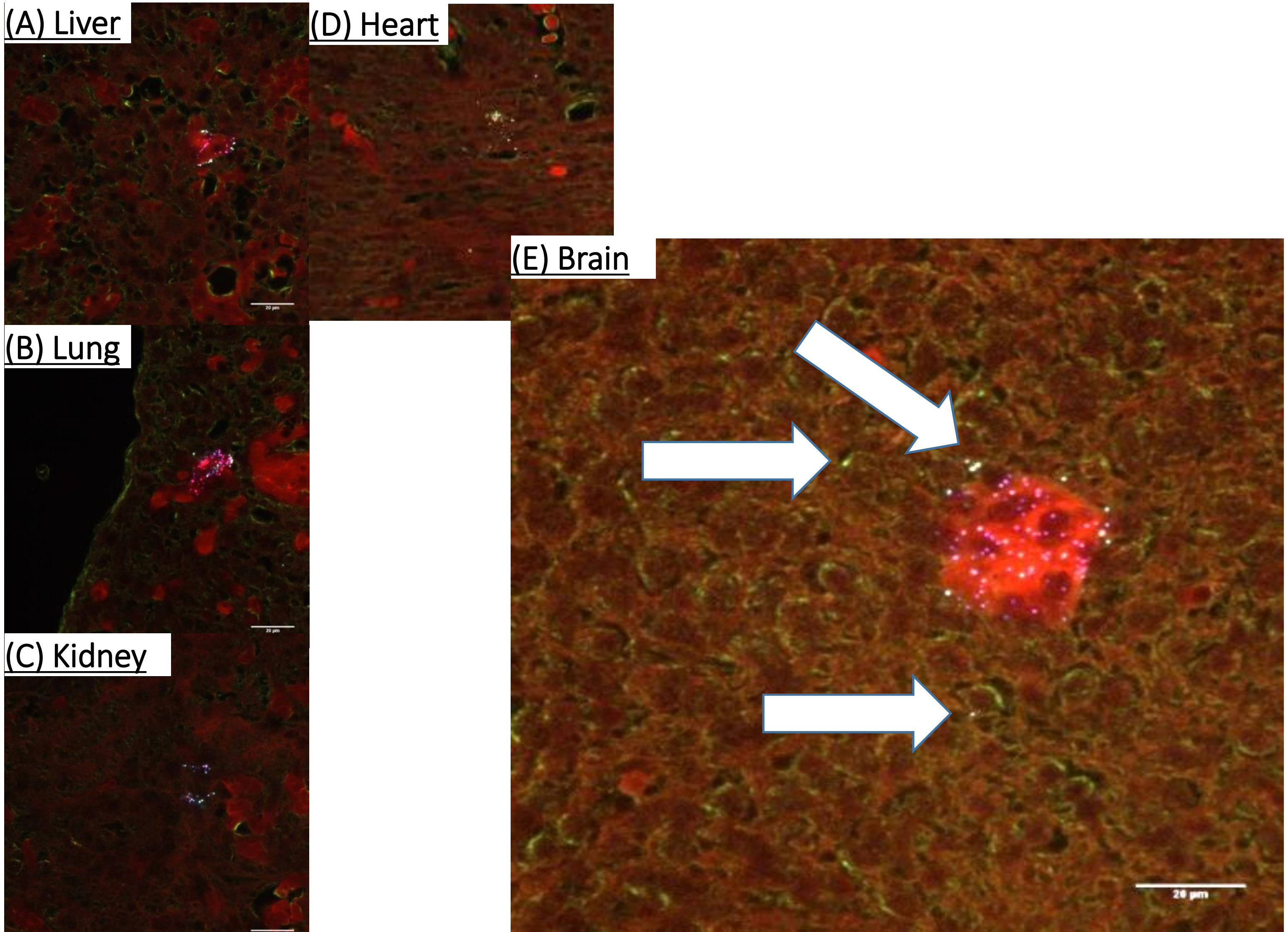
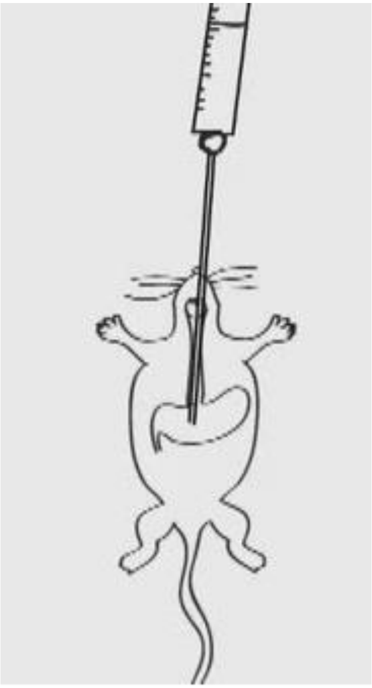


