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Heterogeneity in toxicity of particulate matter collected across Europe

Flemming R. Cassee

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Particulate Matter:
Properties Related to Health Effects

Outline

- Studies with PM collected across Europe
  - RAIAP project
  - HEPMEAP project
  - PAMCHAR project
- Conclusions

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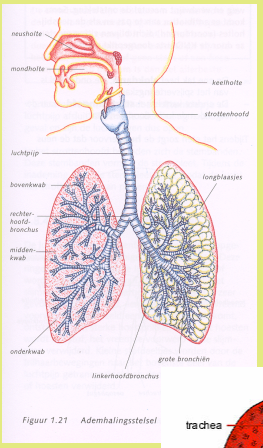
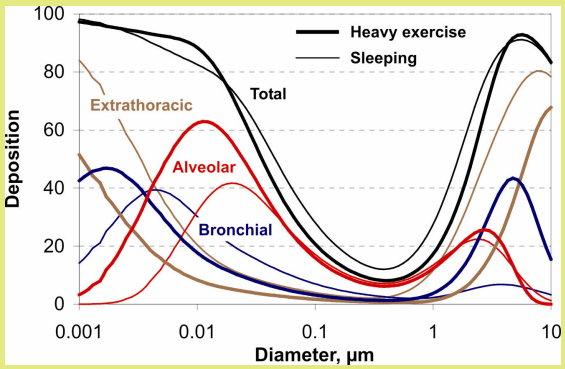
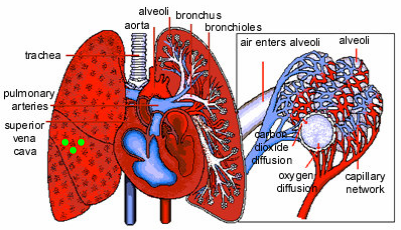
Size affects deposition and translocation







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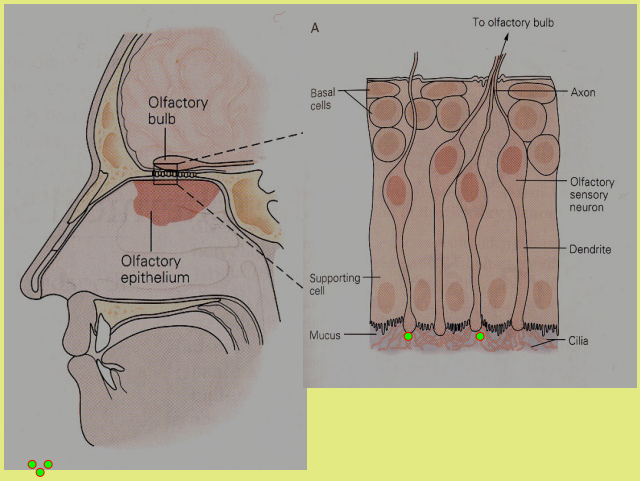
Size affects deposition and translocation



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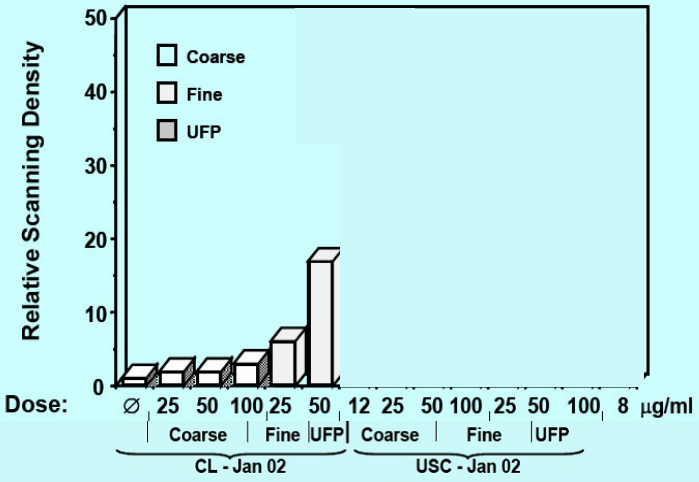
Heamoxygenase as oxidative stress indicator

Hazard of PM differs per size fraction and source!!



