Air pollution and ultrafine plastic particles: Breathing for two”

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Genetic and Environmental Toxicology Association (GETA) of Northern California Spring Symposium

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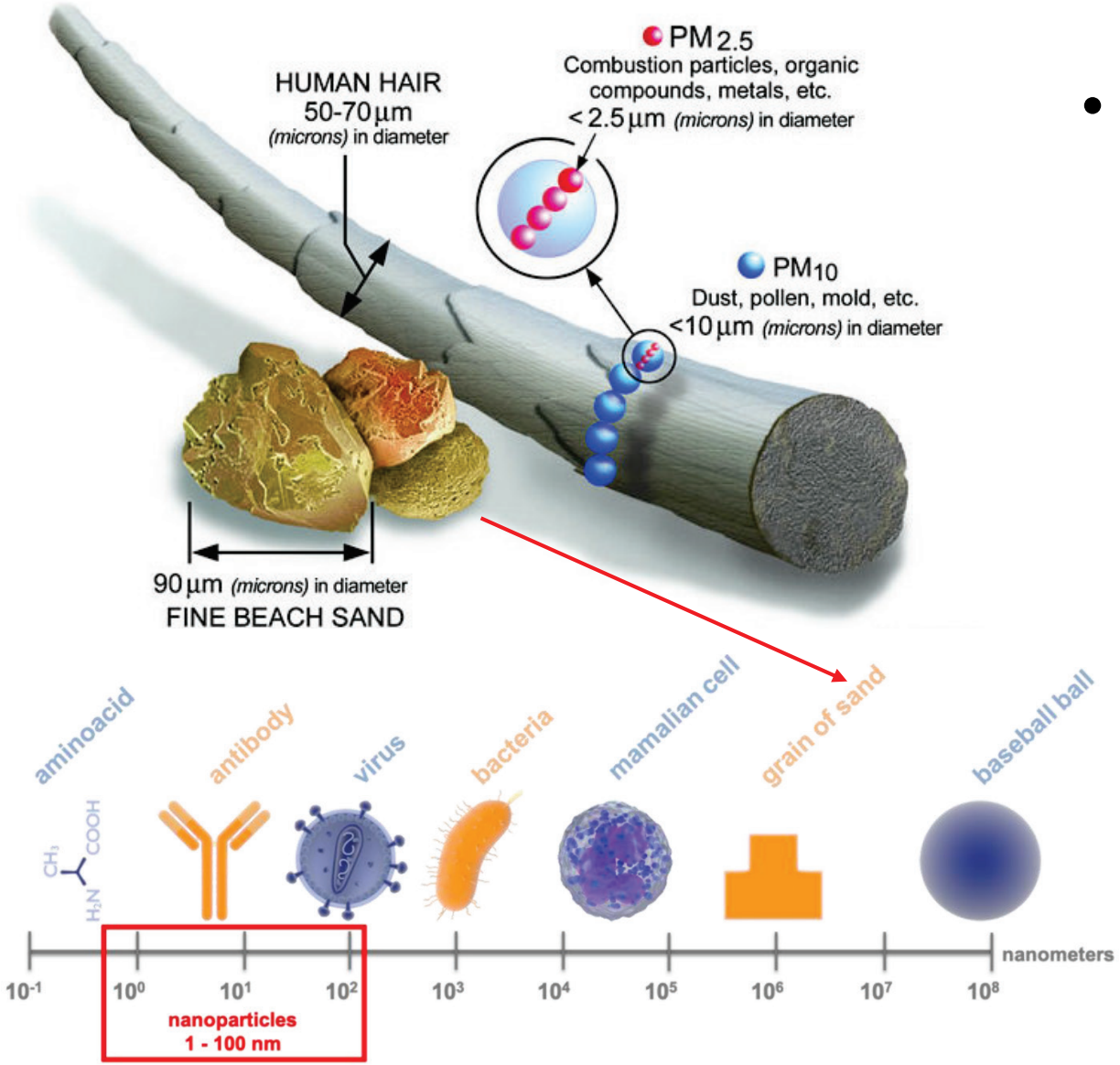
Air Pollution and Particulate Matter (PM) - Epidemiological Studies

- Epidemiologic evidence of cardiovascular (not pulmonary) effects of particulate air pollution.[1]
- Increased incidence of myocardial infarction within 24 hours of inhaled particulate pollution.[2]
- Increased risk of intrauterine growth restriction (IUGR) and/or fetal growth restriction (FGR) from exposure during pregnancy.[3,4]
- Overall, exposure to fine and ultrafine particulate air pollution has adverse effects on cardiopulmonary health.[5,6]

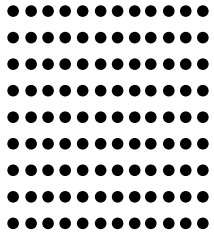
San Francisco, Camp Fire wildfires, 2018

[1.] Dockery, 2001; [2.] Peters, 2001;
[3.] Nobles, 2019; [4.] Liu, 2007
[5.] Pope, 2015; [6.] Van Eeden, 2002

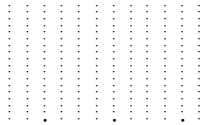
Aerosolized Particles: Particulate Matter (PM)



- Particulate Matter – term for solid particles and liquid droplets in the air



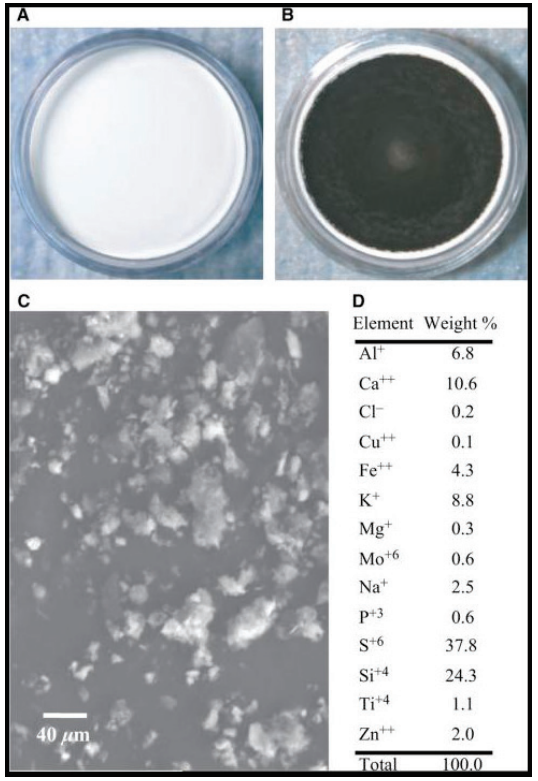
Course PM
PM_{10}: <10µm diameter



Fine PM
$PM_{2.5}$: <2.5µm diameter

Ultrafine PM
$PM_{0.1}$: <0.1µm diameter (also "nanoparticles")

Chemical Constituents



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

Table IV : *Detection limits in μg/g particulate material for 6 analytical techniques. Comparison with average concentrations in urban aerosol (W. Maenhaut, 1989).*

Element	Detection limits						Conc. in urban aerosols
	INAA	ED-XRF[a]	PIXE[a]	ETA-AAS[b]	ICP-AES[b]	ICP-MS[b]	
As	40	40	4	0.2	35	0.04	62
Cd	100	60	100	0.003	1.7	0.06	46
Cr	10	160	8	0.01	4	0.06	150
Cu	1000	60	3	0.02	3.5	0.32	2000
Hg	5	70	10	2	17	0.02	15
In	1		140		40	0.07	2.5
Mn	6	120	6	0.01	0.95	0.10	750
Mo	2000	50	19	0.02	5.5	0.04	32
Ni	500	50	4	0.2	6.5	0.10	200
Pb		80	11	0.05	30	0.05	12000
Sb	10	80	140	0.1	20	0.05	93
Se	10	20	4	0.5	50	0.79	25
Sn		80	160	0.1	17	0.06	200
Tl			11	0.1	25		0.5
V	10	200	13	0.2	3.5	0.03	500
Zn	50	50	3	0.001	1.2	0.21	5200

[a] A particulate loading of 100 μg/cm^2 on the filter was assumed
[b] For solutions, containing 0.1 % dissolved particulate material

Table 2. Statistical summary of PM_{10} and Particle bound chemical constituents at Jogannapalem and Parawada sites.

	Jogannapalem				Parawada			
	Min.	Max.	Mean	Stdev.	Min.	Max.	Mean	Stdev.
PM_{10}	34.8	109.7	65.4	17.9	32.3	137.3	74.7	26.2
Al	1109.7	8873.2	4079.5	1980.9	729.1	9877.9	3828.0	1923.5
Ca^{2+}	223.1	6399.9	2361.1	1371.1	300.0	6880.0	2501.5	1137.5
Cr	0.8	31.1	7.4	6.7	0.9	53.9	9.6	9.5
Cu	0.6	20.8	3.5	3.2	0.2	53.4	9.9	9.9
Ni	0.7	34.8	6.2	6.8	0.8	28.3	7.3	4.8
Pb	1.6	27.6	9.1	4.7	1.1	83.2	23.0	15.7
Mn	7.1	797.6	154.2	153.9	0.3	62.8	18.2	13.2
Zn	79.9	1909.2	676.8	407.4	60.4	3686.8	927.5	692.2
V	0.3	16.2	3.5	3.1	0.6	18.3	5.2	3.4
Fe	63.9	7538.5	2741.0	1406.5	287.6	5646.9	2350.8	1270.9
As	0.2	7.3	2.5	1.6	0.2	24.3	5.3	5.3
F^-	0.5	177.0	54.3	31.1	4.8	1260.0	127.5	141.5
Cl^-	105.7	4951.5	1805.3	1394.5	306.9	2584.3	948.4	384.8
NO_3^-	386.0	1669.0	840.3	291.9	400.3	4256.0	1833.3	840.5
SO_4^{2-}	1199.0	5336.0	2854.6	1056.0	717.2	7336.0	3194.8	1432.0
K^+	398.4	11,716.5	3156.2	2323.5	240.0	5874.0	2361.2	1061.1
Na^+	88.3	2971.9	1229.7	672.6	226.8	1980.1	710.1	291.5
Mg^{2+}	85.1	963.6	351.1	201.6	55.0	760.0	287.9	151.7
Cd	<0.01	<0.01	<0.01	<0.01	0.04	8.0	1.9	1.6

*Chemical species values are expressed in ng/m^3; PM_{10} values are in μg/m^3.

Knuckles, 2013; Adams, 2002; Police, 2016

Indoor Exposures

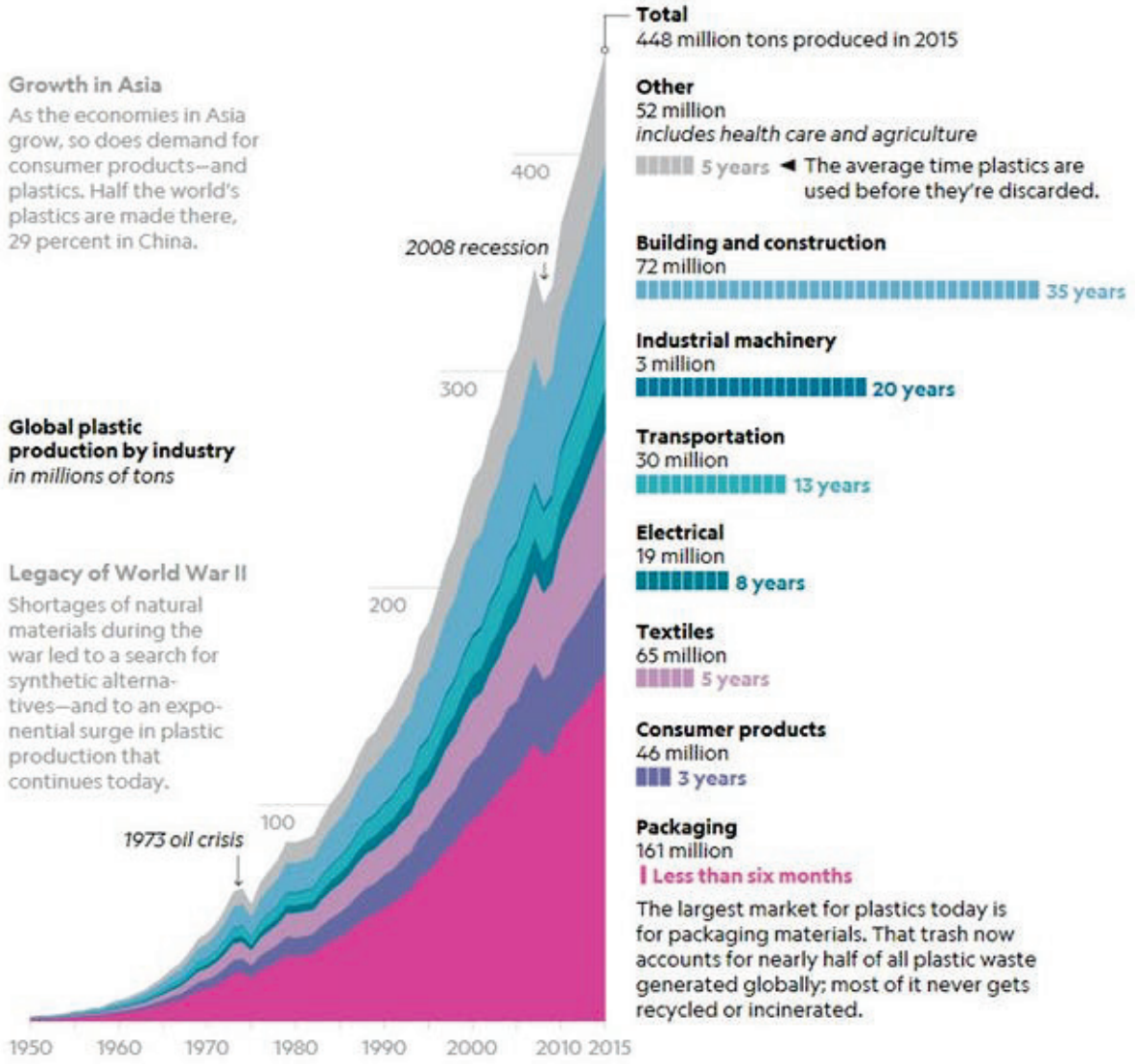
Furniture/Carpeting/Clothing
Coatings
Containers

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

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

A LIFETIME OF PLASTIC

The first plastics made from fossil fuels are just over a century old. They came into widespread use after World War II and are found today in everything from cars to medical devices to food packaging. Their useful lifetime varies. Once disposed of, they break down into smaller fragments that linger for centuries.



