

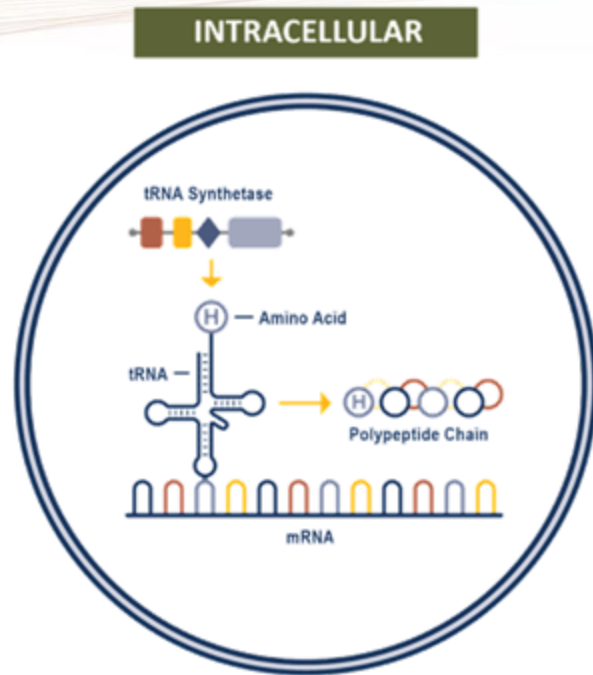


ATYR0101

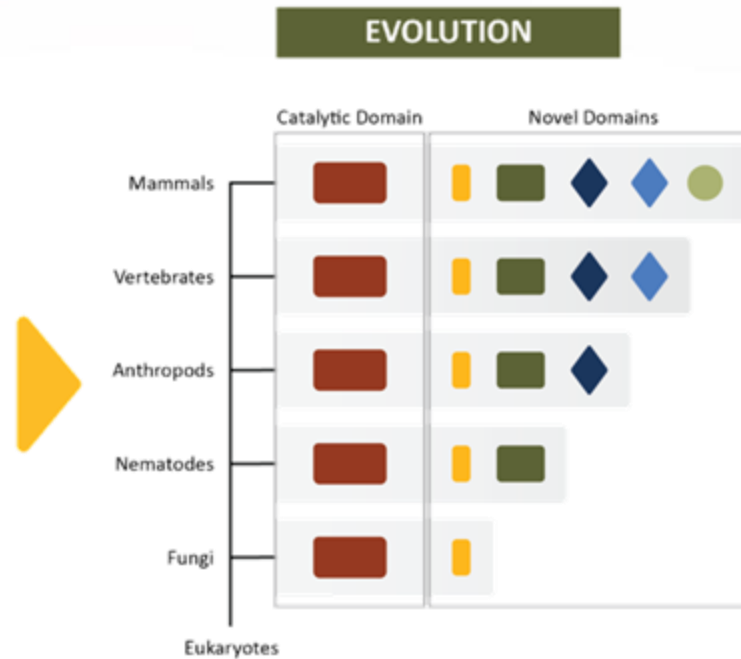
A New Approach to Fibrosis

May 17th, 2025

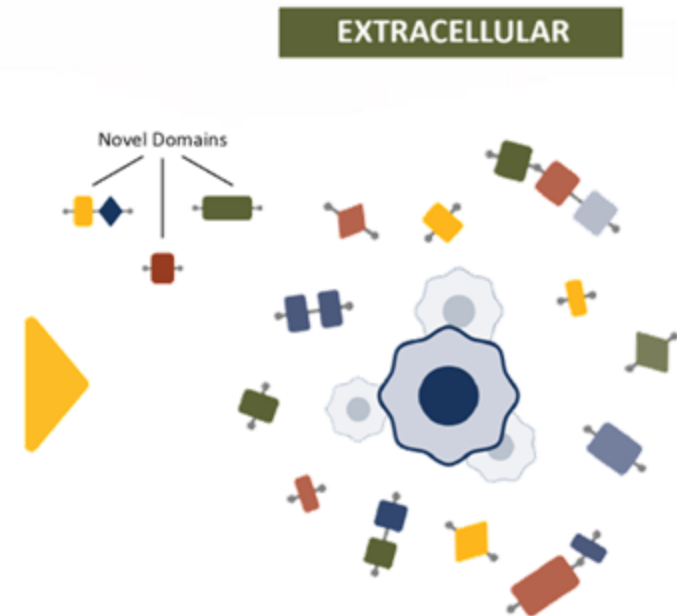
Extracellular tRNA Synthetases Regulate Homeostasis Through Novel Pathways



- **Ancient, essential enzymes** that catalyze protein synthesis by conjugating amino acid to tRNA



