GIST reveals treatment for pulmonary fibrosis caused by COVID-19... Identifying the effectiveness of existing drugs and suggesting new treatment targets

- Identification of the core gene group of macrophages in pulmonary fibrosis... Construction of an interaction network of genes related to pulmonary fibrosis in macrophages and presentation of the upstream regulator 'GRN gene' as a new treatment target

▲ (From left) Professor Chang-Myung Oh, Dr. Ji-Hwan Park, and integrated master's and doctoral program student Yumin Kim

Pulmonary fibrosis, which can occur as a sequela of COVID-19, has a different mechanism from general pulmonary fibrosis such as idiopathic pulmonary fibrosis*, so research is needed to confirm whether existing drug treatment methods have the same efficacy.

* Idiopathic Pulmonary Fibrosis (IPF): It is an interstitial pneumonia that is localized to the lungs and occurs when chronic inflammatory cells infiltrate the alveolar walls. It mainly occurs in the elderly. Treatment to relieve symptoms through drug treatment such as anti-fibrotic drugs is available. It is the most popularly used.

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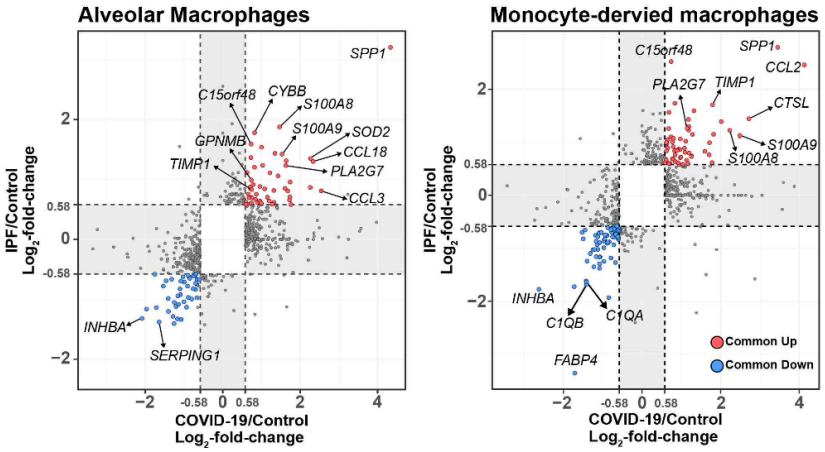
The Gwangju Institute of Science and Technology (GIST) announced that a research team led by Professor Chang-Myung Oh of the Department of Biomedical Engineering, together with domestic and international research teams including Roswell Park Comprehensive Cancer Center in the U.S., analyzed lung macrophages* that cause pulmonary fibrosis in the aftermath of COVID-19 and found that existing drug treatment methods are effective.

* macrophage: A major cell responsible for innate immunity, it is a type of white blood cell that acts as a phagocyte to absorb and digest non-proteins present in the healthy body, such as cellular tissue, foreign substances, microorganisms, and cancer cells.

The research team observed significant changes in the distribution of lung macrophages through analysis of lung single cell transcriptome data (lung macrophages and their gene groups) from patients with severe COVID-19 and idiopathic pulmonary fibrosis (IPF).

The research team studied patients with severe COVID-19 and idiopathic pulmonary fibrosis and found that the number of lung macrophages decreased and monocyte-derived macrophages increased.

Additionally, changes in the metabolic system of lung macrophages (increased lipid metabolism and glucose metabolism) were identified through gene expression analysis of lung macrophages. Changes in immune response and increased expression of lysosome-related genes were associated with the induction of pulmonary fibrosis.



▲ Analysis of lung macrophage transcriptome data from COVID-19 patients and idiopathic fibrosis patients: Among lung macrophages, gene expression of alveolar macrophages and monocyte-derived macrophages was confirmed through comparison with the comparison group.

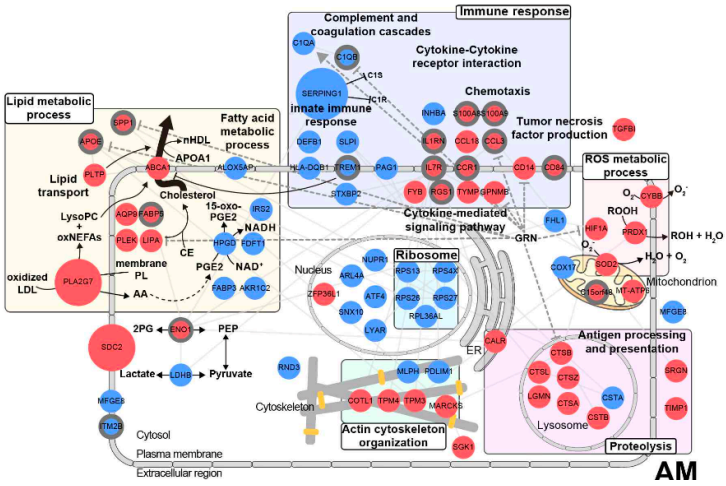
The research team utilized transcriptome data analysis of a pulmonary fibrosis-induced mouse model treated with anti-fibrotic drugs and analyzed gene expression patterns to evaluate the potential responsiveness of lung macrophages to anti-fibrotic drugs.

The research team injected three anti-fibrotic drugs (nintedanib, pirperidone, and sorafenib) into a mouse model that induced pulmonary fibrosis using protein (TGFβ-1)* and obtained transcriptome data 72 hours after injecting pulmonary fibrosis. They comparatively analyzed transcriptome data from patients with COVID-19 and idiopathic pulmonary fibrosis and, as a result, found that anti-fibrotic drugs used for idiopathic pulmonary fibrosis can also be an effective treatment for pulmonary fibrosis caused by COVID-19.

* TGFβ-1 (transforming growth factor beta-1): A protein that plays an important role in cell growth, differentiation, and various physiological functions and is known to induce fibrosis in the lung.

In addition, an interaction network of genes related to pulmonary fibrosis in macrophages was constructed using a protein-protein interaction database. Based on this, the GRN gene*, which acts as an upstream regulator of the relevant genes, was proposed as a new treatment target.

* GRN (Granulin Precursor) gene: A gene that codes for the Granulin Precursor protein. It is known to be involved in cell differentiation, inflammatory response, and protein homeostasis, but its exact function is not yet known.



▲ Gene network model of alveolar macrophages: Network model based on interaction and gene function within gene groups showing common gene expression with the comparison group through analysis of single cell transcriptome data of lungs from COVID-19 patients and idiopathic pulmonary fibrosis patients.

Professor Chang-Myung Oh said, "This study confirmed the effectiveness of existing anti-fibrotic drugs to treat pulmonary fibrosis, which has become a social problem due to the aftereffects of COVID-19, while also suggesting a new treatment target. We expect to speed up the development of new treatments for pulmonary fibrosis, and through follow-up research, we plan to confirm how GRN, predicted to be an upstream regulator, is involved in the metabolic system and immune response."

This research, conducted by GIST Professor Chang-Myung Oh's team, the Korea Research Institute of Bioscience & Biotechnology, Dr. Ji-Hwan Park's research team at the University of Science and Technology, and Professor Dae-Kyum Kim's research team at Roswell Park, USA, was supported as a joint research project of the Korea Advanced Institute of Science and Technology, the National Research Foundation of Korea, and the GIST Institute for Life Science Convergence, and was published online on November 15, 2023 in JMV: Journal of Medical Virology, an international journal in the field of virology.

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