



# Hazard assessment of inhaled particulate matter – clinical aspects and experimental designs to study immune effects

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# Historical background

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## 1952 London Smog Episode



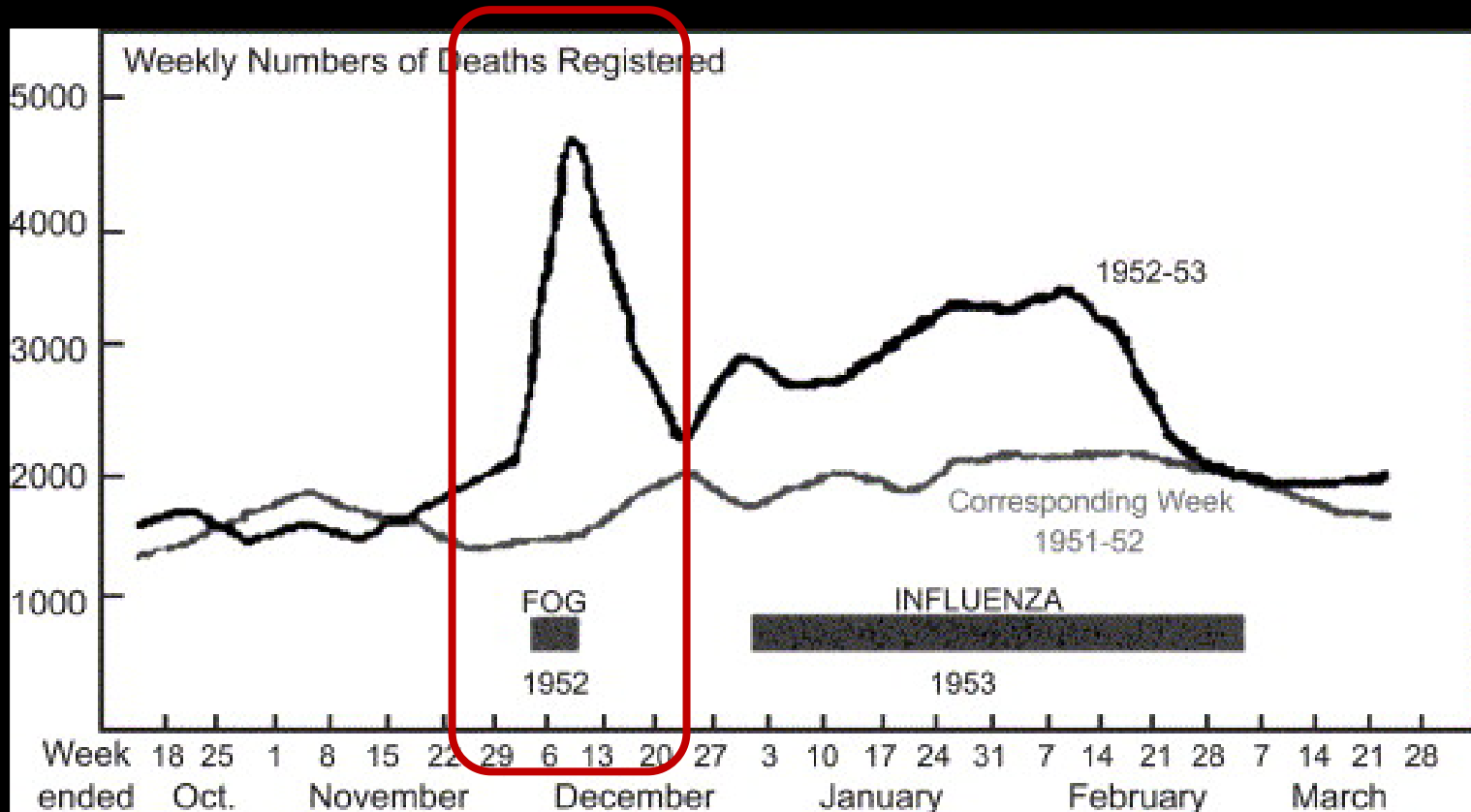
www.huffingtonpost.co.uk

## Intense Period of Air Pollution in London



# Historical background

## 1952 London Smog Episode



Whittaker et al. (2004). *Sci. Total Environ.* 334-335, pp. 435



# Adverse health effects of air pollution

## Epidemiological Studies

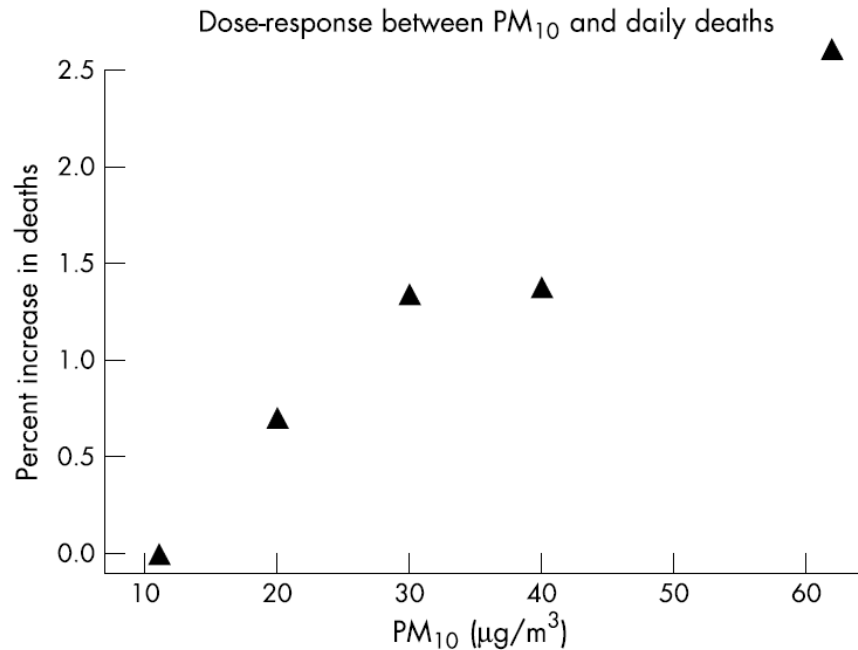
- Conducted in the 1990s
- A positive correlation between the level of particulate air pollution and increased morbidity and mortality rates
  - Schwartz. *Occ Environ Med* (1994)
  - Dockery et al. *New Eng J Med* (1993)
  - Pope and Dockery. *Air Pol Health* (1999)
  - Pope et al. *N Engl J Med* (2009)

