# RESPIRE: Unraveling Maternal Vulnerabilities to Indoor Air Pollution

**UK Clean Air Conference 2nd October 2024**

Sophie Reed

Swansea University

**PI: Prof. Cathy Thornton**

**R**elating

**E**nvironment-use

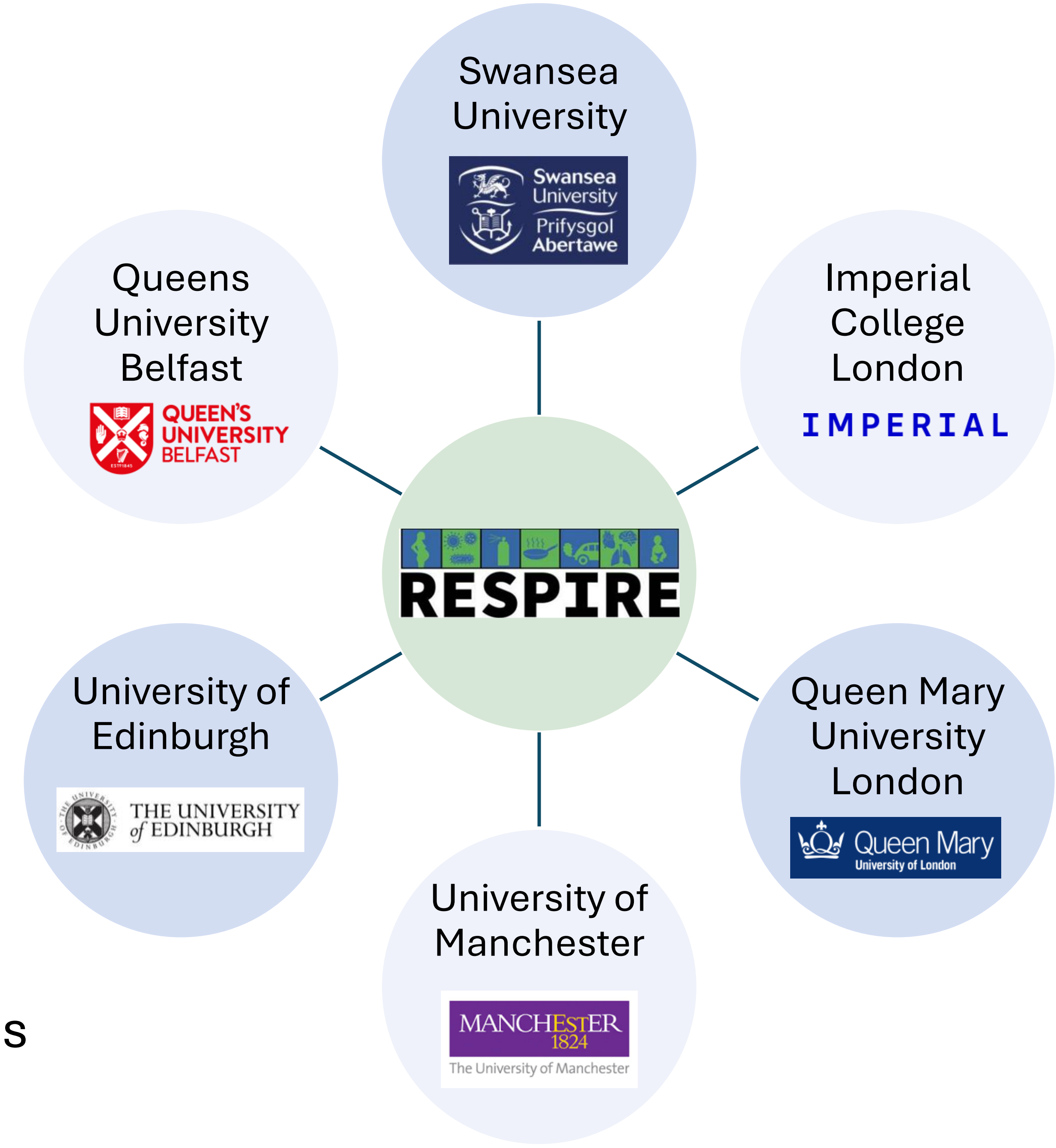
**S**cenarios in

**P**regnancy/

**I**nfanthood and

**R**esulting airborne material

**E**xposures to child health outcomes



# Climate change & pregnancy

**Climate change** is the single largest threat facing humanity today

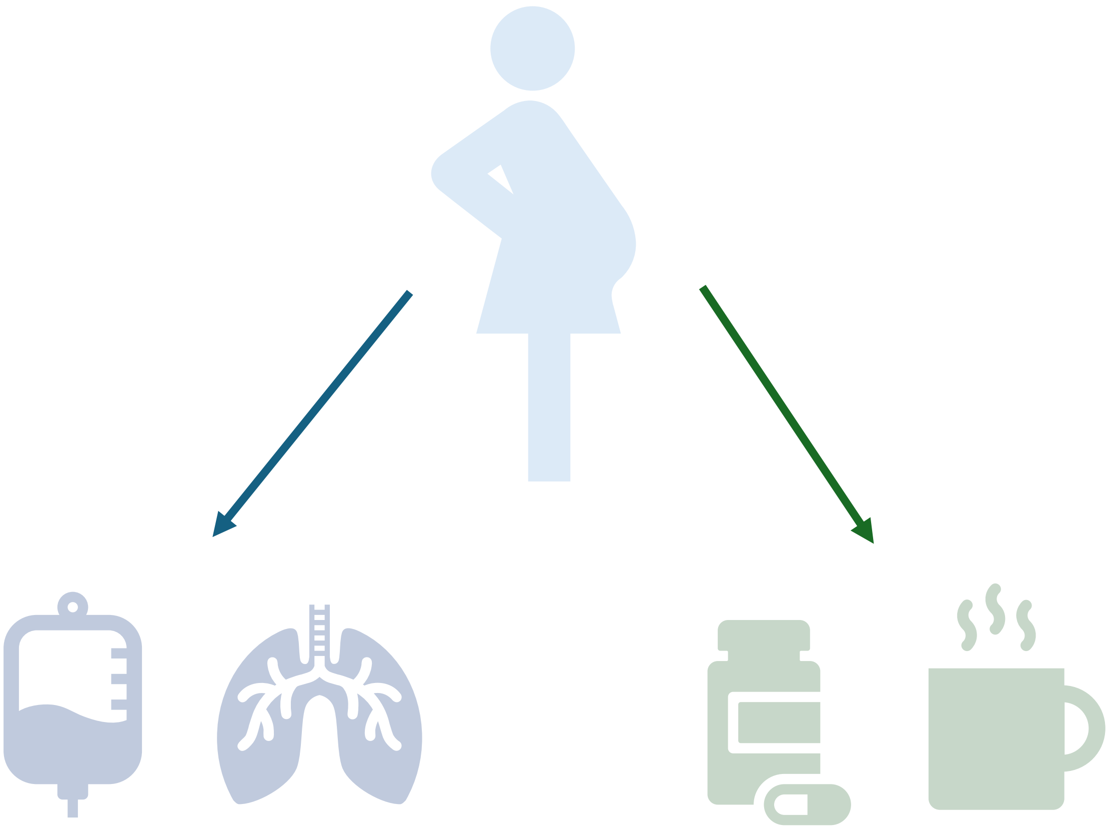


- 1/10 deaths in children under 5 and 1/5 deaths in newborns are attributed to air pollution (WHO).

WHO: www.who.int/news/item/29-10-2018-more-than-90-of-the-worlds-children-breathe-toxic-air-every-day

