**EFFECT OF ULTRAFINE PARTICLE MATTER ON HUMAN PERIPHERAL BLOOD MONONUCLEAR CELLS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS: INVOLVEMENT OF THE INFLAMMASOME**

1)Colarusso C. 2)De falco G. 3)Terlizzi M. 4)Imitazione P. 5)Commodo M. 6)Sirignano M. 7)D'anna A. 8)Aquino RP. 9)Pinto A. 10)Molino A. 11)Sorrentino R.

*Dept.of Pharmacy,University of Salerno*

Inflammation is one of the main feature of chronic obstructive pulmonary disease (COPD), which is caused by inhalation of noxious particles or gas, especially cigarette smoke (CS) that represents the first risk factor for this respiratory disorder (Lee at al., 2016). It is believed that lung inflammation in COPD patients reflects the site of deposition of irritants from CS and particles of air pollution (Perez-Padilla et al., 2010), which can cause chronic inflammation in a long-term manner (Hosseinian et al., 2015). Emerging scientific evidence suggests that persistent Nod-like Receptor 3 (NLRP3) inflammasome activation may be involved in the onset of COPD pathogenesis (De Nardo et al., 2014), in fact high levels of IL-1-like cytokines are detected in the sputum and broncho-alveolar lavage (BAL) of COPD patients. In order to understand the role of inflammasome in COPD, we isolated PBMCs from healthy volunteers distinguished as smoker and non-smoker, and COPD patients and treated them with Ultrafine particles (UFP) generated by combustion processes to mimic the effects of inhaled combustion particles (UFP, <50nm).

We found that, PBMCs from COPD patients were less susceptible to UFP treatment than smokers-derived PBMCs, in fact IL-1α, IL-18 and IL-33 release is pronounced in smokers, to equal treatment. These data were confirmed by lower production of mitochondrial-derived reactive oxygen species (mtROS) by stimulation of COPD-derived PBMCs respect to PBMCs from smokers. Moreover, PBMCs of smokers presented higher levels of associated OGG1, a DNA repair enzyme, which is involved in oxidative stress repair. In contrast, after UFP treatment levels of IL-33, an alarmin of the IL-1 family that is crucial for the innate immune response, were higher in COPD-derived PBMCs than healthy no smokers, as well as smokers-derived PBMCs; interestingly IL-33 release in COPD patients was not caspase-1/8 dependent.

In conclusion, our data suggest that despite UFP are able to active inflammasome triggering IL-18 release in healthy smokers, have not influence on IL-18 release in COPD patients. However, PBMCs from COPD patients release IL-33 in a caspase-1/8-independent manner opening new perspectives for evaluation of the role of inhaled combustion particles and inflammasome involvement in COPD patients.

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