Could plastic production be driving lung cancer rates?

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Lost at Sea: Where Is All the Plastic?

Richard C. Thompson,[1]* Ylva Olsen,[1] Richard P. Mitchell,[1] Anthony Davis,[1] Steven J. Rowland,[1] Anthony W. G. John,[2] Daniel McGonigle,[3] Andrea E. Russell[3]

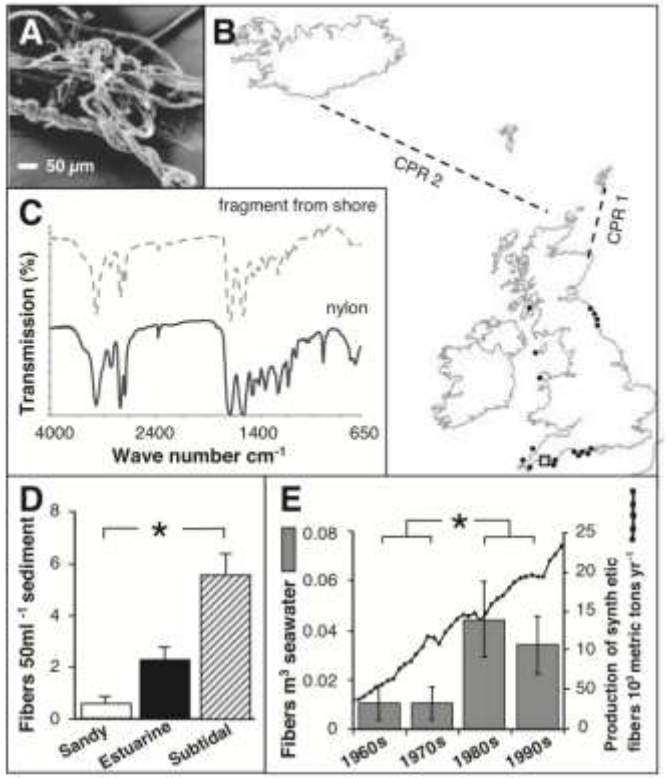


Fig. 1. (**A**) One of numerous fragments found among marine sediments and identified as plastic by FT-IR spectroscopy. (**B**) Sampling locations in the northeast Atlantic. Six sites near Plymouth (□) were used to compare the abundance of microplastic among habitats. Similar fragments (●) were found on other shores. Routes sampled by Continuous Plankton Recorder (CPR 1 and 2) were used to assess changes in microplastic abundance since 1960. (**C**) FT-IR spectra of a microscopic fragment matched that of nylon. (**D**) Microplastics were more abundant in subtidal habitats than on sandy beaches (*, $F_{2,3} = 13.26$, $P < 0.05$), but abundance was consistent among sites within habitat types. (**E**) Microscopic plastic in CPR samples revealed a significant increase in abundance when samples from the 1960s and 1970s were compared to those from the 1980s and 1990s (*, $F_{3,3} = 14.42$, $P < 0.05$). Approximate global production of synthetic fibers is overlain for comparison. Microplastics were also less abundant along oceanic route CPR 1 than along CPR 2 ($F_{1,24} = 5.18$, $P < 0.05$).

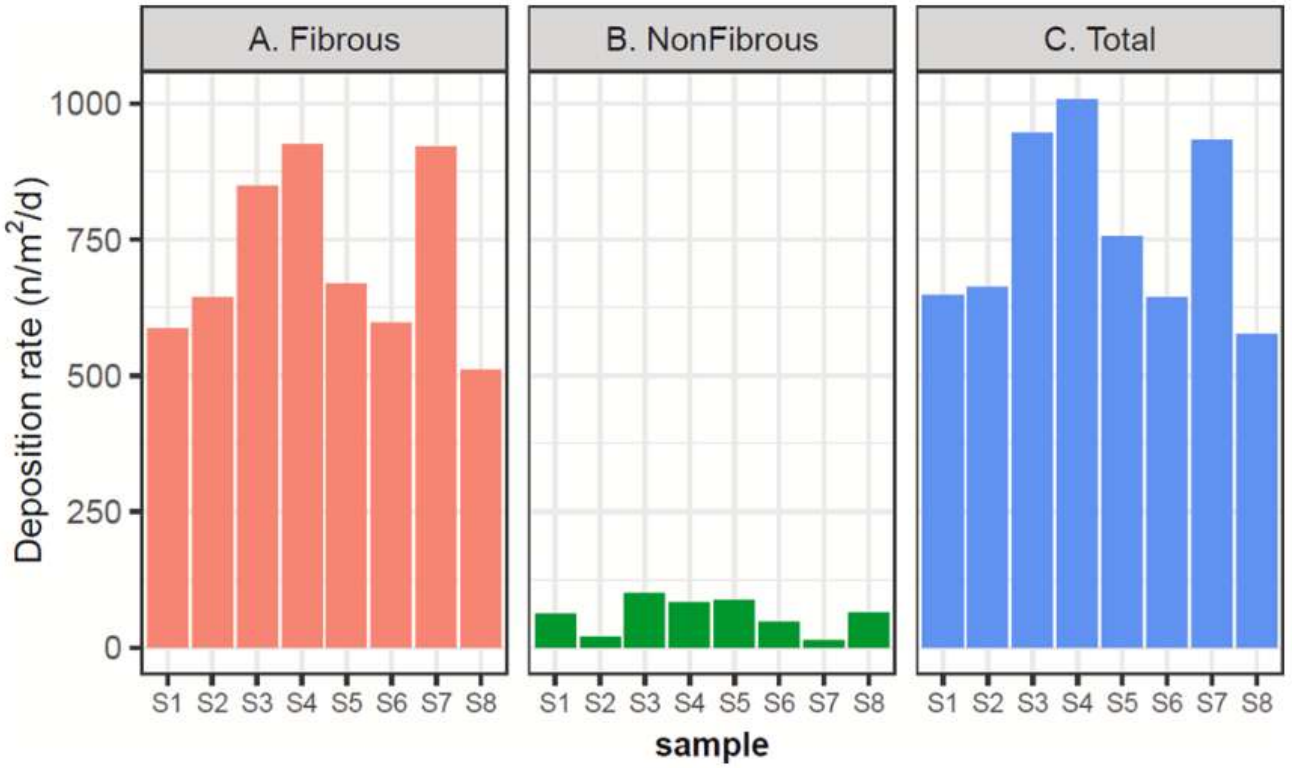
Overview of the Recommendations for a Definition and Classification of Plastic Debris (Wiki MP = 1 to 5000µM)

IV: Size	▪ Nanoplastics: 1 to <1000 nm ▪ Microplastics: 1 to <1000 µm ▪ Mesoplastics: 1 to <10 mm ▪ Macroplastics: 1 cm and larger The largest dimension of the object determines the category. Comprehensive reporting of multiple dimensions is preferred (e.g., for fibers).
V: Shape and structure	Spheres: Every surface point has the same distance from the center Spheroid: Imperfect but approximate sphere Cylindrical pellet: Rod-shaped, cylindrical object Fragment: Particle with irregular shape Film: Planar, considerably smaller in one than in the other dimensions Fiber: Significantly longer in one than wide in two dimensions Additional information on the structure (e.g., porosity) can be included.
VI: Color	Not crucial but useful in some biological contexts. Use a standardized color palette.
VII: Origin (optional)	Primary: Intentionally produced in a certain size Secondary: Formed by fragmentation in the environment or during use Origin should only be used if the primary origin can be established.

Hartmann NB et al. Environ. Sci. Technol. 2019, 53, 1039−1047

Time-series of deposition rates (n/m2/d) for (A) fibrous,(B) non-fibrous and (C) total microplastics in London

Threshold for analysis = 20μM: The smallest identified particle (high-density PE) was 25 μm



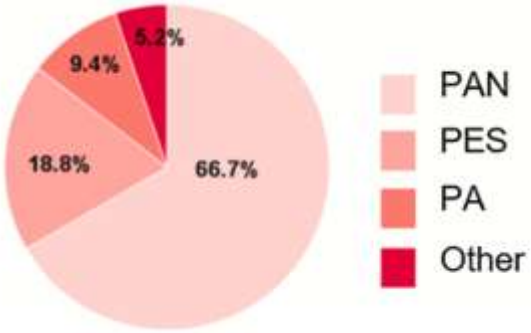
The deposition rate of fibrous microplastics was calculated to range from 510 to 925 fibrous microplastics/m2/d, with an average of 712 ± 162microplastics/m2/d(mean ± SD).

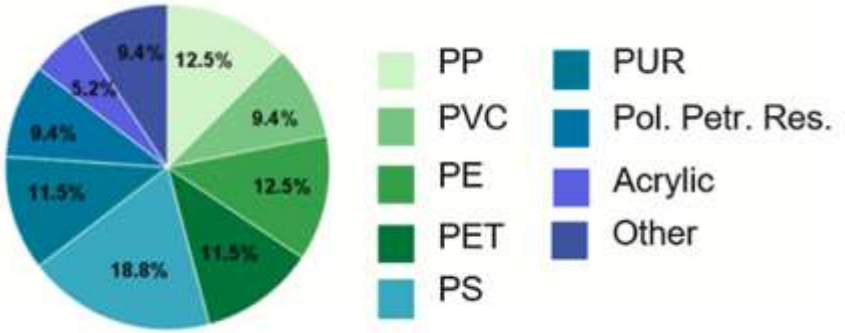
The non-fibrous microplastic deposition rate ranged from 12 to 99 microplastics/m2/d, with an average of 59 ± 32 non-fibrous microplastics/m2/d.

The average deposition rate of synthetic fibres and non-fibrous microplastics combined (total) was 771 ± 167 particles/m2/d

Wright SL et al. Environ Int. 2020 Mar;136:105411.

The petro-chemical composition of microplastics in total atmospheric deposition





Wright SL et al. Environ Int. 2020 Mar;136:105411.

PAN = polyacrylonitrile
PES = polyester
PA = polyamide
PP = polypropylene
PVC = polyvinylchloride
PE = polyethylene
PET = polyethyleneterephthalate
PS = polystyrene
PUR = polyurethane
Pol. Petr. Res = polymerised petroleum resin.

Presence of airborne microplastics in human lung tissue

31 synthetic polymer particles and fibres were observed in thirteen of the twenty autopsied decedents, of which 87.5% were particles (all fragments) and 12.5% were fibres (length to width ratio >3).

Approximately 0.56 MP particles/g of lung tissue. Mean weight of a set of normal adult lungs is approximately 840 g: 470 particles in both lungs.