Total
448 million tons produced in 2015

Other
52 million
includes health care and agriculture
5 years ◄ The average time plastics are used before they're discarded.

Building and construction
72 million
35 years

Industrial machinery
3 million
20 years

Transportation
30 million
13 years

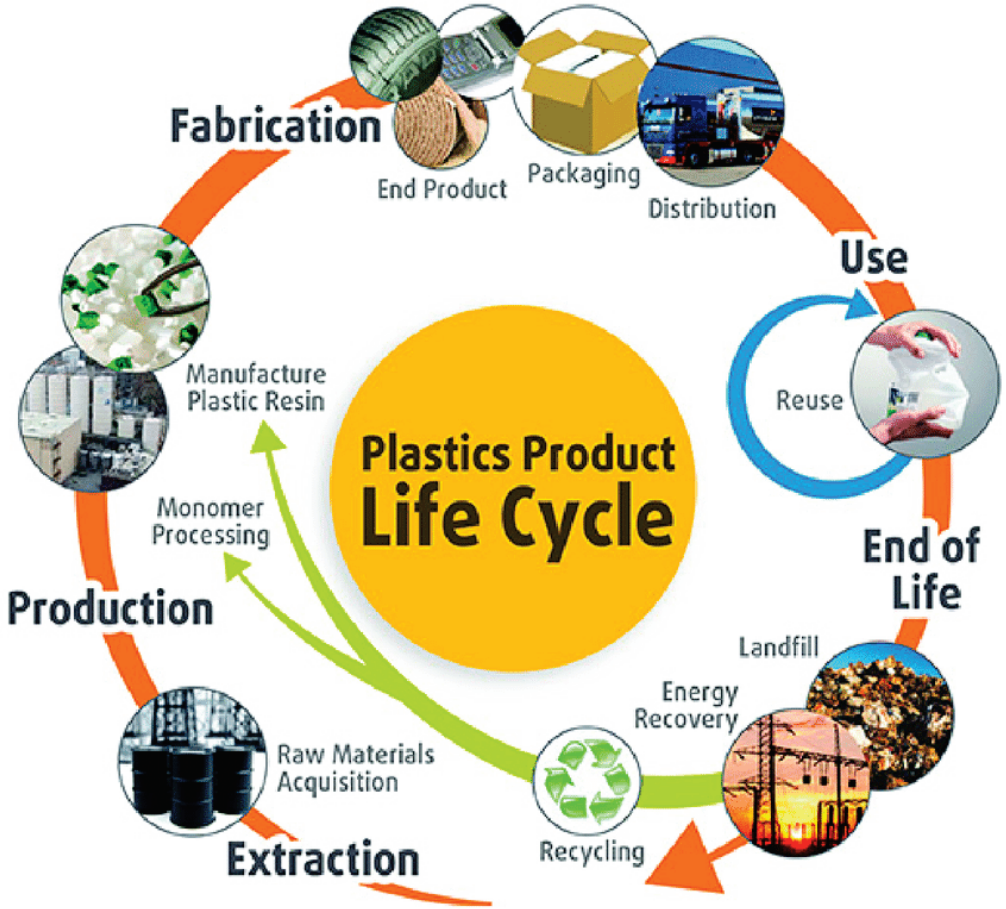
Electrical
19 million
8 years

Textiles
65 million
5 years

Consumer products
46 million
3 years

Packaging
161 million
Less than six months

The largest market for plastics today is for packaging materials. That trash now accounts for nearly half of all plastic waste generated globally; most of it never gets recycled or incinerated.



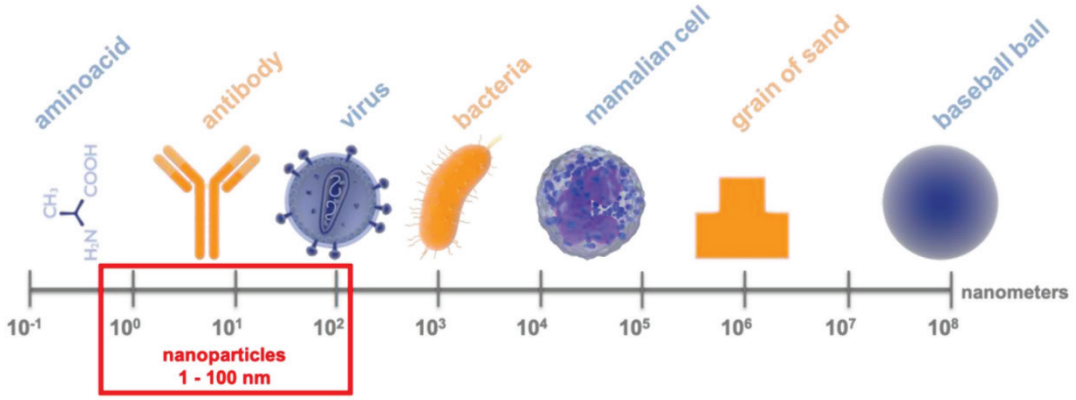
<10 %

Breakdown of plastics ranges from 10 – 1000 years.

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

Unfortunately, this concept of decomposition is unclear. Not always referring to chemical degradation. May refer to particle size.

Micro- and nanosized particles



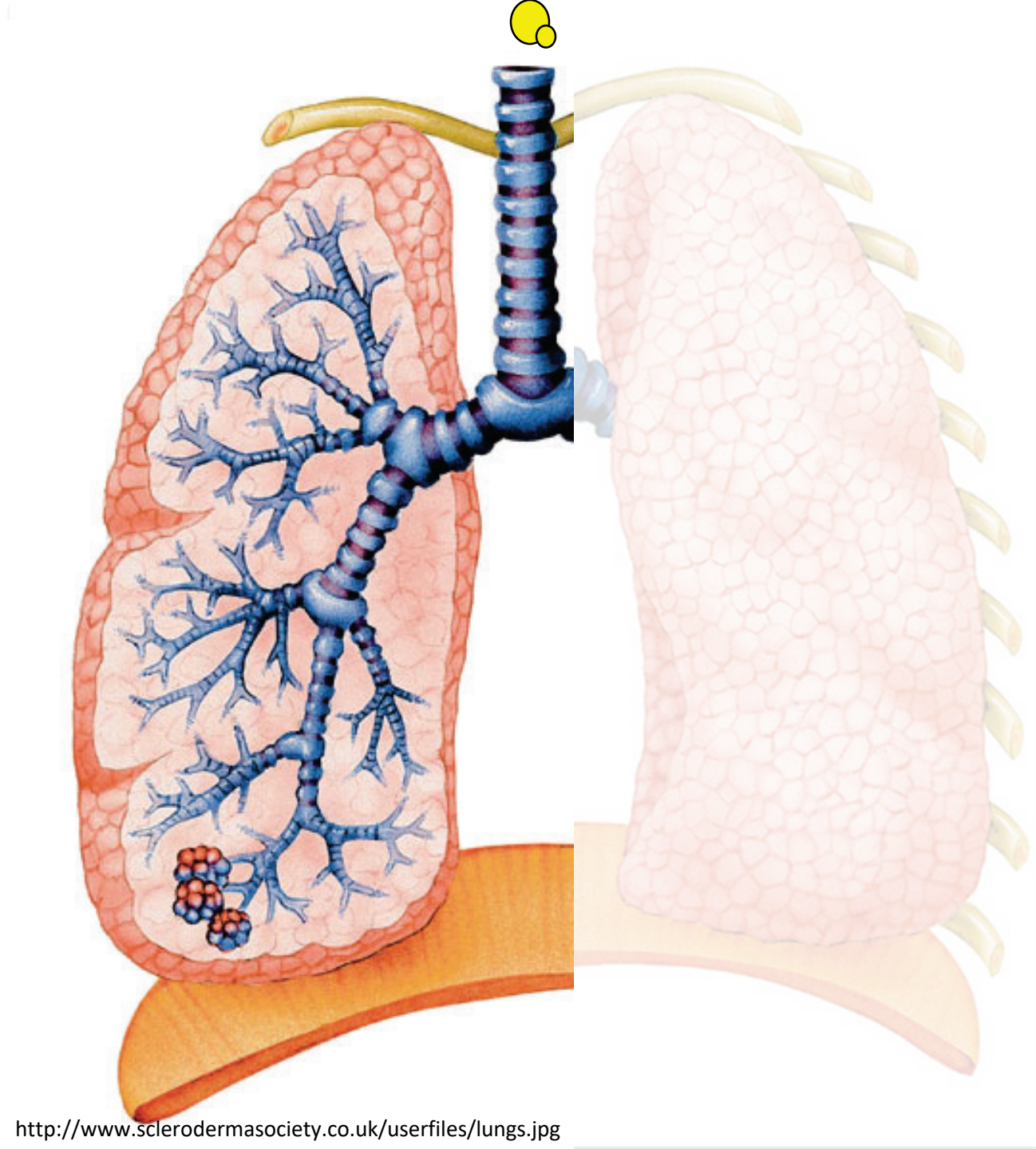
Microplastics are not a specific kind of plastic, but rather any type of plastic fragment that is less than 5 mm in length.

(Sesame Seed)

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



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

Pulmonary Ultrafine/Nanoparticle Exposure

- Pulmonary particle retention in the lung[1]
- Pulmonary inflammation leading to systemic inflammation following exposure[2]
- Sympathetic neural activation[3]
- Particle translocation from the lungs to systemic organs[4]

Animation – Dr. Cody Nichols

[1]Husain, 2013

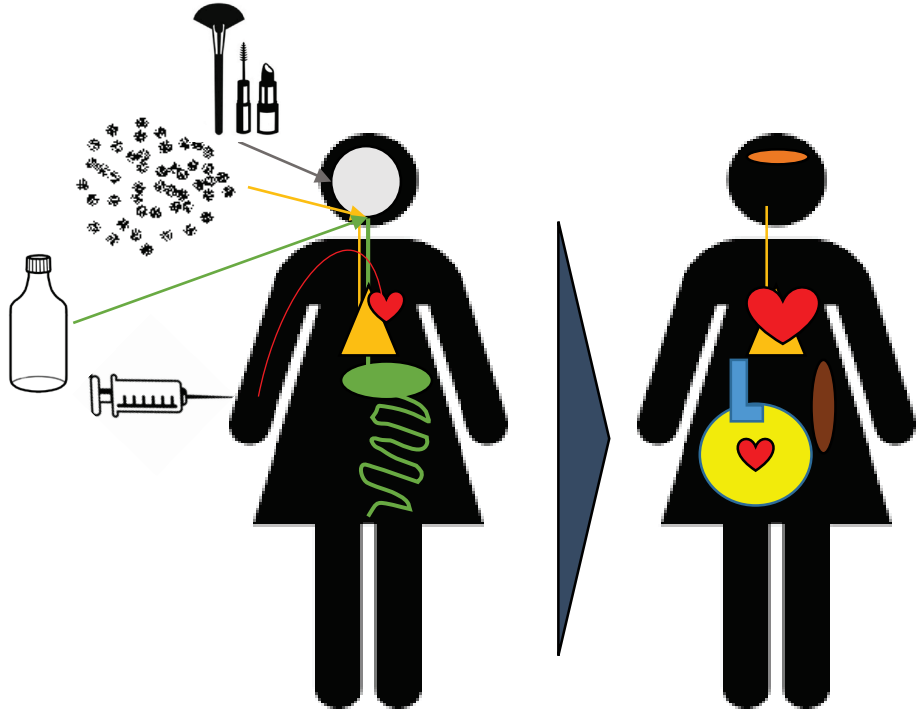
[2]Baisch, 2014

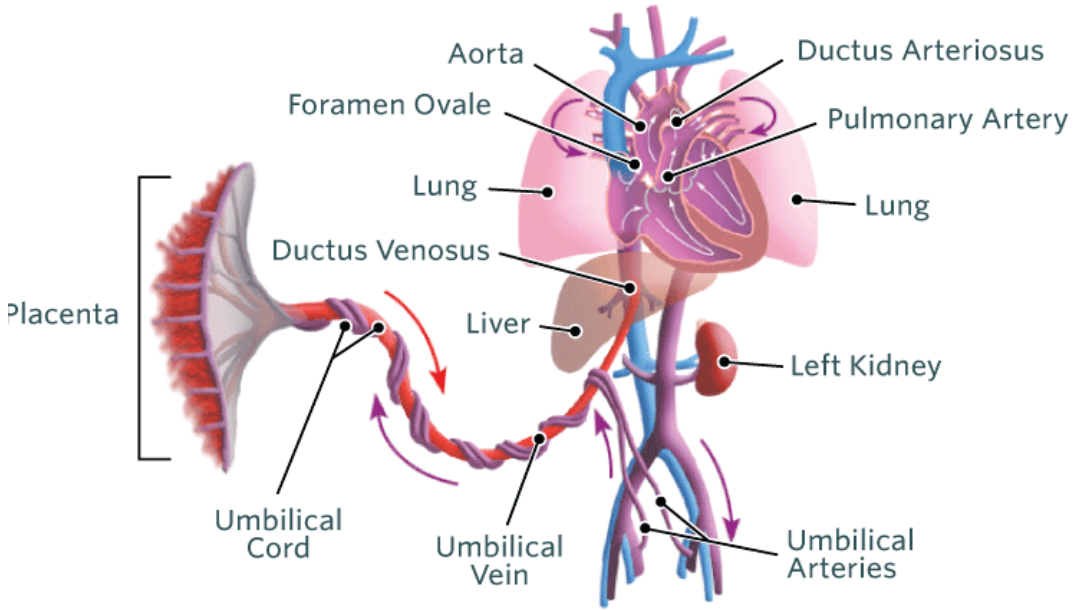
[3]Knuckles, 2012; Stapleton, 2015

[4]Elder, 2006; Stapleton, 2012

Maternal-Fetal Model

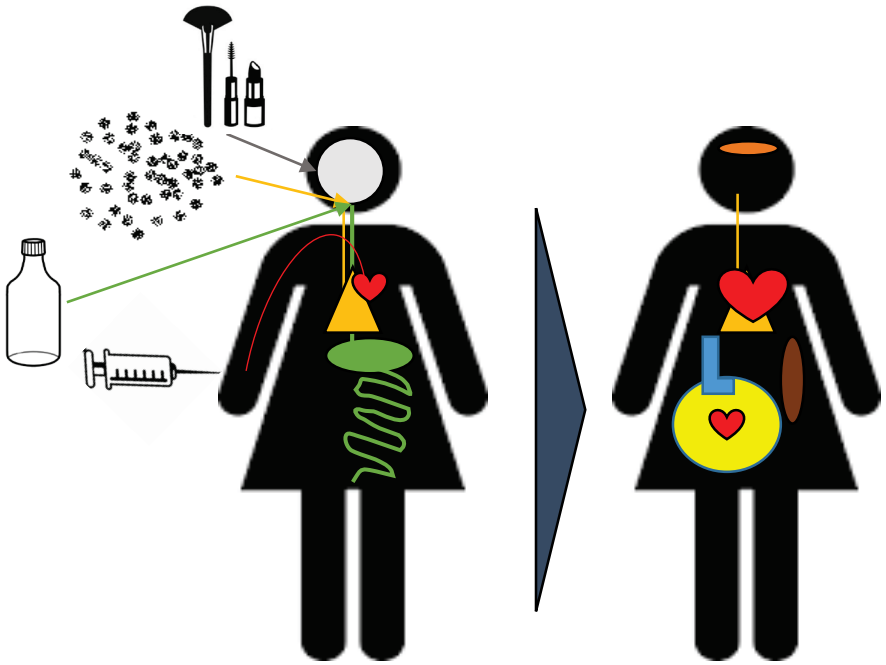
- Complex and widely understudied model
  - Rapid and precise development
  - Hormonal variation
  - Physiological disparities (normal)
    - Increased Blood Volume
    - Increased Heart Size
    - Increased Tidal Volume
  - Maternal Health
  - Placental Barrier
  - Fetal/Progeny Health