### ORIGINAL ARTICLE

The effects of particulate air pollution on daily deaths: a multi-city case crossover analysis

J Schwartz

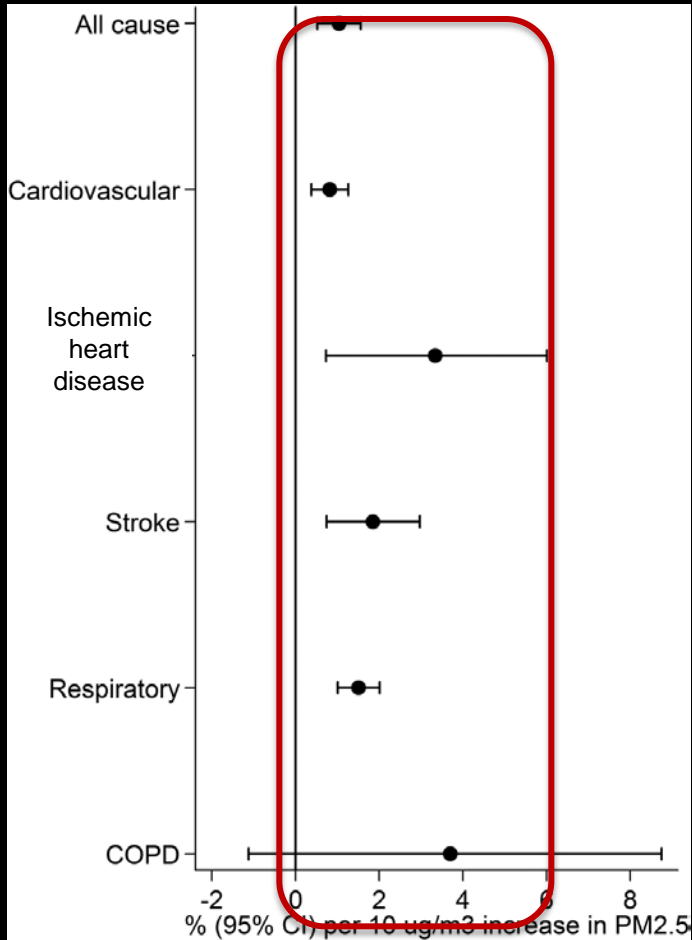
*Occup Environ Med* 2004;61:956–961. doi: 10.1136/oem.2003.008250



**Figure 1** shows the percent increase in the risk death on days with PM<sub>10</sub> concentrations in the ranges of 15–24 µg/m<sup>3</sup>, 25–34 µg/m<sup>3</sup>, 35–44 µg/m<sup>3</sup>, and 45 µg/m<sup>3</sup> and greater, compared to a reference of days when concentrations were below 15 µg/m<sup>3</sup>. Risk is plotted against the mean PM<sub>10</sub> concentration within each category.



# PM<sub>2.5</sub> - daily mortality and hospital admissions



A systematic review and **meta-analysis** of 110 peer-reviewed time series studies

=> Adverse health effects of short-term exposure to PM<sub>2.5</sub>: **10 µg/m<sup>3</sup> increment** associated with **1.04%** (95% CI 0.52% to 1.56%) **increase in the risk of death**