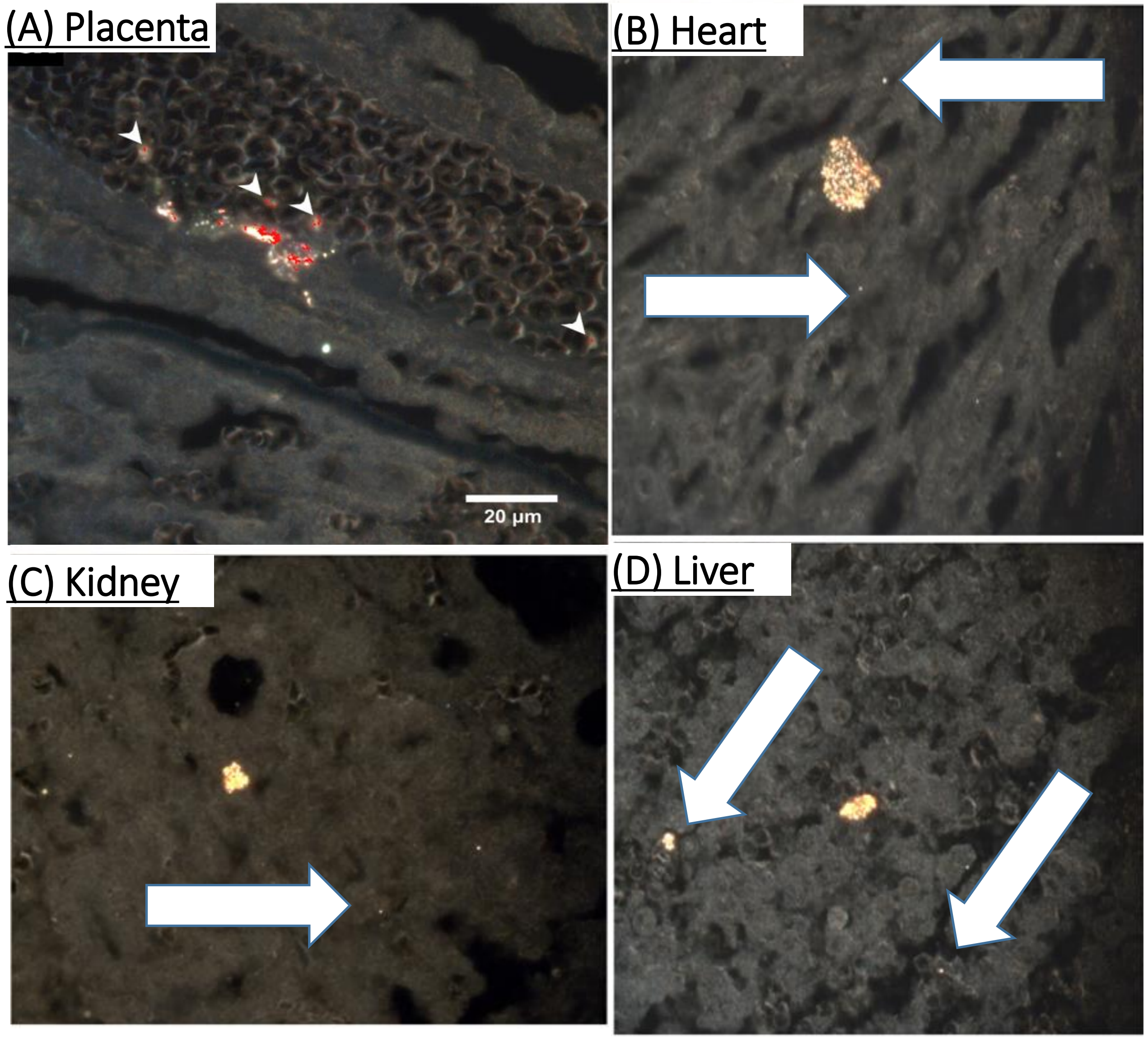
Fournier, 2020

MNP Exposure and Translocation 24h after exposure



Material:
25 nm Carboxylated polystyrene bead
(G) 250 µg/mL, 10 mL/kg

Nanopolystyrene Gavage



Cary, 2023
Pan-Montojo, 2010