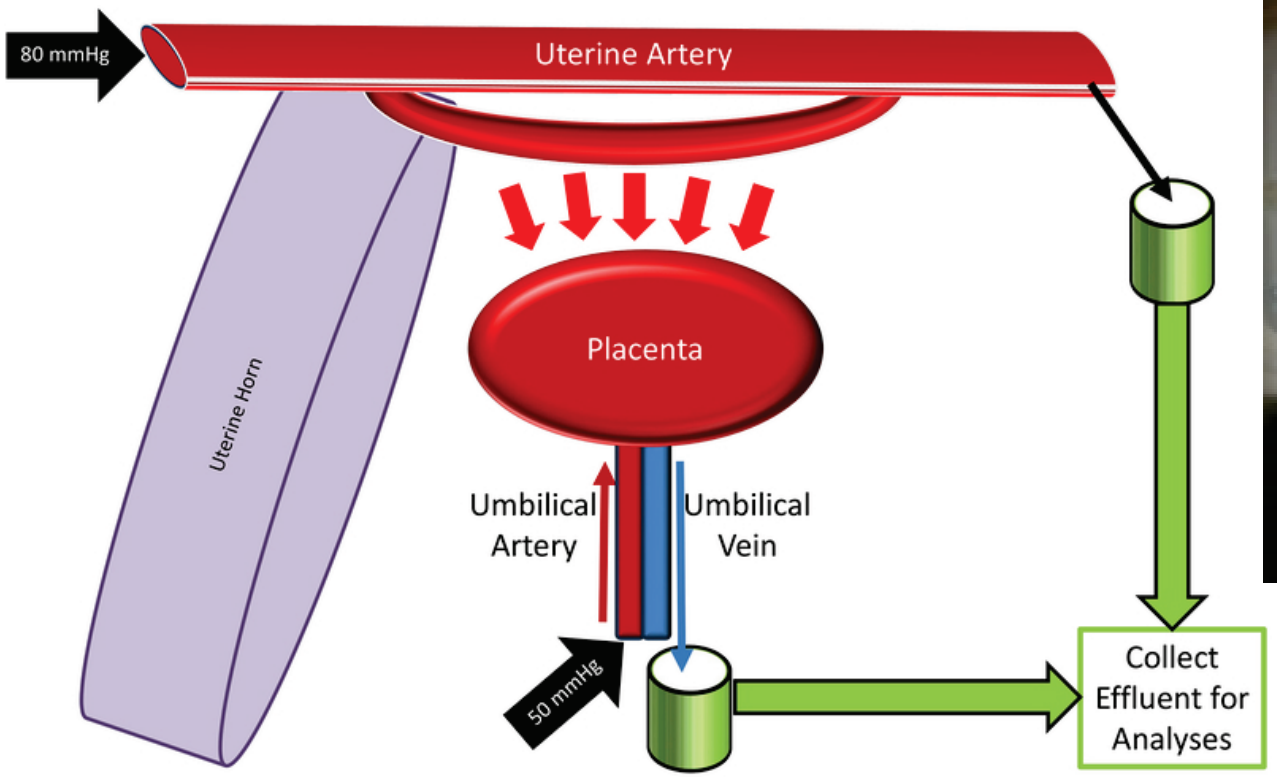
Stapleton, 2019; Campagnolo, 2017; Hougaard, 2015

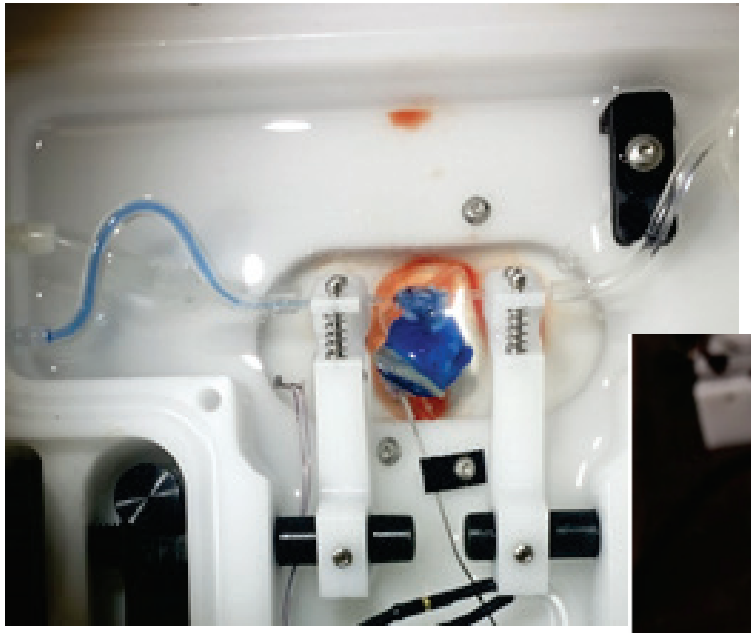
<u>Hypothesis</u>: Nanoplastic particles can migrate from the mother's lungs to fetal tissues after pulmonary exposure.

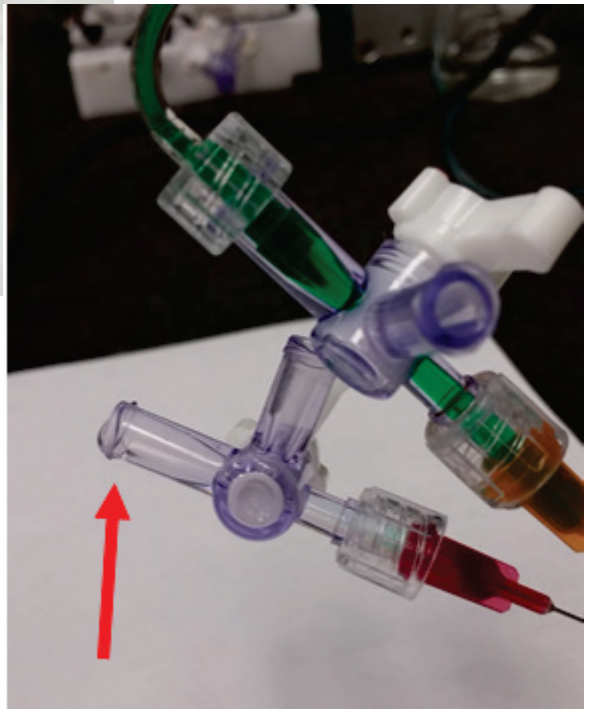


Can the placenta act as a barrier to nanoplastic particles?

Developed a Placental Perfusion Technique

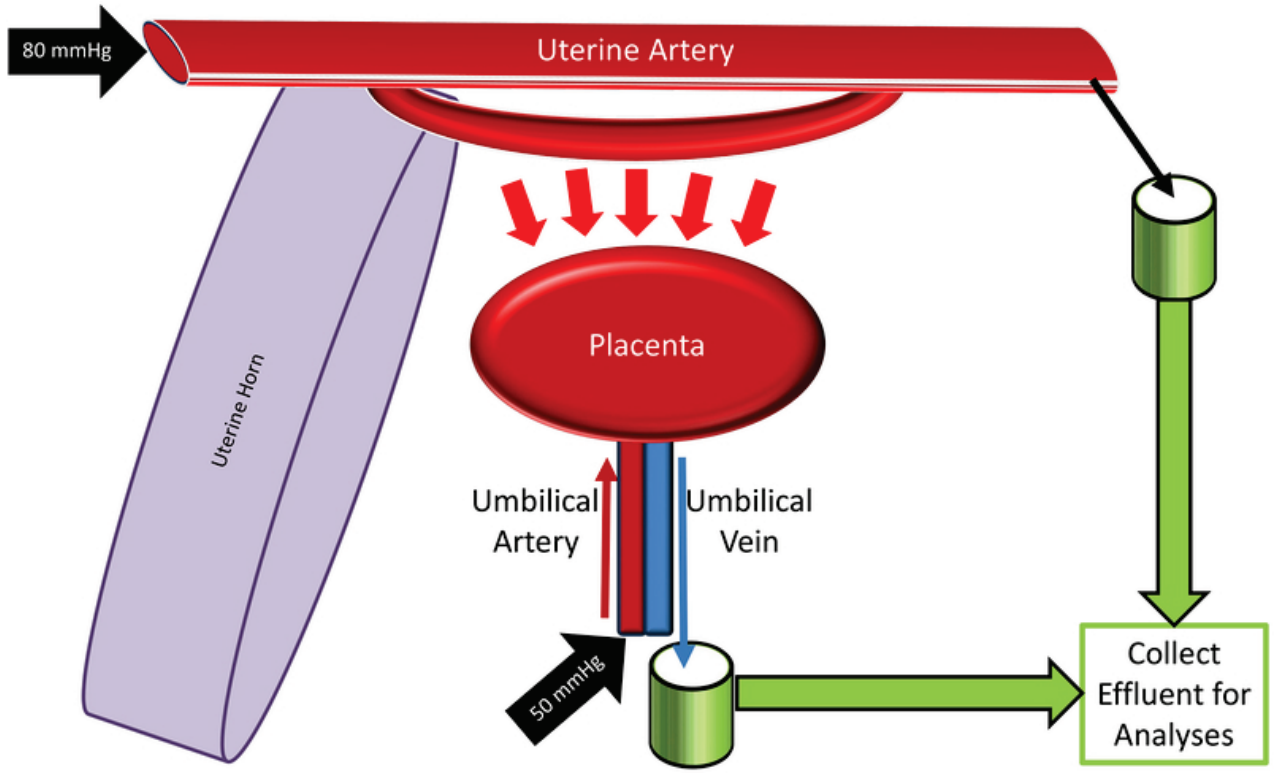






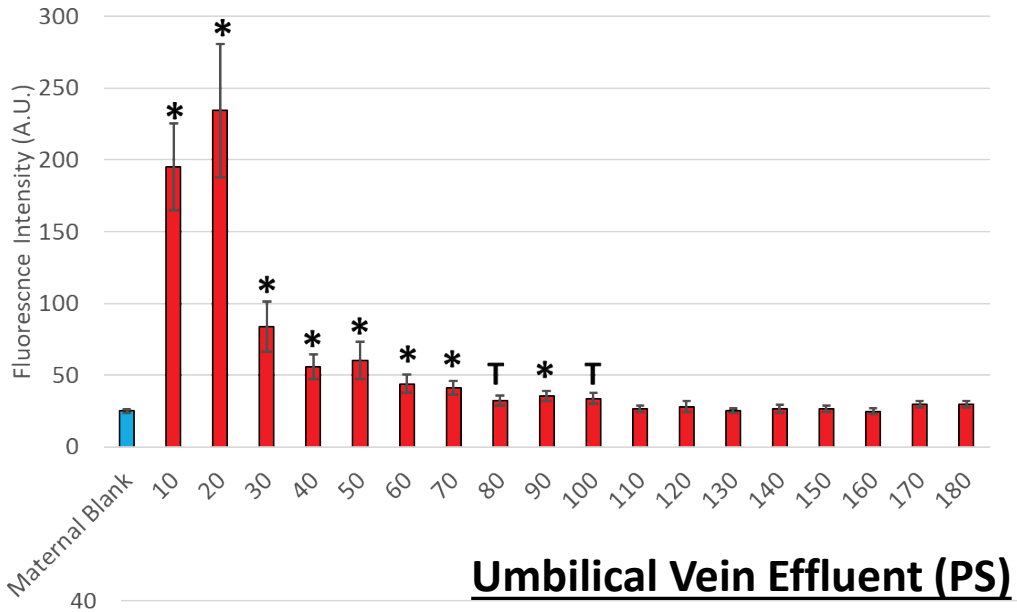
D'Errico, 2019a

Can the placenta act as a barrier?