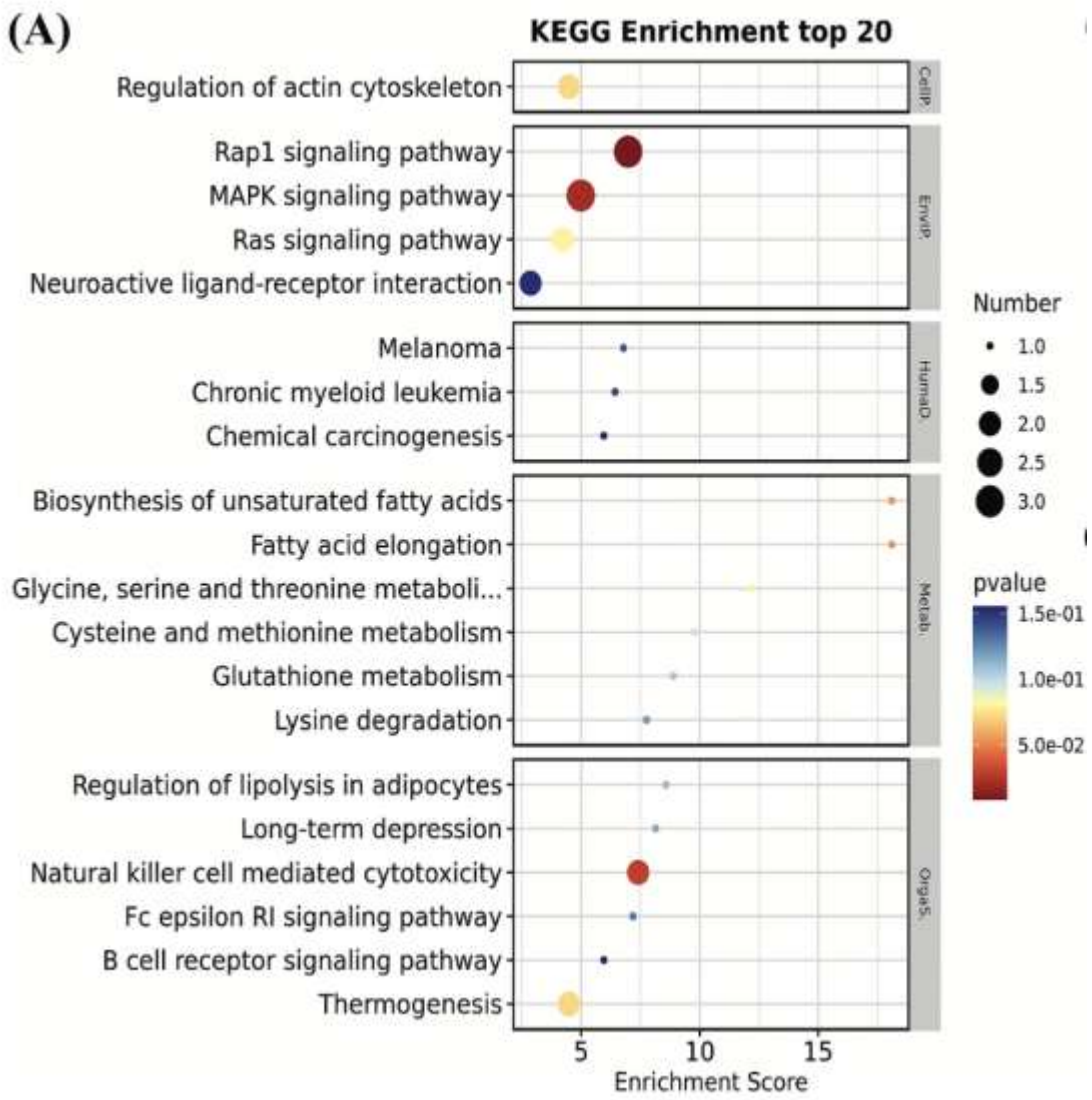
The mean particle size was 3.92 (±0.67) µm, ranging from 1.60 to 5.56 µm, while the mean fibre length was 11.23 (±1.96) µm, ranging from 8.12 to 16.80 µm.

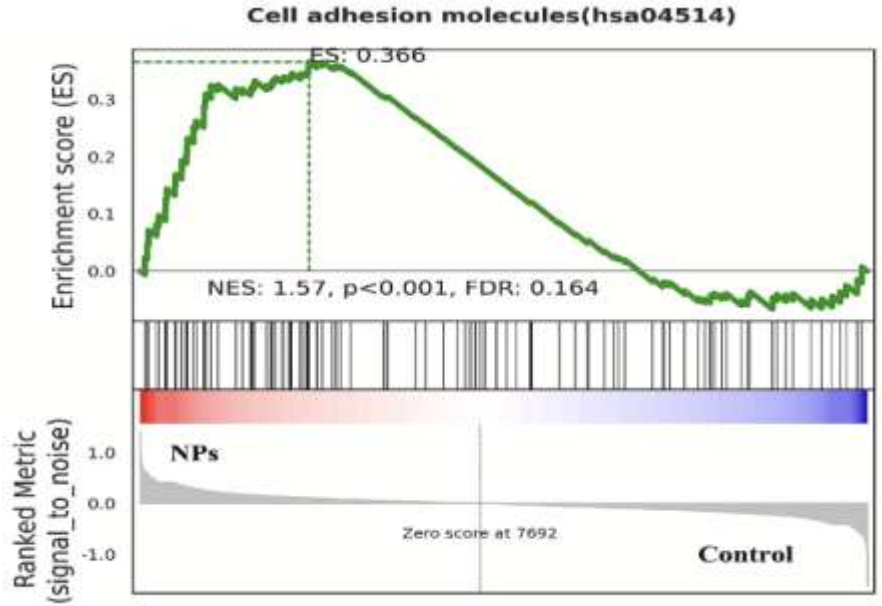
Particles found in this study ranged from 1.60 to 5.58 µm in size have the capability to reach the bronchial-alveolar regions by mechanisms of inertial impaction and sedimentation.

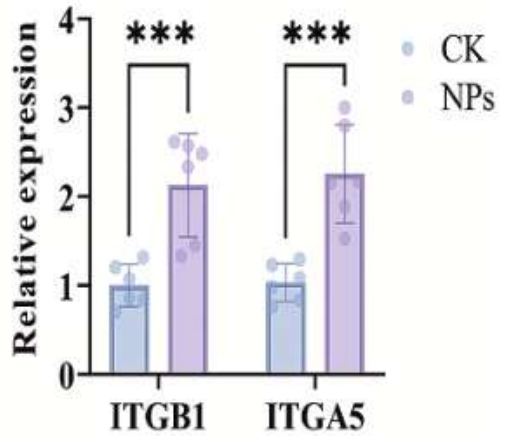
Polypropylene was the most frequent polymer (35.1%), followed by **polyethylene** (24.3%); cotton (16.2%); **polyvinyl chloride** and cellulose acetate (5.4%); and polyamide, polyethylene co polypropylene, **polystyrene**, polystyrene-co-polyvinyl chloride, and polyurethane (2.7%).

Amato-Lourenço LF et al. Journal of Hazardous Materials 416 (2021) 126124

Transcriptomic analysis of BEAS-2B cells exposed to PS-NPs (80nM) for 24 h.

