



Oxidized ultrafine particles induce the activation of the inflammasome in human peripheral blood mononuclear cells obtained from chronic obstructive pulmonary disease (COPD) patients

°Chiara Colarusso, #Gianluigi De Falco, °Michela Terlizzi, # Mario Commoto, *Mariano Sirignano, *Andrea D'Anna, °Rita P Aquino, ° Aldo Pinto, §Antonio Molino and °**Rosalinda Sorrentino**.

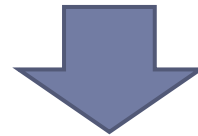
° Department of Pharmacy (DIFARMA), ImmunePharma s.r.l., University of Salerno, Fisciano, 84084, Italy; # Department of Chemical Engineering, University of Naples; # National Research Center (CNR)-Istituto di Ricerche sulla Combustione, Naples, Italy; §Department of Respiratory Medicine, Respiratory Division, University of Naples Federico II.

Risk Factors and Chronic inflammation in COPD

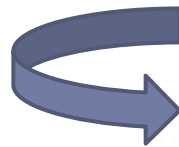
Indoor and outdoor pollution



Smoking

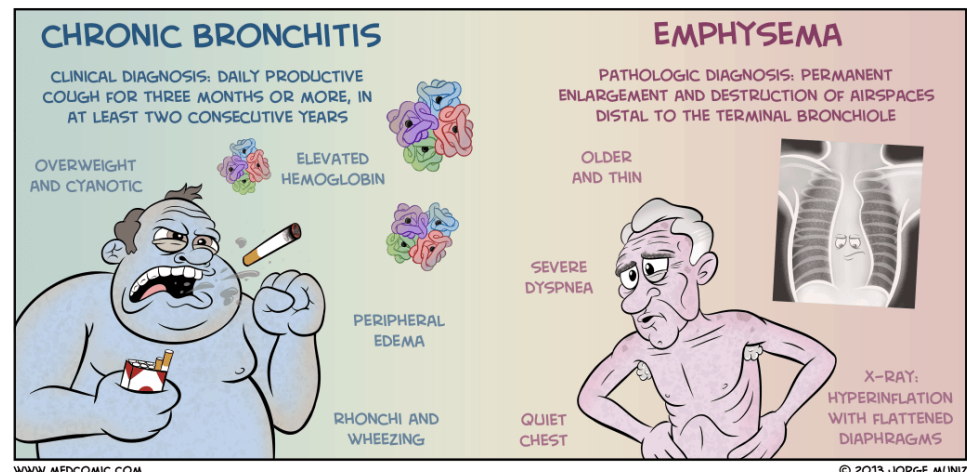


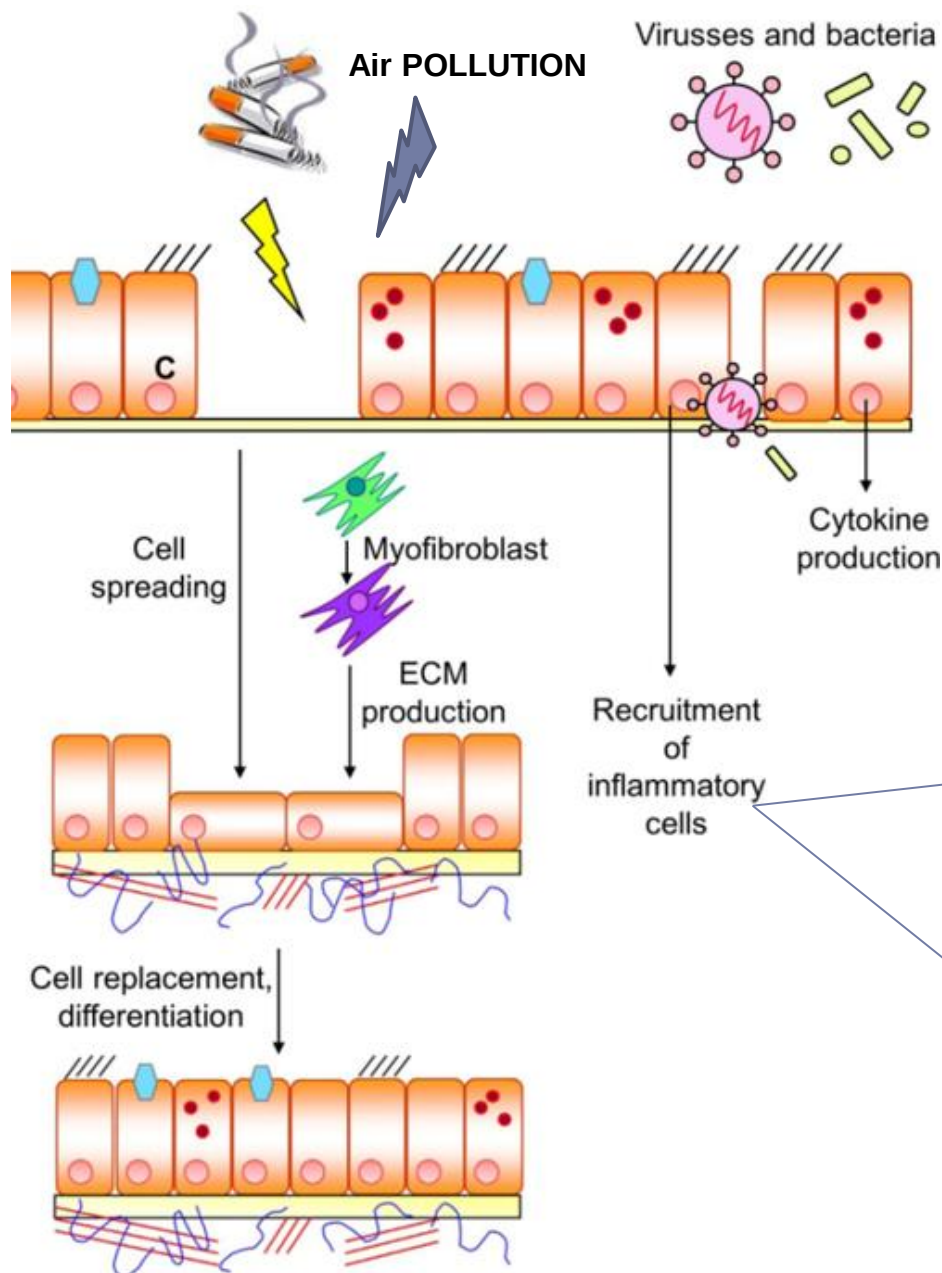
LUNG CHRONIC INFLAMMATION



COPD
(CHRONIC OBSTRUCTIVE
PULMONARY DISEASE)