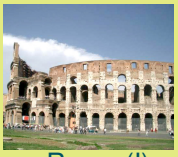
Li et al., Environ Health Perspect. 2003

Respiratory Allergy and Inflammation Due to Ambient Particles (RAIAP)

coordinated by Erik Dybing

- Coarse (2.5-10 um) and fine (0.15-2.5 um) particles
- Collected during the spring, summer and winter
- Immunology (cytokines) and toxicology in vitro
- Screened for allergenic and inflammatory potential in vivo
- Analyses of overall response pattern in the bioassays

Amsterdam (NL) Lodz (PL)



Oslo (N) Rome (I)

RAIAP

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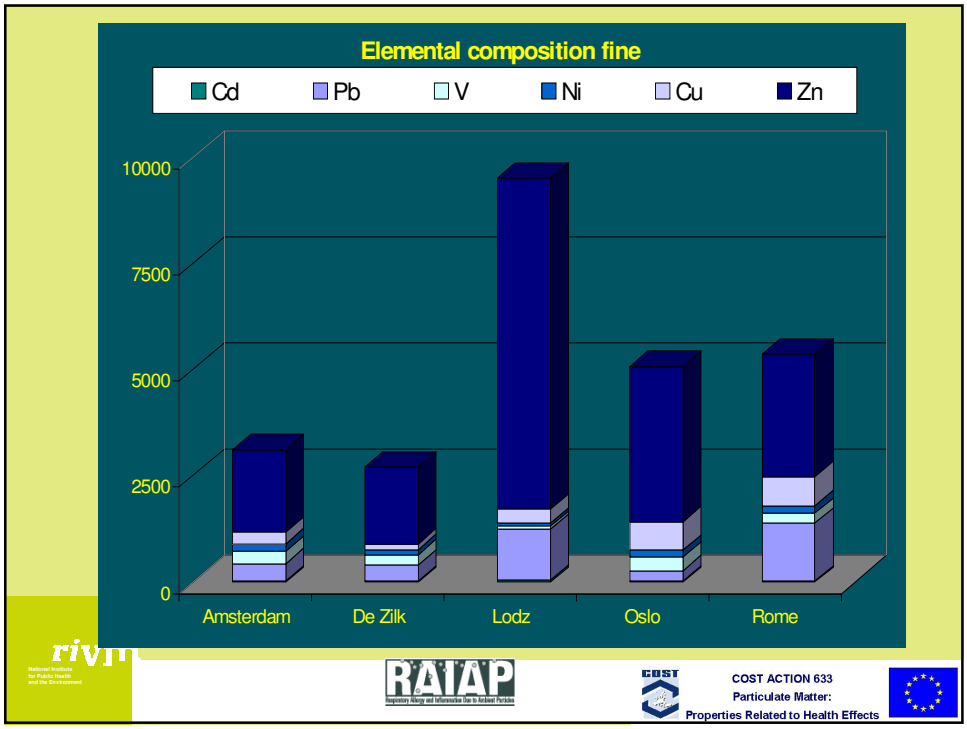
Elemental composition fine
Cd
Pb
V
Ni
Cu
Zn
10000
7500
5000
2500
0
Amsterdam
De Zilk
Lodz
Oslo
Rome
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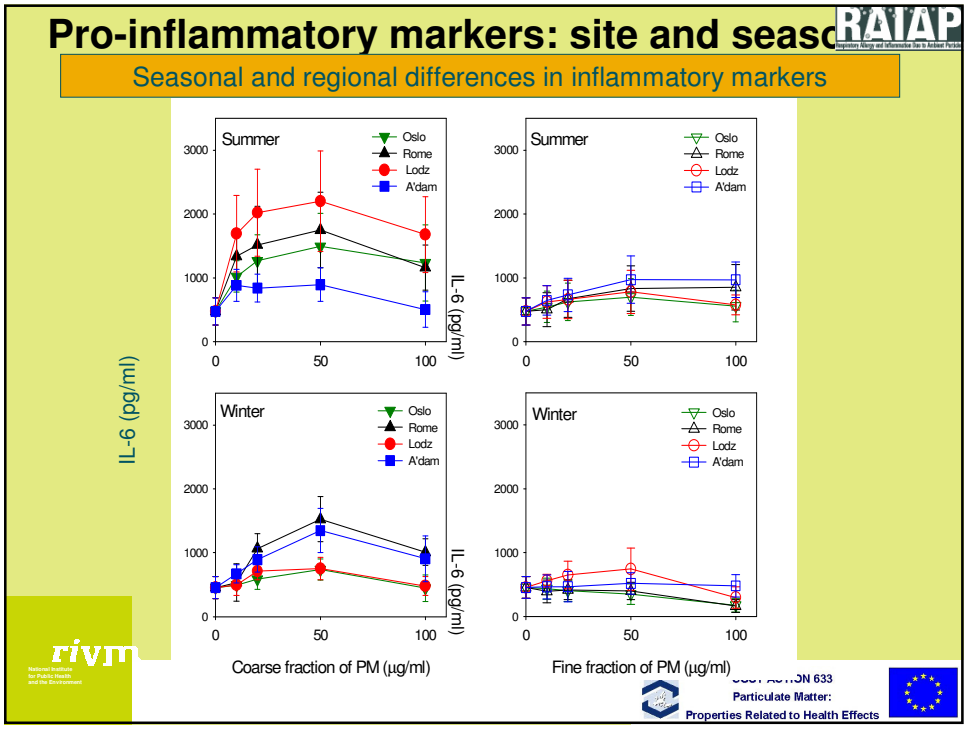
Pro-inflammatory markers: site and seasc
RAIAP
Seasonal and regional differences in inflammatory markers
IL-6 (pg/ml)
Summer
Winter
Oslo
Rome
Lodz
A'dam
3000
2000
1000
0
0
50
100
Coarse fraction of PM (µg/ml)
Fine fraction of PM (µg/ml)
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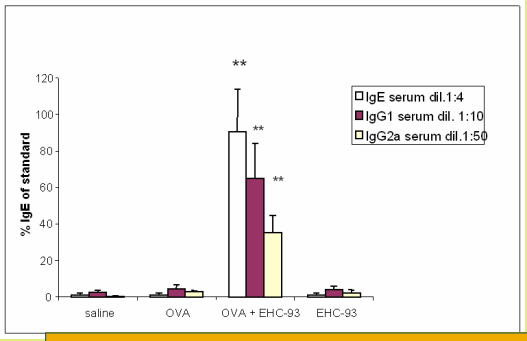
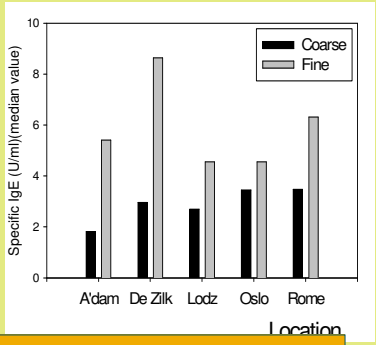
Antibody response after co-exposure to allergen and PM