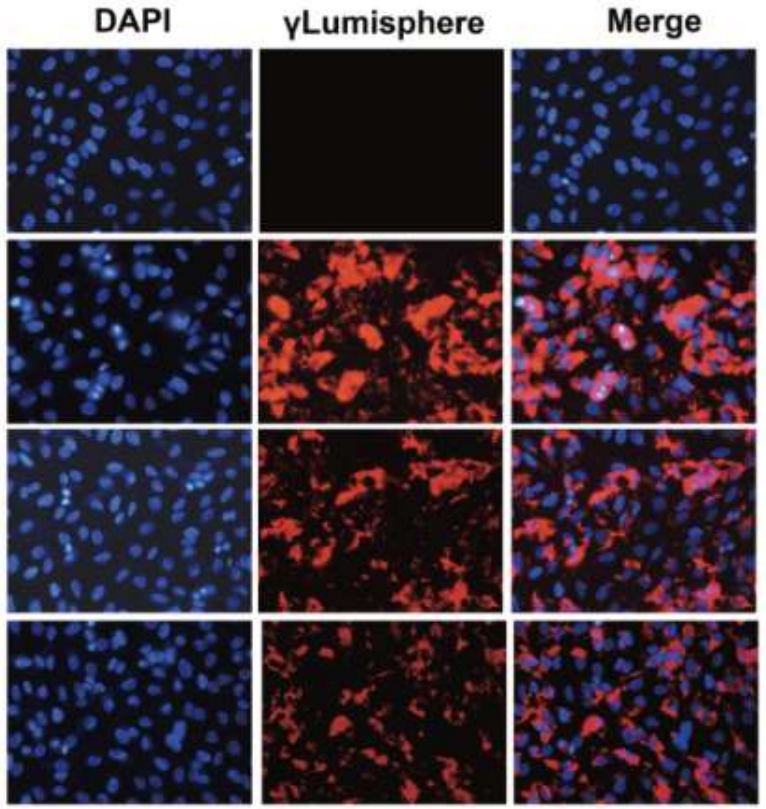


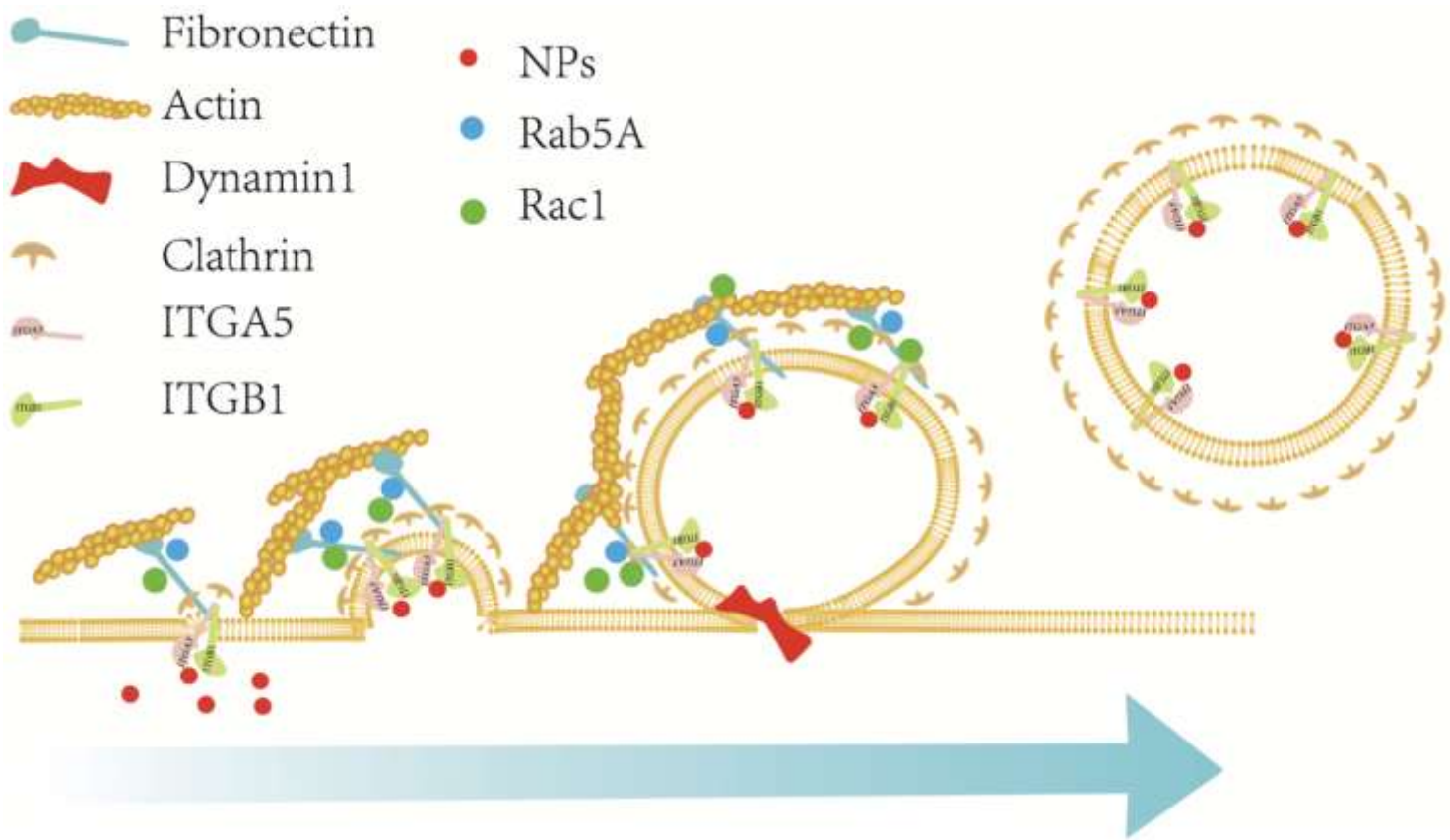




Han M et al. Sci Total Environ 2024 Nov 25:953:176017.

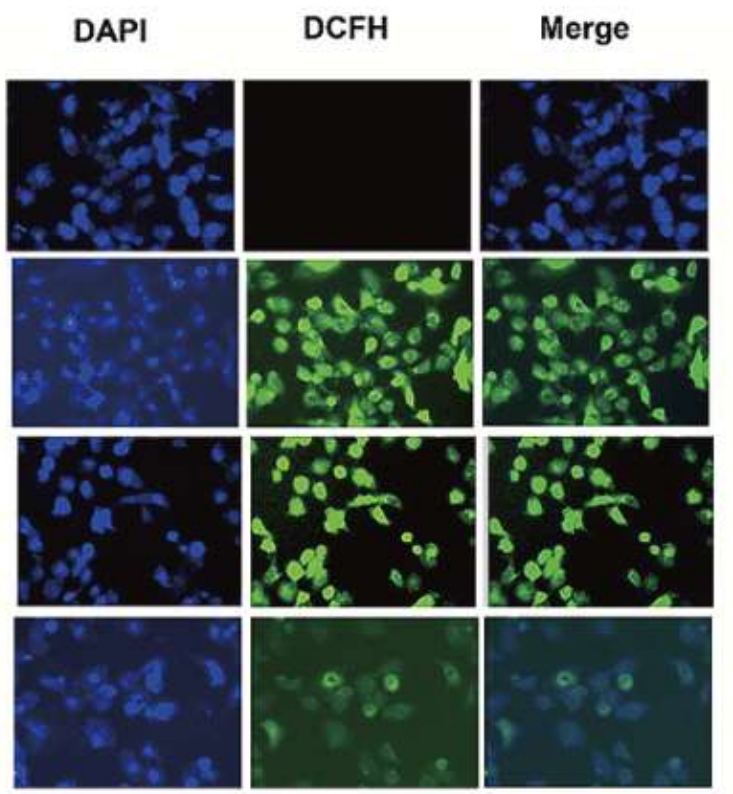
The progress of integrin A5B1 promote PS-NP ingestion.

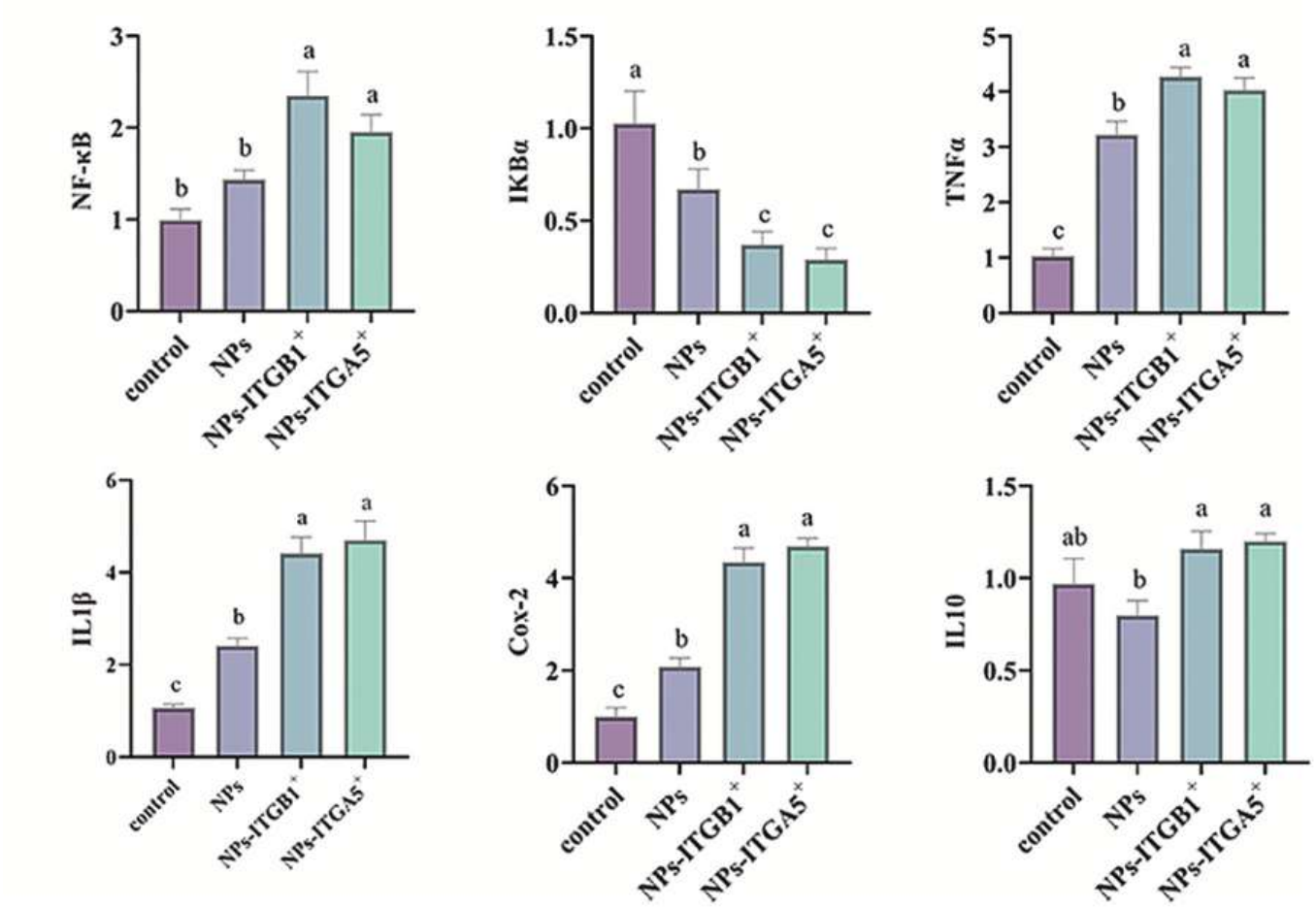




Han M et al. Sci Total Environ 2024 Nov 25:953:176017.

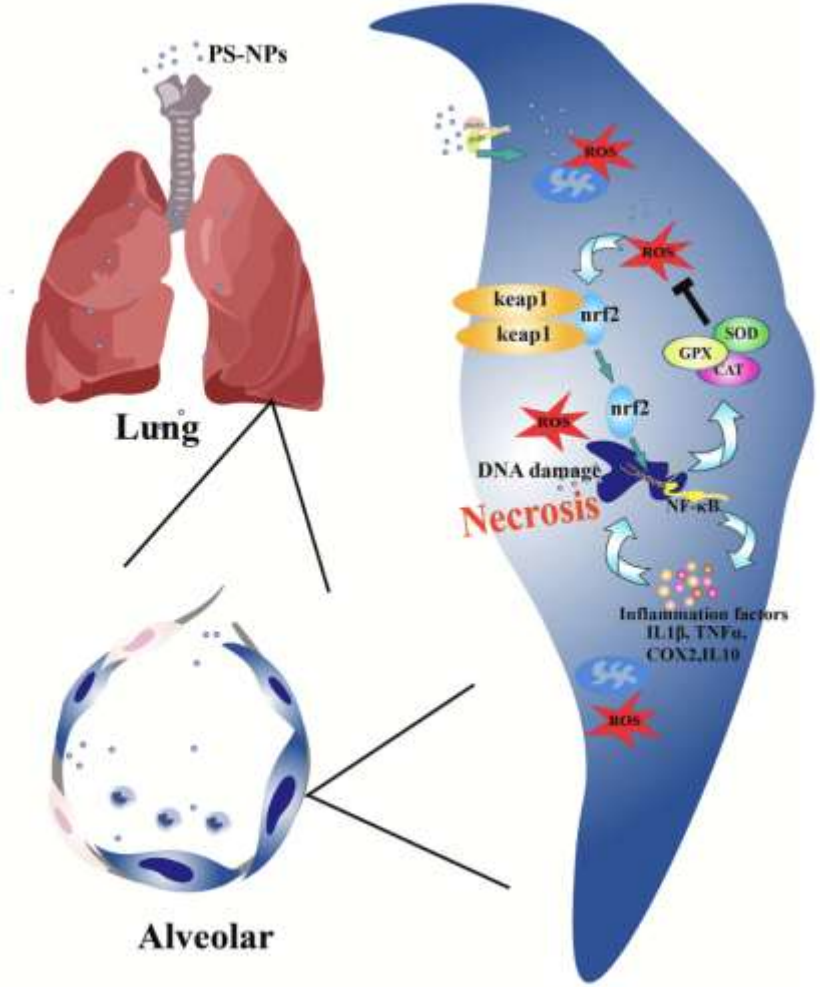
Integrin A5B1 promotes ROS production and inflammation under PS-NPs exposure.