Disruption of lung parenchyma
Lung dysfunction



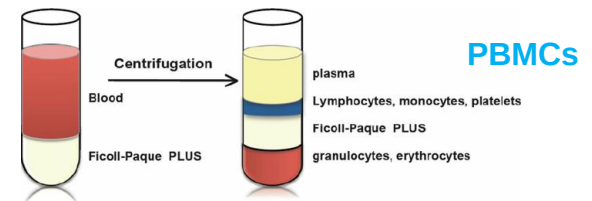


Smoking and Air Pollution are HIGH RISK FACTORS for CHRONIC LUNG INFLAMMATION:

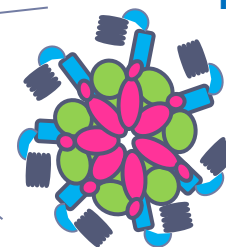
•what is the role of hematopoietic cells?

Groups of Subjects

- Healthy non-smokers
- Healthy smokers
- COPD patients



INFLAMMASOME



Pro-Caspase-1

Active Caspase-1

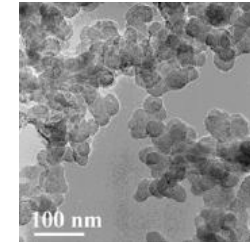
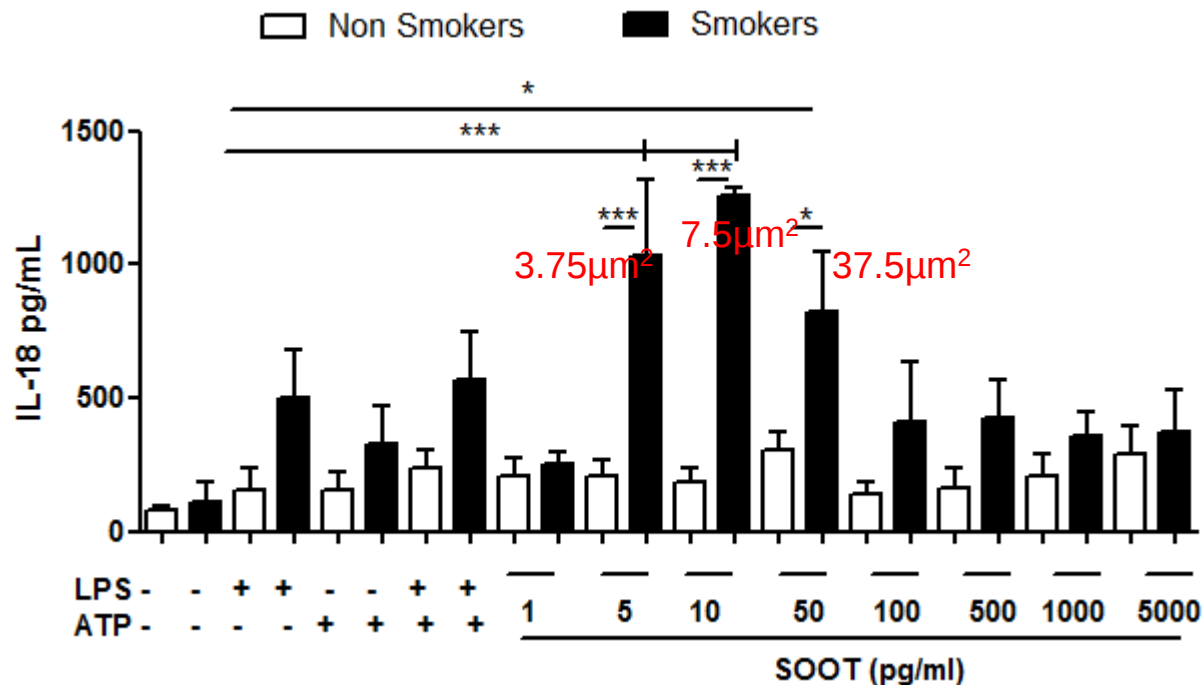


Pro-IL-1 β

Pro-IL-18

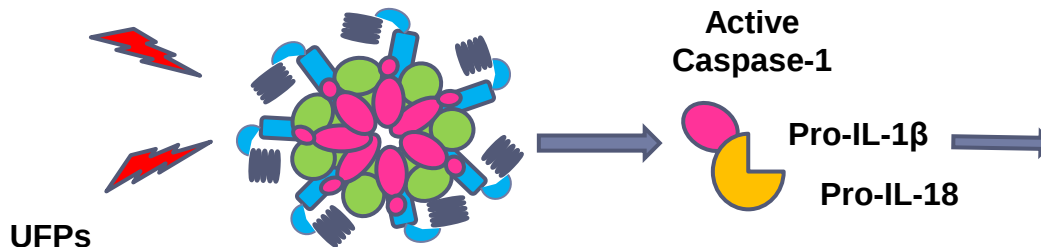
Smokers are more susceptible to soot-mediated inflammation

PBMCs from
healthy non-smokers and smokers



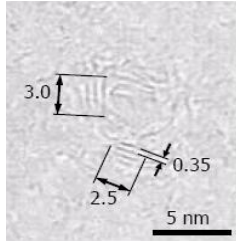
Aggregates of ~20-100 nm
%C=96%
%H= 2.5-2.8%

Cigarette smoke



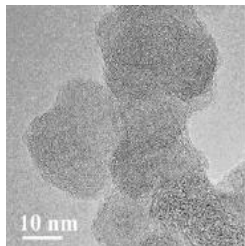
INFLAMMATION
..BUT LATENT INFLAMMATION!!!