# Climate change & pregnancy

**Climate change** is the single largest threat facing humanity today



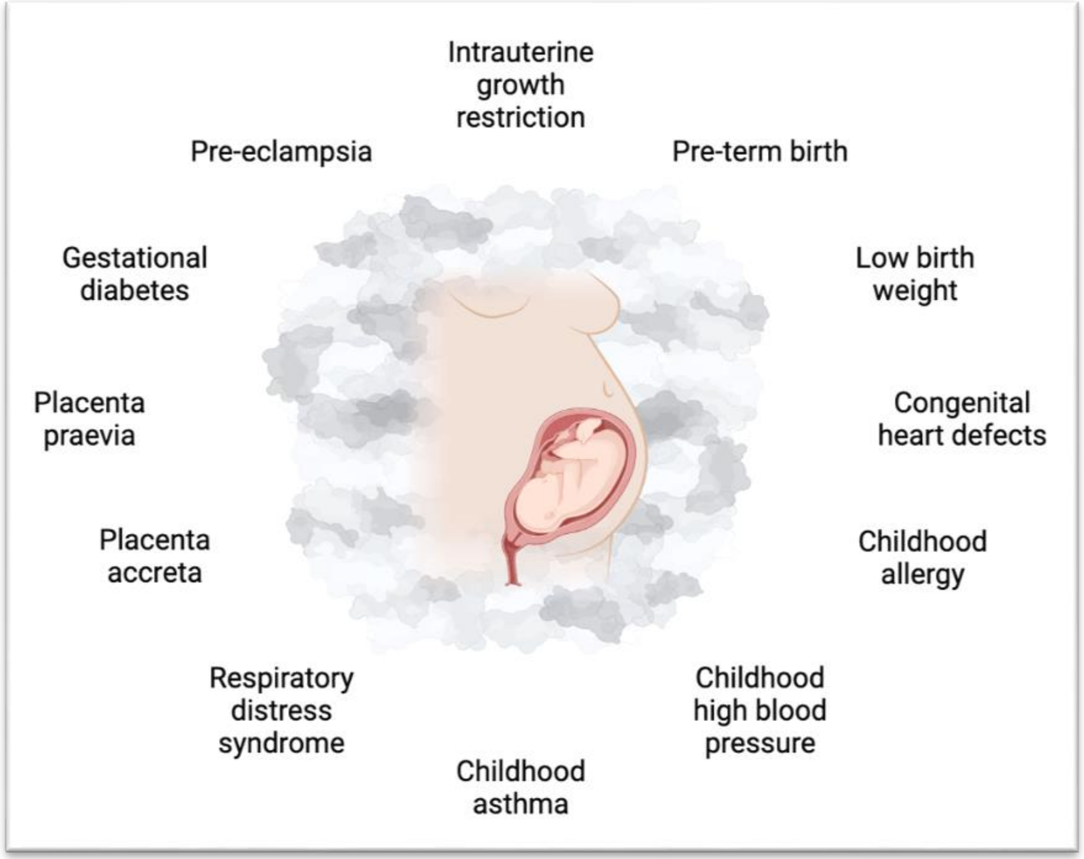
- 1/10 deaths in children under 5 and 1/5 deaths in newborns are attributed to air pollution (WHO).

- Pregnant women are a uniquely vulnerable population.
  - Biological changes.
  - Child health programming.

WHO: www.who.int/news/item/29-10-2018-more-than-90-of-the-worlds-children-breathe-toxic-air-every-day

# Climate change & pregnancy

**Climate change** is the single largest threat facing humanity today



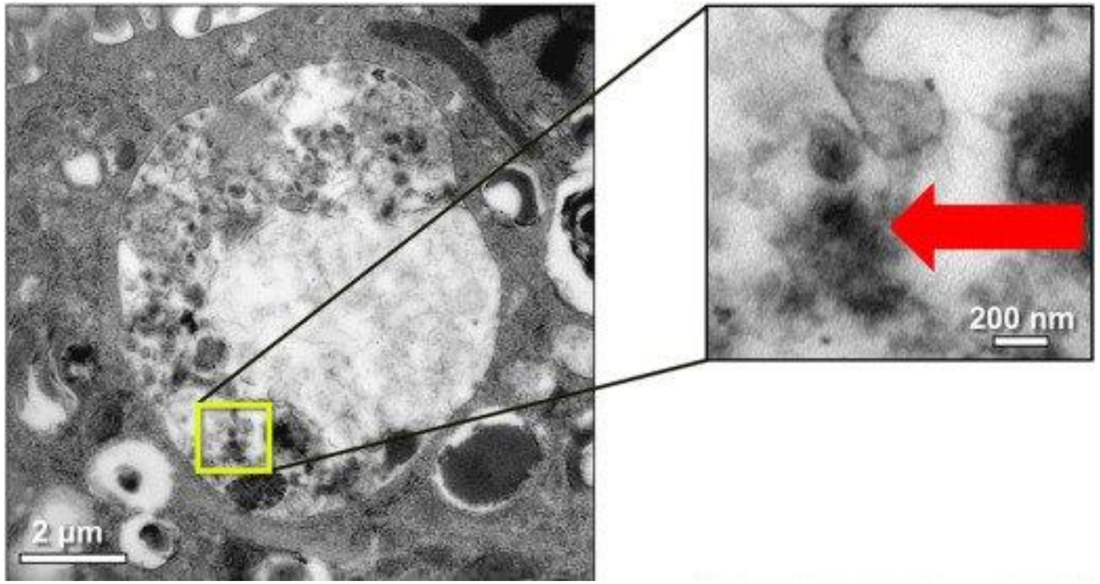

- 1/10 deaths in children under 5 and 1/5 deaths in newborns are attributed to air pollution (WHO).

