Human Peripheral blood mononuclear cells (PBMCs) from idiopathic pulmonary fibrosis patients release IL-1-like cytokines in an inflammasome independent manner.

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Idiopathic pulmonary fibrosis (IPF) is a fibrosing interstitial pneumonia of unknown aetiology, characterized by progressive respiratory dysfunction, chronic inflammation and collagen deposition from lung fibroblasts, culminating in death from respiratory failure. Inflammation likely plays a role; however, the molecular mechanisms is far to be elucidated. Recent studies showed that IPF-derived fibroblasts had lower expression of inflammasome-dependent proteins (Plantier et al., 2016). Similarly, IPF-derived alveolar macrophages showed lower activity of NLRP3 after LPS+ATP stimulation (Lasithioki et al., 2016). According to the direct inflammation hypothesis (Bringardner et al., 2008), inflammatory cells directly damage lung tissues in that fibroblasts are instructed to deposit collagen. Therefore, in order to understand the role of the inflammasome in IPF, we isolated peripheral blood mononuclear cells (PBMCs), treated for 5 hours with well-known NLRP3 and AIM2 activators. We found that the activation of NLRP3 in IPF-derived PBMCs, by means of LPS+ATP, did not induce the release of IL-1b, IL-18 and IL-1a compared to healthy PBMCs. Interestingly, we found that the activation of AIM2, another inflammasome receptor, induced the release of IL-18, but not of IL-1b, in a caspase-1/8-dependent manner from IPF-derived PBMCs, similarly to healthy PBMCs. In contrast, the release of IL-1a after AIM2 triggering was not caspase-1/8-dependent as in healthy PBMCs, but rather it was calpain I/II-dependent. In conclusion, our data imply that while NLRP3 inflammasome is impaired, the activation of AIM2 inflammasome occurs in a canonical- and non-canonical manner, opening new perspectives on the biology of AIM2 inflammasome in IPF, focusing on the instructing information released by circulating immune cells.

Plantier, L., Renaud, H., Respaud, R., Marchand-Adam, S. & Crestani, B. (2016) Int. J. Mol. Sci. 17.

Lasithiotaki, I. et al. (2016) Eur. Respir. J. 47, 910–918.

BRINGARDNER, B. D., BARAN, C. P., EUBANK, T. D. & MARSH, C. B. (2008) Antioxid. Redox Signal. 10, 287–301.