Nanoparticles in a premixed flame



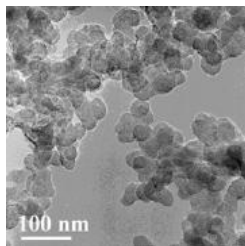
NOC

Nanoparticles of Organic Carbon
dimension 2-5 nm
stacked PAHs containing sub-units
with aliphatic/aromatic bonds
 $H/C \geq 0.5$



Soot

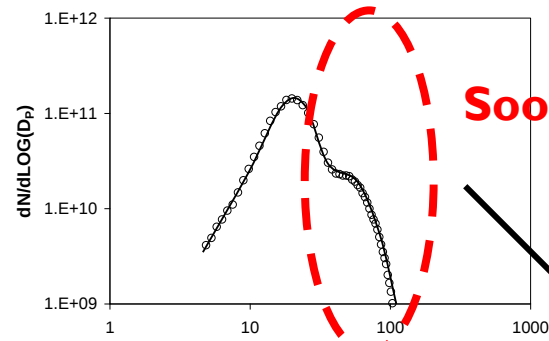
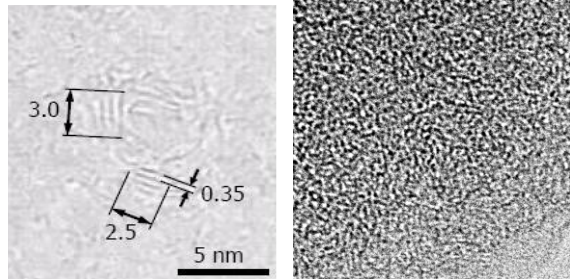
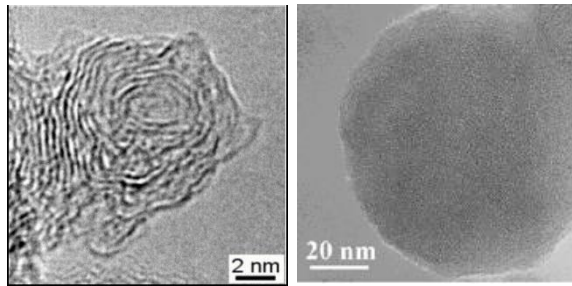
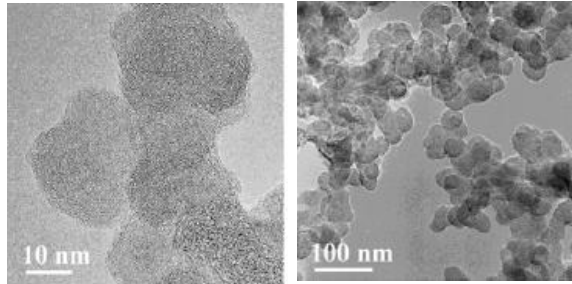
primary particles and chain like agglomerates
dimension primary particles 20-40 nm
dimension chain-like agglomerates > 100 nm
elemental carbon structures
 $H/C \sim 0.2 - 0.3$



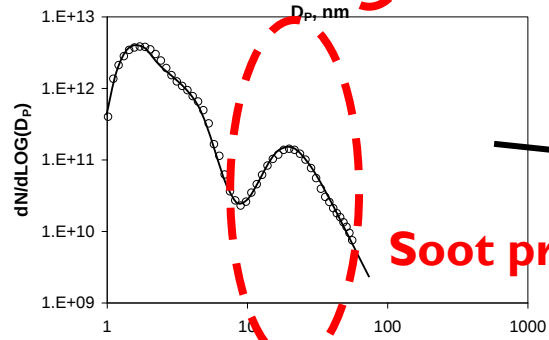
Pyrolysis Soot

chain-like agglomerates
dimension chain-like agglomerates > 100 nm
graphitic carbon structures
 $H/C \sim 0.1 - 0.05$

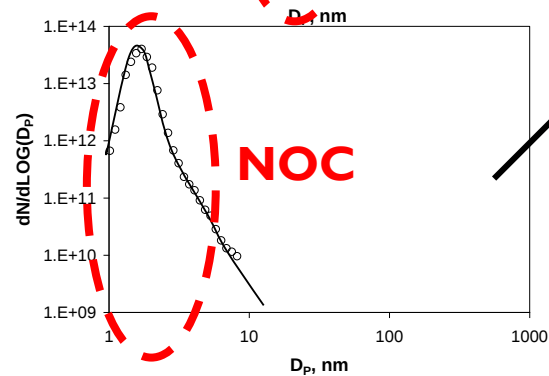
Nanoparticles in a premixed flame



Soot agglomerates



Soot primary

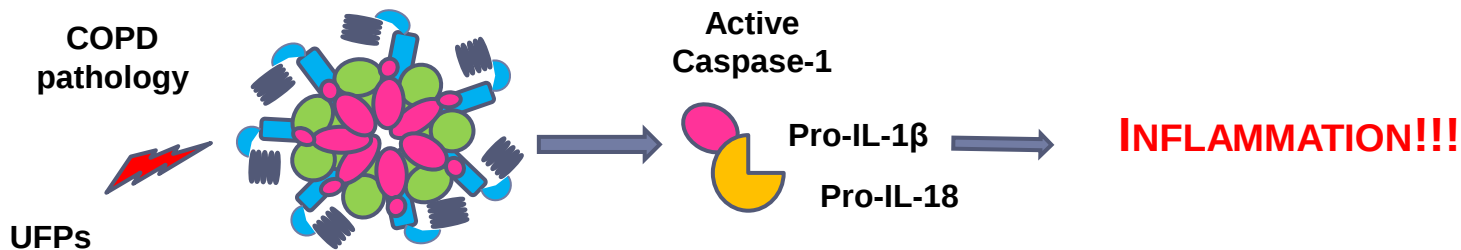
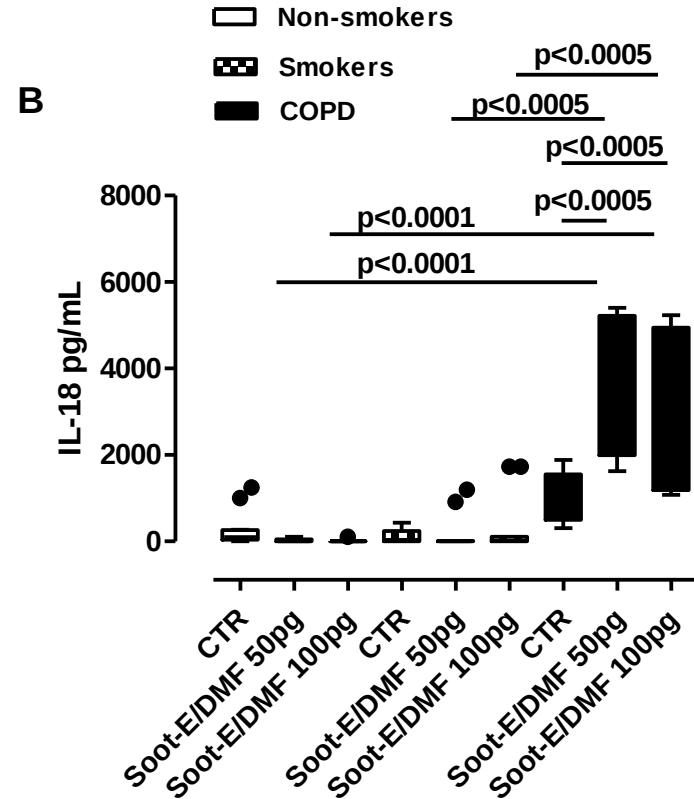
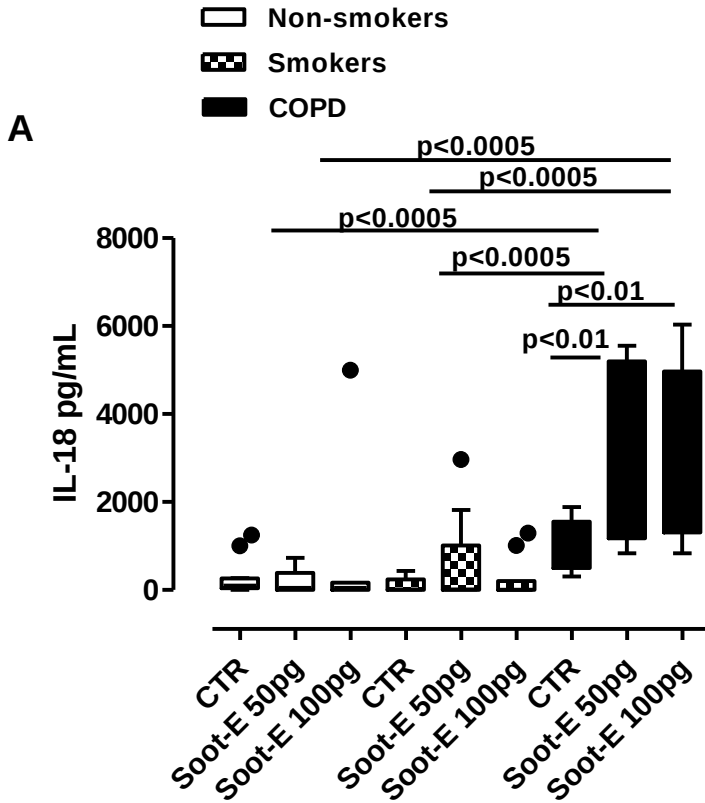