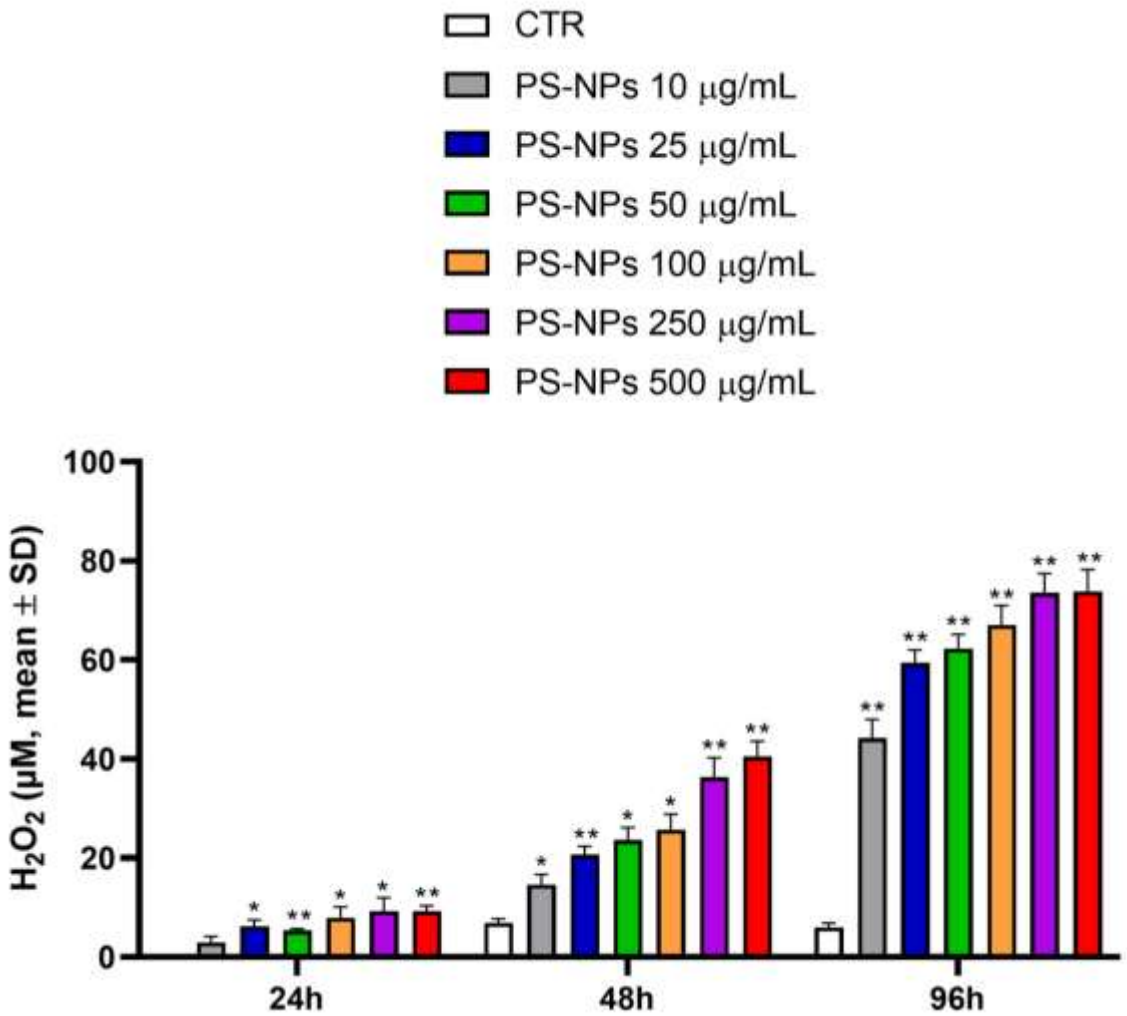
Han M et al. Sci Total Environ 2024 Nov 25:953:176017.

The integrin A5B1 promote PS NP ingestion, and then induce oxidative damage and necrosis



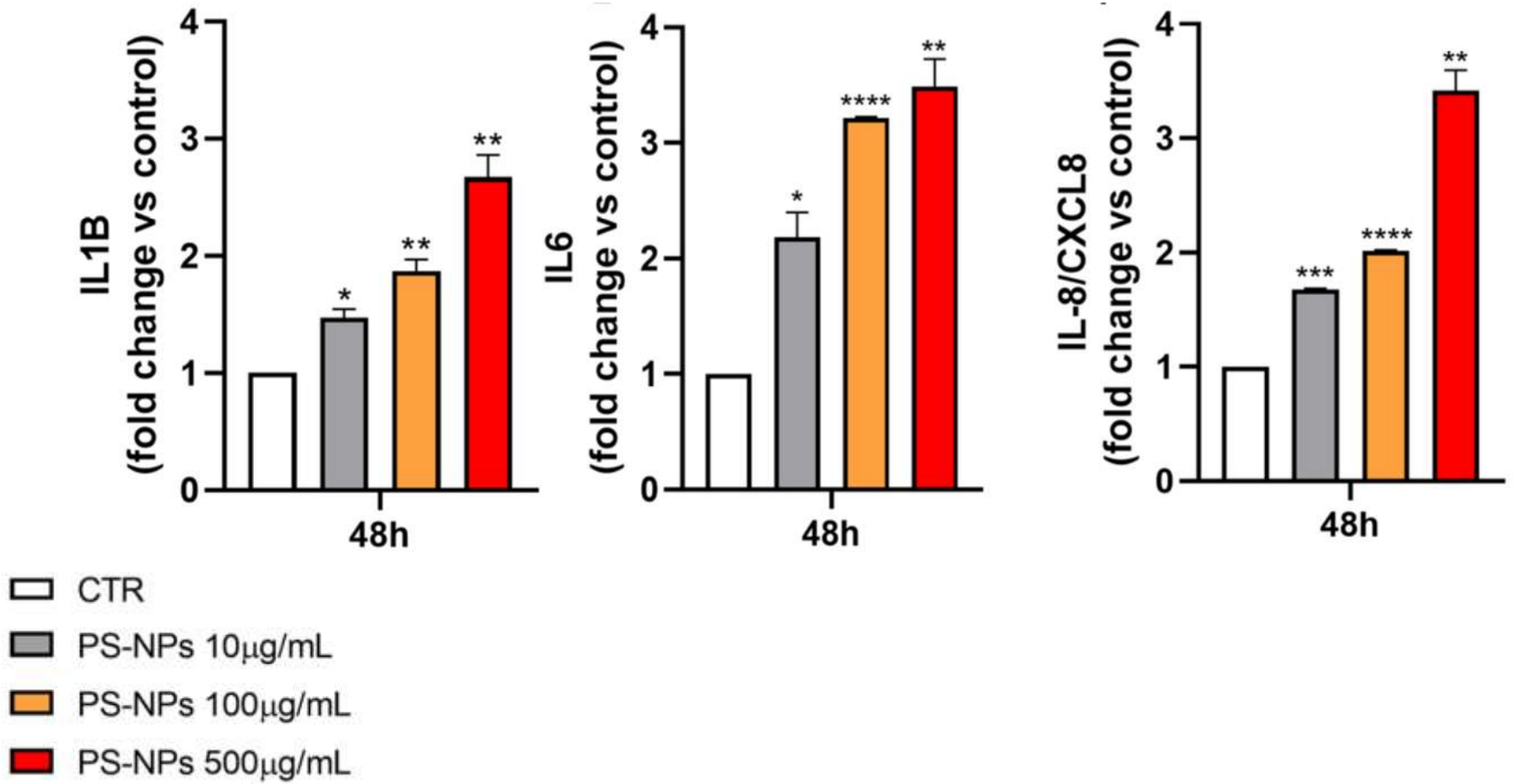
Han M et al. Sci Total Environ 2024 Nov 25:953:176017.

Effects of PS-NPs (0.8μM) on the intracellular generation of reactive oxygen species in A549 cells.



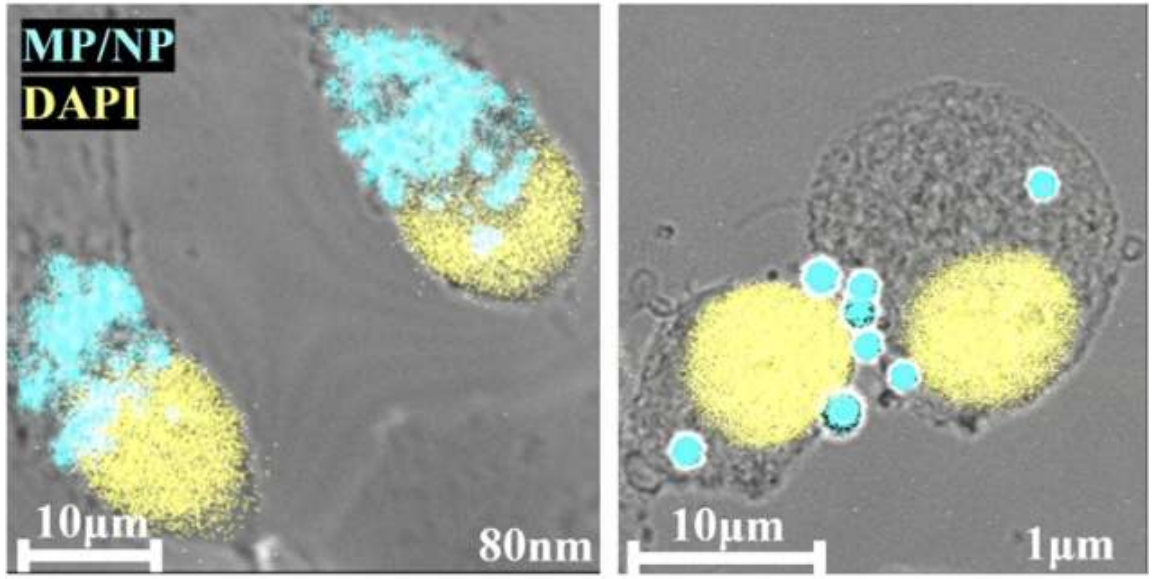
Milillo C et al. Front. Public Health 12:1385387

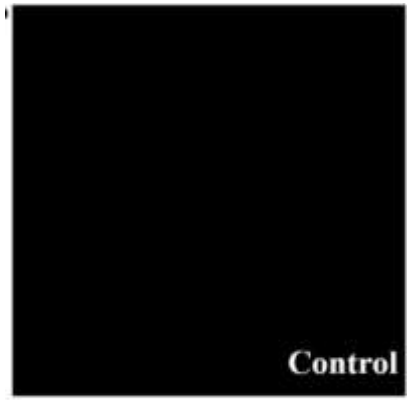
Effects of PS-NPs (0.8μM) on the cytokine expression in A549 cells.

