EUROPEAN RESPIRATORY SOCIETY
INTERNATIONAL CONGRESS 2023
MILAN Italy, 9-13 September

Anti-fibrotic effect of FGF21 in pulmonary fibrosis

M. Ghanem (Paris, France), G. Archer (Paris, France), A. Justet (Paris, France), M. Hachem (Paris, France), T. Boghanim (Paris, France), A. Vadel (Paris, France), N. Poté (Paris, France), A. Cazes (Paris, France), P. Mordant (Paris, France), Y. Castier (Paris, France), H. Mal (Paris, France), M. Jaillet (Paris, France), A. Mailleux (Paris, France), B. Crestani (Paris, France)

Introduction

FGF21, an endocrine FGF that acts through the FGFR1/KLB pathway, prevents liver fibrosis in mice. In human, PEGylated FGF21 analog (PEG-FGF21) was shown to reduce liver fibrosis in NASH. We asked whether FGF21 could modulate bleomycin-induced pulmonary fibrogenesis in mice.

Methods

We determined in vivo the mRNA expression of Fgf21, Klb and Fgfr1 in lung by qPCR, at D3, 7, 14, 21 and 28 after bleomycin intra-tracheal injection. We studied the development of pulmonary fibrosis in Fgf21 deficient mice compared to their Wild Type (WT) littermates, after a unique intra-tracheal injection of bleomycin. Mice were sacrificed at D14. We determined the effect of repeated subcutaneous injections of PEG-FGF21 at D7, 10, 14 and 17 after bleomycin on the development of pulmonary fibrosis. Mice were sacrificed at D21.

Results

Fgf21 mRNA expression was induced at all timepoints in the lung after bleomycin injection as compared to saline, whereas Fgfr1 and Klb were not modulated. Fgf21 KO mice presented an increased sensitivity to bleomycin, with higher histological injury score, increased fibrosis markers (Fn1, Col3a1, Col14a1) and increased Tgfb1 mRNA lung content as compared to WT littermates. The overexpression of FGF21 by PEG-FGF21 treatment prevented lung fibrogenesis, with lower injury score, decreased Col1a1 mRNA and protein content, and decreased pro-fibrotic mediators mRNA expression (Pai-1 and Ctgf) as compared to the control group receiving the diluent.

Conclusion

Fgf21 lung mRNA expression was increased after bleomycin. FGF21 overexpression prevented bleomycin-induced pulmonary fibrosis, whereas Fgf21 deletion was associated with an increased fibrosis. Our data indicate a possible antifibrotic effect of FGF21 in the lung.