residence time

Fuel/Air mixture

Combustion-generated UFPs induce the activation of the inflammasome

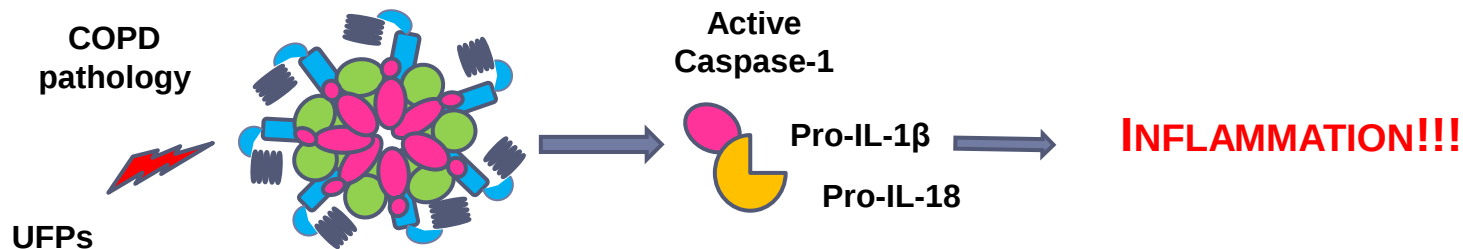
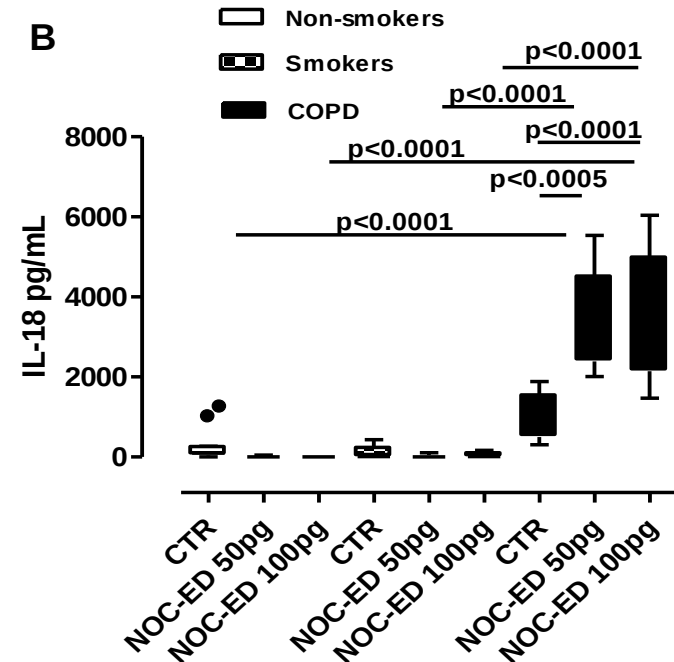
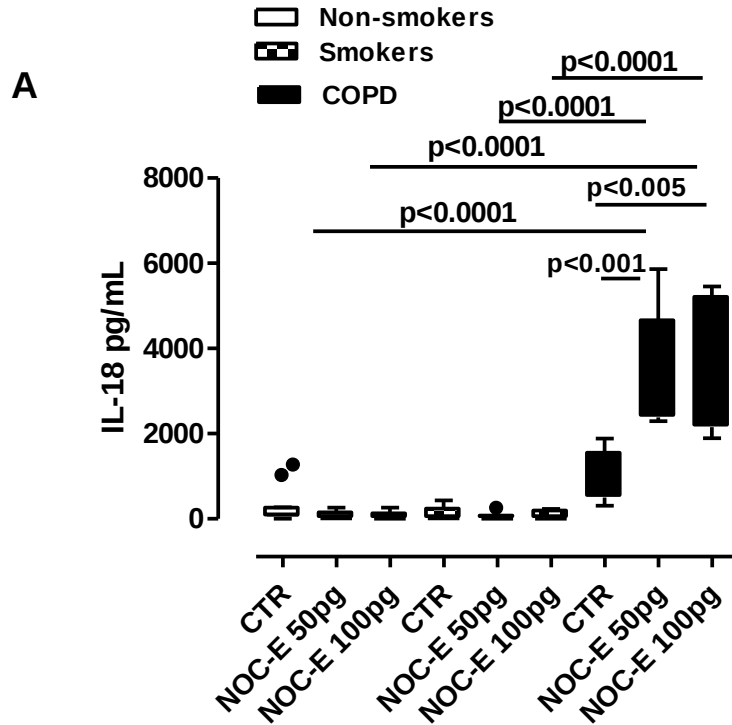
UFP tested: **SOOT E/DMF** of 20-30 nm diameter; Area (50-100pg/ml)= $1.1\text{E-}4$ - $2.2\text{E-}4$ cm^2/ml
Cytokine release: IL-18 and IL-33 release



