

## Thyroid hormone therapy heals lung fibrosis in animal study

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Thyroid hormone therapy significantly resolves resolution of fibros significantly less fi significantly less fi fact that they were study shows. These provide a novel insight into the development of pulmonary fibrosis and could lead to alternative treatment for this serious condition, according to the researchers.

The study was published in Nature Medicine.

A type of <u>lung</u> disease, <u>pulmonary fibrosis</u> causes scarring of the lungs, which impairs breathing. One form of this lethal illness, <u>idiopathic pulmonary fibrosis</u> (IPF), is steadily increasing in the United States and leads to death within three to five years of diagnosis in half of patients.

Using profiles of all the genes expressed in the lungs, the Yale-led team of investigators identified a gene that was increased in the lungs of people with IPF; this gene also activates the <a href="mailto:thyroid">thyroid</a> hormone.

To examine the link between the thyroid hormone and IPF, the research team tested the effect of the hormone in two different mice models. The thyroid hormone therapy, delivered systemically or in an inhaled form, significantly blocked the <u>fibrosis</u> in the IPF mice compared to control animals. The researchers observed the same effect in human epithelial cells, which line the airways, after treatment with the hormone in cell culture.

The beneficial effects of thyroid hormone were observed even though fibrosis was established in the mice, said senior author Naftali Kaminski, M.D., professor of medicine and chief of the Section of Pulmonary, Critical Care, and Sleep Medicine at Yale School of Medicine.

"Giving the hormone systemically causes signs of hyperthyroidism," Kaminski said. "But when we delivered the hormone by aerosol, it was not increased in the blood; yet it enhanced the resolution of fibrosis, so the animals treated had significantly less fibrosis than controls despite the fact that they were treated during the established phase of fibrosis."

The findings also revealed an unexpected insight into fibrosis. It has recently been suggested that in fibrosis, mitochondria—small organelles that regulate cell metabolism—do not function well. The Yale-led team discovered that thyroid hormone-normalized mitochondria function in epithelial cells that line the air sacs in the lungs. They believe that this normalization of metabolism protects the epithelial cells from damage and allows resolution of fibrosis.

The study has practical implications for future research. "Our data support further study of the potential role of aerosolized thyroid hormone as a therapy for fibrosis," Kaminski said. But additional studies focusing on determining the hormone dose, delivery, and demonstrating safety and efficacy in humans are required, he noted, adding that it is likely the aerosolized version could avoid potential side effects of therapy.

**More information:** Thyroid hormone inhibits lung fibrosis in mice by improving epithelial mitochondrial function, *Nature Medicine* (2017). nature.com/articles/doi:10.1038/nm.4447

Provided by Yale University



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