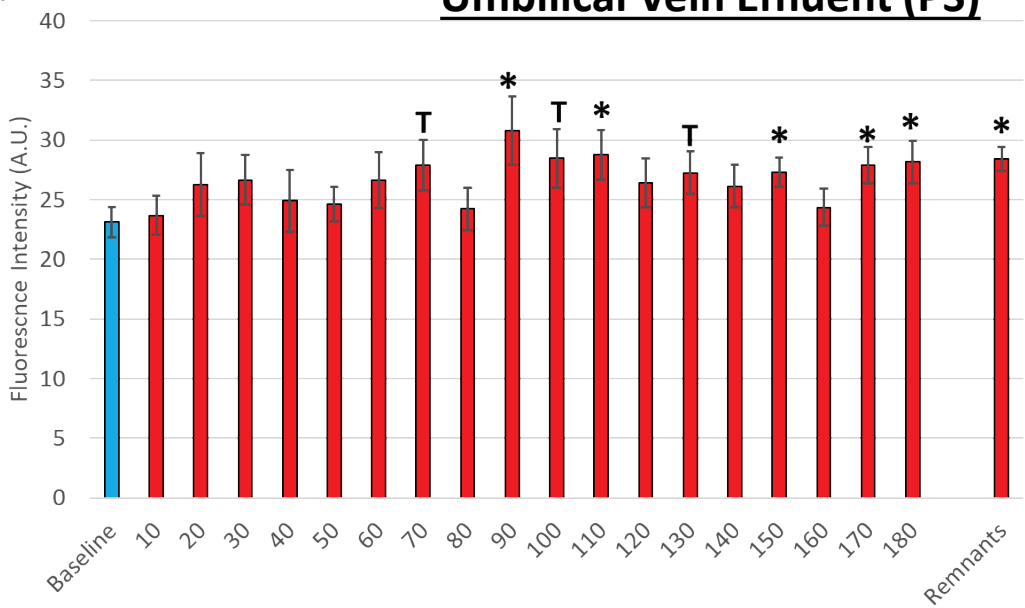


POLYSTYRENE ENM

Uterine Artery Effluent (PS)



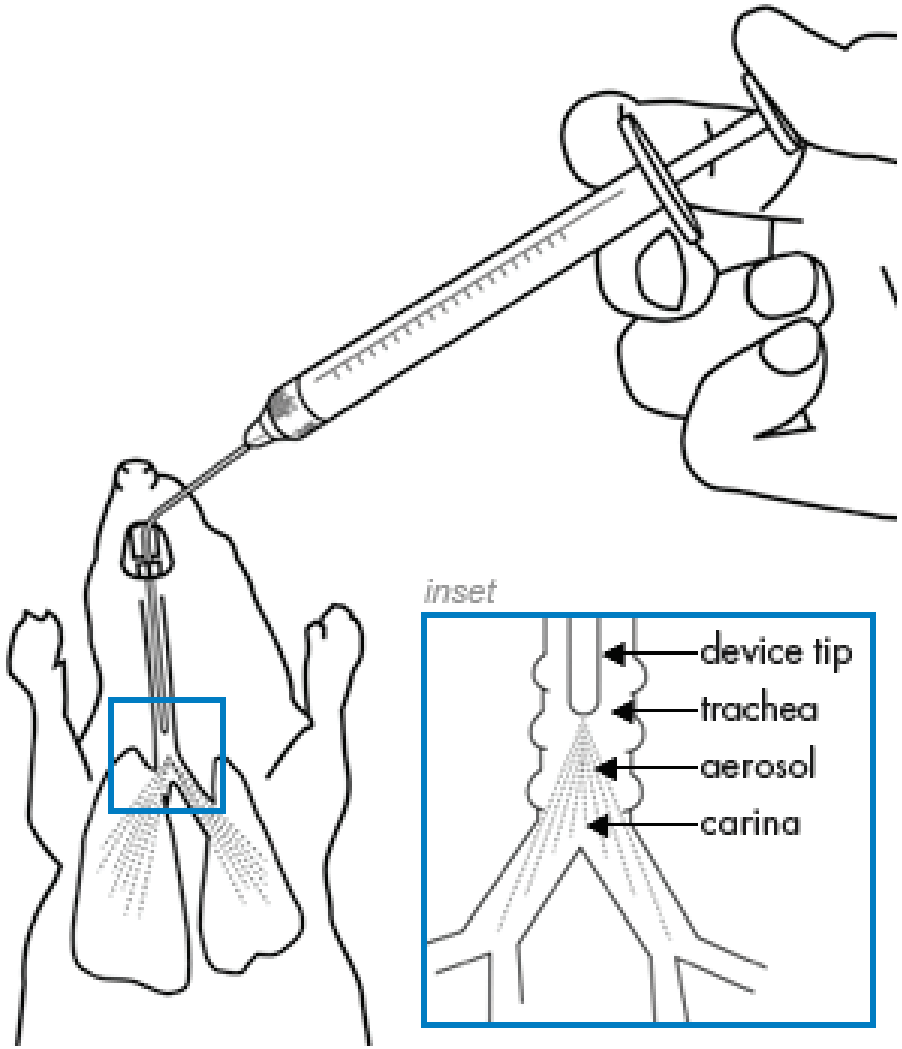
Umbilical Vein Effluent (PS)



Placenta* does not *act as a barrier to nanoplastic particles ex vivo.

D'Errico, 2019; Fournier, 2020

Experimental Design: *In Vivo Exposure*



- **Dosimetry – Particle Dosage**
- ***Particle Characterization – Confirmation of Manufacturing***
- **Intratracheal Instillation – Exposure**

- Maternal/Litter Characteristics – Overall Health
- Optical Imaging – Visualize Material
- DarkField Microscopy – Visualize Material

- Exposure on Gestational Day 19 – single dose
- Control: 300 µL of sterile saline

- Exposure: 300 µL of Rhodamine-Labelled polystyrene beads containing 2.64×10^{14} nanoplastic particles

- Sacrifice Gestational Day 20

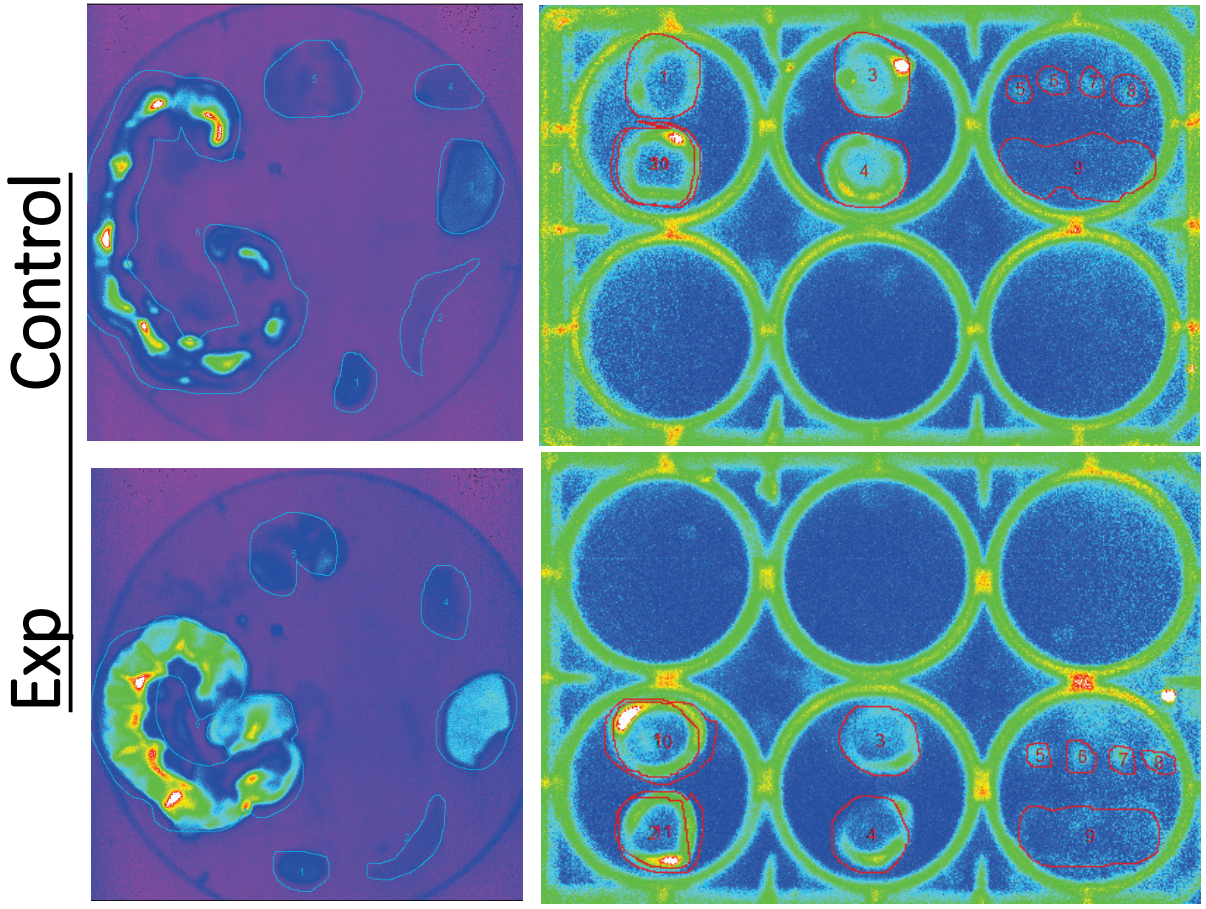
Maternal Characteristics at 24h

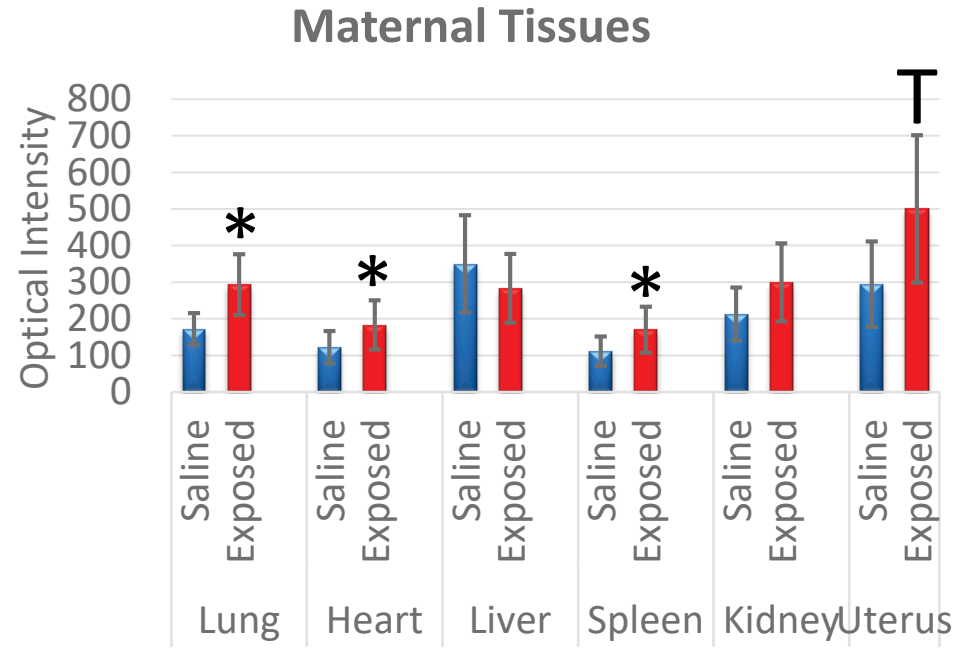
	Pregnant (Saline)	Pregnant (Nano-polystyrene)
Maternal Weight (g)	302 ± 6	302 ± 14
MAP (mmHg)	74.4 ± 1.5	**85* ± 3.8**
Maternal Heart Weight (g)	0.74 ± 0.02	**0.88*± 0.05**
Maternal Heart Weight to Body Weight (%)	0.24 ± 0.004	**0.29*± 0.02**
Number of Reabsorption Sites	0.63 ± 0.25	**1.83* ± 0.47**
Number of Pups	9.56 ± 0.63	8.33 ± 0.76
Pup Weight (g)	4.52 ±.0.05	**4.32* ± 0.10**

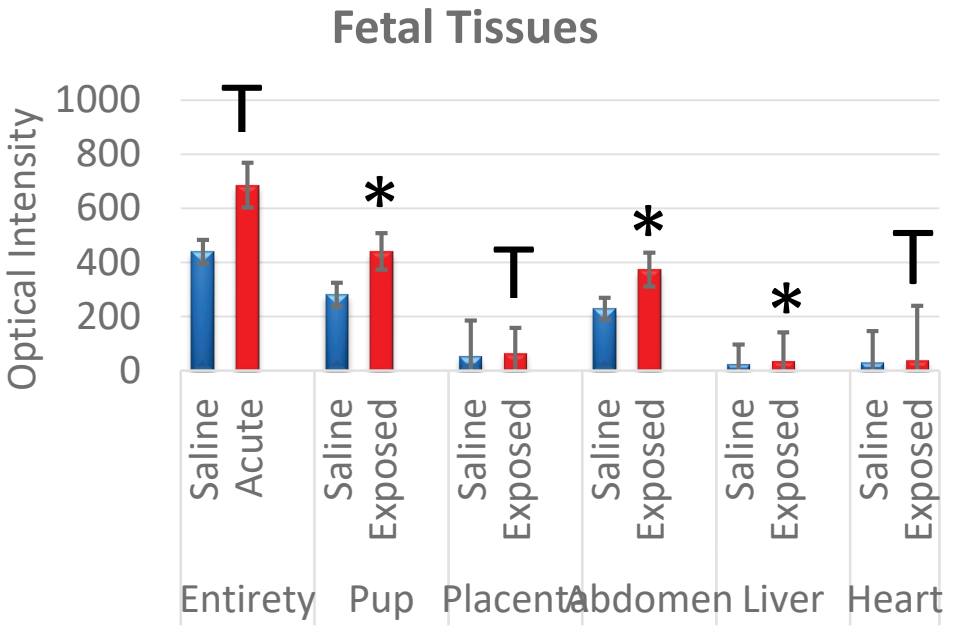
*** $p < 0.05$**

Nanoplastic Translocation to the Fetal Compartment

- *In Vivo* Translocation (Optical Imaging)





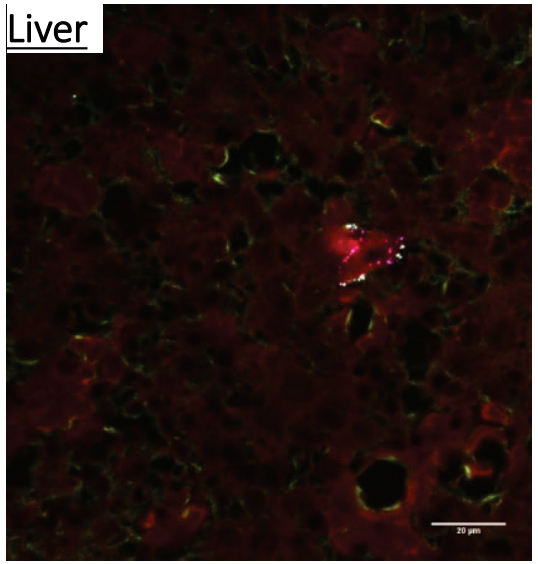


Fournier, 2020

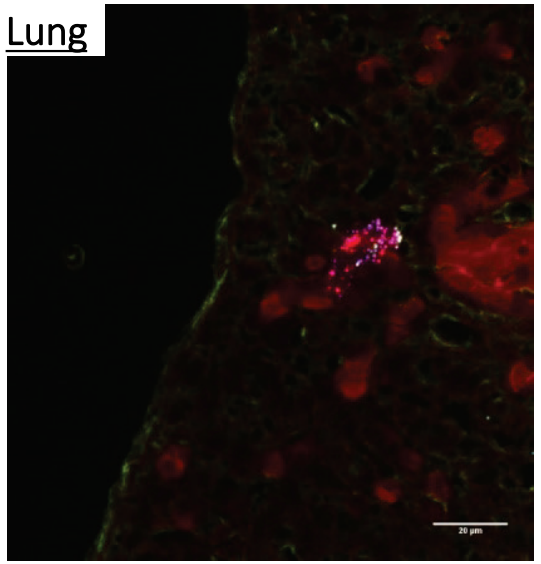
Nanoplastic Translocation to the Fetal Compartment