One Way Anova followed by Tukey's multiple comparison test

Combustion-generated UFPs induce the activation of the inflammasome

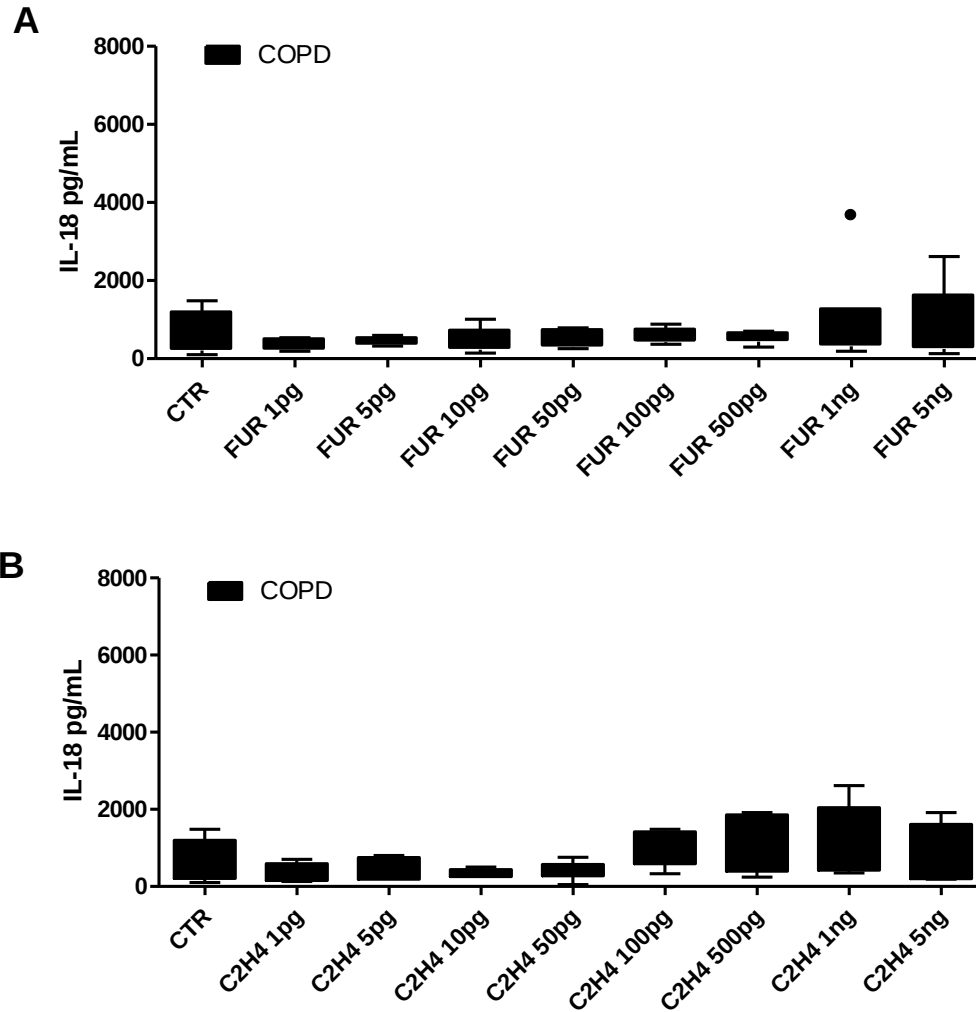
UFP tested: **NOC-E** and **NOC-ED** of 2-5 nm diameter; Area (50-100pg/ml)=1.0E-3 – 2.0E-3 cm²/ml
Cytokine release: IL-18 and IL-33 release



One Way Anova followed by Tukey's multiple comparison test

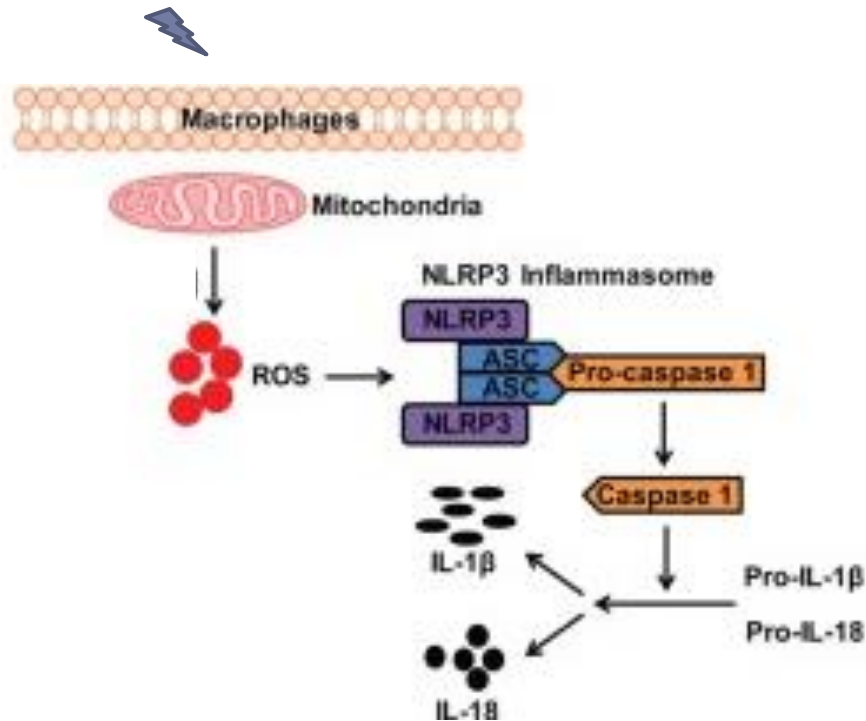
...BUT

Soot/ethylene-dimethylfuran agglomerates DID NOT induce the activation of the inflammasome in COPD-derived PBMCs