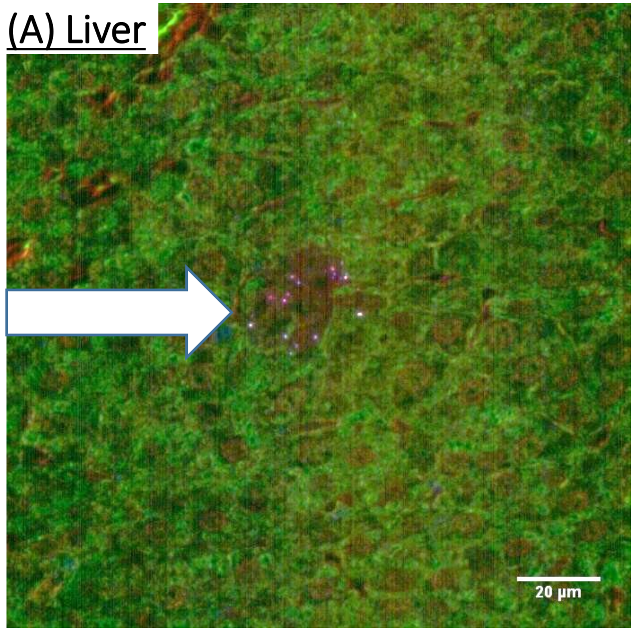
MNP Maternal Transfer to Offspring

Maternal MNP Inhalation
Polyamide-12

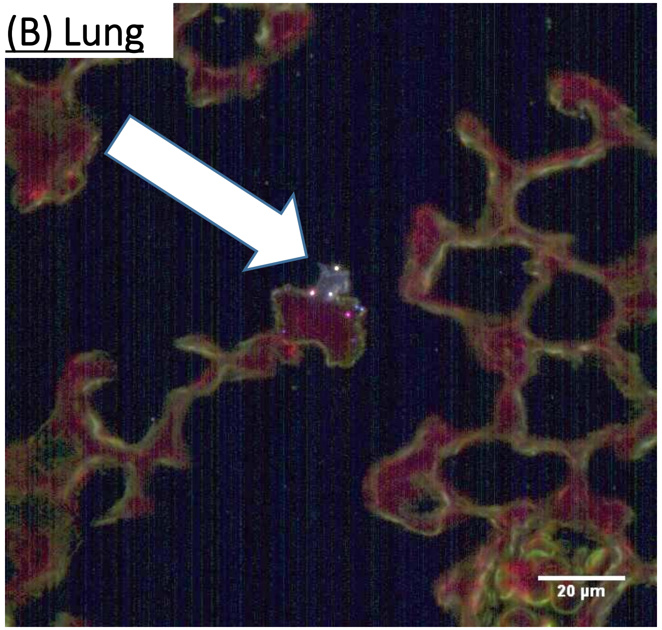
Offspring

2 Weeks of Age

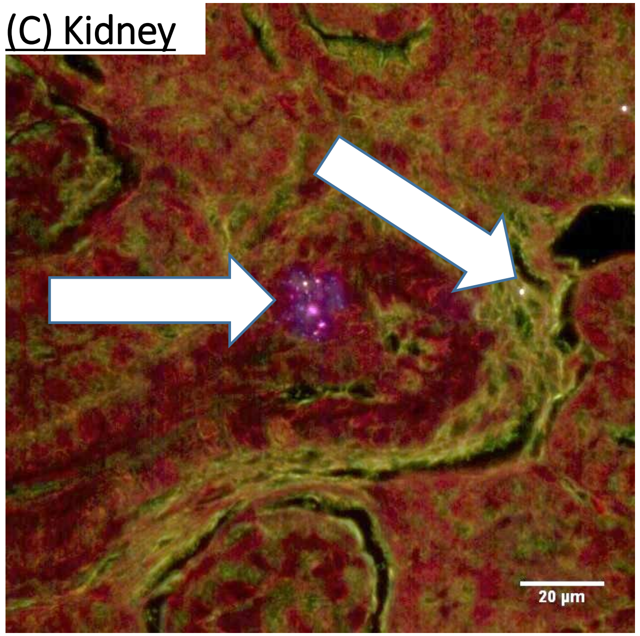
(A) Liver