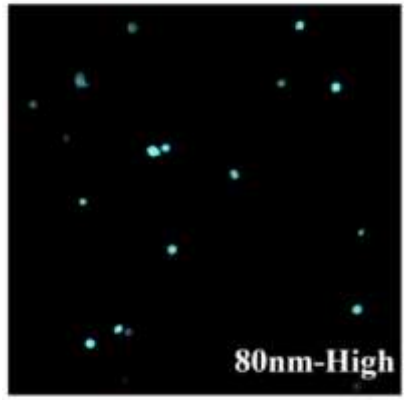


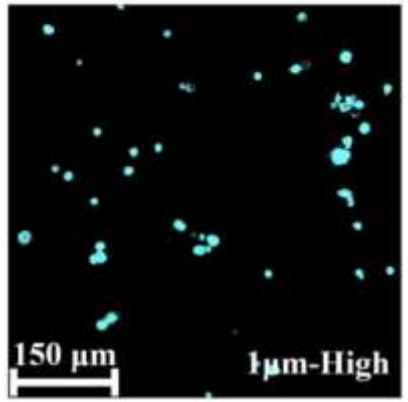
Milillo C et al. Front. Public Health 12:1385387.

Macrophage NP/MP phagocytosis and ROS production (NR8383 AM in vitro)



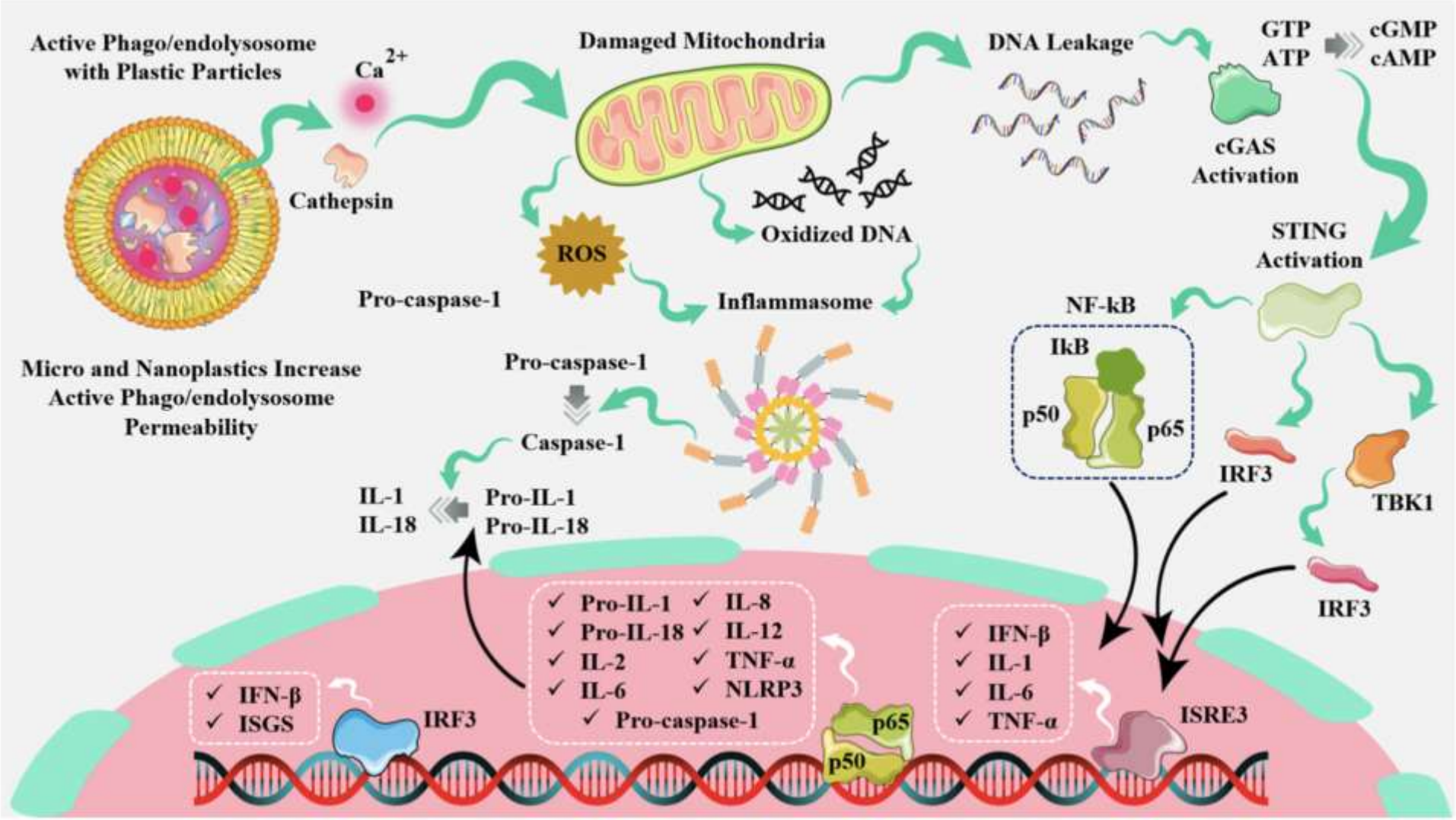






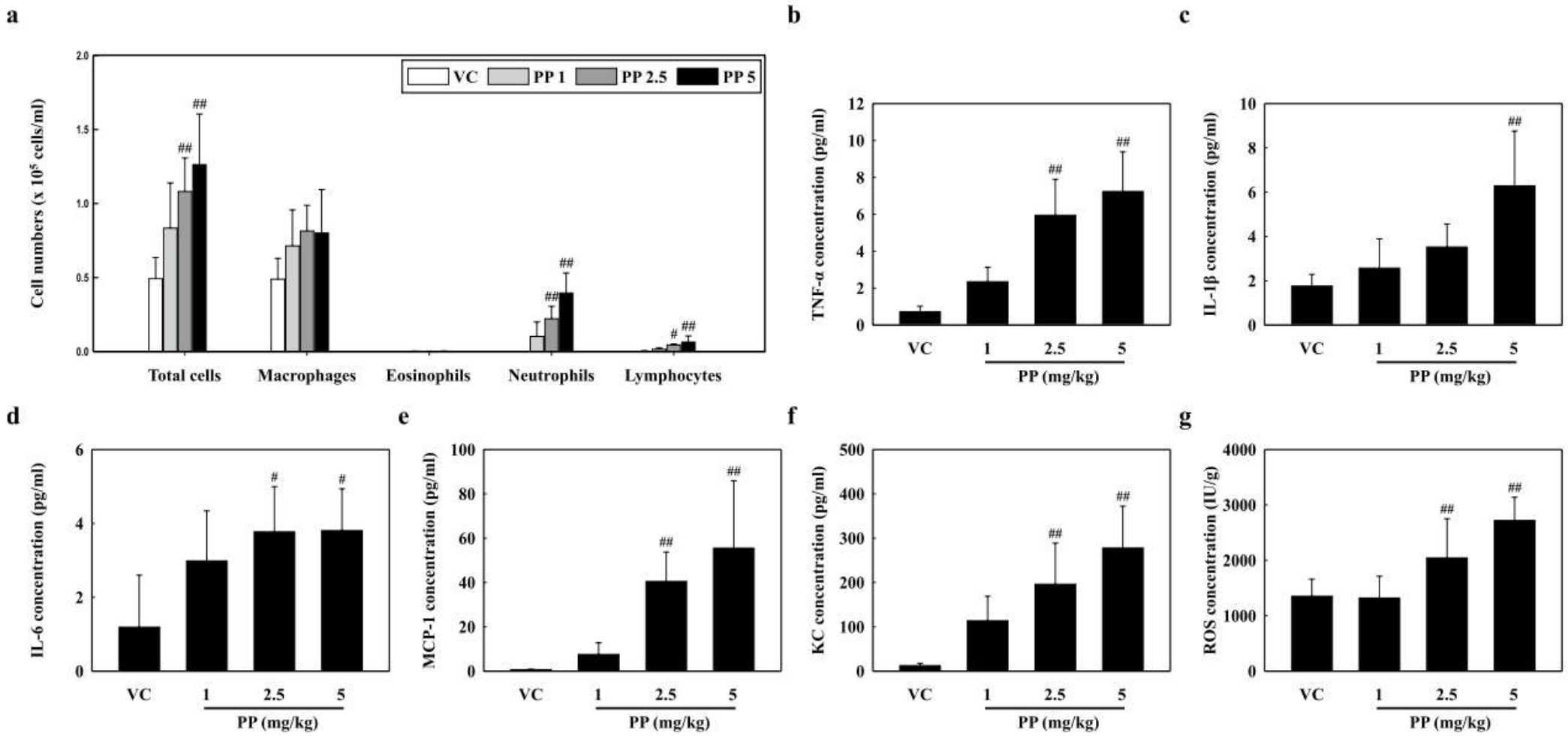
Chen L et al. Environ Sci Technol. 2025 Apr 15;59(14):6993-7003.

Effects of micro- and nanoplastic exposure on macrophages: a review of molecular and cellular mechanisms



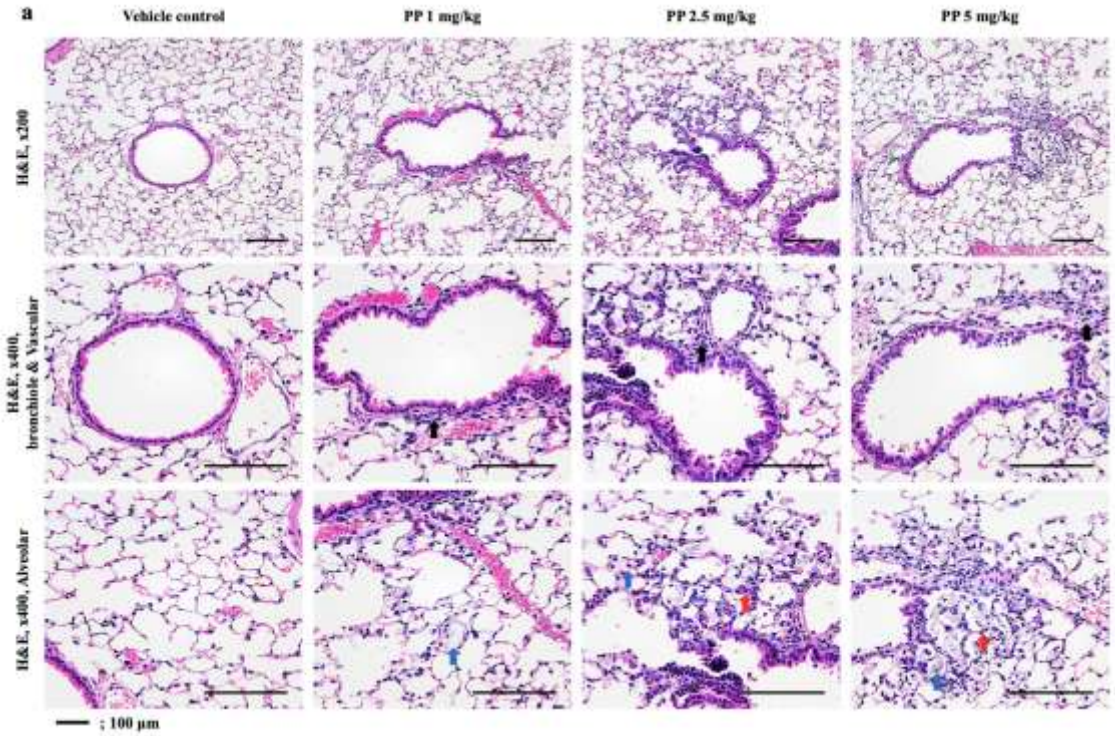
Ahmadi P et al. Toxicol Mech Methods 2025 May 20:1-24.