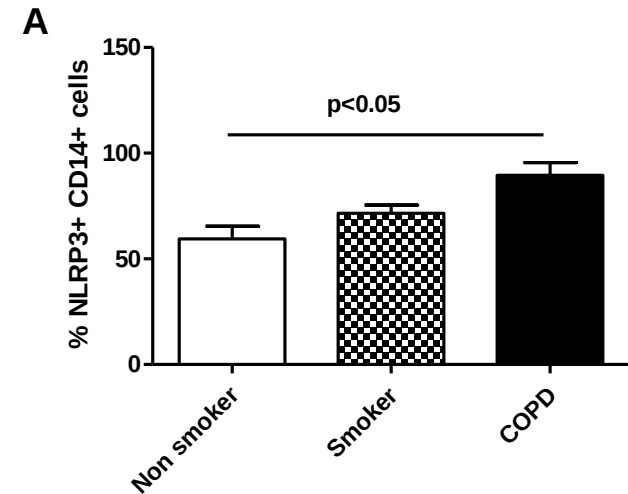


Combustion-generated ultrafine particles increased oxidative stress

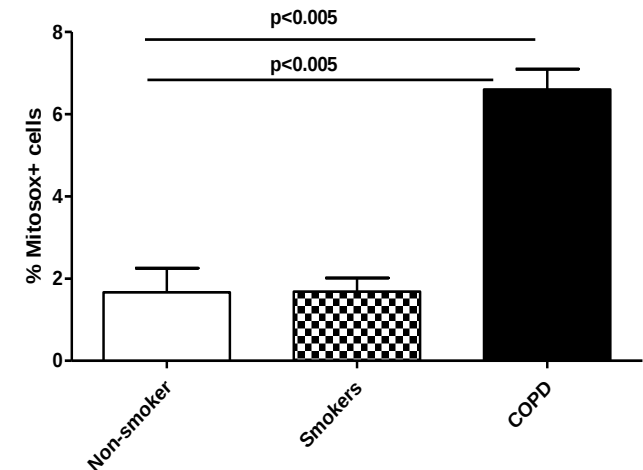
Pro-inflammatory Stimulus



NLRP3 expression

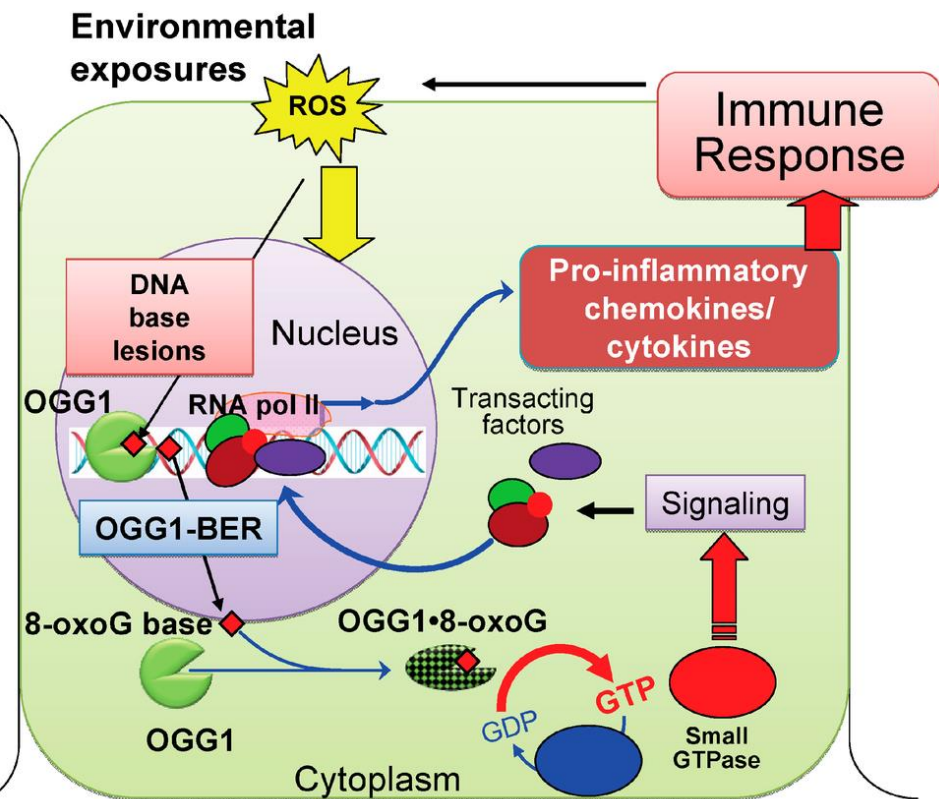


B mtROS release

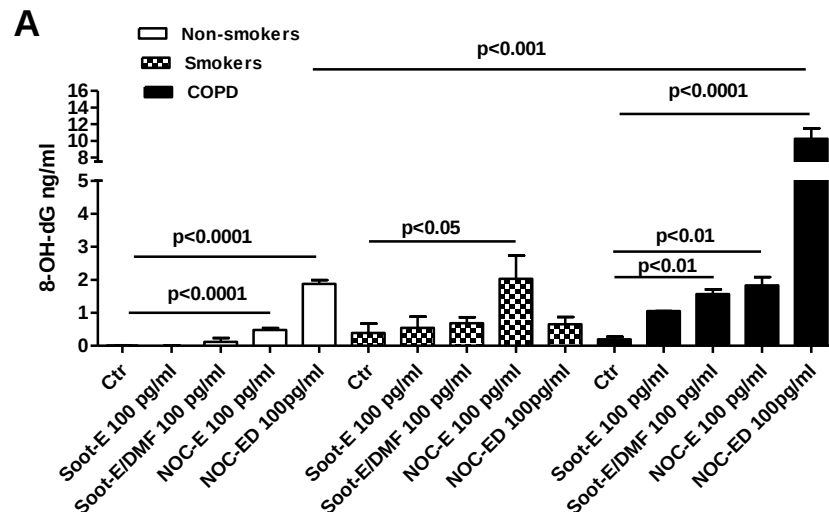


Combustion-generated ultrafine particles increased oxidative stress in COPD-derived PBMCs