- Pregnant women are a uniquely vulnerable population.
  - Biological changes.
  - Child health programming.

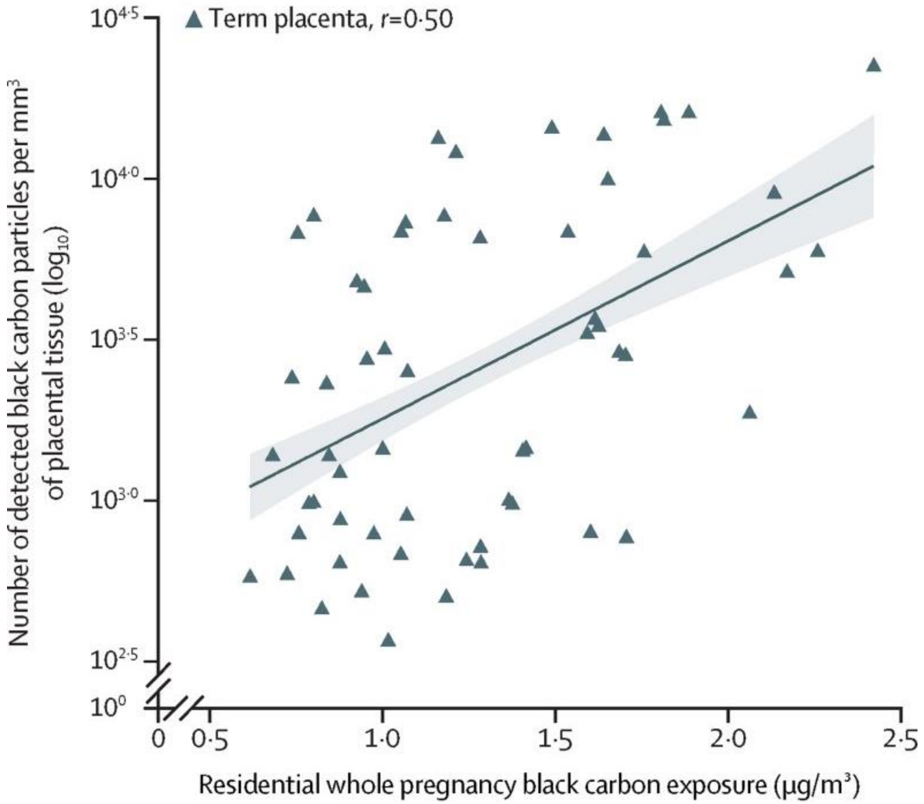
- Unfavourable birth and child health outcomes associated with pollution (& extreme heat exposure) in pregnancy.

# Pollutants in the placenta and fetus

Black carbon & inhaled ultrafine particles <0.1μm detected in placenta




Liu et al, *Sci Total Environ*, (2021).

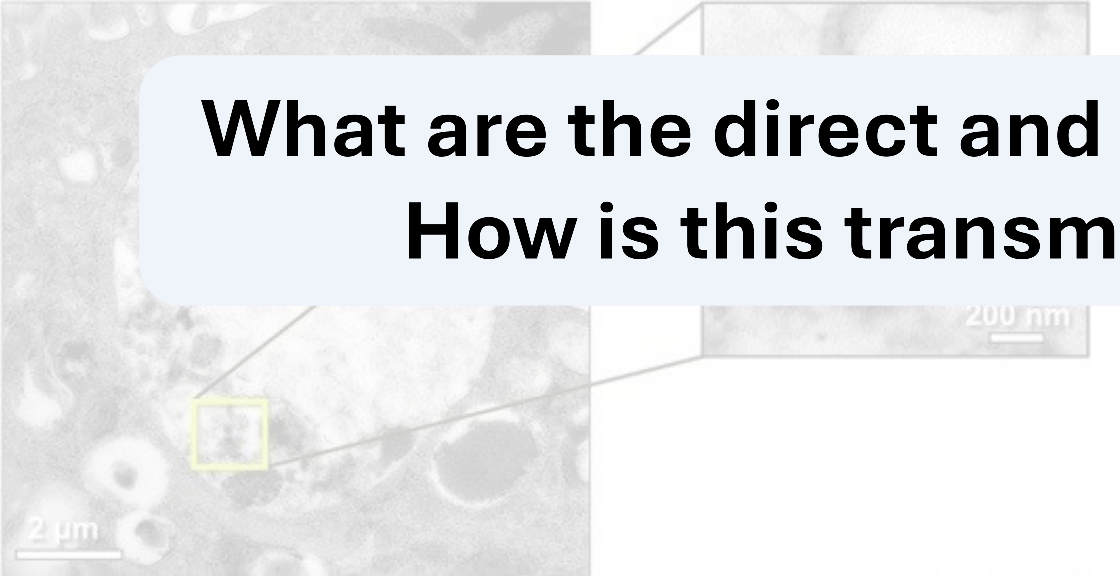



Bongaerts et al, *Lancet Planet Health*, (2022).