Atkinson et al. Thorax 2014



# Adverse health effects of air pollution



<https://en.wikipedia.org>



<http://inhabitat.com/>



<http://www.digitaljournal.com>



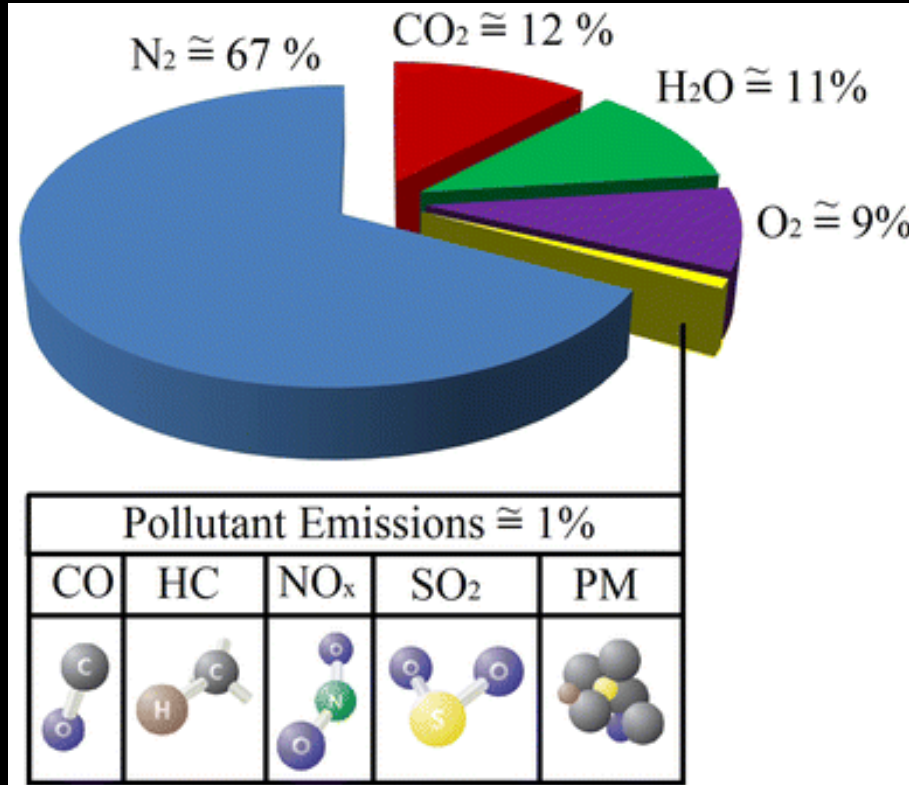
<http://www.mia.mk>



<http://amudu-gowripalan.blogspot.ch>



# Diesel engine exhaust components



Five main pollutant emissions from diesel engines:

- Carbon monoxide (CO)
- Hydrocarbons (HC)
- Particulate matter (PM)
- Nitrogen oxides (NO<sub>x</sub>)
- Sulphur dioxide (SO<sub>2</sub>)

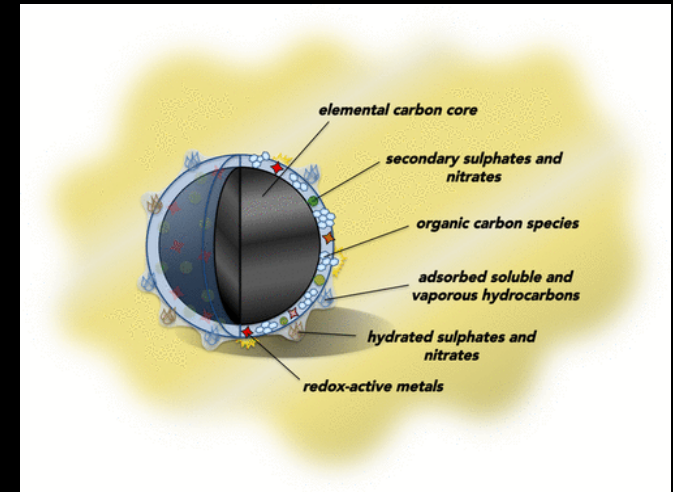
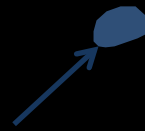
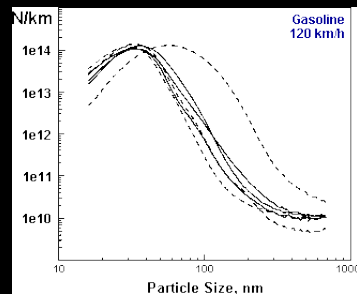
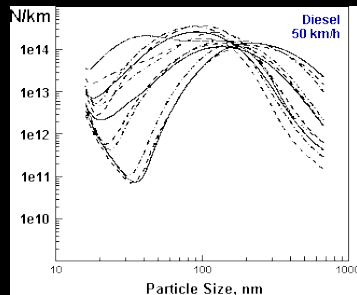
Reşitoğlu et al. Clean Technologies and Environmental Policy 2015



# Diesel engine exhaust components

- Diesel particle emissions can be divided into three main components
  - Soot
  - Soluble organic fraction
  - Inorganic fraction
- Inhalation of these particles may cause to important health problems such as premature death, asthma, lung cancer, and other cardiovascular issues.

Reşitoğlu et al. Clean Technologies and Environmental Policy 2015



Steiner et al. Arch Tox 2016

Stone et al. Env Health Persp 2017

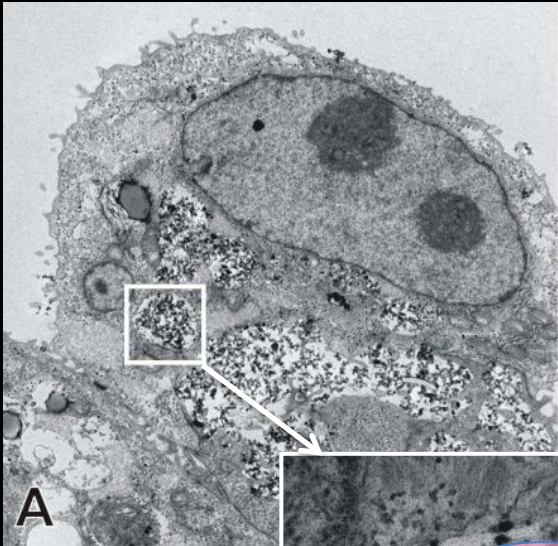
[https://www.dieselineet.com/tech/dpm\\_size.php](https://www.dieselineet.com/tech/dpm_size.php)



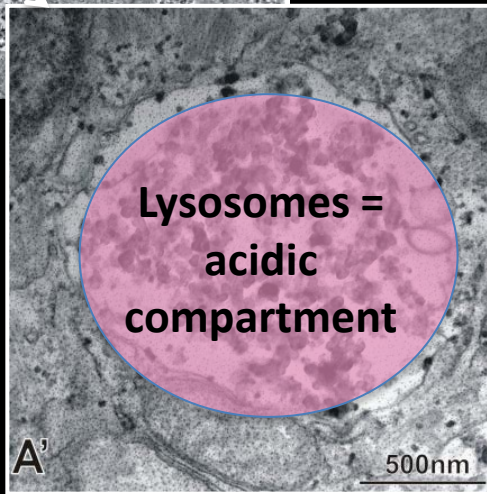


# Adverse effects of diesel exhaust particles

Macrophage



A



A'

500nm

Lehmann et al. Part  
Fibre Toxicol 2010

Gene



ulation  
uction)