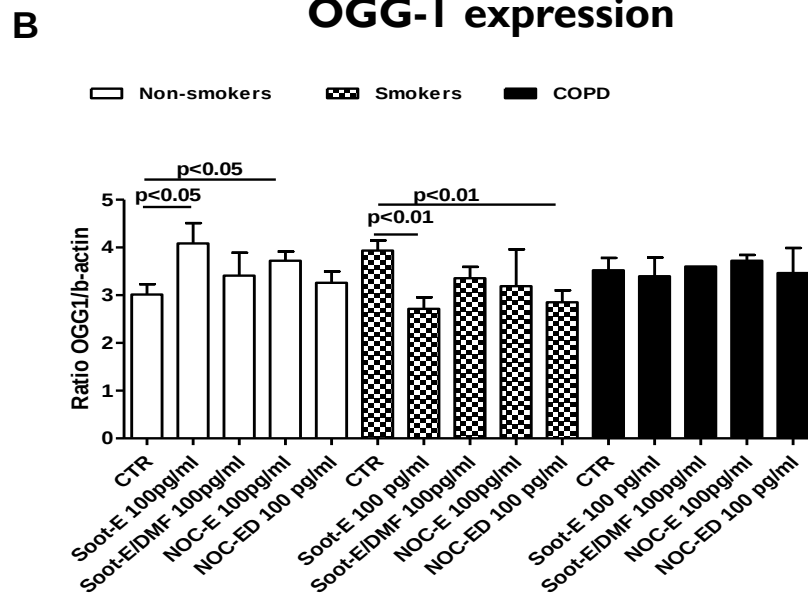
Soot-E and NOC



8-OH-dG levels

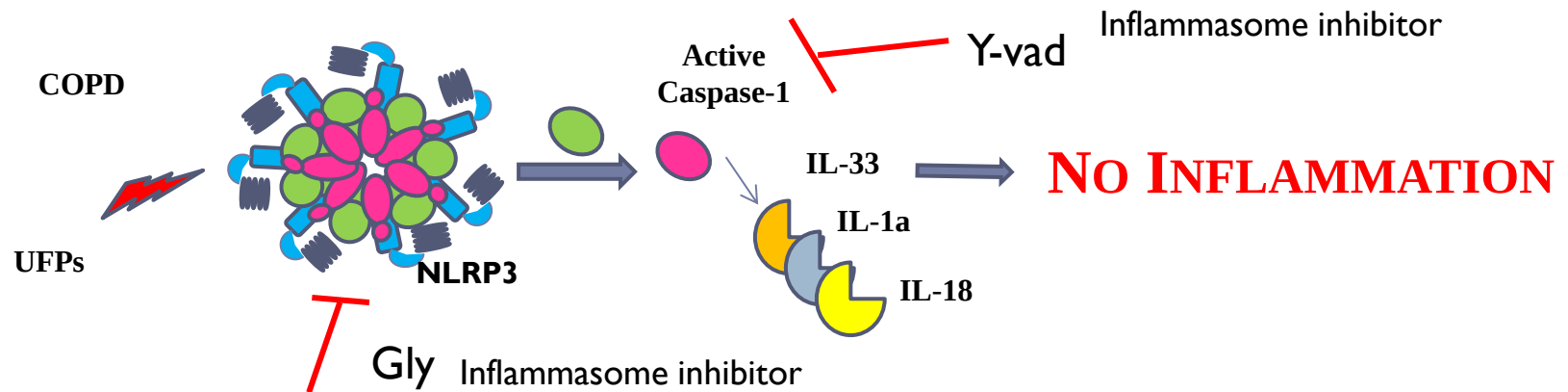


OGG-I expression

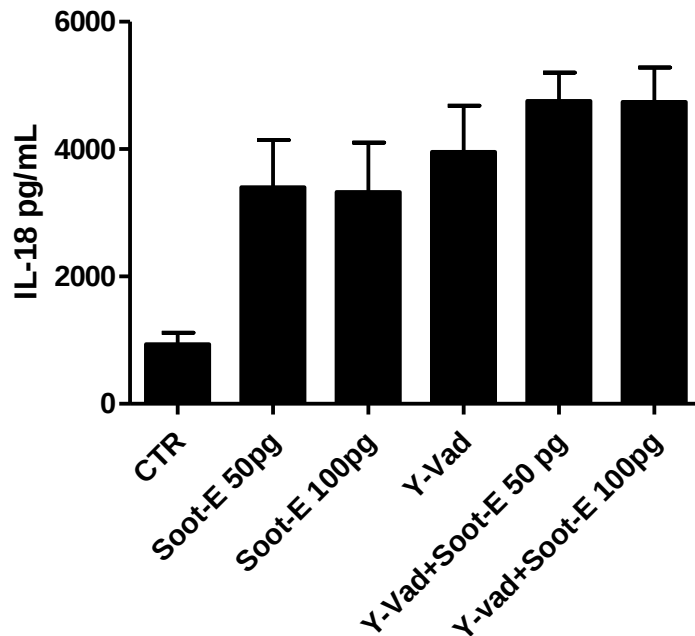


Combustion-generated ultrafine particles induced IL-18 release in an inflammasome-independent manner