(Dark-Field Microscopy)

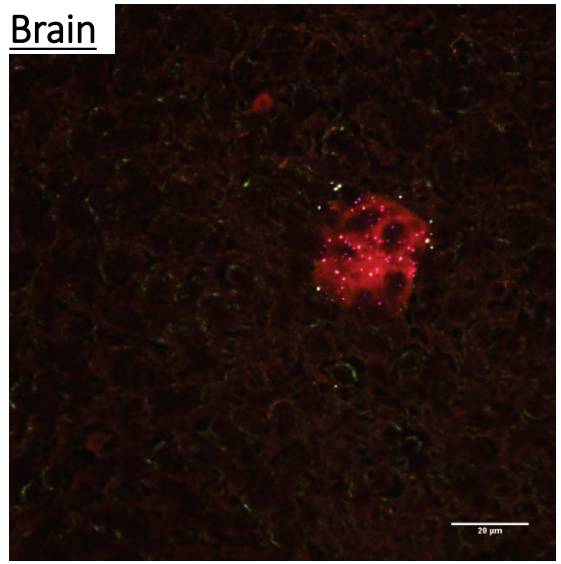
Liver



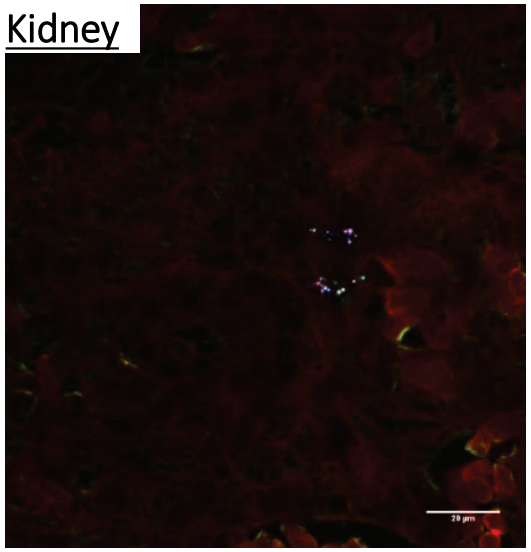
Lung



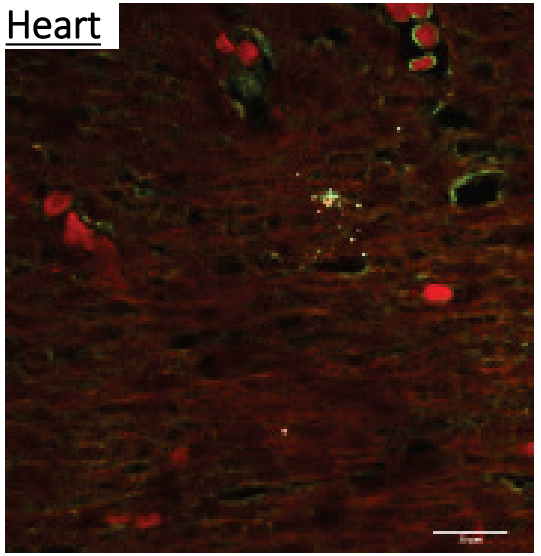
Brain

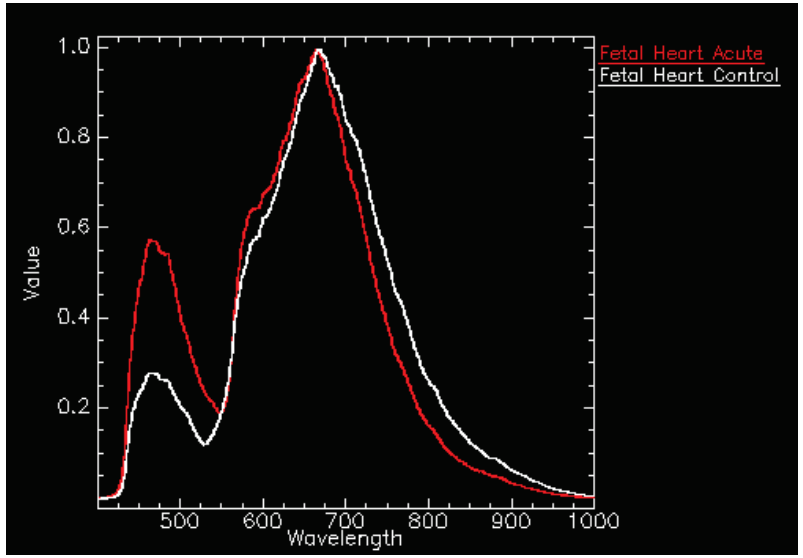


Kidney



Heart

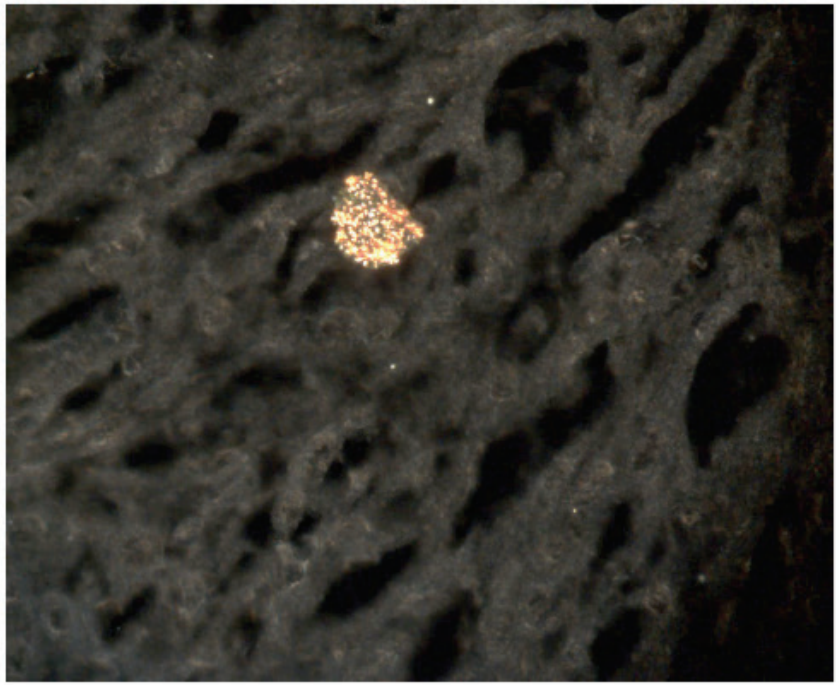




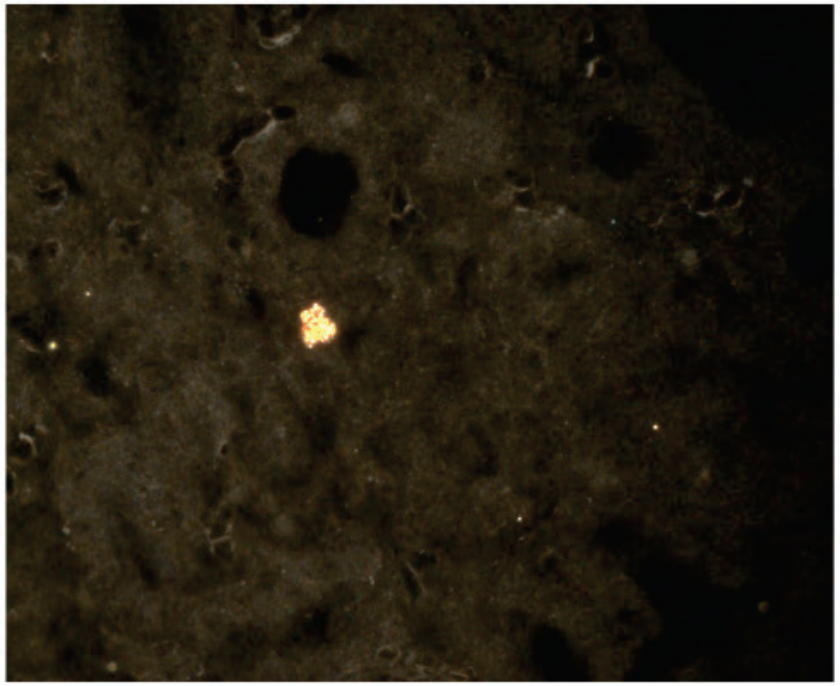
Fournier, 2020

And through ingestion… to the fetal _____

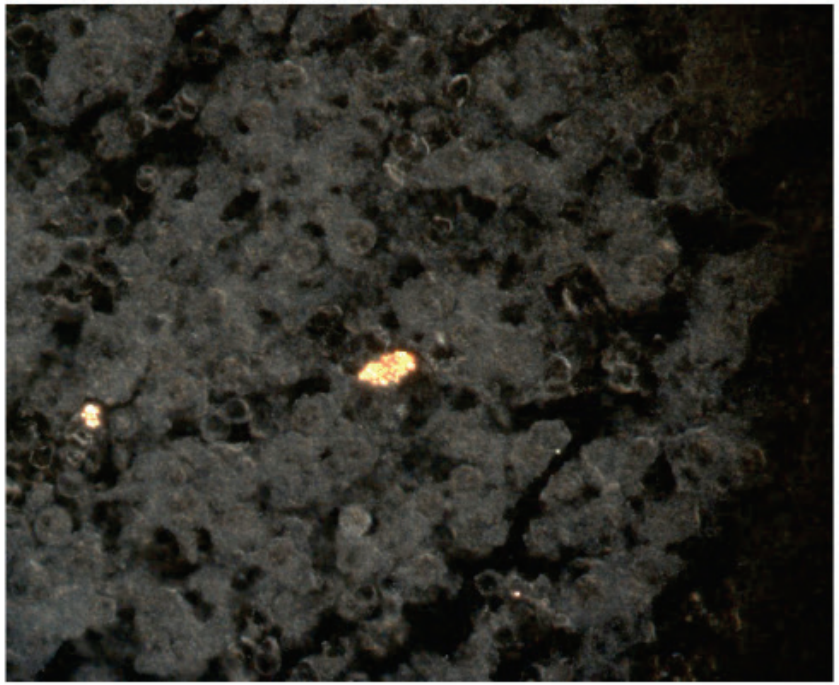
CytoViva®



Heart



Kidney

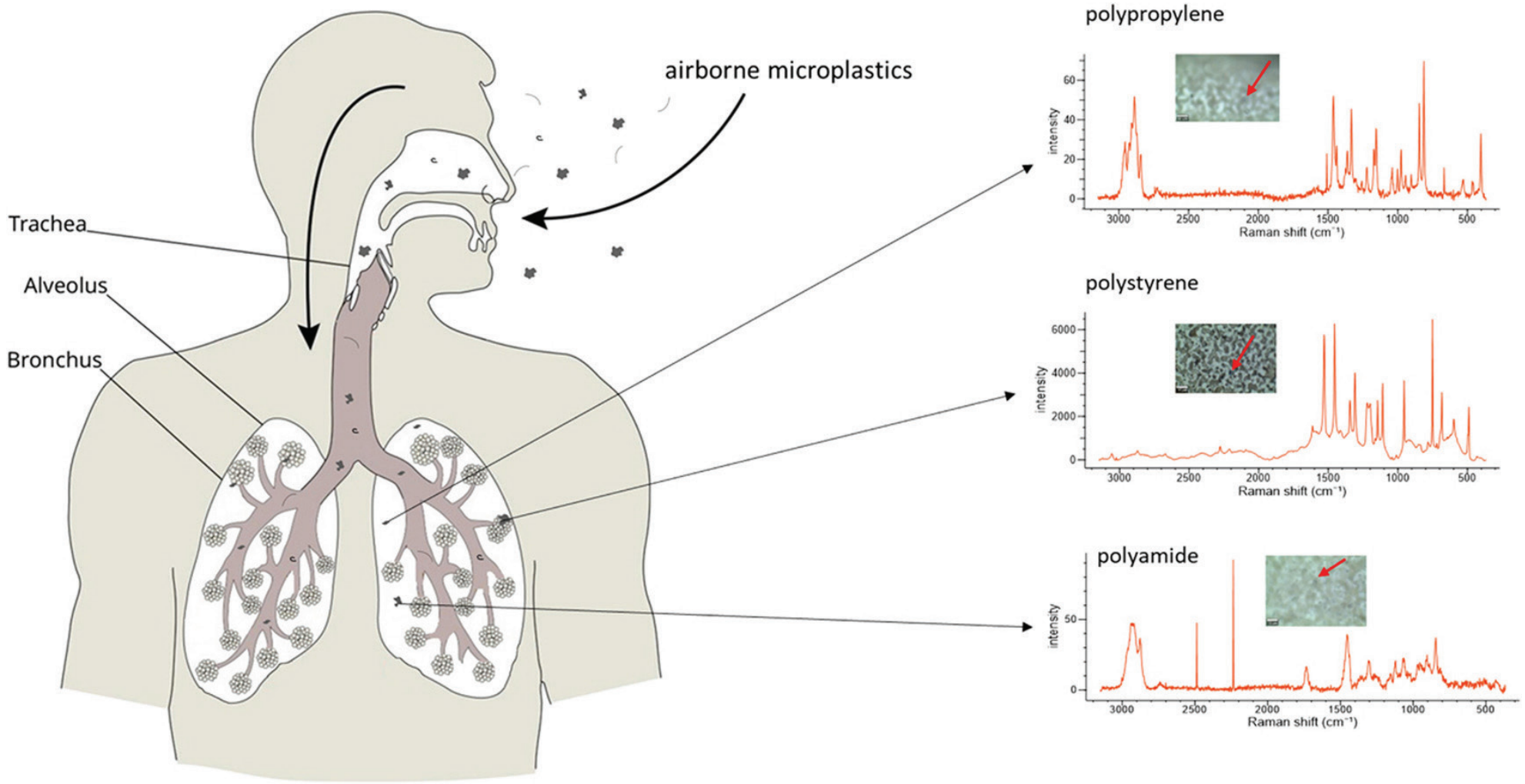


Liver

Cary, in preparation

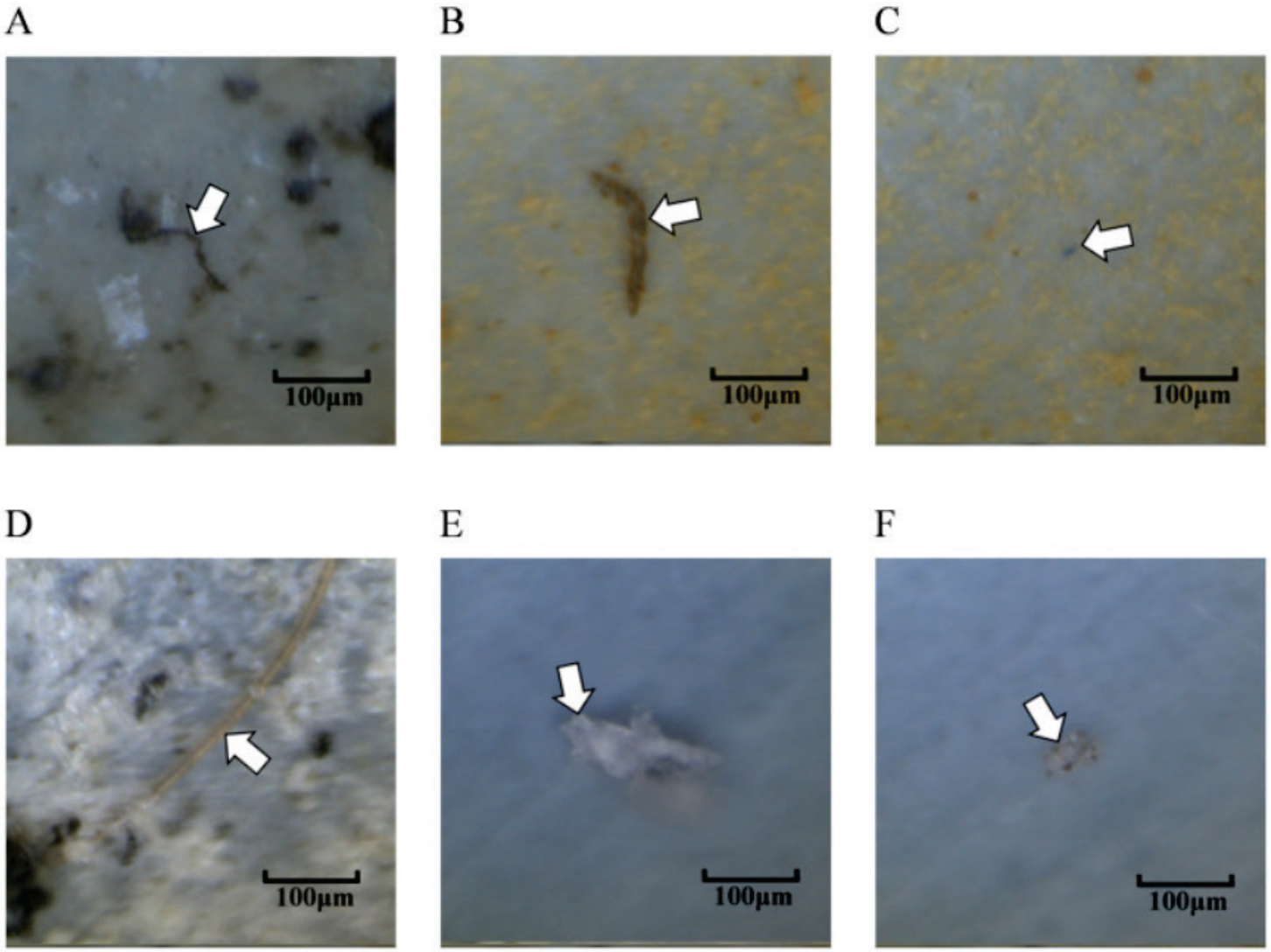