2007



# Effects of diesel exhaust particles on the immune system

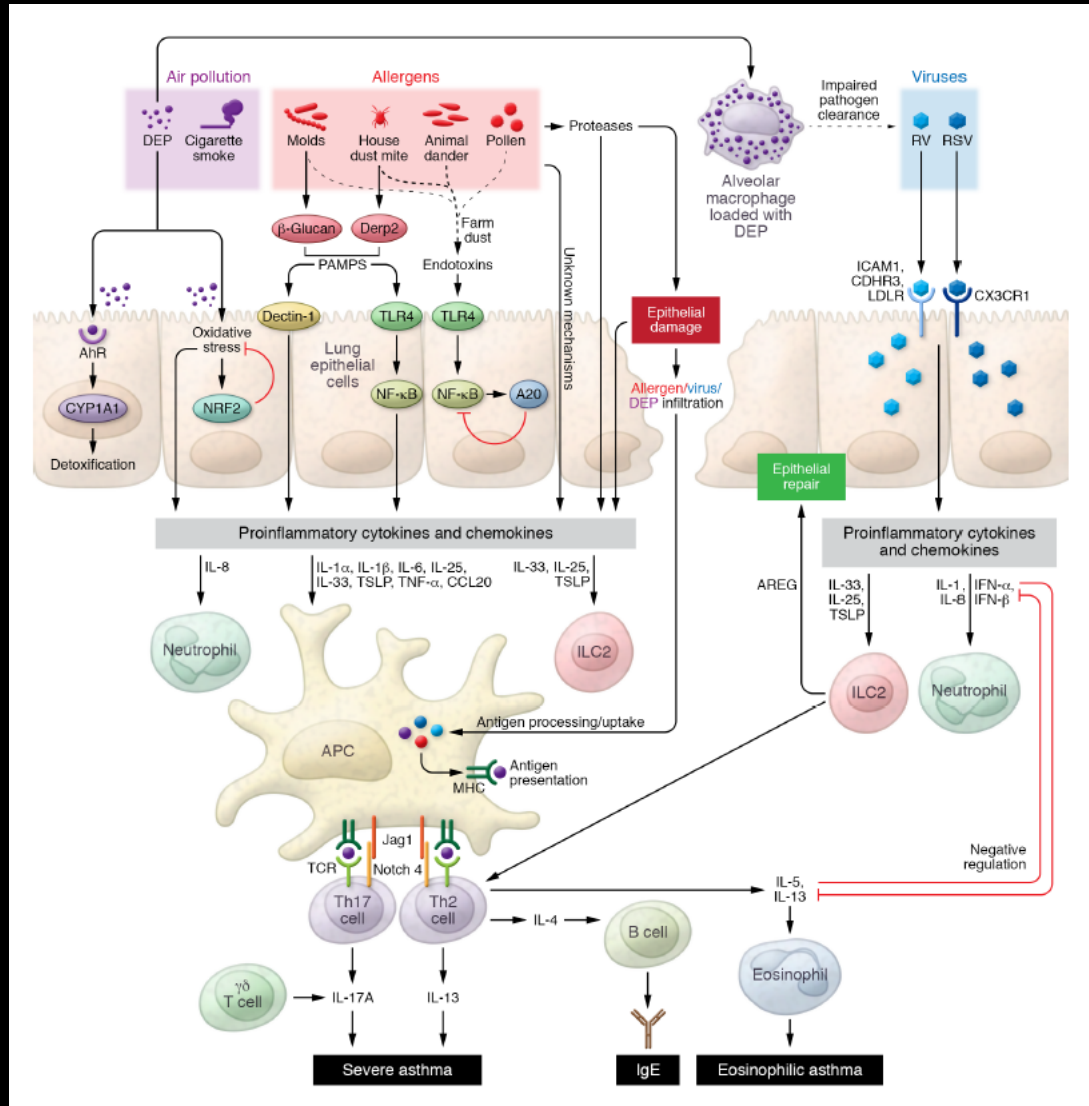
REVIEW SERIES: ALLERGY  
Series Editor: Karl Nadeau

The Journal of Clinical Investigation

## Environmental exposures and mechanisms in allergy and asthma development

Liza Bronner Murrison,<sup>1,2</sup> Eric B. Brandt,<sup>1</sup> Jocelyn Biagini Myers,<sup>1,2</sup> and Gurjit K. Khurana Hershey<sup>1,2</sup>

<sup>1</sup>Division of Asthma Research, Cincinnati Children's Medical Center, Cincinnati, Ohio, USA; <sup>2</sup>Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, Ohio, USA.





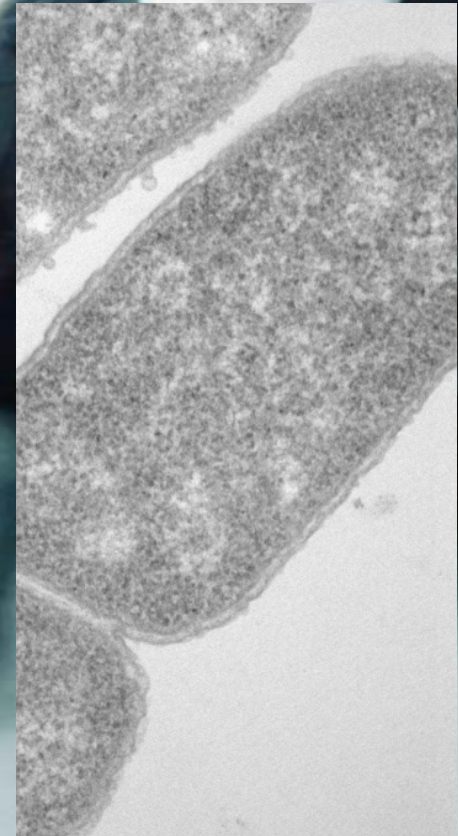
# Models to study effects of complete engine exhaust



