MicroRNAs (miRNAs) are a class of 19-22 nucleotides non-coding small RNAs that control the expression of a large number of genes by binding to the 3'UTR of targets and blocking translation or by causing degradation of target mRNA.

MicroRNAs have emerged as an important class of small RNAs encoded in the genome, acting as master regulators of gene expression at post-transcriptional level. Recent studies have indicated that microRNAs appear to be associated with many disease processes. Because they are thought to be single molecular entities that dictate the expression of fundamental regulatory pathways, microRNAs represent potential drug targets for controlling many biologic and disease processes.

Yale University researchers are studying a potential new treatment that reverses the effects of pulmonary fibrosis, a respiratory disease in which scars develop in the lungs and severely hamper breathing. The treatment uses a microRNA mimic, miR-29, which is delivered to lung tissue intravenously. In mouse models, miR-29 not only blocked pulmonary fibrosis, it reversed fibrosis after several days.

The microRNA-29 family is a well-established regulator of extracellular matrix genes. Accumulating studies have demonstrated that miR-29 family participates in the development of liver fibrosis, renal fibrosis, pulmonary fibrosis, cardiac fibrosis. It was also known the comprehensive role of miR-29 family in modulating profibrotic effect and its potential as therapeutic approach to fibrosis diseases. The expression of the three miR-29 family members is consistently downregulated in a number of pathological fibrotic conditions, including cardiac, renal, hepatic, and pulmonary fibrosis, as well as systemic sclerosis. Numerous studies in cell-culture and genetic replacement in rodents have also demonstrated the potential of miR-29 normalization to correct many drivers of pathological fibrosis. The Yale University study is the first one showing the potential therapeutic of miR-29 in vivo. The findings were recently published in the journal EMBO Molecular Medicine.

Another group of researchers from the People’s Republic of China found that another microRNA type, the 26a family, is fundamentally down-regulated during pulmonary fibrosis. Over-expression of microRNA-26a is able to contrast the experimental pulmonary fibrosis induced by bleomycin inhibiting the nuclear translocation of p-Smad3 through directly targeting Smad4, which determines the nuclear translocation of p-Smad2/Smad3. So, also microRNA-26a could be a new promising molecular treatment to reverse pulmonary fibrosis.
miRs in fibrotic lung diseases is not well understood. In this study, we found downregulation of miR-26a in the lungs of mice with experimental pulmonary fibrosis and in IPF, which resulted in posttranscriptional derepression of connective tissue growth factor (CTGF), and induced collagen production. More importantly, inhibition of miR-26a in the lungs caused pulmonary fibrosis in vivo, whereas overexpression of miR-26a repressed transforming growth factor (TGF)-β1-induced fibrogenesis in MRC-5 cells and attenuated experimental pulmonary fibrosis in mice. Our study showed that miR-26a was downregulated by TGF-β1-mediated phosphorylation of Smad3. Moreover, miR-26a inhibited the nuclear translocation of p-Smad3 through directly targeting Smad4, which determines the nuclear translocation of p-Smad2/Smad3. Taken together, our experiments demonstrated the antifibrotic effects of miR-26a in fibrotic lung diseases and suggested a new strategy for the prevention and treatment of IPF using miR-26a. The current study also uncovered a novel positive feedback loop between miR-26a and p-Smad3, which is involved in pulmonary fibrosis.