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Caspase-11 and AIM2 Inflammasome are Involved in Smoking-Induced COPD and Lung Adenocarcinoma

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Abstract : Cigarette smoking is the main cause and the most common risk factor for both COPD and lung cancer. In our previous studies, we proved that caspase-11 in mice and its human analogue, caspase-4, are involved in lung carcinogenesis and that AIM2 inflammasome might play a pro-cancerous role in lung cancer. Therefore, the aim of this study was to investigate potential crosstalk between COPD and lung cancer, focusing on AIM2 and caspase-11-dependent inflammasome signaling pathway. To mimic COPD, we took advantage of an experimental first-hand smoking mouse model and, to confirm what was observed in mice, we used human samples of lung adenocarcinoma patients stratified according to the smoking and COPD status. We demonstrated that smoke exposure led to emphysema-like features, bronchial tone impairment, and release of IL-1-like cytokines (IL-1α, IL-1β, IL-33, IL-18) in a caspase-1 independent manner in C57Bl/6N. Rather, a dysfunctional caspase-11 in smoke-exposed 129Sv mice was associated to lower bronchial inflammation, collagen deposition, and IL-1-like inflammation. In addition, for the first time, we found that AIM2 inflammasome is involved in lung inflammation in smoking and COPD, in that its expression was higher in smoke-exposed C57Bl/6N compared to 129Sv smoking mice, who instead did not show any alteration of AIM2 in both macrophages and dendritic cells. Moreover, we found that AIM2 expression in the cancerous tissue, albeit higher than non-cancerous tissue, was not statistically different according to the COPD and smoking status. Instead, the higher expression of AIM2 in non-cancerous tissue of smoker COPD patients than smokers who did not have COPD was correlated to a higher hazard ratio of poor survival rate than patients who presented lower levels of AIM2. In conclusion, our data highlight that caspase-11 in mice is associated to smoke-induced lung latent inflammation which could drive the establishment of lung cancer, and that AIM2 inflammasome plays a role at the crosstalk between smoking/COPD and lung adenocarcinoma in that its higher presence is correlated to lower survival rate of smoker COPD adenocarcinoma.

Keywords : COPD, inflammasome, lung cancer, lung inflammation, smoke
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