<https://blog.bhf.org.uk/esc-congress-highlights-part-one-e6079efde0e>



<https://www.datasci.com/products/inhalation-and-exposure-systems/buxco-inhalation-exposure-system>



Steiner et al. Env Sci Technol 2014

<https://auto.howstuffworks.com/diesel-isnt-always-worse-polluter-than-gasoline.htm>



# Models to study effects of complete engine exhaust

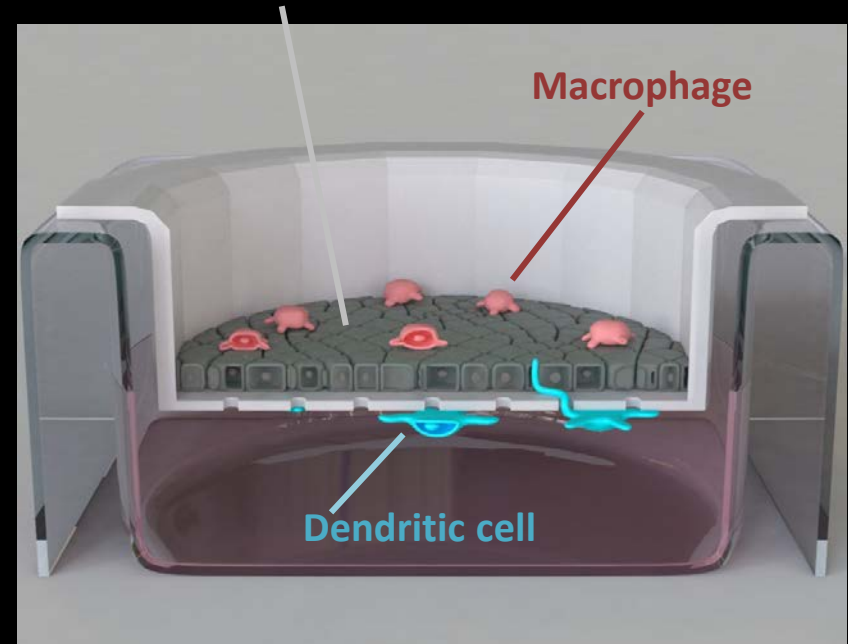
## Air-liquid interface lung cell models



<http://www.modifica.com.br/pele-humana-laboratorio-alternativa-testes-em-animais/#.Wqhbe43ruk8>

Voisin et al. Bull Eur Physiopathol Respir (1977)

## Epithelial cells (A549/16HBE14o-/primary cells)

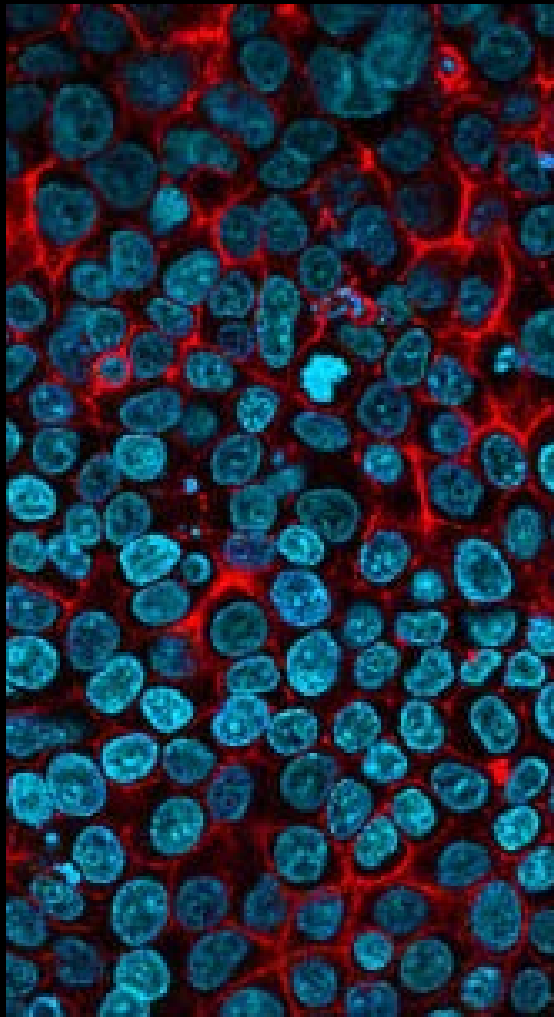


Fytianos et al. Nanomedicine (Lond) 2016  
Rothen-Rutishauser et al. Am J Respir Cell Mol Biol 2005;  
Blank et al. Am J Respir Cell Mol Biol 2007  
Rothen-Rutishauser et al. Review, Exp Opin Drug Metab Toxicol 2008  
Lehmann et al. Eur J Pharm Biopharm 2010