Coarse and fine differ in their allergy enhancing capacity

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RAIAP Respiratory Allergy and Inflammation Due to Ambient Particles

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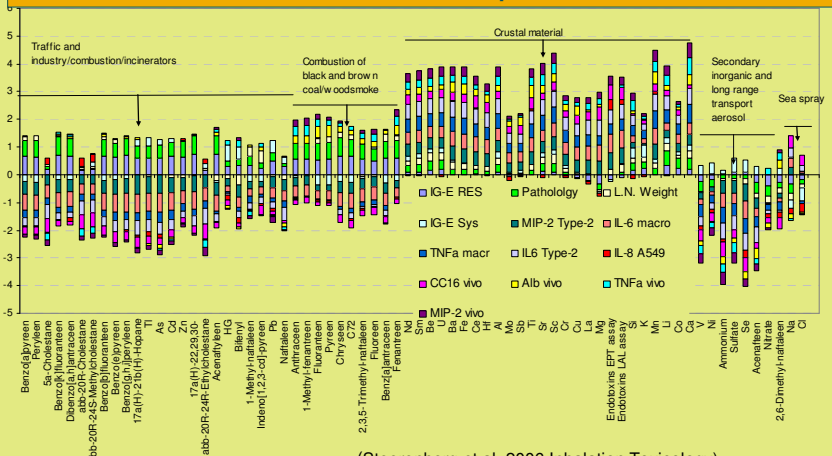
Response pattern clustering

