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

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**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.