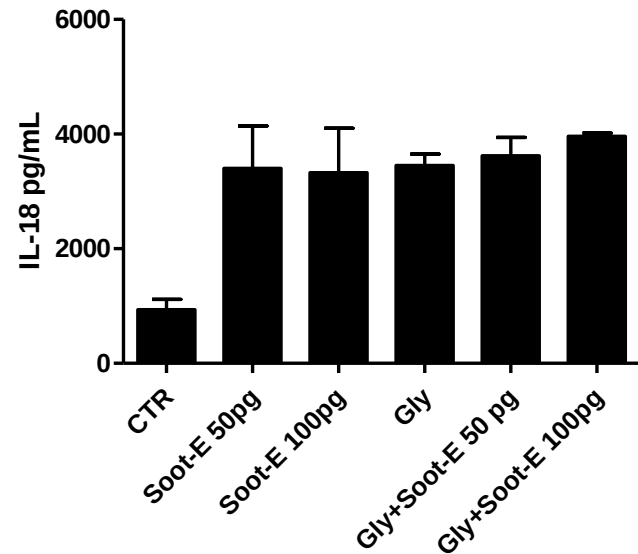
Soot-E



A

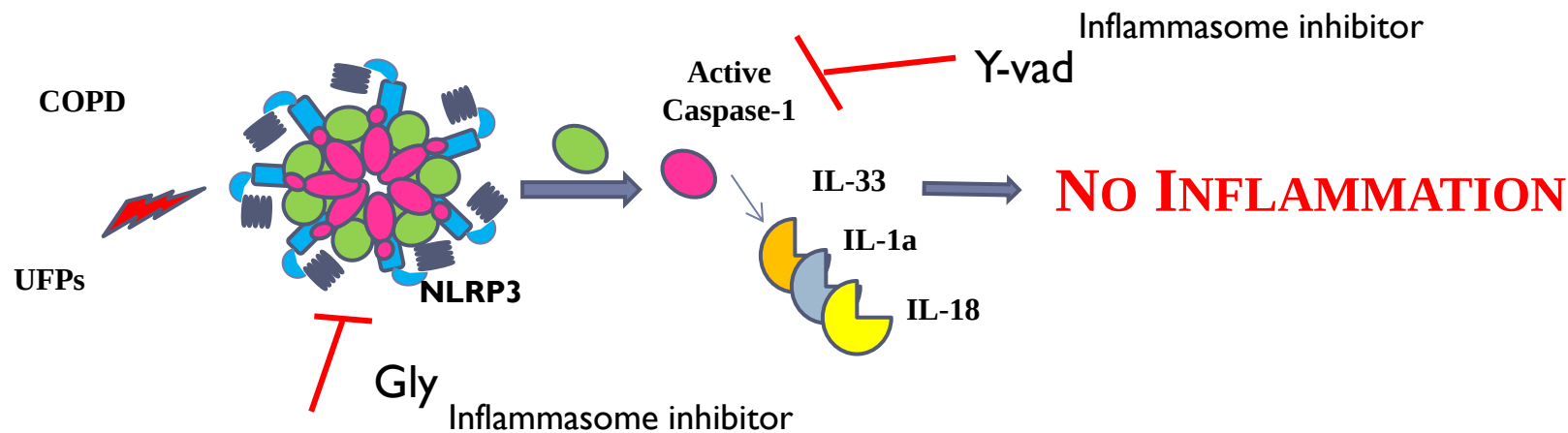


B

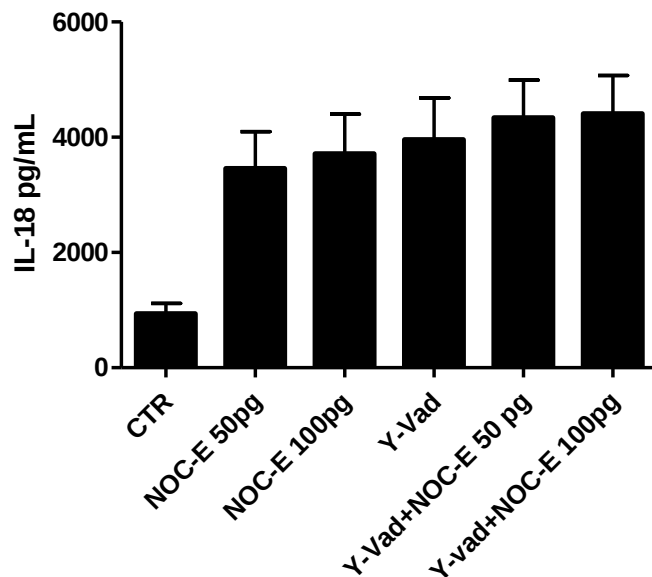


Combustion-generated ultrafine particles induced IL-18 release in an inflammasome-independent manner

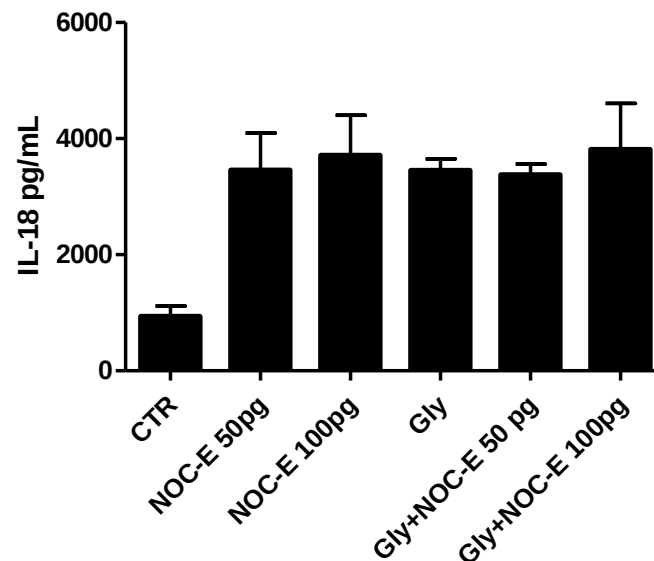
NOC-E and NOC-ED



A



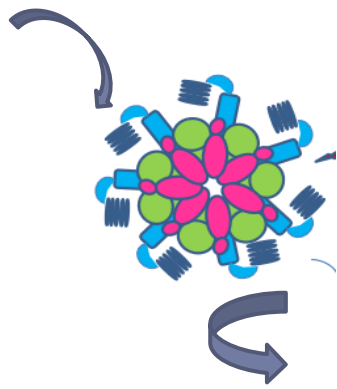
B



UFPs
SOOT-E and NOC
LOW CONCENTRATIONS (50-100pg/ml)
Higher superficial Area (cm²/ml)



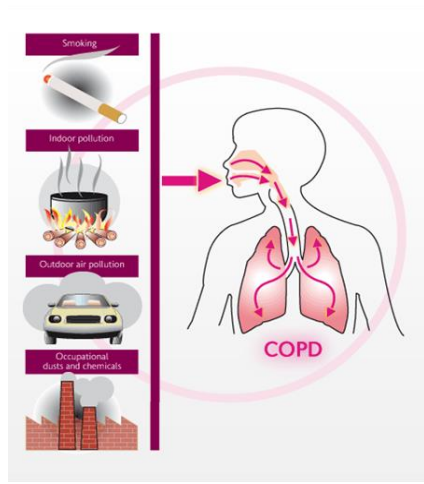
Immune System Activation



IL-18, IL-33

LUNG INJURY

**Cell transformation:
LUNG CANCER????**



UFPs
Soot-E Agglomerates
Lower superficial Area (cm²/ml)



SMOKERS:
De Falco et al., Scientific Reports 2016

BUT NOT IN COPD

??? Work in progress

THANKS FOR YOUR ATTENTION!