Sources can be related to specific toxic effects



(Steerenberg et al, 2006 Inhalation Toxicology)

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RAIAP Respiratory Allergy and Inflammation Due to Ambient Particles

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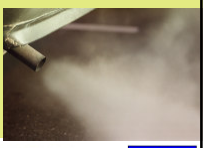
RAIAP conclusions

- **Coarse** PM consistently more potent than **fine** for inflammation, but could not be related to any specific source
- The **fine** ambient fractions have a stronger adjuvant effect on the IgE antibody responses than the **coarse** ones
- **Seasonal** and **spatial** variability in toxicity per mg PM due to chemical composition
- Different source emissions result in different effects in animals and cell cultures



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RAIAP Respiratory Allergy and Inflammation Due to Ambient Particles

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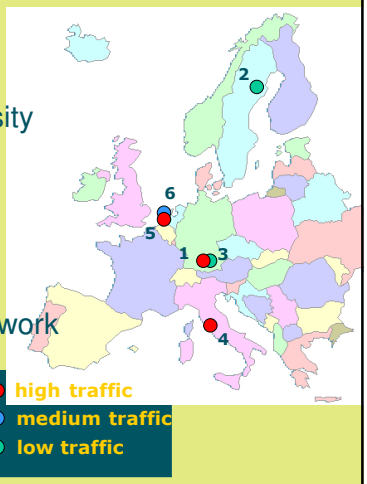
Health effects of particles from motor engine exhaust and ambient air pollution (HEPMEAP)

Coordinated by Thomas Sandström

- Compare the toxicity of various ambient derived PM samples collected throughout Europe at sites with contrast in traffic density
  - **Coarse** and **fine** PM fraction
  - **Six** PM samples from six different locations with contrast in traffic contribution
  - In vitro tests guide for selection in vivo work



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HEPMEAP

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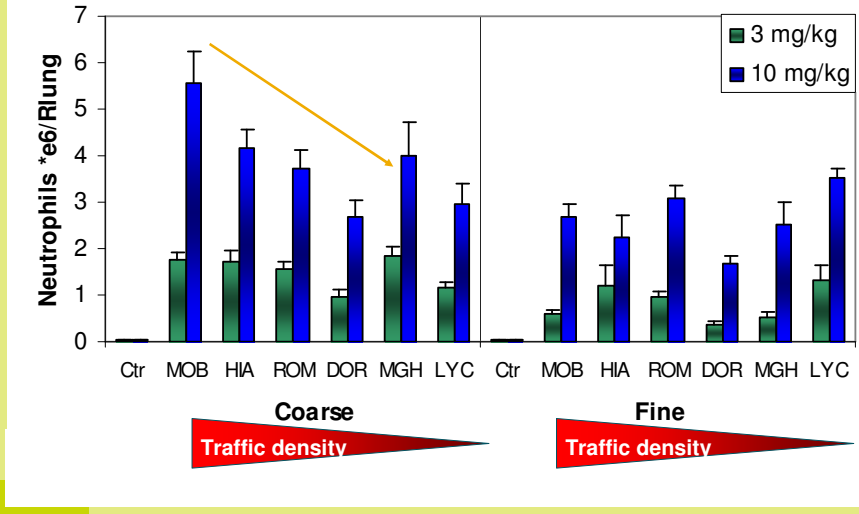
PM induced inflammation in rat lungs