Real World Considerations: Rat to Human

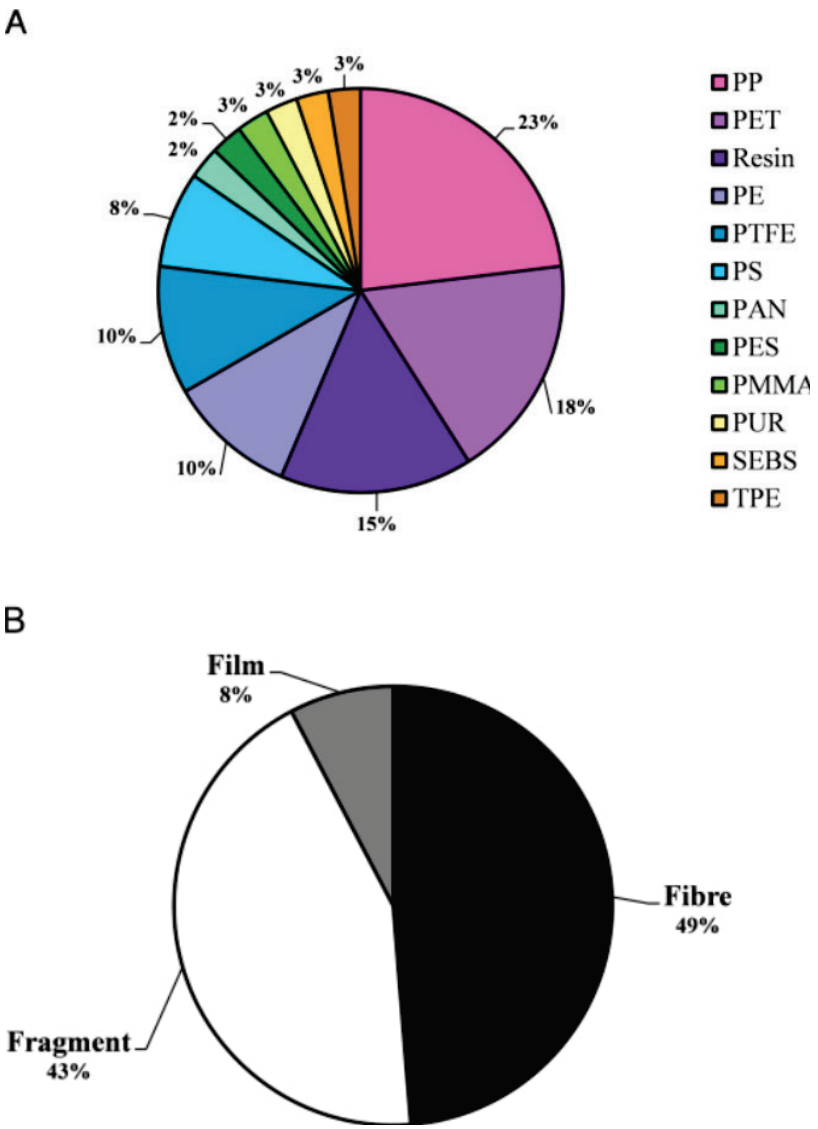
Microplastic identified in human lung tissue



Amato-Lourenço, 2021 – Raman spectrometry (scatters radiation) – cadaver samples

Microplastic identified in human lung tissue





Jenner, 2022 - µFTIR spectroscopy (absorbs radiation) – live patient samples

Microplastic particle migration to the human placenta after **real-world** exposure

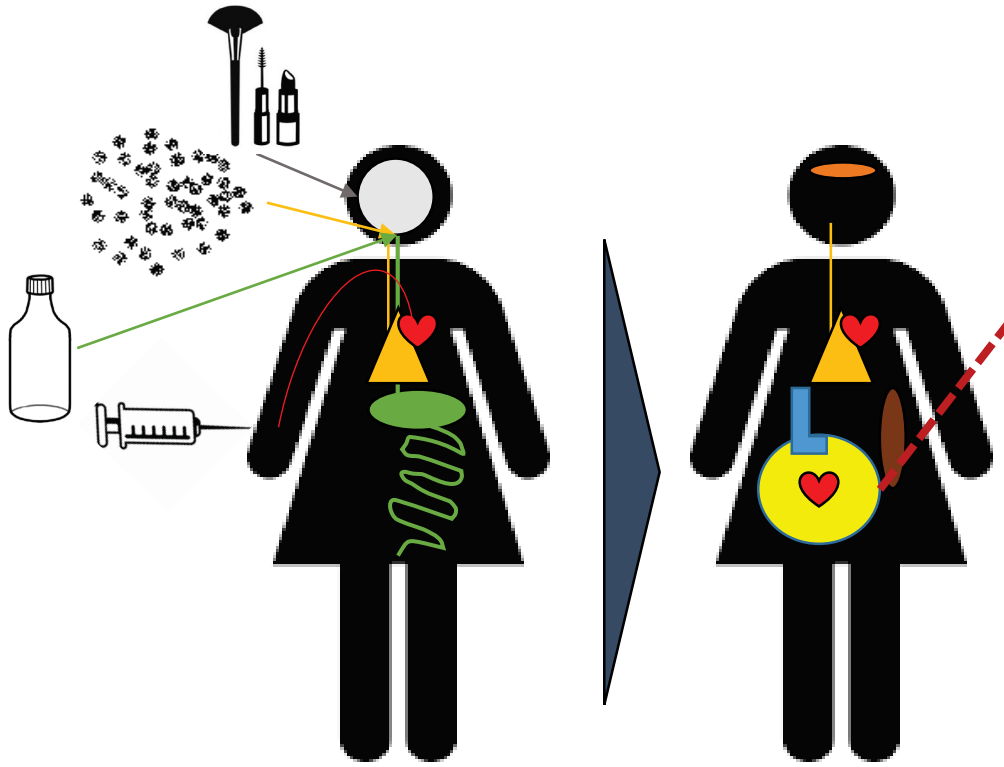


Figure 2

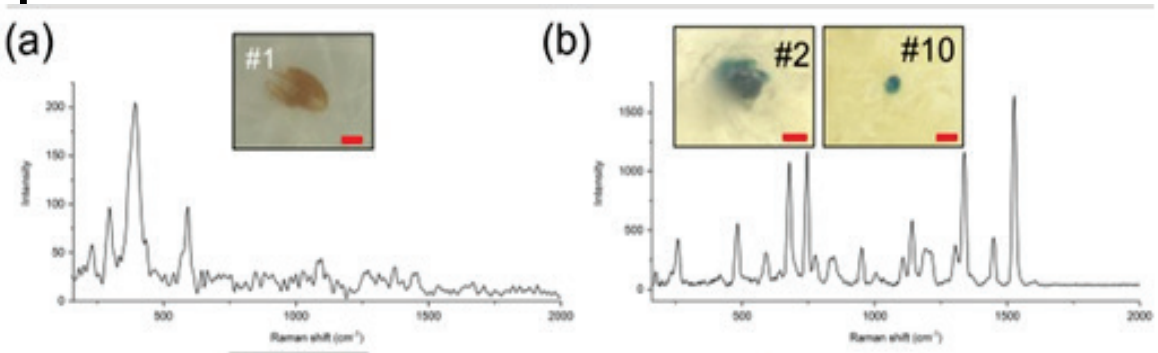
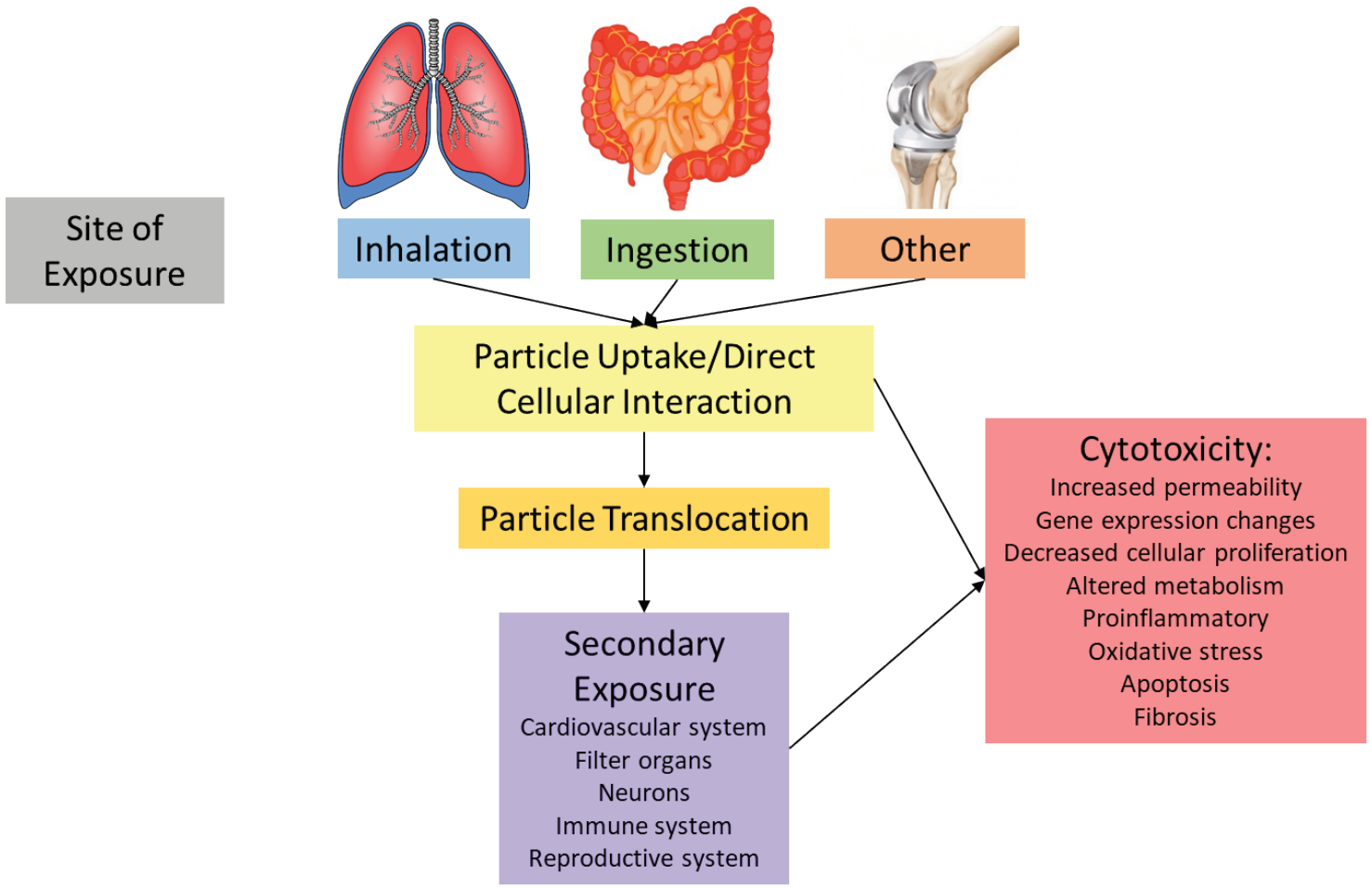