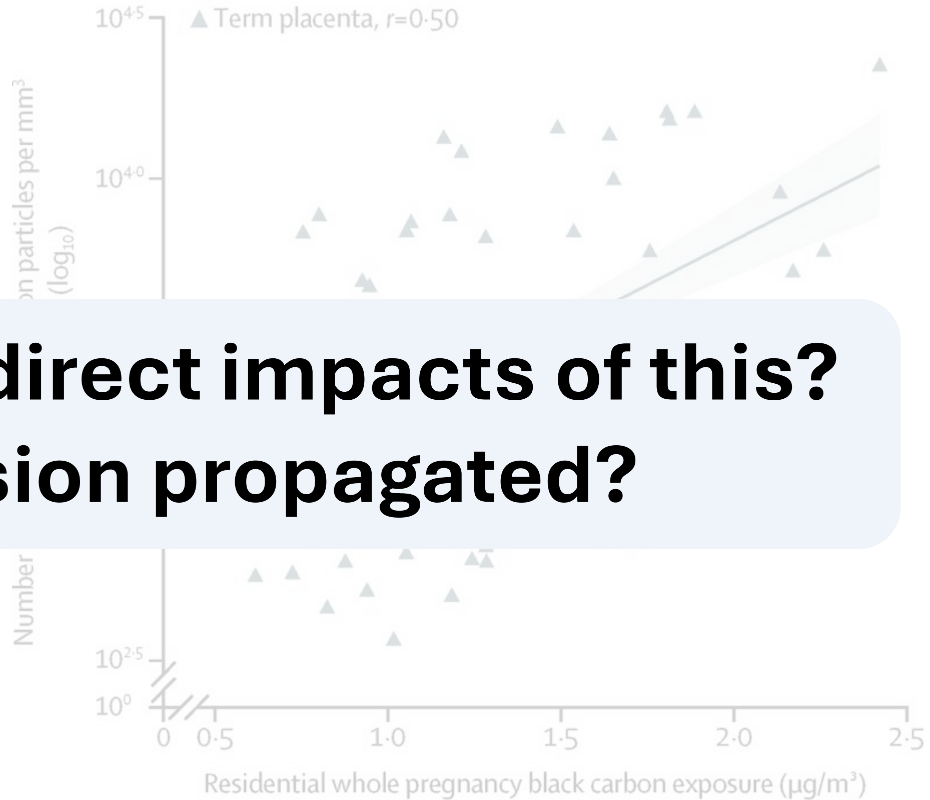
Positive correlation between maternal black carbon exposure and placental black carbon

# Pollutants in the placenta and fetus

Black carbon & inhaled ultrafine particles <0.1μm detected in placenta




Liu et al, *Sci Total Environ*, (2021).




Bongaerts et al, *Lancet Planet Health*, (2022).

**What are the direct and indirect impacts of this?**
**How is this transmission propagated?**

Positive correlation between maternal black carbon exposure and placental black carbon

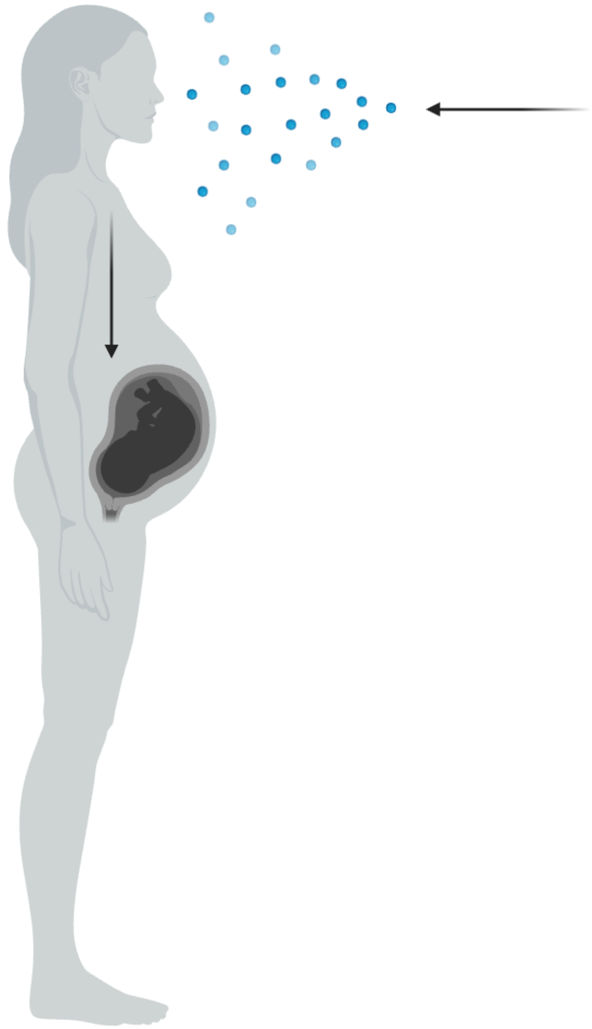
Swansea University
Prifysgol Abertawe

# RESPIRE project aims

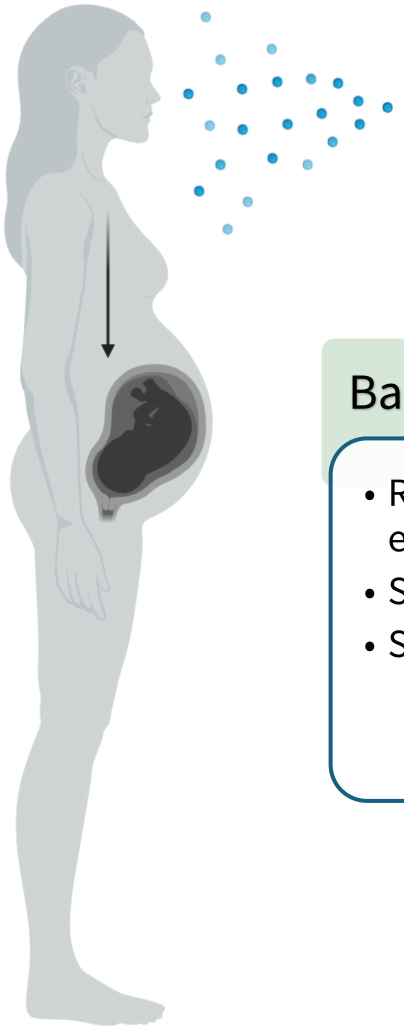
Identify the toxicological impact of direct airborne material exposures (AMEs) on the maternal respiratory tract.

Elaborate the systemically propagated direct and indirect toxicological effects of AMEs.

Reveal the effects of gestation, BMI and ethnicity on responses to AMEs.