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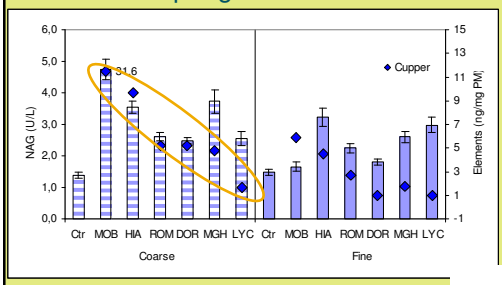
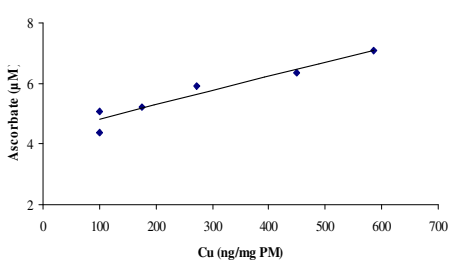
The role of cupper

Macrophage activation



Good correlation between Cu (and Ba) and toxicity in coarse PM ➔brake ware

Oxidative stress



Gerlofs-Nijland et al, Inhalation Tox, 2007

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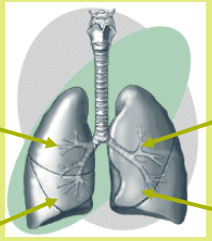
Human experiments with coarse vs. fine PM

Bronchial instillation of PM followed by lavage at 6 or 18 hours



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Results

- Fine and Coarse PM induced IL-6 and lymphocytosis in proximal and distal lavage samples, compared with saline.
- Fine PM increased neutrophils, mast cells and macrophages only in the proximal aliquot vs. saline (AM also vs. Coarse)
- Coarse PM fraction differed by inducing a pronounced neutrophilia and mastocytosis vs. both saline and the Fine fraction in the distal airway lavage aliquot.

Notably, bronchial instillation of **Coarse and Fine PM** resulted in **diverging inflammation** and differences in **regional airway responses**

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HEPMEAP Summary

- As a general rule samples from locations with high **traffic** densities induced greater responses than those from low traffic sites. However that two low traffic density sites also appeared to induce relatively large toxic responses
- Ba and Cu (*brake wear*) were associated with **cytotoxicity** in the coarse fraction and **inflammation** in the fine fraction; no positive correlation with *tailpipe* emissions
- **Zn** was associated with pulmonary toxicity (not pathology) in the fine fraction; K (wood smoke?) in fine fraction was linked with the overall pathology score

Coarse and fine differ in inflammatory potency possible driven by chemical composition (sources??)

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HEPMEAP

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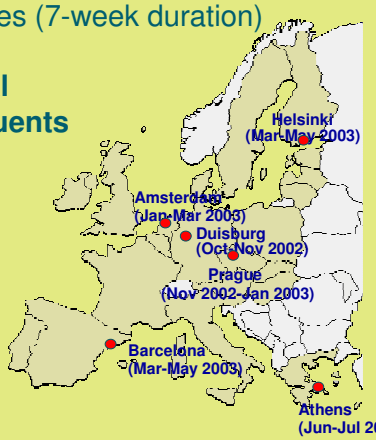
Chemical and biological characterisation of ambient air coarse, fine, and ultrafine particles for human health risk assessment in Europe (PAMCHAR)

Coordinated by Raimo Salonen

Sampling campaigns in 6 European cities (7-week duration)

Identifying **causative physicochemical characteristics** and **chemical constituents** of ambient air PM10 focussing on