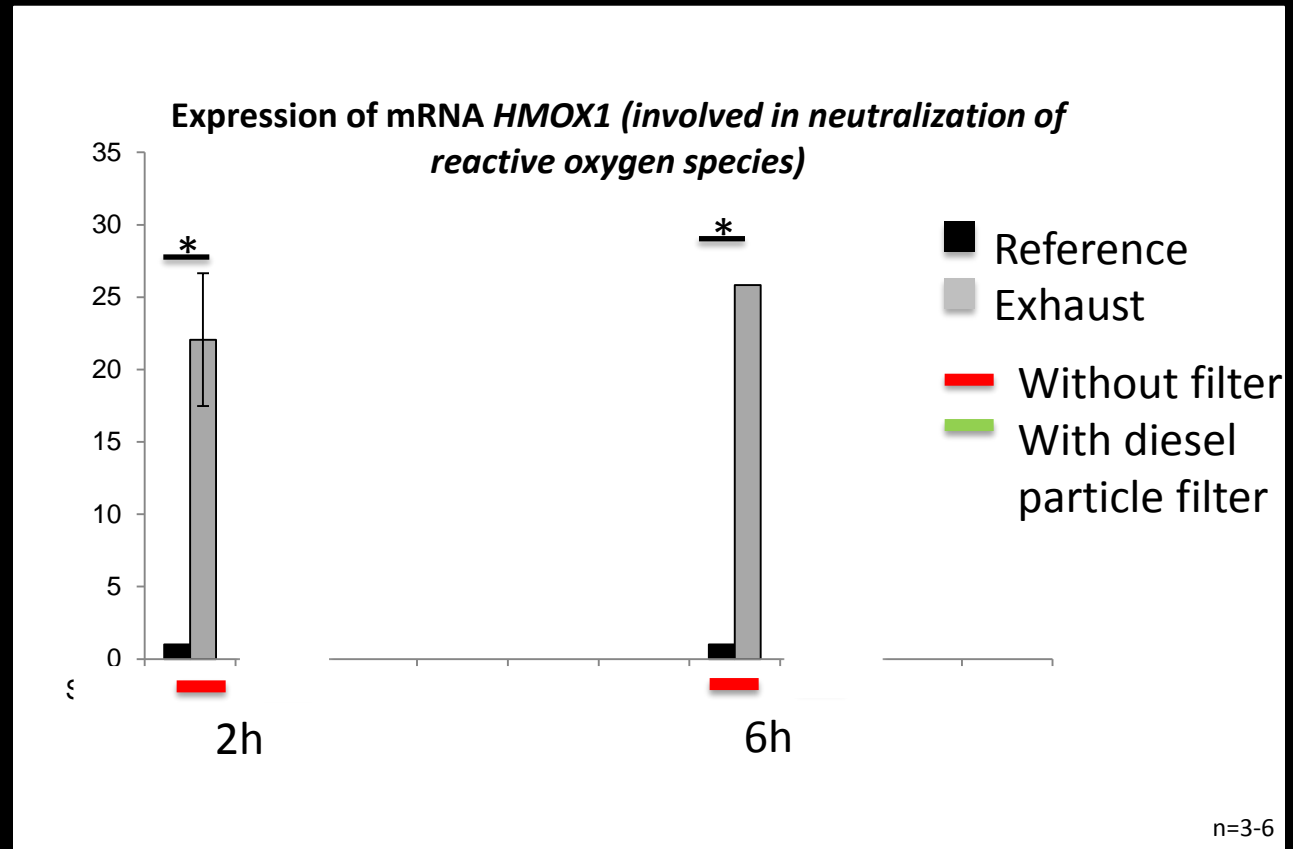


# Exposure of 3D lung cultures to complete engine exhaust

3D lung cell model

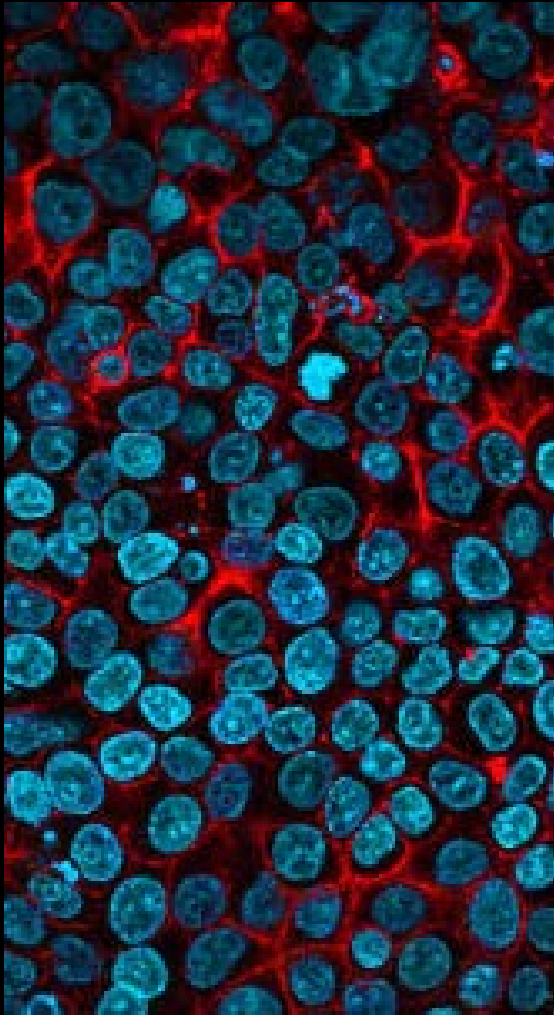


Oxidative stress response





# Exposure of 3D lung cultures to complete engine exhaust



	Without filter (Gas and particles)	With filter (Gas)
Cytotoxicity	No	No
Oxidative stress (GSH and <i>HMOX1</i> )	↑	↑
Pro-inflammatory reactions (TNF $\alpha$ , IL8)	↑	No