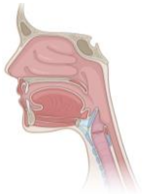
# Transmission of AMEs from mother to foetus



**Primary** effects (direct transmission between organs)

**Secondary** effects (systemic inflammation)

**Barrier surfaces**
- Respiratory tract (Nasal epithelium, NELF)
- Saliva
- Skin

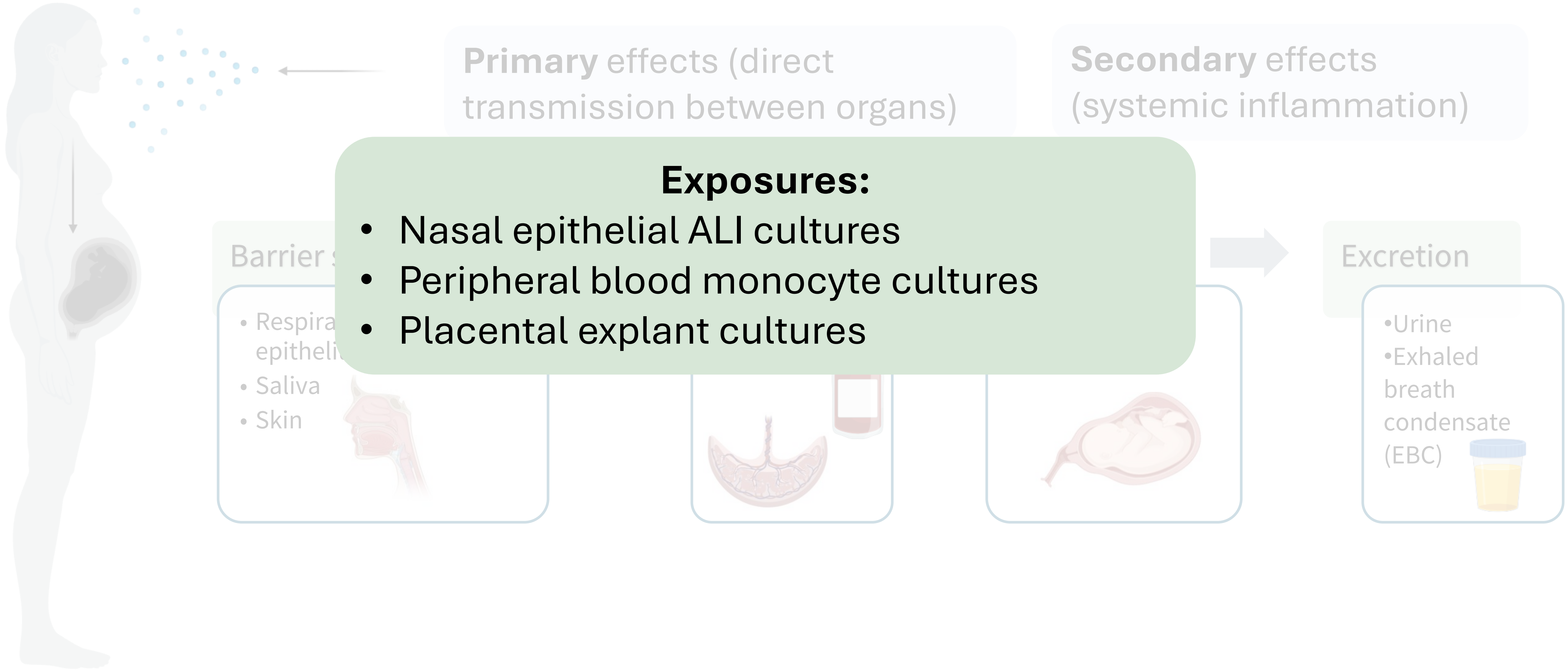


**Intermediate**
- Blood
- Placenta

**Foetus**
- Umbilical cord blood

**Excretion**
- Urine
- Exhaled breath condensate (EBC)

# Transmission of AMEs from mother to foetus




**Exposures:**

- Nasal epithelial ALI cultures
- Peripheral blood monocyte cultures
- Placental explant cultures