- cytotoxicity
- inflammatory and
- genotoxicity



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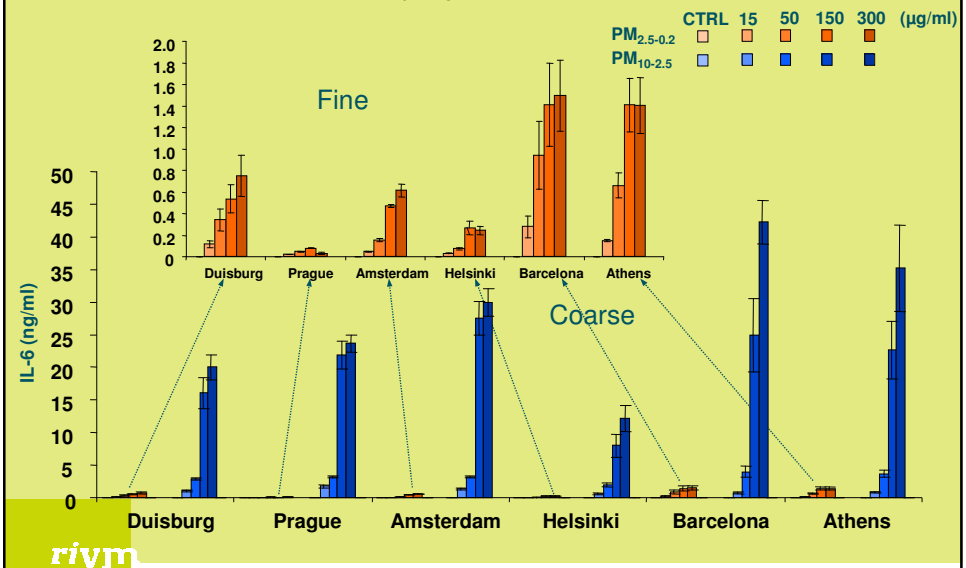
Inflammatory potential in cell cutures

IL-6 in mouse RAW264.7 macrophage cultures at 24 h



Jalava et al. Inhal Toxicol 2007;19(3):213-225

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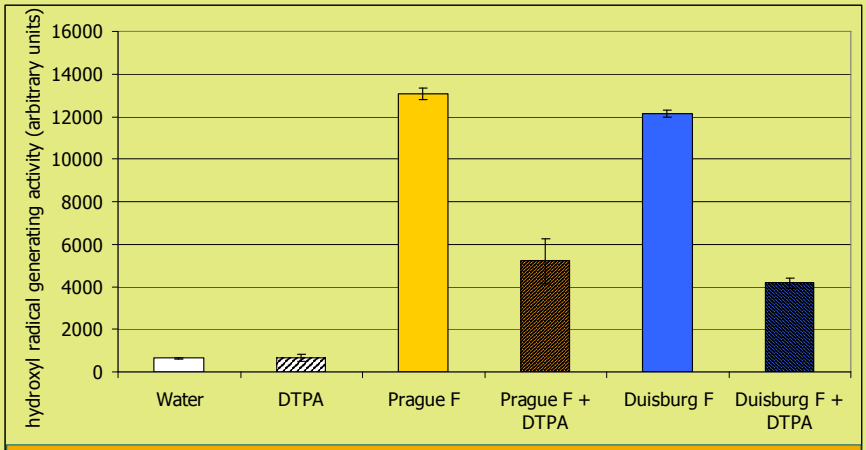
Role of metals on hydroxyl radical activity



Reduction of activity by removing metals

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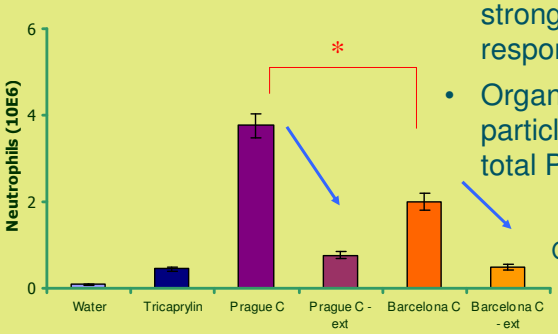
Role of PAHs in inflammation *in vivo*



- PM Prague coarse 12x higher PAHs ➔ stronger inflammatory response
- Organic extracts (w/o particles) ≤ inflammation total PM

Gerlofs et al, in prep.

Particles act as carriers

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PAMCHAR

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Summarizing conclusions

- Evidence that **metals and organic** have their own unique role in inducing toxicity or enhancing existing diseases
- **Coarse** PM, albeit the lower deposited dose in the lower respiratory tract compared to fine PM, has potential to induce health effects and that this can be related to e.g. brake ware
- There was more **heterogeneity** in inflammatory responses due to fine than to coarse PM
- PM mass is not the best **metric** to predict the associated health effects

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What we need to know or do better

- Are suggested alternative metrics such as oxidative potential, black smoke/elemental carbon really an improvement to predict human heath impact of PM?
- Combination of hazard identification and exposure assessment to perform proper risk assessment next to the epidemiological data
- Source oriented hazard identification

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Acknowledgement

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