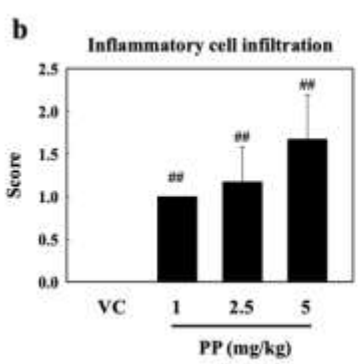
Cellular changes in the BALF obtained from intratracheal administration of PP NPs: NP size = 0.66μM

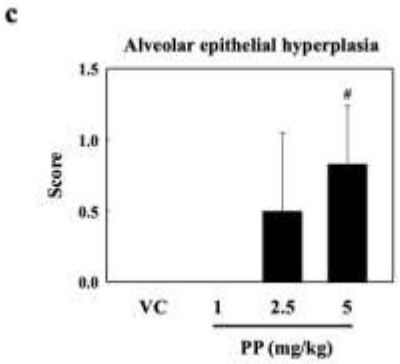


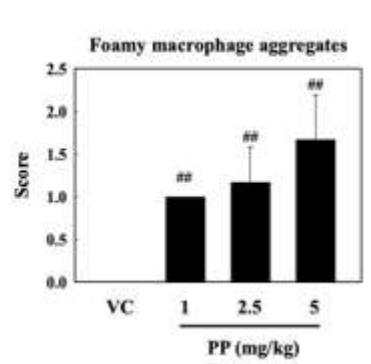
Woo J-H et al. Part Fibre Toxicol 2023 Jan 10;20(1):2.

PP induces inflammation and ROS production in the lung of mice



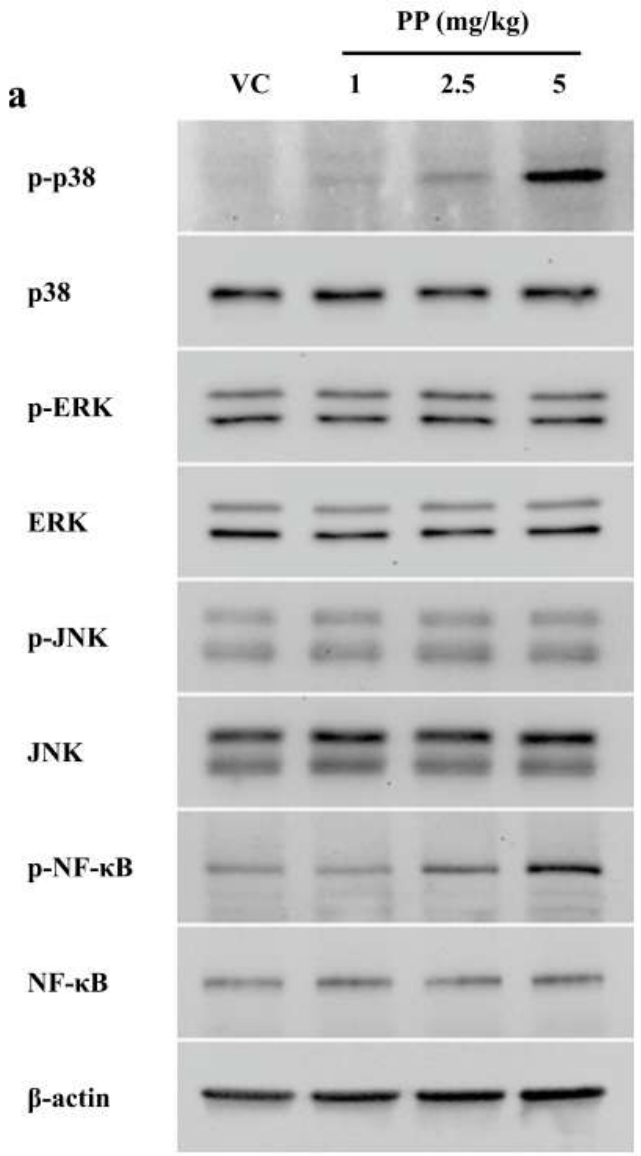


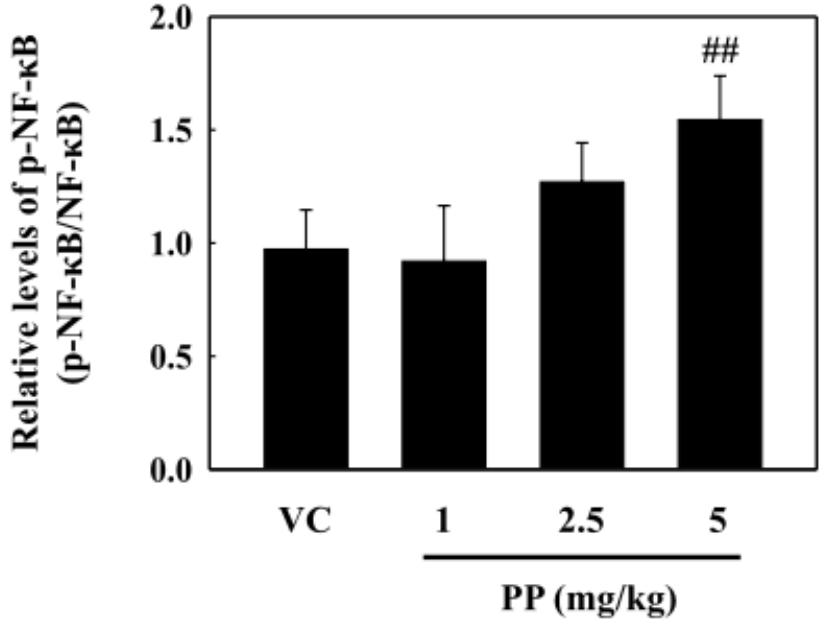




Woo J-H et al. Part Fibre Toxicol 2023 Jan 10;20(1):2.

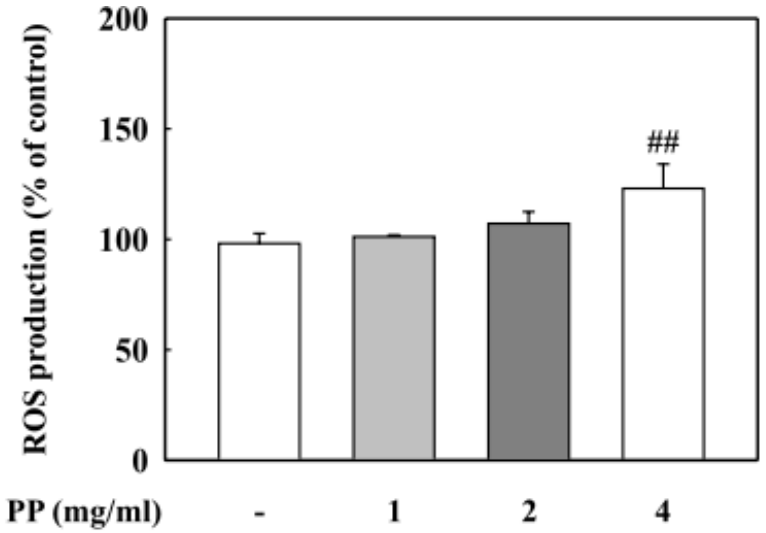
PP-instilled mice regulate p38 and NF-κB activation

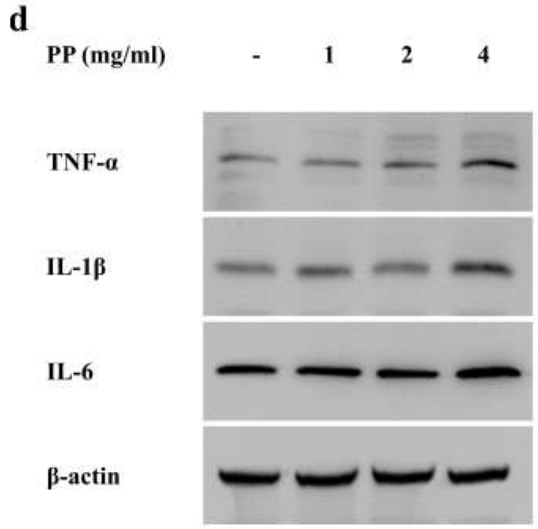


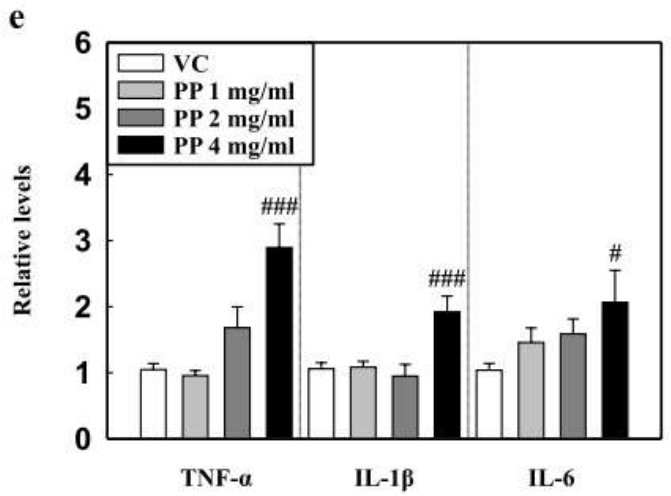


Woo J-H et al. Part Fibre Toxicol 2023 Jan 10;20(1):2.