Table 1

Particle	Placenta Portion	Microparticles				
		Size	Color	Polymer matrix	Pigment	
					Generic name	Molecular formula and IUPAC name
#1	FS	~10 μm	Orange	n.d.	Iron hydroxide oxide yellow (Pigment Yellow 43; C.I. Constitution 77492)	FeO(OH) iron(III) oxide hydroxide
#2	CAM	~10 μm	Blue	Polypropylene	Copper phthalocyanine (Pigment Blue 15; C.I. Constitution 74160)	$C_{32}H_{16}CuN_8$ (29H,31H-phthalocyaninato(2 –)-N29,N30,N31,

Ragusa, 2020; Stapleton, 2019

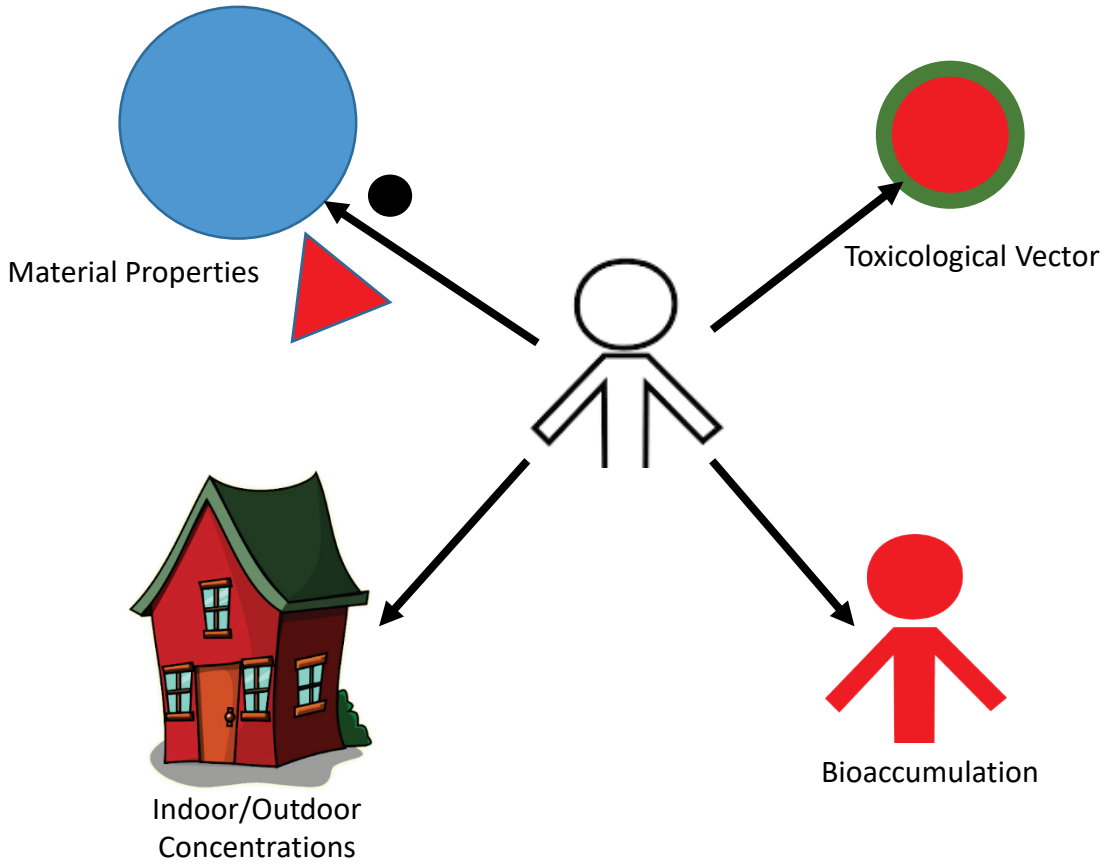
Plastic particles - What we know



- Gain access to and accumulate within primary and secondary tissues.
- Direct ***cellular interactions*** may lead to cellular uptake and local effects including inflammation, oxidative stress, altered metabolism, and gene expression changes.
- Clearance or excretion of the migrated particles remains unknown.

Stapleton, 2021

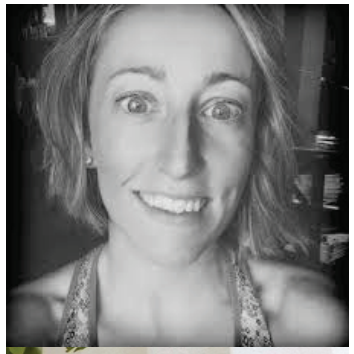
What don’t we know?

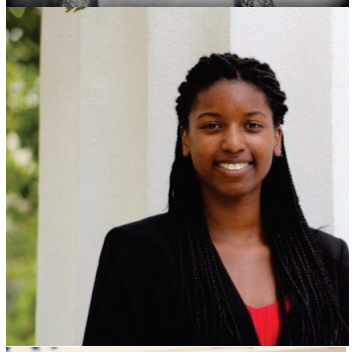


Stapleton, 2021

Study Considerations in Toxicology:

- Doses: Laboratory dose-responses and real-world exposure concentrations
- Material Properties
  - Size: Micro- vs Nano- plastics
  - Chemical
  - Shape
- Toxicological Vector (e.g., internalized plasticizers, “corona”, and/or environmental contaminants)
- Tissue bioaccumulation and biological transport mechanisms
- Exposure population (e.g. children, men, women, aged, disease, pregnancy)





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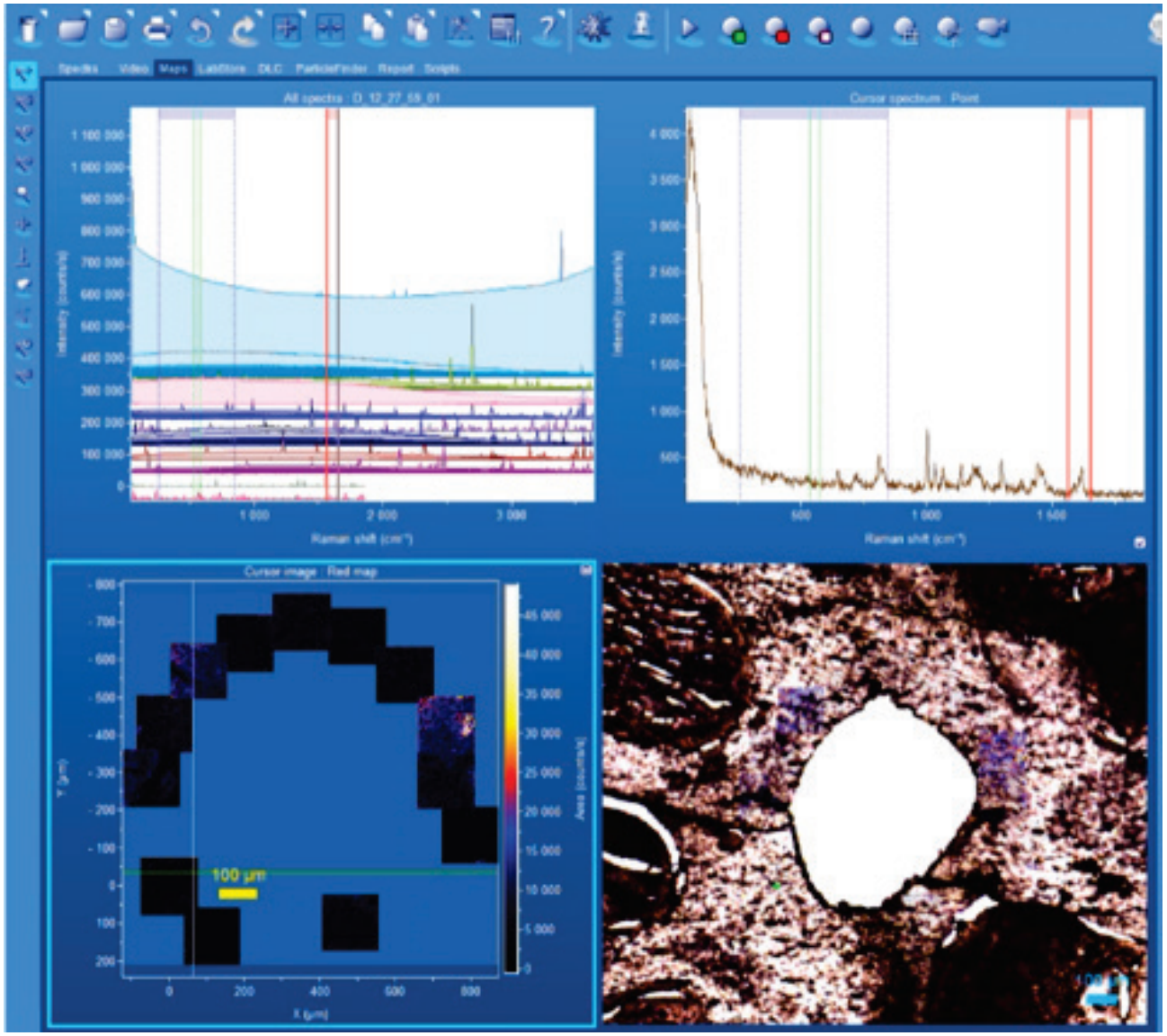
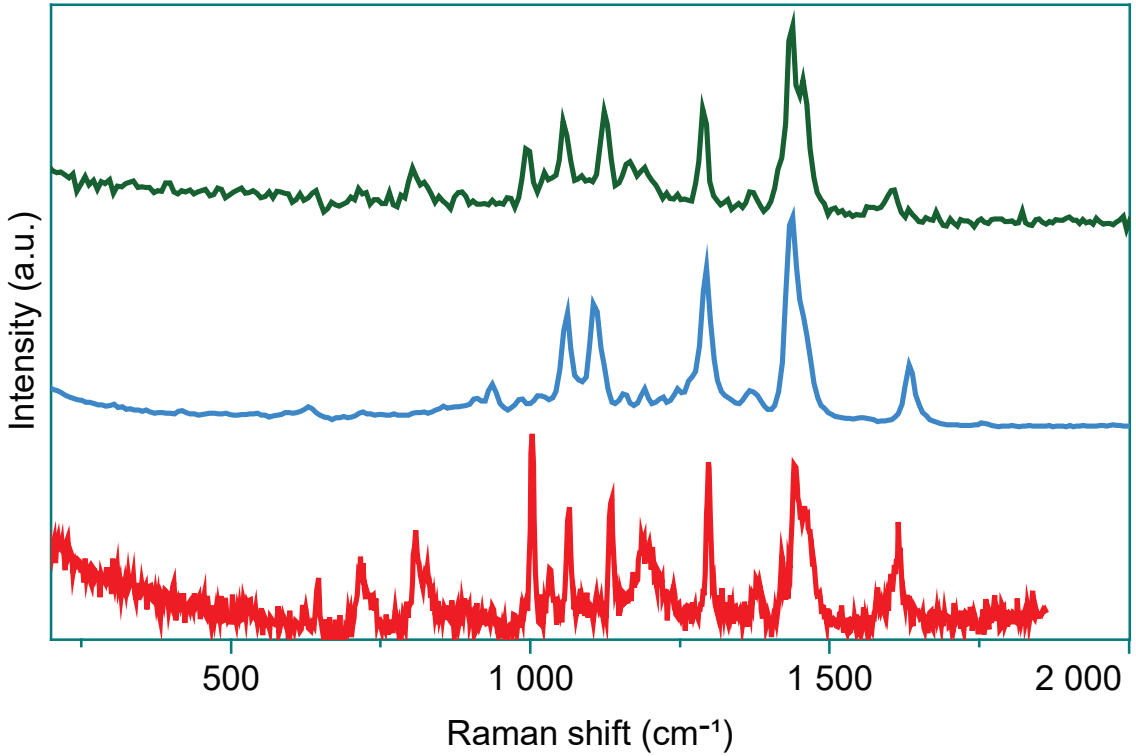




Dosimetry – Estimate of Exposure

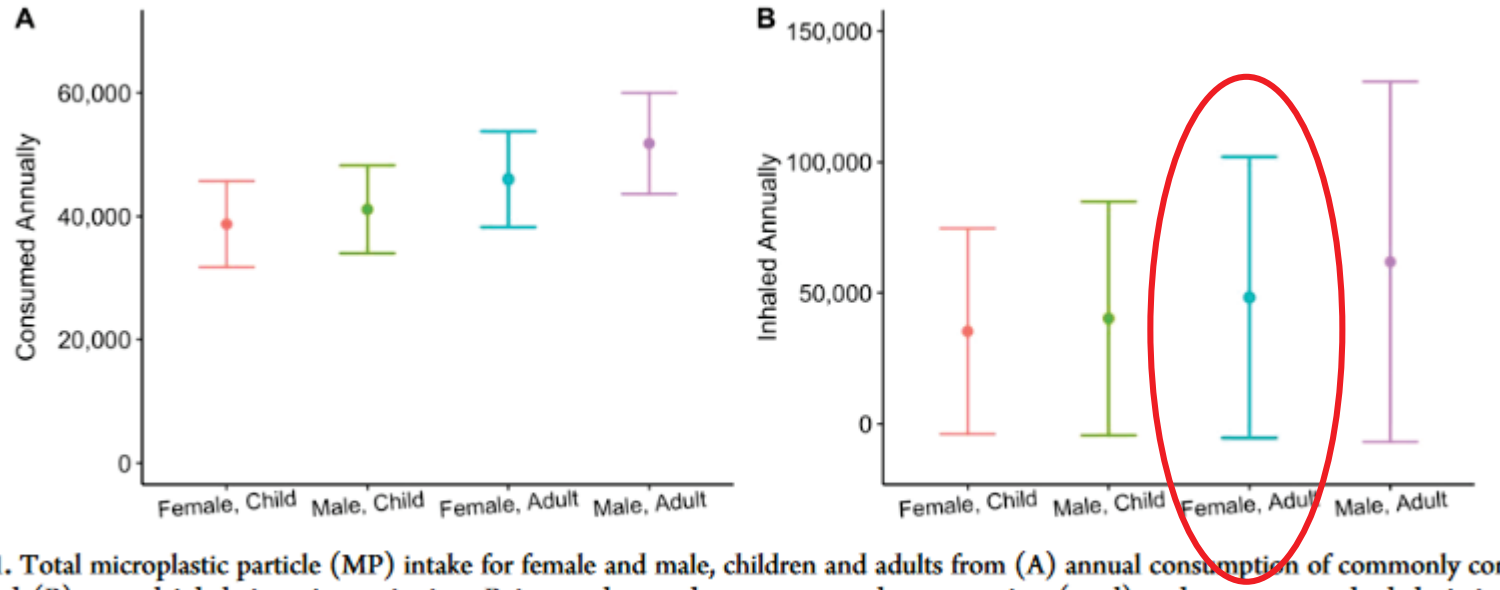


Figure 1. Total microplastic particle (MP) intake for female and male, children and adults from (A) annual consumption of commonly consumed items and (B) annual inhalation via respiration. Points and error bars represent the summation (total) and average standard deviation of all microplastics consumed.

