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# Activation of the AIM2 Inflammasome in Peripheral Blood Mononuclear Cells (Pbmcs) from Idiopathic Pulmonary Fibrosis Patients Leads to the Release of Pro-Fibrotic Mediators

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Idiopathic pulmonary fibrosis (IPF) is a chronic fibro-proliferative disease characterized by poor prognosis, with a mean survival of ~2–3 years after definite diagnosis. The cause of IPF is still unknown but it is a heterogeneous condition in which the aberrant deposition of extracellular matrix leads to extensive lung remodeling. This remodeling is a consequence of inflammatory responses, but the mechanisms involved are poorly understood. In this study, we first analyzed a bleomycin-induced mouse model, which showed that higher expression of IL-1β, but not IL-18, was correlated to pulmonary cell infiltration and fibrosis. Then, we found that peripheral blood mononuclear cells (PBMCs) from IPF patients released higher levels of IL-1α and IL-18 in a NLRP3- and calpain-independent manner after LPS±ATP. Instead, the activation of the AIM2 inflammasome induced the release of IL-1α in a caspase-1/-8 independent manner; whereas IL-18 release was caspase-1-dependent. These effects correlated with the release of the pro-fibrotic TGF-β, which was induced by AIM2 activation in a caspase-1- and TLR4-independent manner, but dependent on IL-1α. In this context, the activation of AIM2 induced the release of caspase-4 from IPF-derived PBMCs, which correlated with the mRNA levels of this caspase that was higher in IPF than in healthy PBMCs.

In conclusion, our findings identify a novel molecular mechanism whereby the activation of AIM2 could lead to the activation of the non-canonical inflammasome (caspase-4-dependent), that induces the release of IL-1α responsible for the release of TGF-β from PBMCs of IPF patients.

**Biography:**

Dr. Rosalinda Sorrentino, PhD, is actually a Tenure Track Research Scientist at the University of Salerno. During her PhD training, Dr. Sorrentino joined Prof. Jane Mitchell's laboratory at Imperial College-NHLI (UK) as a visiting scientist. In 2007 Dr. Sorrentino obtained a PostDoctoral Position at Cedars Sinai Medical Center, USA. In 2008 she moved to Italy to establish her own research project to understand how chronic inflammation in the lung favors malignancy.