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Scarred lungs leave trail of beta arrestins

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Targeting a family of signaling proteins called beta arrestins may stop the life-threatening scarring and thickening of lungs associated with pulmonary fibrosis, reports a new *Science* study in mice.

If a drug that blocks the function of beta arrestins proves to be effective and safe in humans, patients and doctors will be able to add another treatment option to the currently sparse shelf of pulmonary fibrosis therapies. Under normal circumstances, the formation of scar tissue is the result of the body's own team of cellular doctors and nurses, rushing to help to seal up wounds with fibrous connective tissue and prevent infection.

But sometimes the formation of scar tissue can go haywire; progressive scarring and stiffening that occurs in the lungs of pulmonary fibrosis patients it increasingly difficult for affected individuals to breathe. The massive buildup of scar tissue can't be reversed, and no treatment has been able to stop progression of the disease. Most patients die within a few years of diagnosis. Discouragingly, no one knows what causes pulmonary fibrosis or even why some people get it while others don't.

Because pulmonary fibrosis appears later in life and without warning, creating an animal model that directly mimics disease onset has been difficult. The standard way to study pulmonary fibrosis is to treat mice with an antibiotic that causes lung scarring similar to that found in the lungs of pulmonary fibrosis patients. Here, Paul Noble and colleagues show that deleting beta arrestin genes in mice protected the animals from developing antibiotic-induced fibrosis, without affecting normal wound

healing.

The team also determined that beta arrestins regulate the ability of fibroblasts—cells that build collagen and connective tissue—to invade and damage lung tissue. By blocking beta arrestins' ability to invade and degrade lung tissue, the researchers were able to halt the development of lung fibrosis in mice. Noble and colleagues also found that similarly, blocking the function of beta arrestins in fibroblast cells from pulmonary fibrosis patients reduced damage to lung tissue.

The results point to beta arrestins as a possible drug target for pulmonary fibrosis.

More information: "Beta-Arrestin Deficiency Protects Against Pulmonary Fibrosis in Mice and Prevents Fibroblast Invasion of Extracellular Matrix," by A.K. Lovgren *Science* (2011)

Provided by AAAS