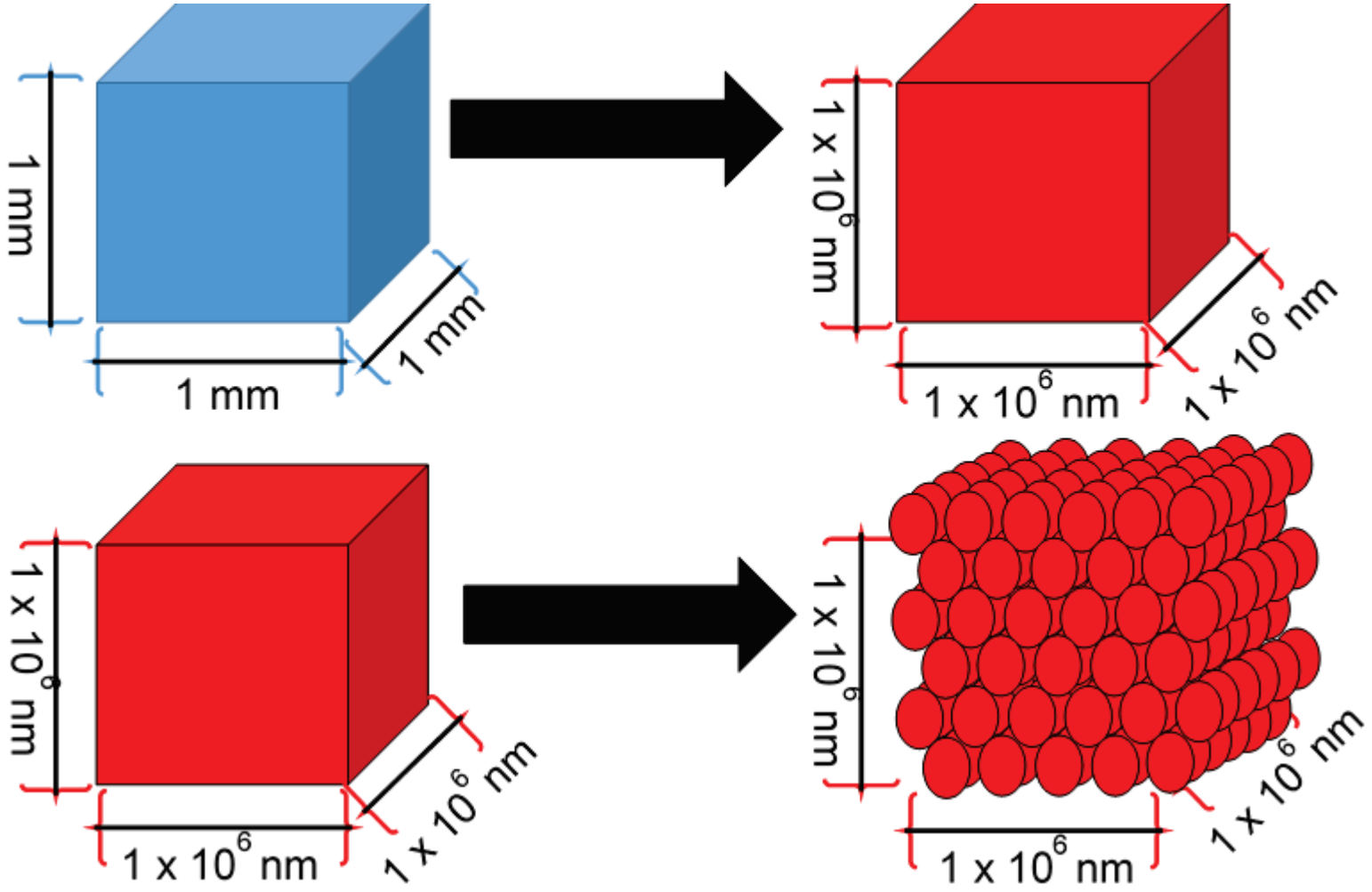
Table 1. Daily and Annual Consumption and Inhalation of Microplastic Particles for Female and Male, Children and Adults[a]

	Daily		Annual		Total	
	Consumed	Inhaled	Consumed	Inhaled	Daily	Annually
Male Children	113	110	41106 ± 7124	40225 ± 44730	223	81331
Male Adults	142	170	51814 ± 8172	61928 ± 68865	312	121664
Female Children	106	97	38722 ± 6977	35338 ± 39296	203	74060
Female Adults	126	132	46013 ± 7755	48270 ± 53676	258	98305

[a]Points and error bars represent the summation (total) and average standard deviation of all microplastics consumed.

Cox, 2019

Dosimetry: Microplastics verses Nanoplastics

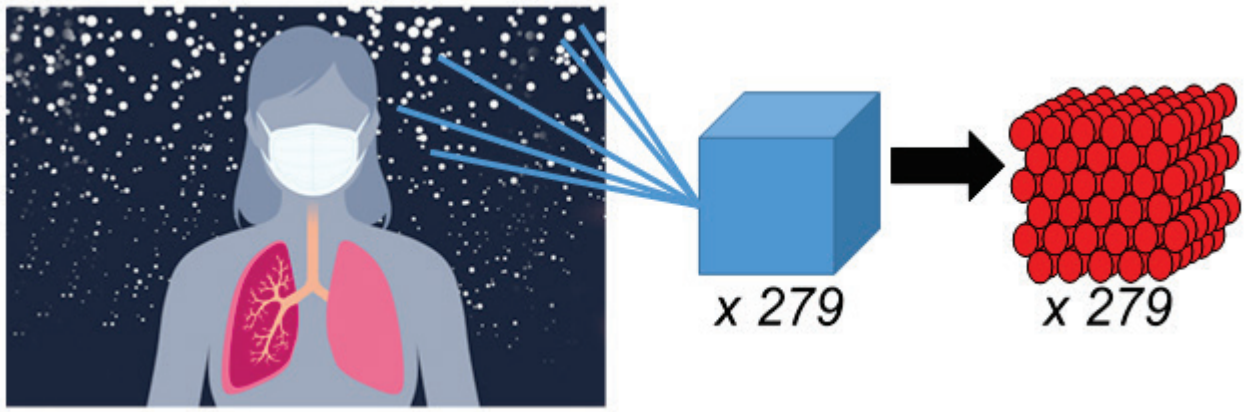


$\mathbf{1\ mm^3 = (1\ x\ 10^6\ nm)^3 = 1\ x\ 10^{18}\ nm}$

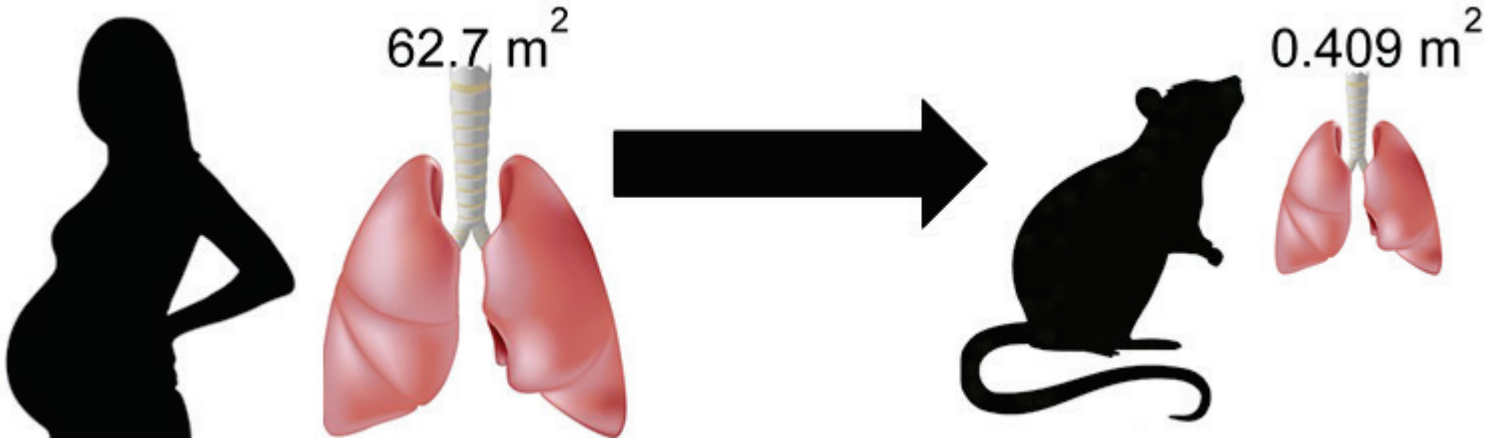
$\frac{4}{3}\pi r^3 = \frac{4}{3}\pi(10nm)^3 = 4188.79\ nm^3$

$1\ x\ 10^{18}\ nm \div 4188.79\ nm =$
$2.39\ x\ 10^{14}\ \textbf{\textit{nanoplastic particles}}$

Dosimetry: Human to Rat



$$(2.39\ x\ 10^{14})\ x\ 279 = 6.66\ x\ 10^{16}\ nanoplastics/day$$

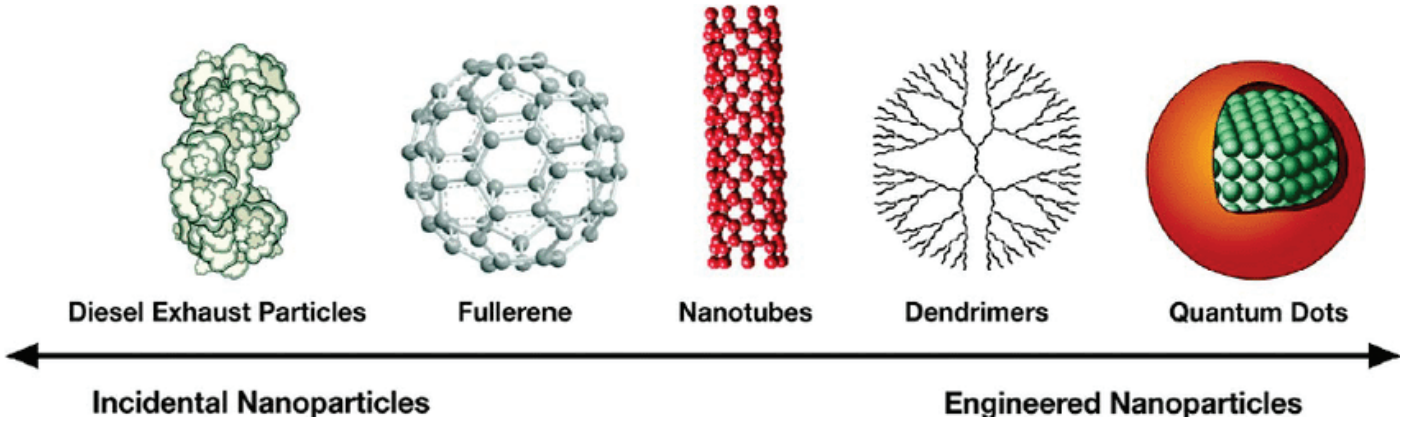


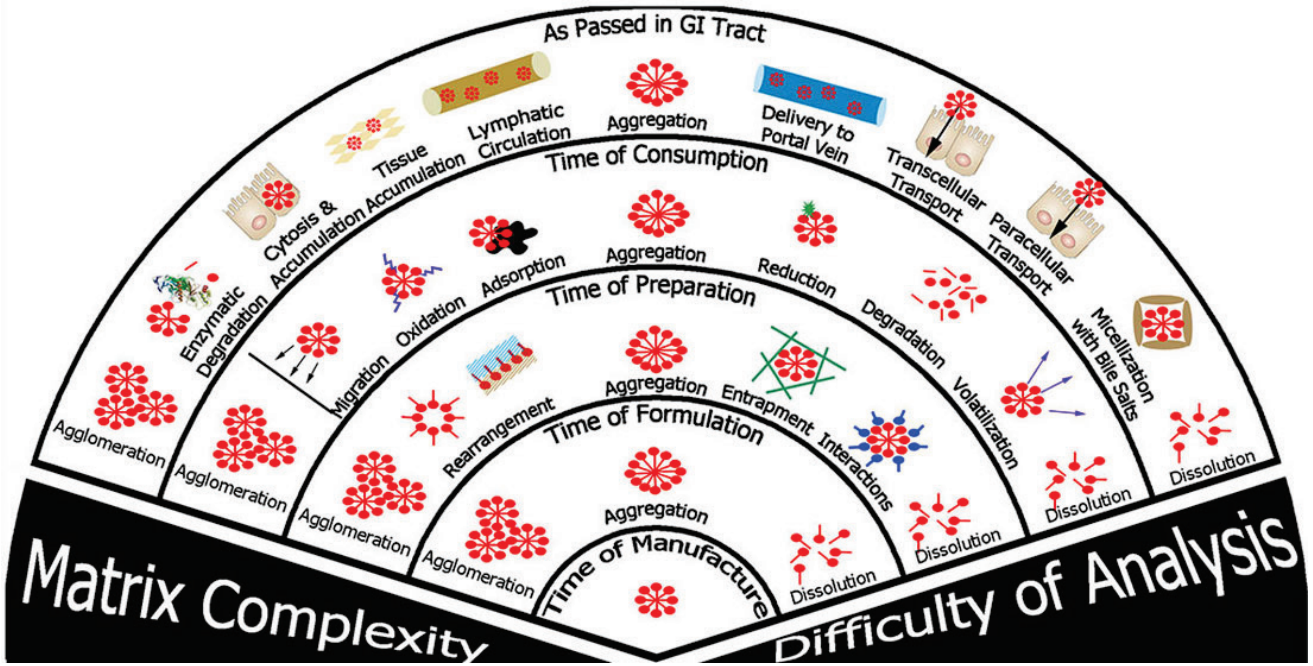
$$\frac{(6.66\ x\ 10^{16})\ x\ 0.409\ m^2}{62.7\ m^2} = 4.34\ x\ 10^{14}\ nanoplastic\ particles$$

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

Cox, 2019

Ultrafine/Nano-sized Particles





Physicochemical Properties:

- ✓ Chemical (Mixtures)
- ✓ Size
- ✓ Shape
  - ✓ Surface Area
- ✓ Charge
- ✓ Solubility/Aggregation
- ✓ Functional Modifications
- ✓ Protein Corona
- ✓ Surface Energy

Ultrafine/Nano-sized Particles