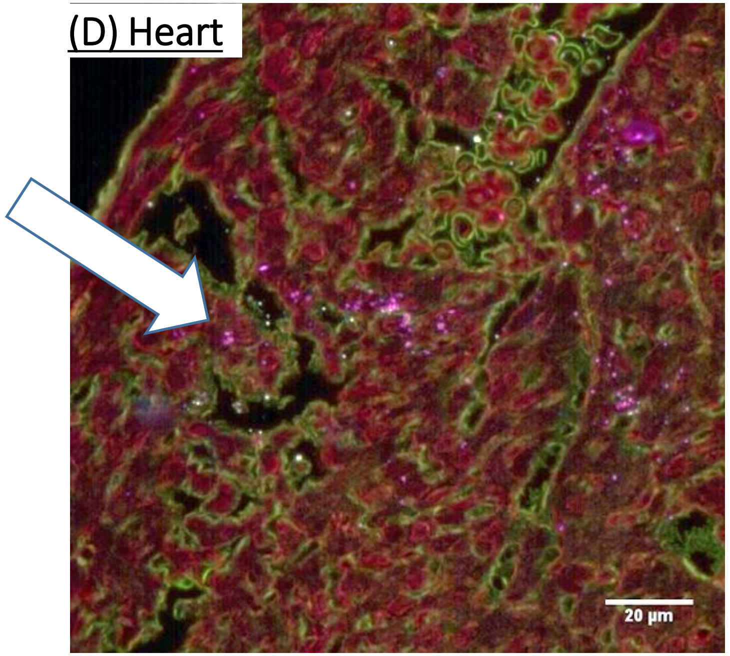
(B) Lung



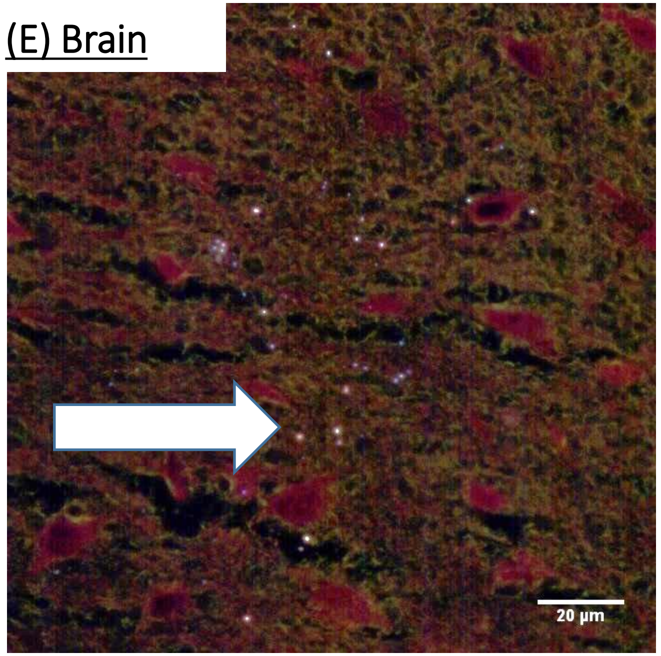
(C) Kidney



(D) Heart



(E) Brain

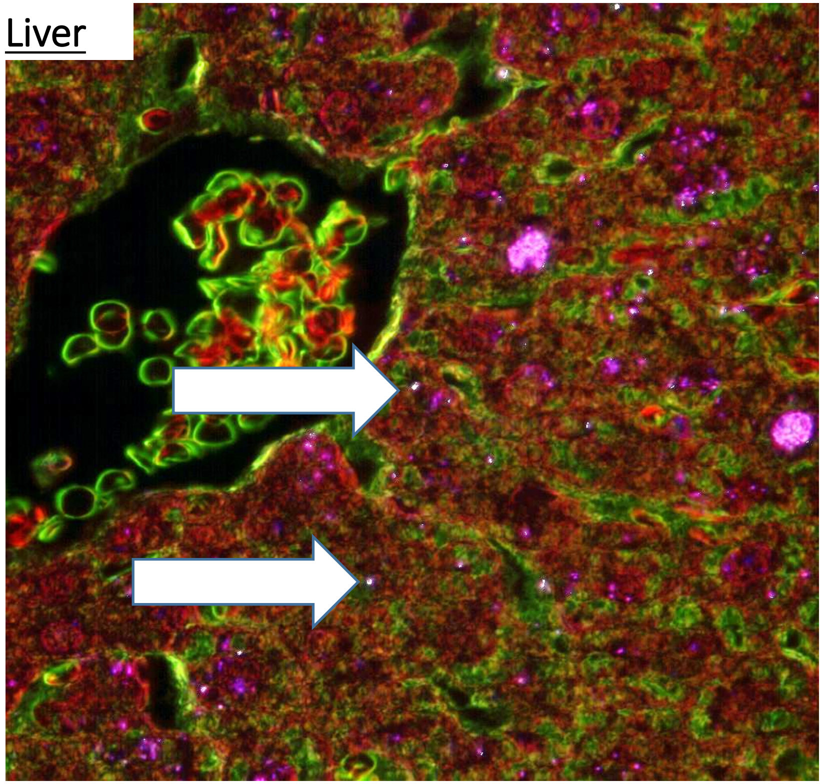


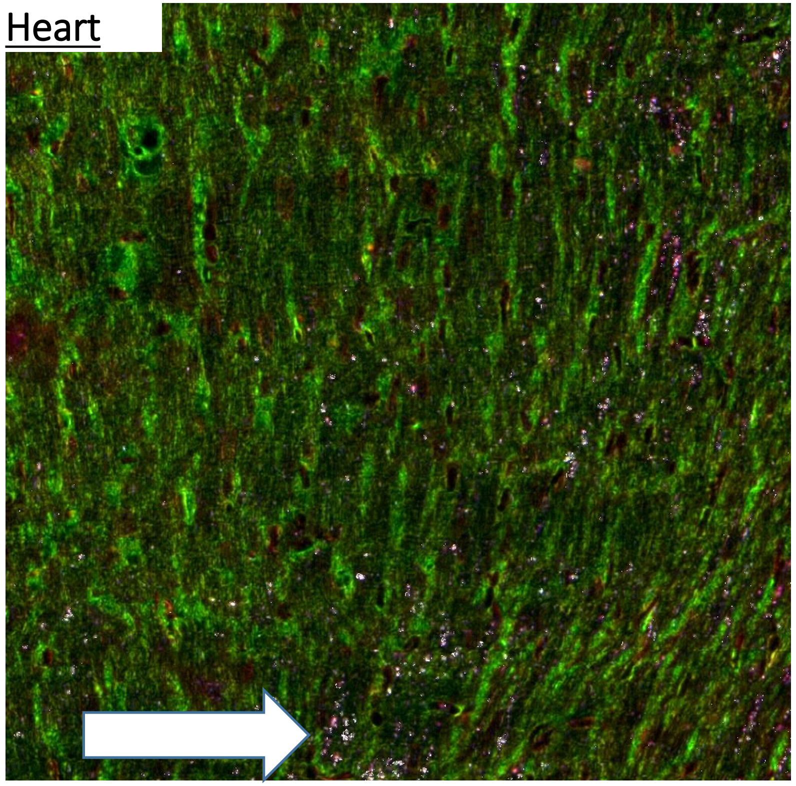
Moreno, 2024

