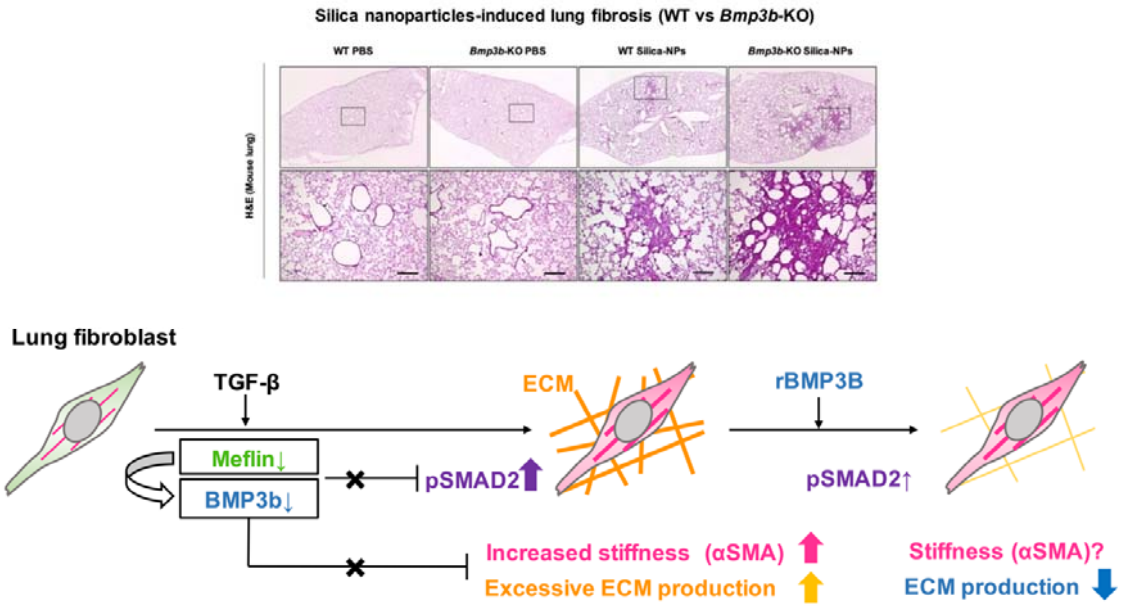


**News Release**

**Title:** BMP3b is a Novel Anti-Fibrotic Molecule Regulated by Meflin in Lung Fibroblasts

**Key Points**

- Pulmonary fibrosis is a chronic progressive fibrotic lung disease with a poor prognosis, and the therapeutic developments are warranted.
- The authors demonstrated that BMP3b specifically expressed in lung fibroblasts is a novel anti-fibrotic molecule regulated by meflin.
- Future studies may explore the clinical benefits of BMP3b in the context of pulmonary fibrosis.

**Summary**

Pulmonary fibrosis is a chronic progressive fibrotic lung disease with a poor prognosis, and the therapeutic developments are warranted. The authors recently reported that meflin is specifically expressed in lung fibroblasts and exhibited an anti-fibrotic effect in murine lung fibrosis model. On the other hand, the exact mechanisms by which meflin prevents lung fibrosis remained unknown.

In the current study, the authors conducted a comprehensive analysis of gene expression in lung fibroblasts using cDNA microarray, and an analysis of single-cell RNA sequence (scRNA-seq) database. In these analyses, BMP3b was specifically expressed in lung fibroblasts similar to meflin, and the expression was strongly regulated by meflin. Furthermore, experiments using a murine pulmonary fibrosis model and lung fibroblasts revealed that BMP3b has anti-fibrotic effects and exerts its function even if meflin is suppressed. These lines of evidence indicates that BMP3b covers anti-fibrotic effects of meflin in part, and a promising molecule for the treatment of pulmonary fibrosis.

**Research Background**

Pulmonary fibrosis is a chronic devastating lung disease with a poor prognosis, and the therapeutic developments are warranted. The authors recently reported that meflin is specifically expressed in lung fibroblasts and exhibited an anti-fibrotic effect in murine lung fibrosis model [1]. On the other hand, the exact mechanisms by which meflin prevents lung fibrosis remained unknown. They assumed that the downstream effector molecules regulated by meflin may have anti-fibrotic effects on lung fibrogenesis.

**Research Results**

In the current study, the authors first conducted a comprehensive gene expression analysis by cDNA microarray using wild-type (WT) and meflin-knockout (meflin-KO) mouse primary lung fibroblasts. The gene expression profiles of meflin-KO lung fibroblasts were significantly different from those of WT lung fibroblasts especially under TGF-β stimulation, which suggested that meflin regulates TGF-β signaling. *Bone morphogenic protein 3b* (*Bmp3b*) (=*Growth differentiation factor 10* [*Gdf10*]) was one of the most down-regulated genes in meflin-KO lung fibroblasts stimulated by TGF-β. In the scRNA-seq databases of mouse and human lungs, BMP3b was specifically expressed in lung stromal cells, similar to meflin. Considering the close relationship between meflin and BMP3b, they focused on the function of BMP3b.

In the functional analyses, primary lung fibroblasts from *Bmp3b*-KO mouse enhanced TGF-β-induced aberrant fibrogenesis, and *Bmp3b*-KO mice exacerbated murine lung fibrosis, suggesting anti-fibrotic effects of BMP3b. Supplementation of recombinant BMP3B was effective on suppression of TGF-β-induced extracellular matrix in lung fibroblasts, even if meflin is suppressed. From these findings, they revealed that BMP3b is a novel anti-fibrotic molecule and partially covers anti-fibrotic effects of meflin in lung fibroblasts.

**Research Summary and Future Perspective**

Further studies will be conducted to confirm the beneficial effects of BMP3b on pulmonary fibrosis aiming to develop potential therapeutics for human lung diseases.

**Publication**

Suzuki A, Sakamoto K, Nakahara Y, Enomoto A, Hino J, Ando A, Inoue M, Shiraki Y, Omote N, Kusaka M, Fukihara J, Hashimoto N. BMP3b is a Novel Anti-Fibrotic Molecule Regulated by Meflin in Lung Fibroblasts. Am J Respir Cell Mol Biol. 2022 Jun 21. doi: 10.1165/rcmb.2021-0484OC.

**References**

[1] Nakahara Y, Hashimoto N, Sakamoto K, Enomoto A, Adams TS, Yokoi T, Omote N, Poli S, Ando A, Wakahara K, Suzuki A, Inoue M, Hara A, Mizutani Y, Imaizumi K, Kawabe T, Rosas IO, Takahashi M, Kaminski N, Hasegawa Y. Fibroblasts positive for meflin have anti-fibrotic properties in pulmonary fibrosis. Eur Respir J. 2021 Dec 23;58(6):2003397. doi: 10.1183/13993003.03397-2020. PMID: 34049947.

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