# Modelling upper respiratory tract responses

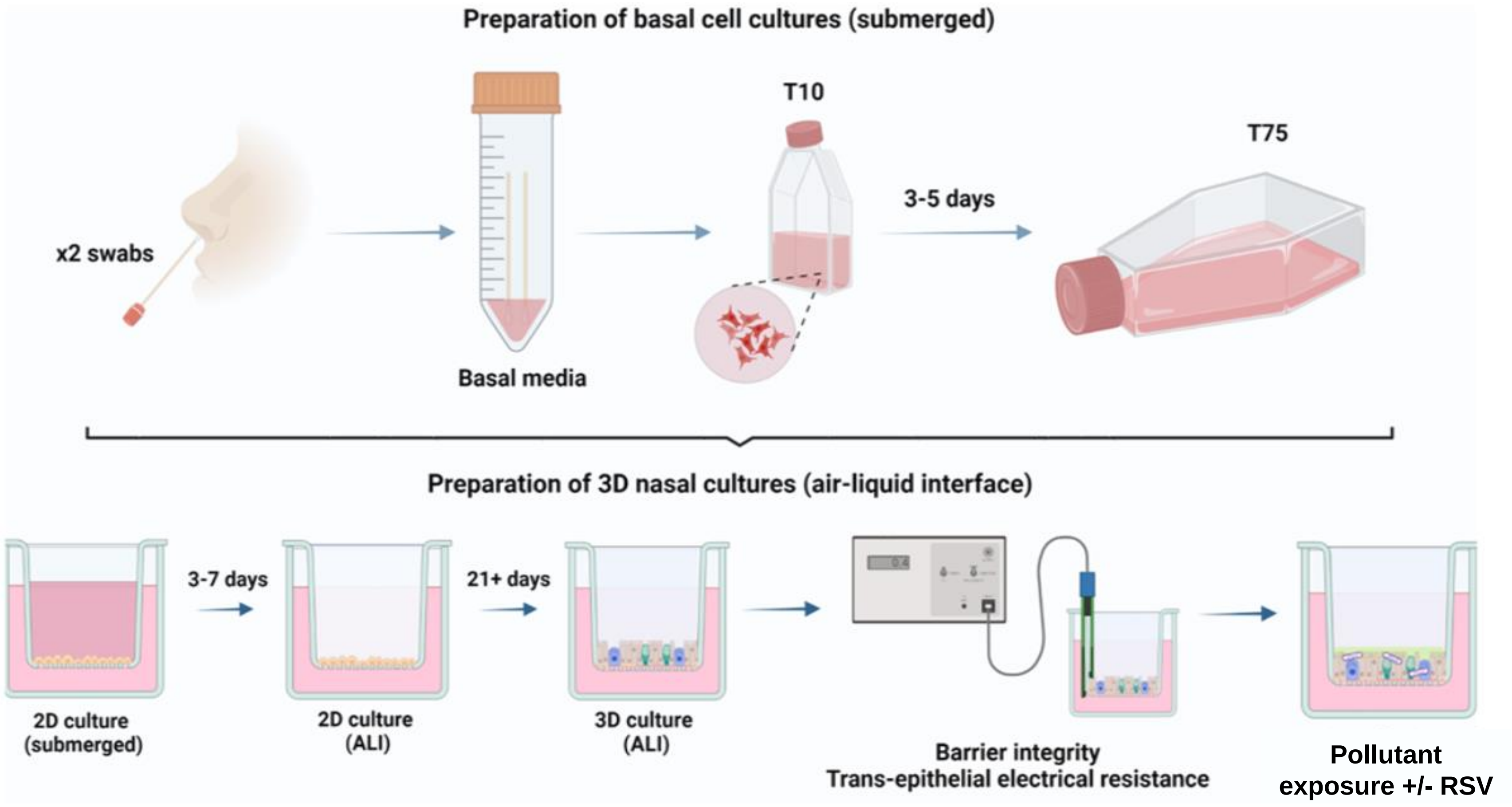



Figure created by Claudia Efstathiou, ICL

# Particulate exposures - ALI cultures

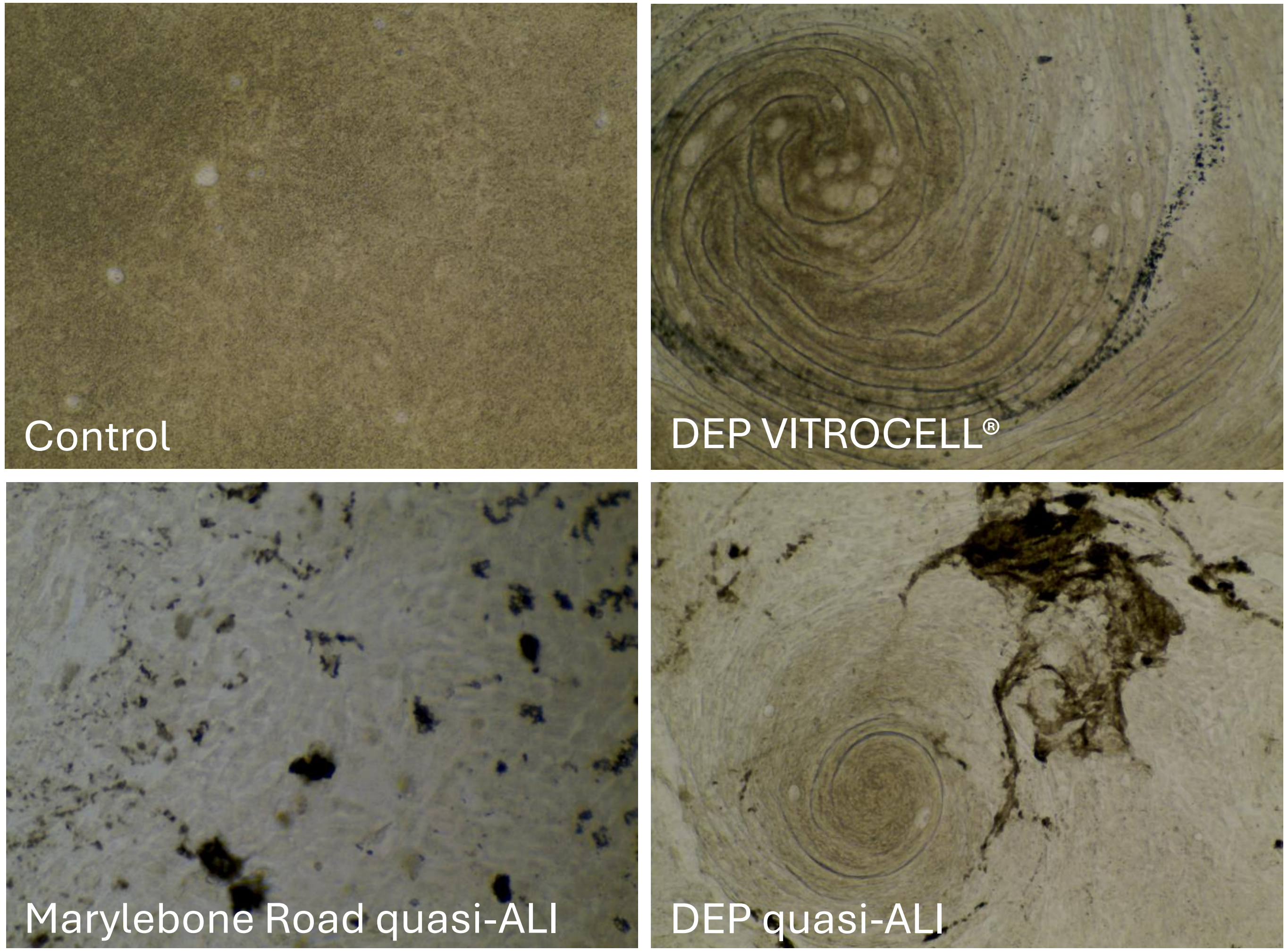
Particulate AMEs of nasal epithelial cell air liquid interface (ALI) cultures –

- VITROCELL® vs quasiALI

Particulates +/- RSV

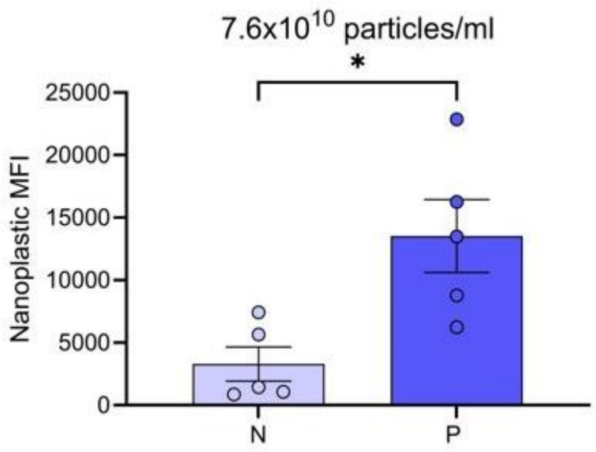
- Claudia Efstathiou, ICL
- Preliminary results showing increased expression of viral sensing genes in nasal epithelium with particulate exposure.