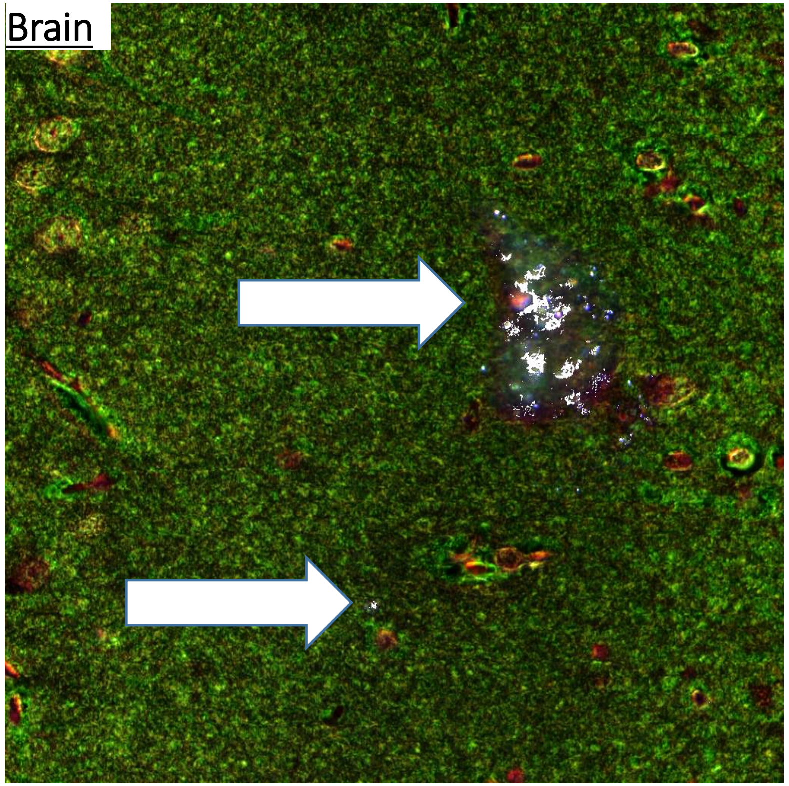
MNP Persistence into Adulthood

Polyamide-12

Offspring at 3 Months of Age



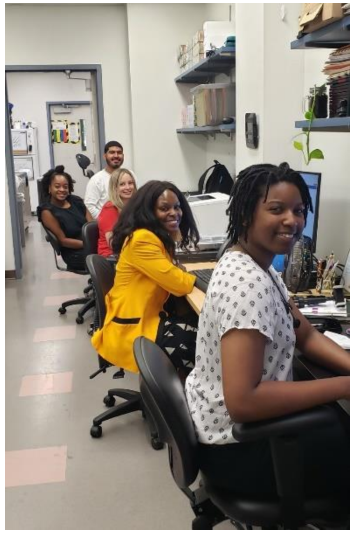




in preparation

Ongoing Projects:

- Understanding Dosimetry Between Exposure Dose and Internal Dose/Bioaccumulation
- Mechanisms of MNP Translocation
- Systemic Toxicities of MNP Exposure and Deposition
- Specific Toxicities of MNP Based on Material Properties



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