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Mitochondrial antiviral signaling protein is crucial for the development of pulmonary fibrosis

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MAVS may play a critical role in the development of pulmonary fibrosis, and targeting MAVS or its signalling by proapoptotic BH3 mimetics may be a feasible strategy for the treatment of IPF. https://bit.ly/31rIsmZ

Cite this article as: Kim S-H, Lee JY, Yoon CM, *et al*. Mitochondrial antiviral signaling protein is crucial for the development of pulmonary fibrosis. *Eur Respir J* 2021; 57: 2000652 [https://doi.org/10.1183/13993003.00652-2020].

ABSTRACT Danger signals, or damage-associated molecular patterns (DAMPs), instigate mitochondrial innate immune responses wherein mitochondrial antiviral signaling protein (MAVS) functions as a key platform molecule to mediate them. The role of MAVS in the pathogenesis of idiopathic pulmonary fibrosis (IPF), however, has not yet been identified. Whether MAVS signalling can be modulated by currently existing drugs has also not been explored.

We used an established model of pulmonary fibrosis to demonstrate that MAVS is a critical mediator of multiple DAMP signalling pathways and the consequent lung fibrosis after bleomycin-induced injury *in vivo*.

After bleomycin injury, MAVS expression was mainly observed in macrophages. Multimeric MAVS aggregation, a key event of MAVS signalling activation, was significantly increased and persisted in bleomycin-injured lungs. A proapoptotic BH3 mimetic, ABT-263, attenuated the expression of MAVS and its signalling and, consequently, the development of experimental pulmonary fibrosis. In contrast, the therapeutic effects of nintedanib and pirfenidone, two drugs approved for IPF treatment, were not related to the modulation of MAVS or its signalling. Multimeric MAVS aggregation was significantly increased in lungs from IPF patients as well.

MAVS may play an important role in the development of pulmonary fibrosis, and targeting MAVS with BH3 mimetics may provide a novel and much needed therapeutic strategy for IPF.