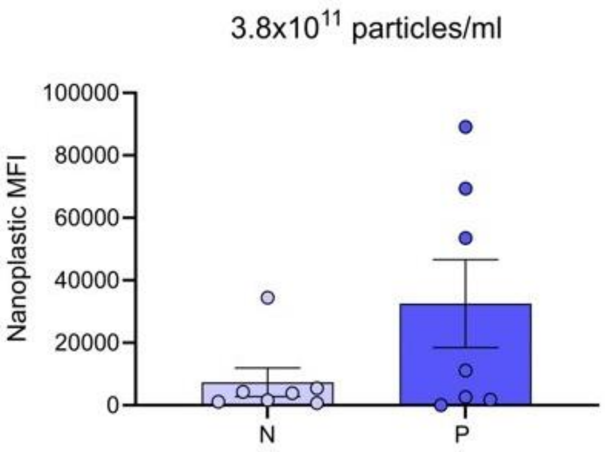
Pregnant vs non-pregnant comparisons underway

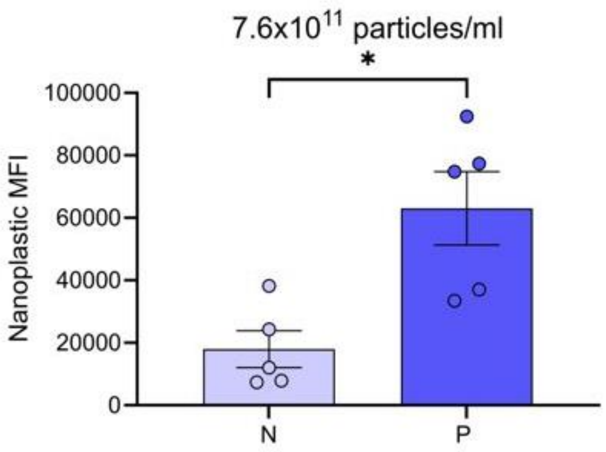



Claudia Efstathiou, ICL, Kirsty Meldrum, SU

# Particulate exposure of blood monocytes

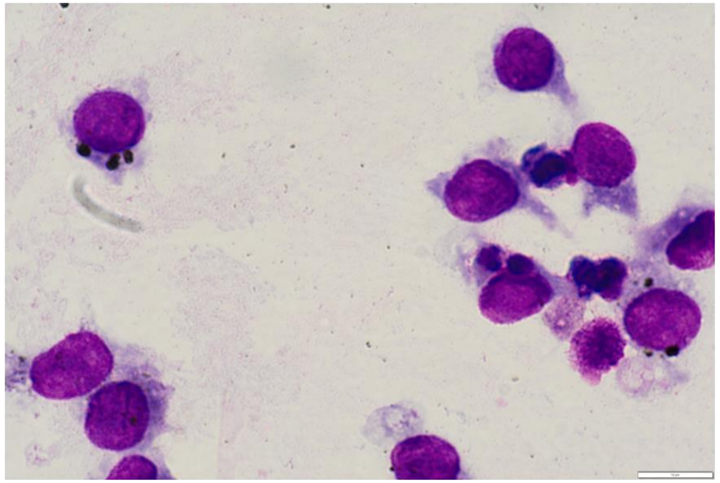



Higher uptake of plastic nanoparticles in pregnant donor blood monocytes, compared to non-pregnant donors.

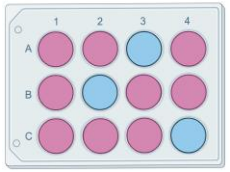
Work ongoing with NIST particulates.



Tyler Joseph, Oliver Richards, SU

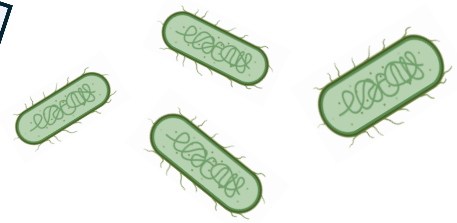
# Placental & fetal membrane explants

1-2 $mm^3$ explant cultures from healthy term placentas (elective c-section)



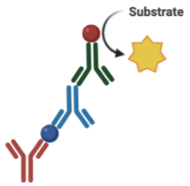
0.8 cm fetal membrane discs from healthy term (elective c-section)

VOC exposure +/- LPS 24 hours



Collect culture supernatants

ELISA for cytokine analysis




LDH cytotoxicity assay

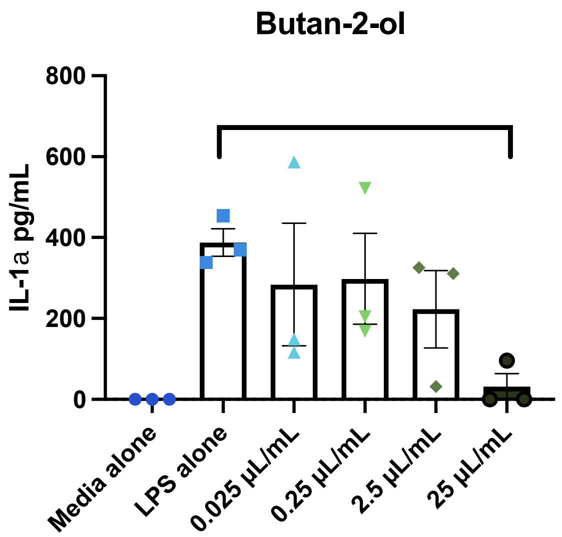
# Placental & fetal membrane explants

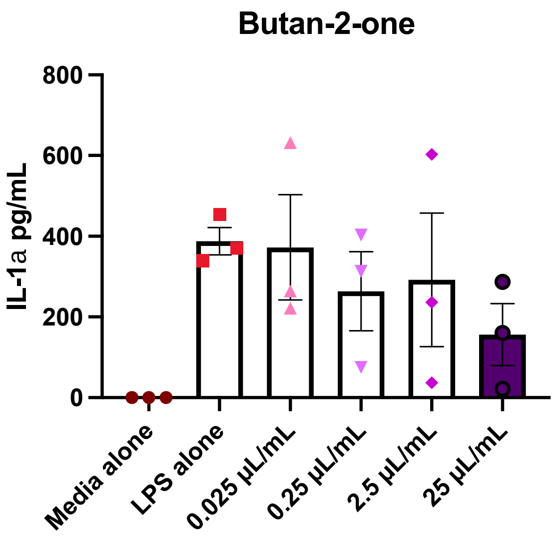
**Table 1**
Individual Volatile Organic Compounds (VOCs) identified through measurements in residences and their calculated Weighted Average Geometric Mean (*WAGM*).

