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Title: The NLRP3 inflammasome in chronic obstructive pulmonary disease

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Body: Background. The inflammasomes are a family of recently described multi-protein cytoplasmic sensors that orchestrate the inflammatory response, of which the NRLP3 inflammasome is the one better characterized so far. We hypothesized that the NRLP3 inflammasome participates in the inflammatory response elicited by tobacco smoking, particularly in smokers with Chronic Obstructive Pulmonary Disease (COPD). Methods. To test this hypothesis, we compared several markers of inflammasome activation in lung and serum of 51 COPD patients, 23 smokers with normal spirometry and 26 non-smokers, using immunohistochemistry, Western blot, ELISA and/or real time PCR. Besides, we tested the in vitro functional response of the NRLP3 inflammasome in these 3 groups of subjects. Results. (1) caspase-1, a core element of several inflammasomes, was widely expressed in lung tissue in all three groups; (2) smoking activates the inflammasome; (3) NLRP3 transcription was significantly up-regulated in COPD patients and related (like that of IL-1β) with the severity of airflow limitation present; (3) the pulmonary levels of IL-1β, IL-1RA and IL-18 were increased in COPD patients despite quitting smoking; (4) in serum, differences between groups were attenuated but, in COPD patients the serum and pulmonary concentrations of caspase-1 were significantly related; and, finally, (5) in vitro the functionality of the NLRP3 inflammasome was not enhanced in COPD, excluding an auto-inflammatory component of the disease. Conclusions. The NLRP3 inflammasome participates in the inflammatory response to smoking and also in the pathobiology of COPD, particularly in patients with more severe airflow limitation. COPD does not have an auto-inflammatory component.