PP stimulation induces ROS and inflammatory response

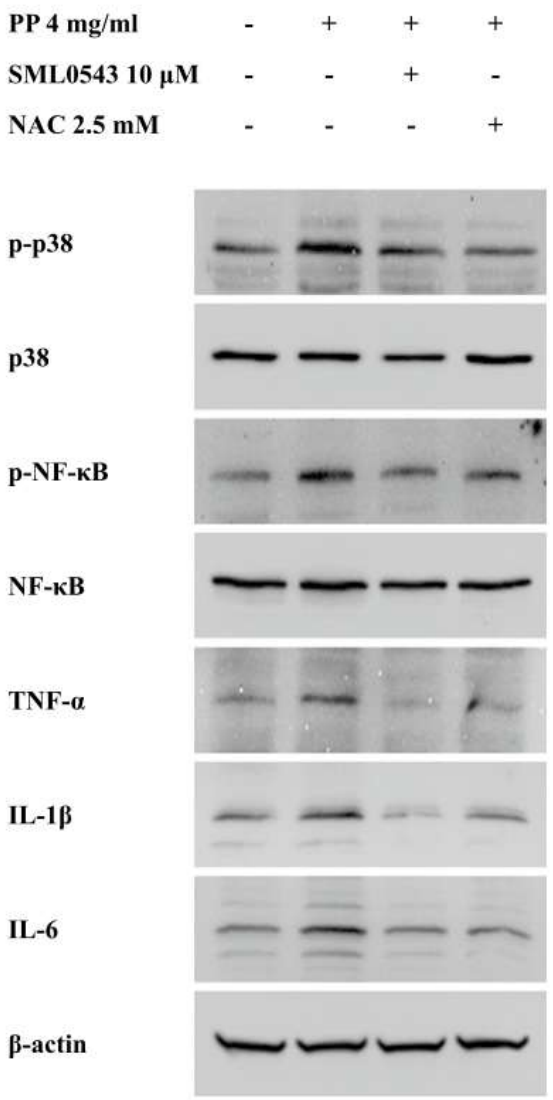


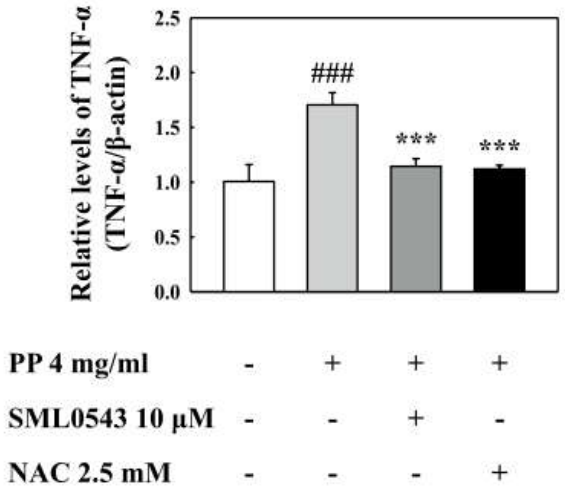


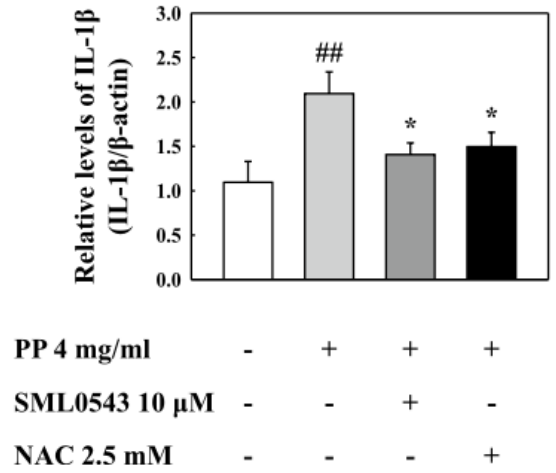


Woo J-H et al. Part Fibre Toxicol 2023 Jan 10;20(1):2.

p38 and NF-κB activation in PP-exposed A549 cells was regulated by inhibition of ROS

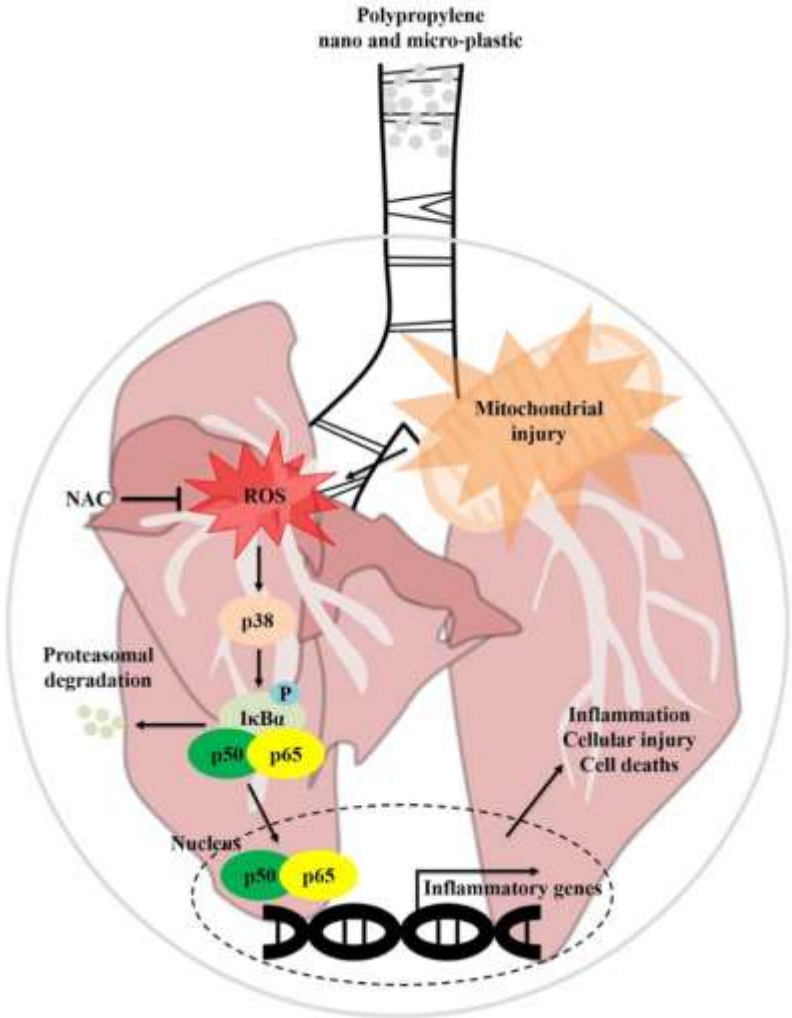






Woo J-H et al. Part Fibre Toxicol 2023 Jan 10;20(1):2.

Pathway by which NF-κB signaling is activated as a result of PP exposure in the lung

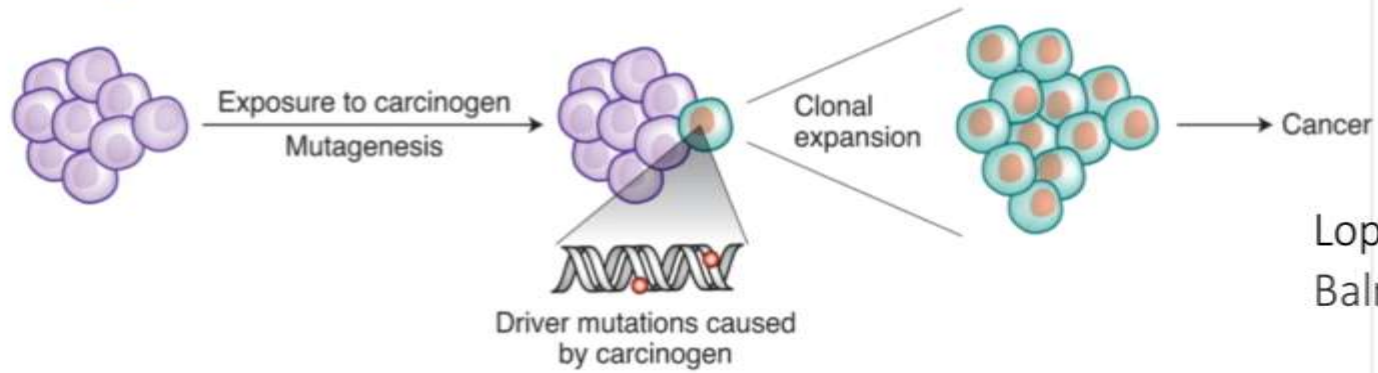


Woo J-H et al. Part Fibre Toxicol 2023 Jan 10;20(1):2.

How do Environmental Carcinogens Cause Cancer?

1. Classical Mutation Model: **Carcinogen → DNA Mutations → Tumour Growth**

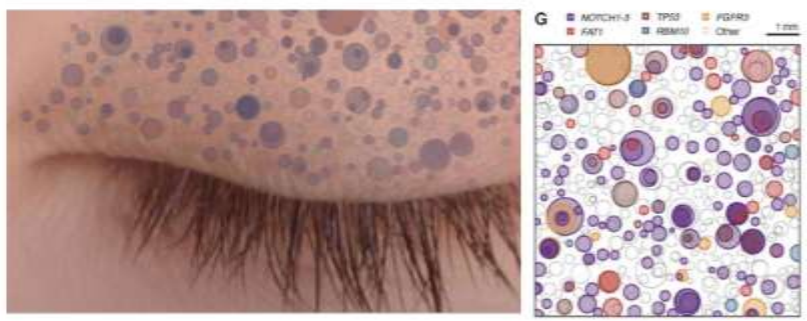
- UV light, Tobacco
- KRAS G12C mutation



Lopez-Bigas 2020
Balmain 2020

Evidence Against this model…:

- BRAF V600E in melanoma is not a UV light induced mutation
- Normal healthy tissue harbours mutant clones with cancer driver mutations with no evidence of cancer (Martincorena 2015)



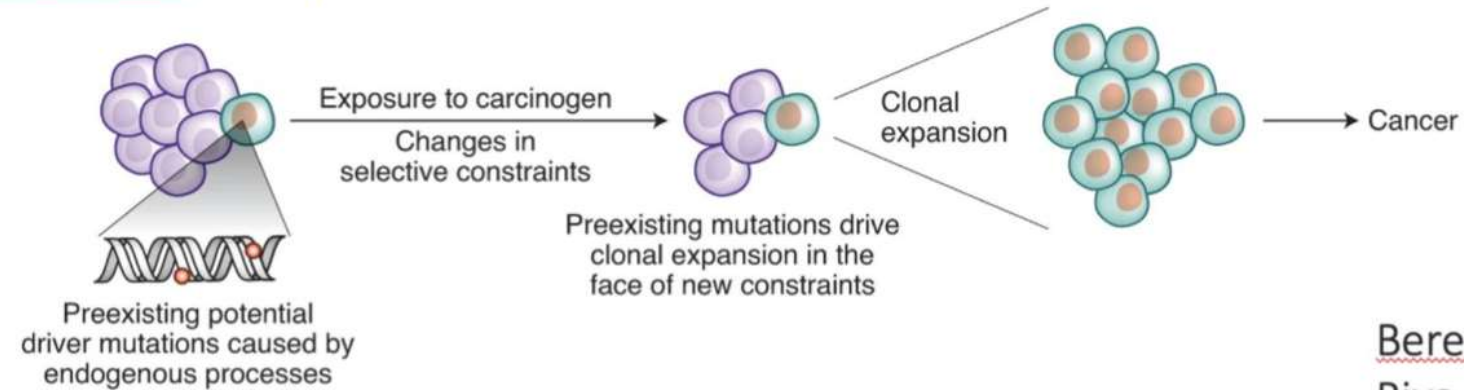
- 17/20 Environmental Carcinogens tested in mice – drive carcinogenesis **without** causing DNA mutations (Riva et al 2020)
- 10% of Smoker associated Lung cancers in TRACERx **do not** have driver mutations driven by tobacco

…. **Need for an alternative model of tumour initiation**

How do Environmental Carcinogens Cause Cancer?

