

European Respiratory Society Annual Congress 2012

Abstract Number: 5173

Publication Number: P3716

Abstract Group: 3.2. Airway Cell Biology and Immunopathology

Keyword 1: Anti-inflammatory **Keyword 2:** Epithelial cell **Keyword 3:** Monocyte / Macrophage

Title: Anti-inflammatory and cytoprotective actions of the endogenous docosahexaenoic acid (DHA) electrophilic derivative 17-oxo-DHA

Dr. Chiara 20455 Cipollina chiacip@hotmail.com^{1,2}, Dr. Stefania 20456 Gerbino stefania1201@libero.it¹, Dr. Serena 20457 Di Vincenzo serenadivincenzo@libero.it¹, Dr. Rosalia 20458 Curto liacurto@alice.it¹, Dr. Mark 20459 Gjomarkaj gjomarkaj@ibim.cnr.it MD¹, Dr. Bruce A. 20460 Freeman freerad@pitt.edu³, Dr. Francisco J. 20466 Schopfer fschopfer@gmail.com³ and Dr. Elisabetta 20468 Pace elisabetta.pace@ibim.cnr.it MD¹. ¹ Istituto di Biomedicina e Immunologia Molecolare (IBIM), Consiglio Nazionale delle Ricerche (CNR), Palermo, Italy ; ² Fondazione Ri.MED, Fondazione Ri.MED, Palermo, Italy and ³ Department of Pharmacology & Chemical Biology, University of Pittsburgh - School of Medicine, Pittsburgh, PA, United States .

Body: Inflammation of the airways is a hallmark of chronic obstructive pulmonary disease (COPD), one of the leading mortality cause worldwide. Bronchial epithelial cells and resident macrophages represent the first barrier in the lung against pathogens and external insults such as cigarette smoke, which is a major risk factor for COPD. Although the activation of the innate inflammatory response is required for defence purposes, uncontrolled activation, typical of COPD, leads to chronic inflammation causing tissue damage and enhanced risk of infection. Currently there is no therapy able to revert disease progression in COPD and therefore the search for new drugs is highly active. Omega-3 derived electrophilic fatty acids have been recently discovered as endogenous anti-inflammatory molecules produced by activated macrophages by the action of cyclooxygenase-2. In the present work, the anti-inflammatory and cytoprotective actions of the electrophilic DHA-derivative 17-oxo-DHA were evaluated in lipopolysaccharide-activated macrophages and in bronchial epithelial cells. We report that 17-oxo-DHA suppresses LPS-induced TNFalpha production in macrophages and increases intracellular glutathione and the expression of heme-oxygenase 1 in both cell types, thus providing protection against oxidative stress caused by cigarette smoke and inflammatory reactions. Although the molecular mechanisms are still under investigation, overall the present results support a role for the electrophilic, omega-3 derived 17-oxo-DHA in limiting inflammatory reactions and modulating the antioxidant response, thus reducing cellular damage and promoting the resolution of inflammation.