| VOC | *WAGM* (μg/m$^3$) | VOC | WAGM (μg/m$^3$) | VOC | *WAGM* (μg/m$^3$) |
|---|---|---|---|---|---|
| Ethanol | 92.00 | Isobutane | 4.01 | 1-Methoxy-2-propanol/propylene glycol methyl ether (PGME) | 1.35 |
| Formaldehyde | 18.04 | 2-Ethylhexanol | 3.70 | 4-Ethyltoluene | 1.33 |
| Toluene | 15.90 | Dodecane/*n*-dodecane | 3.69 | 2-Butoxyethanol | 1.26 |
| Limonene [inc. D-limonene] | 13.65 | Hexane/*n*-hexane | 3.66 | 2-Carene | 1.10 |
| Hexanal/hexaldehyde/ hexanaldehyde | 13.30 | Heptane/*n*-heptane | 3.45 | Methyl-cyclopentane | 1.04 |
| *α*-pinene | 12.10 | Trimethylbenzene (including 1,2,4- Trimethylbenzene) | 3.22 | Isopropanol | 1.00 |
| Butane | 12.00 | Cyclohexane | 2.99 | 3-Ethyltoluene | 0.98 |
| Acetone | 11.40 | 2,2,4-Trimethyl-1,3-pentanediol diisobutyrate (tpddib/TXIB) | 2.94 | 2-Ethyltoluene | 0.94 |
| Acetaldehyde | 10.14 | 2,2,4-Trimethyl-1,3-pentanediol monoisobutyrate (tpdmib/texanol) | 2.78 | Acrolein | 0.92 |
| 2-Methyl-1-propanol | 8.20 | Tetracholorethane | 2.68 | Styrene | 0.82 |
| 2-Methylbutane | 7.80 | Methyl-cyclohexane | 2.68 | Propylbenzene | 0.80 |
| 1-Butanol | 6.16 | Tetrachloroethylene/tetrachloroethene | 2.24 | Tetrachlorocarbon | 0.80 |
| Butylbenzene | 5.72 | Nonane | 2.21 | Trichloroethane | 0.73 |
| Decane/n-decane | 5.27 | Benzene | 1.99 | *p*-Isopropyltoluene/*p*-cymene | 0.56 |
| *m* + *p*-Xylene | 4.57 | Ethylbenzene | 1.84 | Trichloroethene/trichloroethylene | 0.53 |
| Undecane/n-undecane | 4.38 | Propanal/proprionaldehyde | 1.80 | Naphthalene | 0.50 |
| 3-Carene | 4.38 | Tridecane | 1.77 | Chlorobenzene | 0.42 |
| Pentanal | 4.34 | Pentane | 1.69 | Methylbenzoate | 0.33 |
| 2,2,4 Trimethylpentane | 4.33 | *o*-Xylene | 1.57 | 1,3,5- Trimethylbenzene | 0.33 |
| Octanal | 4.30 | *α*-Pinene | 1.56 | Pyridine | 0.12 |
| Ethyl acetate | 4.30 | Benzaldehyde | 1.55 | 1,3-Butadiene | 0.11 |
| *p*-Dichlorobenzene | 3.90 | Octane | 1.54 | 3-Ethenylpyridine/3-vinylpyridine | 0.06 |

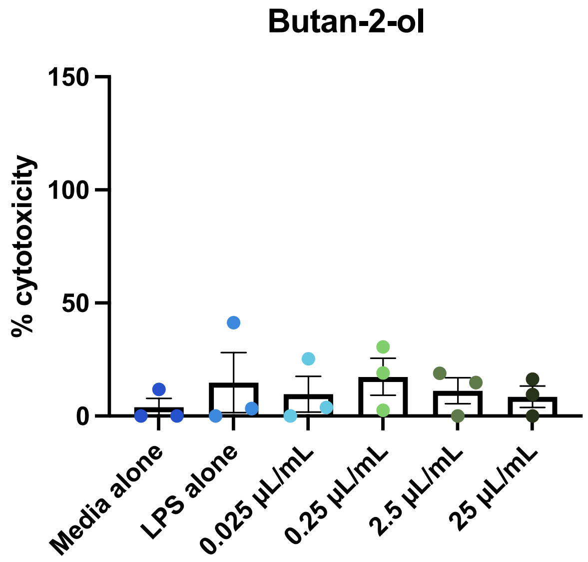
Halios et al, *Sci Total Environ*, (2022).

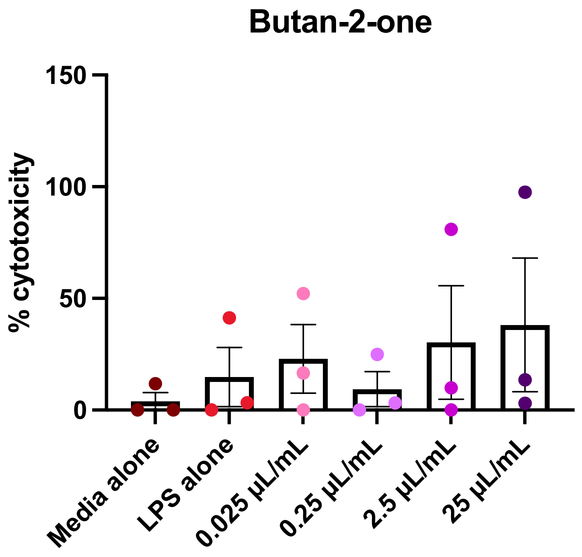
# Cytokine expression




Minimal cytotoxicity, but some with higher concentrations of Butan-2-one




Reduced cytokine expression with higher exposure concentrations of VOCs with LPS co-exposure

Potential negative impacts for pregnancy

# Conclusions & Future work

Air-liquid interface cultures of nasal epithelium exposed to particulates show potential impacts on viral sensing. Comparisons between responses of pregnant and non-pregnant donors underway.

Phagocytic cells isolated from the blood of pregnant women have higher uptake of nanoparticles compared to non-pregnant donors. Uptake mechanisms and cell differentiation are now being investigated with a range of particulates.

Reduced cytokine release from placental explants exposed to higher concentrations of VOCs with LPS co-exposure. VOC metabolism enzyme expression changes in the placenta, nasal epithelium & blood leucocytes during pregnancy are currently being determined.

RESPIRE

UKRI Natural Environment Research Council

Swansea University Prifysgol Abertawe

# Acknowledgments


**Thornton Lab – Swansea University**

Professor Cathy Thornton

Tyler Joseph

Dr April Rees

Dr Oliver Richards

Dr Aisling Morrin

Tiffany Haddow

SWIM

Swansea Immunology Research Lab

**Clift Lab – Swansea University**

Professor Martin Clift

Dr Kirsty Meldrum

**Thwaites Lab – Imperial College London**

Dr Ryan Thwaites

Dr Claudia Efstathiou

**RESPIRE Consortium**

**Research Participants**

Figures created with BioRender.com


Scan QR code for references

X @RESPIREResearch

Clean Air Programme