2. Tumour Promotion Model (Berenblum 1947)

- **Initiator (mutation)**
- **Promoter**



Initiator
DMBA--> mutation

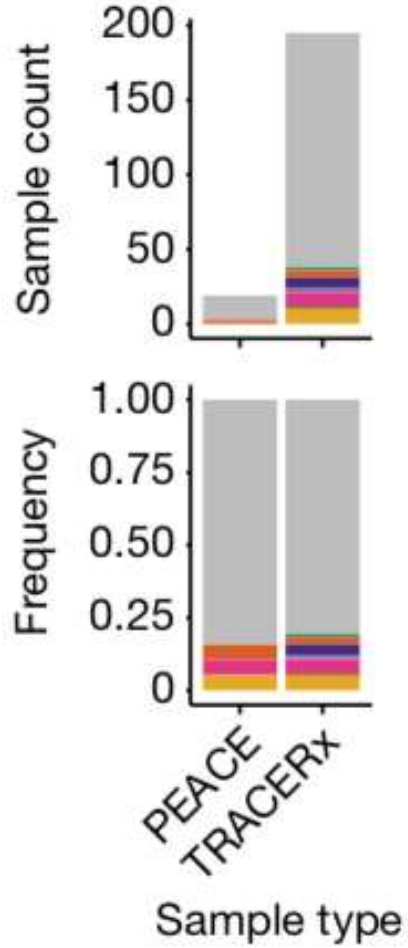
Promoter
TPA → clonal outgrowth

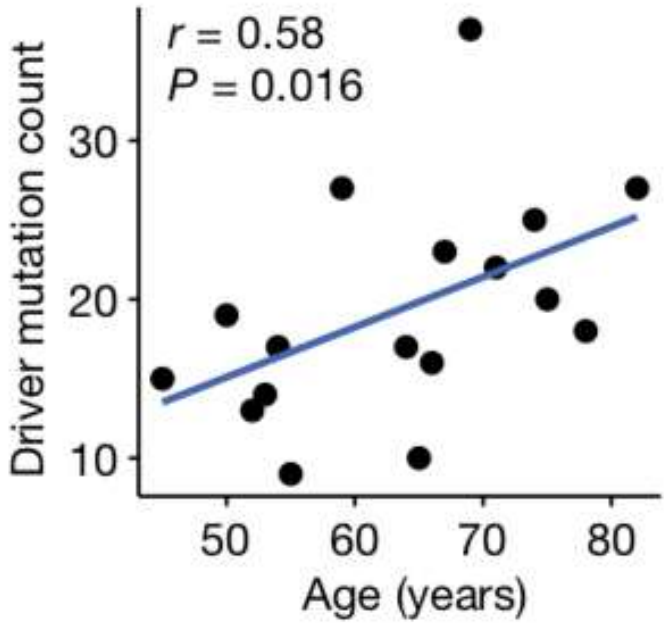
Berenblum 1947
Riva et al., 2020
Lopez-Bigas 2020
Balmain 2020

Air Pollution is known to be associated with lung cancer risk
Lung cancer in never smokers (LCINS) has **no** environmental carcinogen induced DNA mutations

Could Air Pollution Drive Lung Cancer through this Tumour Promotion model?

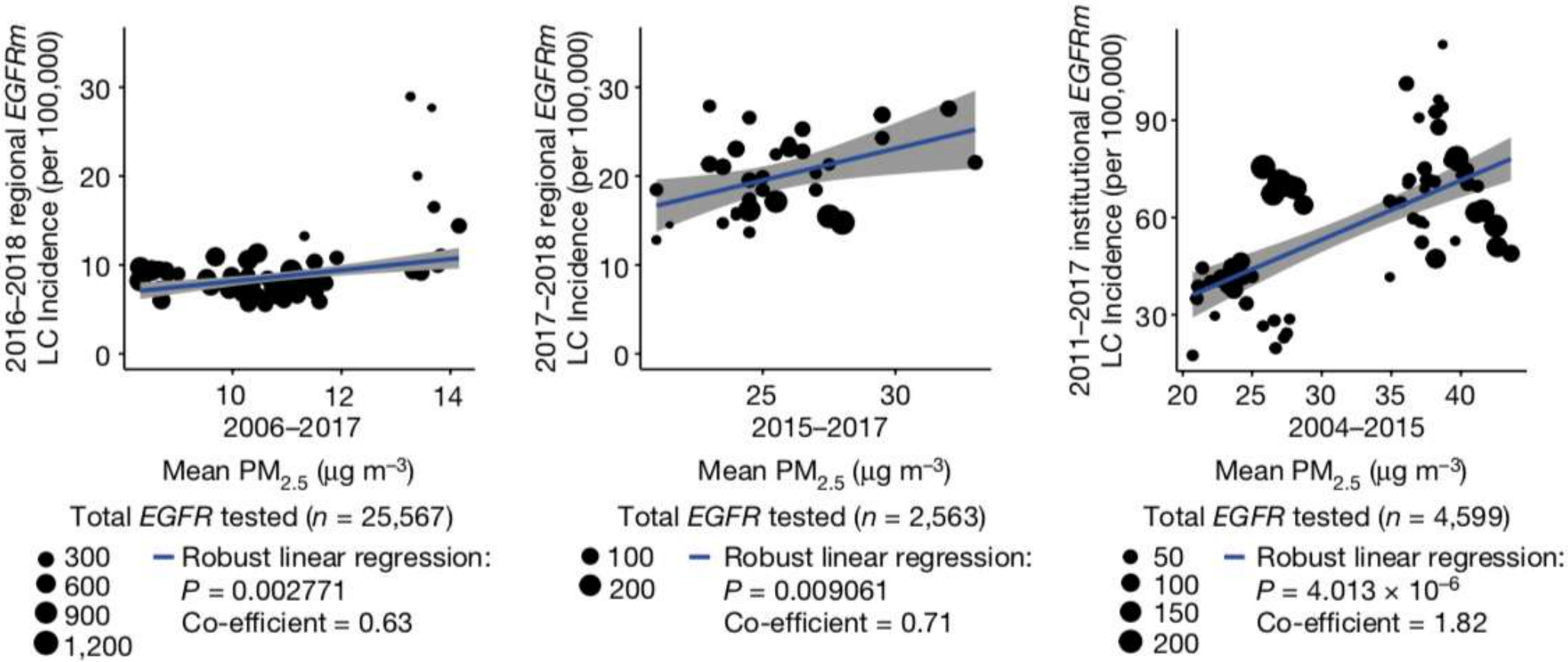
Lung adenocarcinoma promotion by air pollutants.





Hill W et al. Nature. 2023 Apr;616(7955):159-167.

Lung adenocarcinoma promotion by air pollutants.



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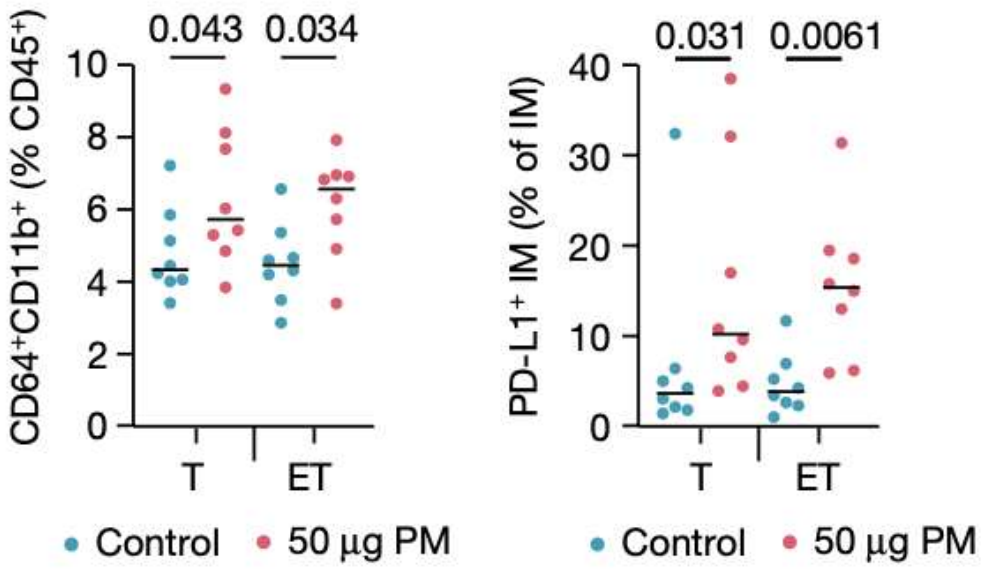

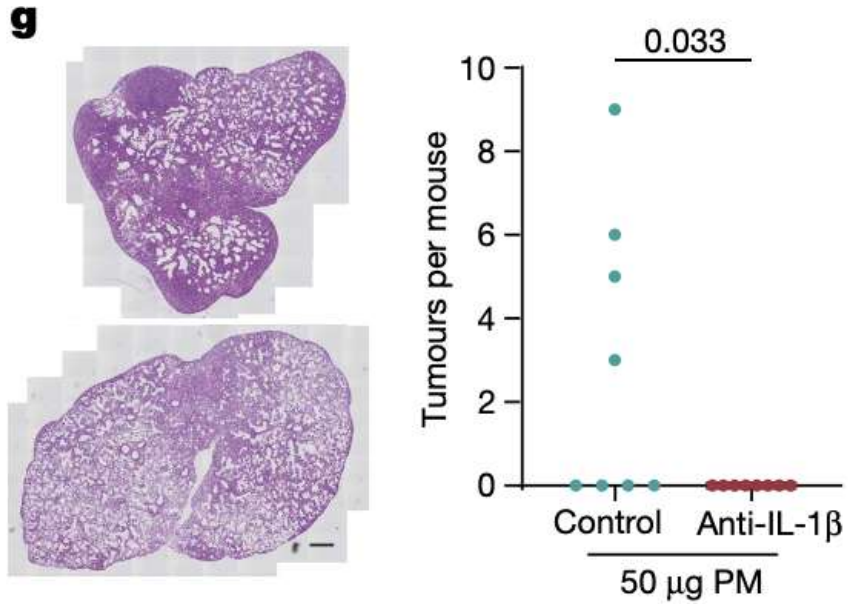

Hill W et al. Nature. 2023 Apr;616(7955):159-167.

A few key questions

What, if any, impact does the reported alveolar deposition of the larger atmospheric MPs have on lung cancer risk?

Are immunostimulatory *nano*plastics and small biactive MPs inhaled in biologically meaningful quantities by humans?

Are NPs deposited and maintained in the alveoli of humans (as they are in mice) in sufficient doses and durations to mediate local biologically meaningful effects?

Will any increase in inflammation mediated by inhaled NPs actively mediate promotion of otherwise dormant oncogenes to drive LCINS?