

Sugar-coated nanoparticles target macrophages, reverse pulmonary fibrosis

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Scientists at the University of Illinois Chicago have developed a treatment for pulmonary fibrosis by using nanoparticles coated in mannose—a type of sugar—to stop a population of lung cells called

macrophages that contribute to lung tissue scarring. The cell-targeting method holds promise for preventing this severe lung scarring disease, which can result in life-threatening complications like shortness of breath.

The researchers say that the treatment is not yet ready to be tested in [clinical trials](#), but its success in relevant animal models is a promising sign that it may be possible to treat the disease—for which there are very limited and imprecise treatments available.

A major cause of lung [fibrosis](#) is the activation of harmful immune cells that cause excessive [inflammation](#).

"The body's inflammatory processes are very complex and finding treatments for diseases that result from lingering or excessive inflammation are very difficult because the treatments that prevent harmful inflammation also—unfortunately—prevent helpful inflammation, which fights infections and heals injuries," said Abhalaxmi Singh, visiting research assistant professor in the department of pharmacology and regenerative medicine at the UIC College of Medicine. "To have a [targeted treatment](#) that addressed a root cause of harmful inflammation work in an animal model is exciting."

The coated nanoparticle treatment stops fibrosis by binding to a subset of [macrophages](#), a type of white blood cell found in all organs, that have a receptor for mannose, a sugar molecule. This receptor, called CD206, is hyper-expressed in patients with [pulmonary fibrosis](#).

The scientists found that the macrophages that cause lung fibrosis have very high levels of mannose. In pulmonary fibrosis, macrophages go through a transition that releases cytokines and promotes scarring. Singh and her colleagues characterized the surfaces of these scar-promoting macrophages and the CD206 mannose receptor and designed a nano-

vehicle to target these receptors.

When the sugar-coated nanoparticle binds to the cell's receptor, it delivers the nucleotide—a fragment of silencing RNA (siRNA) targeting transforming growth factor beta (TGFB)—which the researchers loaded into the nanoparticle. SiRNA targeting TGFB is a cell signaling pathway known to be involved with pulmonary fibrosis. Once in the cell, the nucleotide blocks the macrophage's ability to make excessive amounts of proteins, such as collagen, involved with scar formation.

"Macrophages are exciting, complex cells and the approach Dr. Singh and our team took in coating the nanoparticle with sugar to bind to the mannose receptor is an intriguing and precise way to ensure targeted delivery of a silencing RNA treatment to this subset of cells that contribute to fibrosis," said Asrar Malik, Schweppe Family Distinguished Professor and head of the department of pharmacology and regenerative medicine.

The team has already started testing the treatment in human [lung tissue](#) samples with colleagues at the University of California at San Francisco.

The nanoparticle used in the experiments is formulated from a protein called [albumin](#), and it is a platform the scientists are studying as a tool to deliver therapeutics for a variety of conditions.

Malik's team first discovered that albumin [nanoparticles](#) can be used to suppress inflammation in a precision medicine manner. Their original discovery was reported in a 2014 *Nature Nanotechnology* research article. The inventors subsequently established Nano Biotherapeutics, an independent startup company supported by a National Institutes of Health phase II Small Business Technology Transfer grant to attract the partners and investors needed to bring the innovation to market.

The new research is described in the article "Nanoparticle Targeting of de novo Pro-fibrotic Macrophages Mitigates Lung Fibrosis," which is published in the *Proceedings of the National Academy of Sciences*.

The article is co-authored by Sreeparna Chakraborty, Sing Wan Wong, Nicole Hefner, Andrew Stuart, Abdul Qadir, Amitabha Mukhopadhyay, Kurt Bachmaier, Jae-Won Shin and Jalees Rehman.

More information: Abhalaxmi Singh et al, Nanoparticle targeting of de novo profibrotic macrophages mitigates lung fibrosis, *Proceedings of the National Academy of Sciences* (2022). [DOI: 10.1073/pnas.2121098119](https://doi.org/10.1073/pnas.2121098119)

Zhenjia Wang et al, Prevention of vascular inflammation by nanoparticle targeting of adherent neutrophils, *Nature Nanotechnology* (2014). [DOI: 10.1038/nano.2014.17](https://doi.org/10.1038/nano.2014.17)

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