**Diesel particle filter** significantly **reduces** **(pro-)inflammation** *in vitro* but not oxidative stress

Steiner et al. Atmos Environ 2013

Similar results for gasoline particle filter studies

Bisig et al. Emiss Control Sci Technol 2015, Environ Pollut 2018



## Filtering diesel exhaust could make it worse

For those with allergies, supposedly cleaner fumes can mean worse lung function

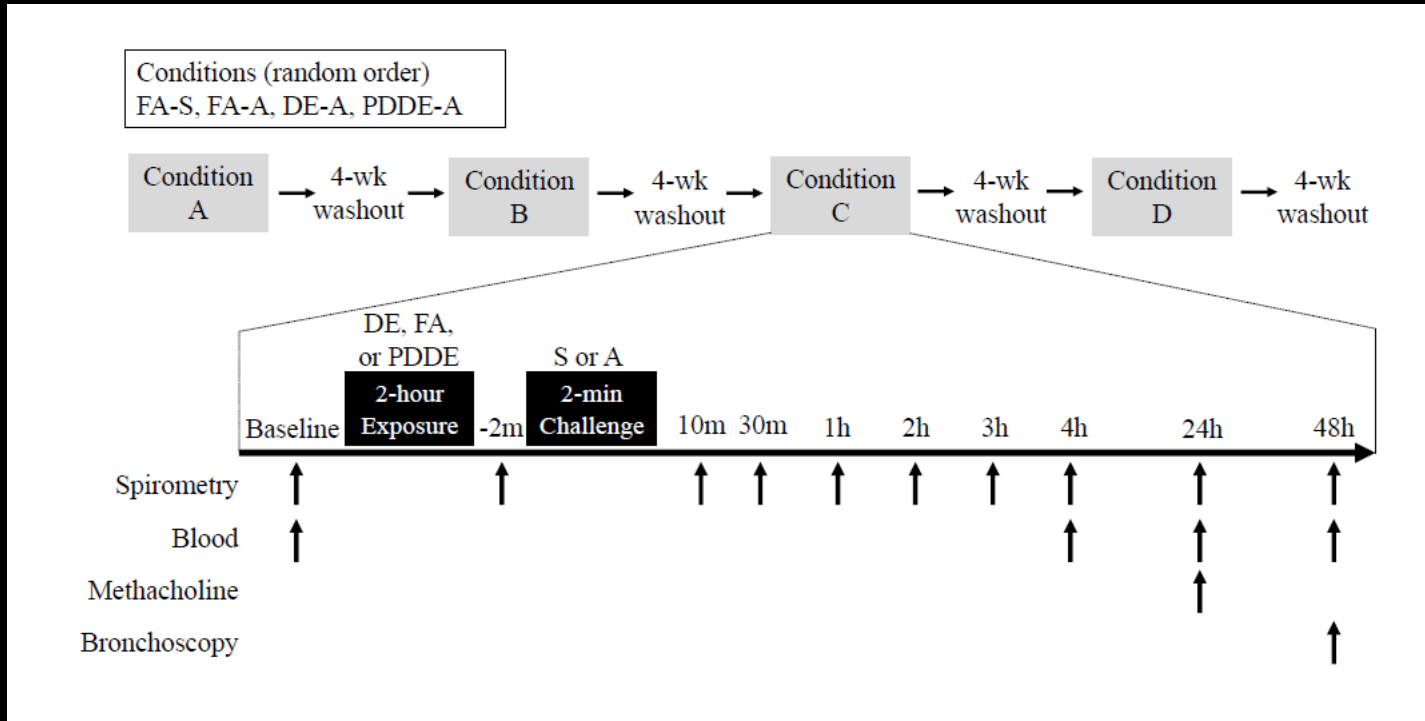
By Ula Chrobak | 18. April 2019

*“Filtration of particles from diesel exhaust is not the perfect solution for preventing adverse health effects,” says John Balmes, a professor of medicine who studies the health impacts of air pollution at the University of California, San Francisco and peer reviewed the paper prior to publication. “We need to reduce exposure to the gaseous components of diesel exhaust.”*

<https://www.popsci.com/diesel-filter-worse-allergies/>



# Exposure of engine exhaust to allergen-sensitized participants



Randomized double blinded crossover study design:

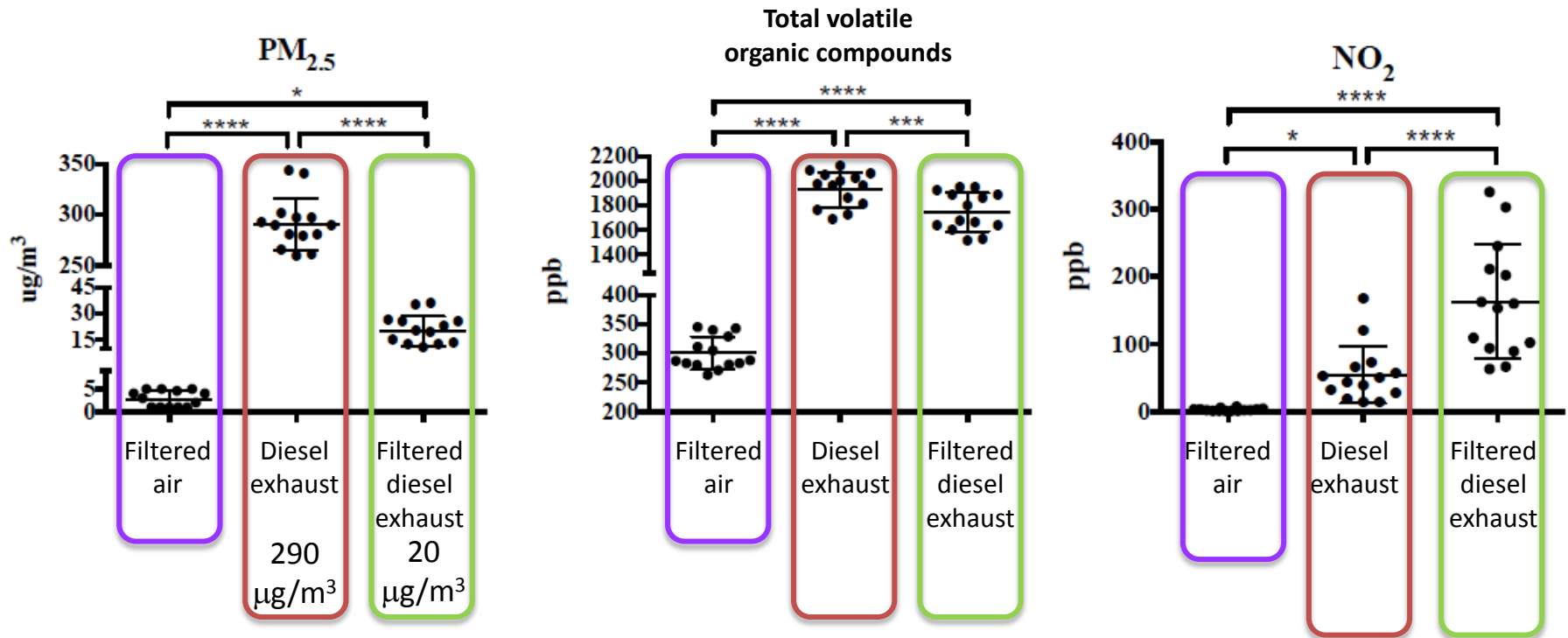
- Filtered air (FA) with or without allergen
- Diesel exhaust (DE) with allergen
- Particle-depleted diesel exhaust (PDDE) enriched with allergen

Wooding et al. Am J Respir Crit Care Med. 2019





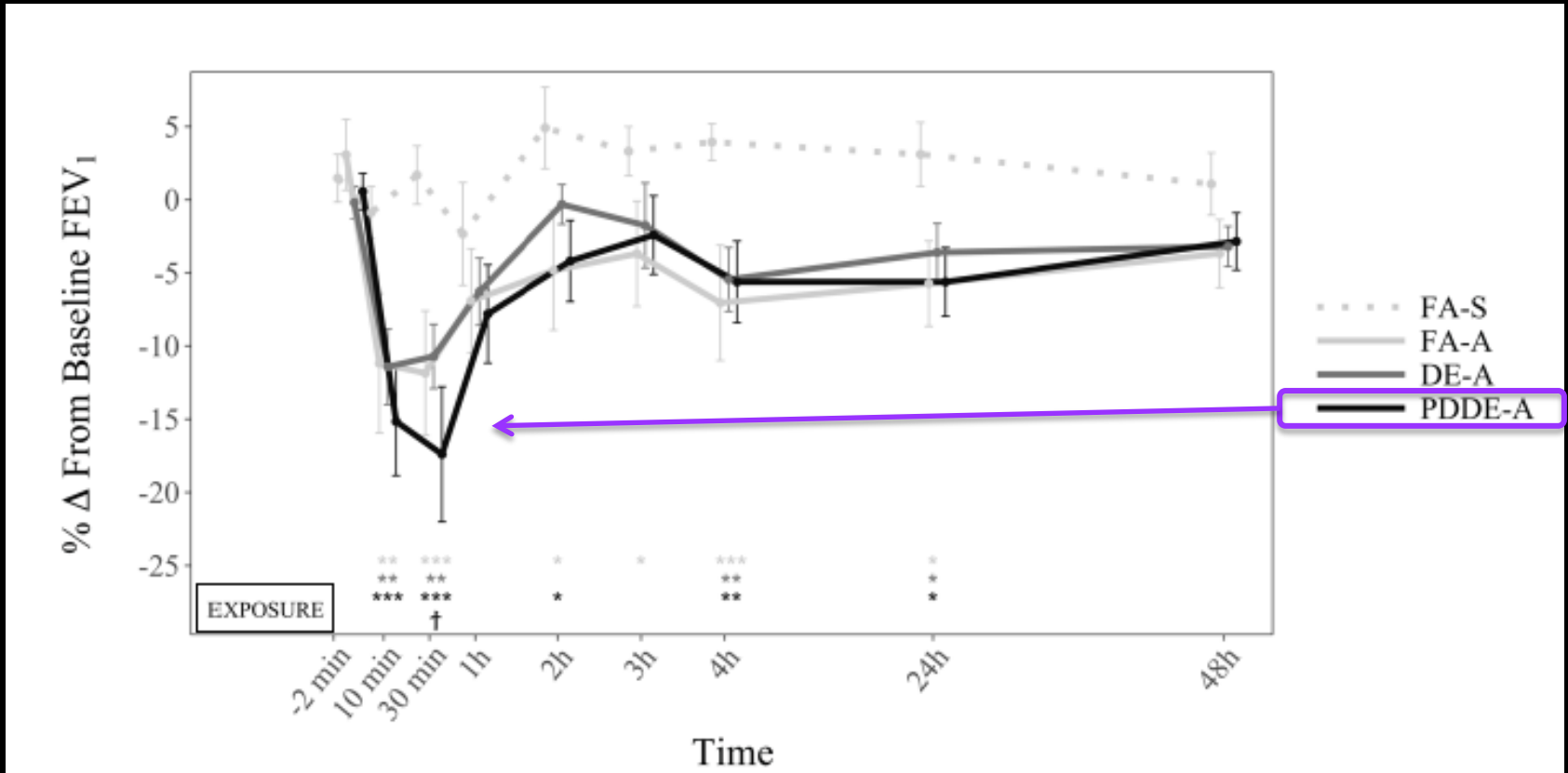
# Exposure of engine exhaust to allergen-sensitized participants



Wooding et al. Am J Respir Crit Care Med. 2019



# Effect on forced expiratory volume in 1 second (FEV<sub>1</sub>)



Wooding et al. Am J Respir Crit Care Med. 2019



# Conclusions

Combustion engine exhaust components result in adverse health / cellular effects

Complete exhaust might lead to a different toxicity than only the single components

Adverse effects persist even after particle depletion suggesting that some diesel particulate-filtering technologies may not protect against the harmful effects of diesel exhaust.

<https://auto.howstuffworks.com/diesel-isnt-always-worse-polluter-than-gasoline.htm>



# Acknowledgments

## BioNanomaterials group



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Christoph Bisig



Sandro Steiner