- Evolved to acquire **novel domains**
- Novel domains **persisted through evolutionary pressure**

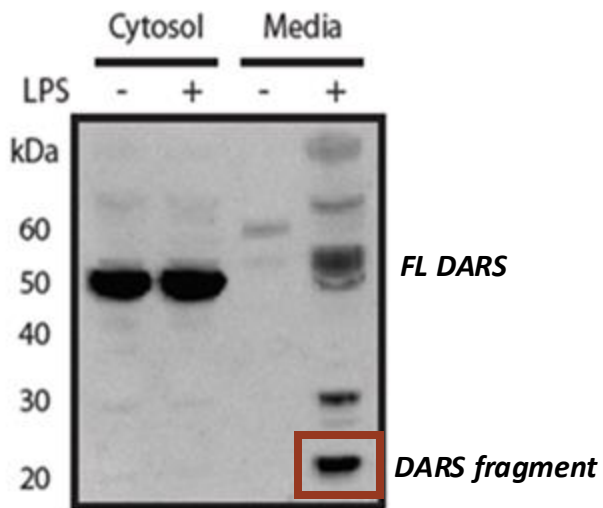
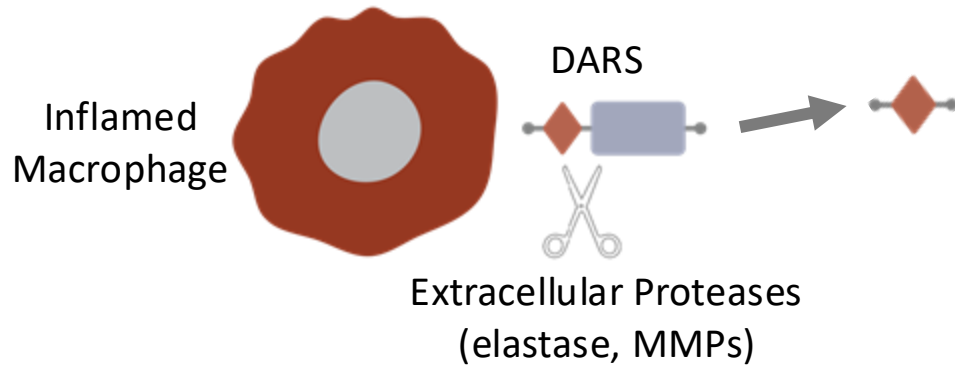


- **Released locally** enabling function as **parallel signaling molecules**
- Liberated by **alternative splicing** or **proteolysis**

Efzofitimod, a HARS-derived therapeutic, is nearing completion of a Phase 3 clinical trial in Pulmonary Sarcoidosis

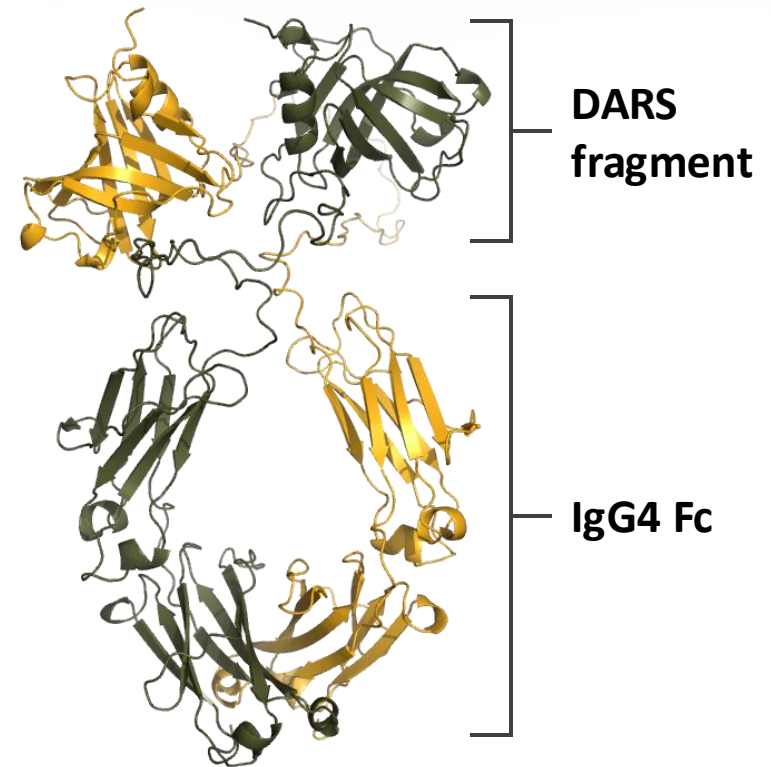
ATYR0101: DARS Synthetase Fragment Modulates LTBP1

DARS Synthetase Fragment Generation



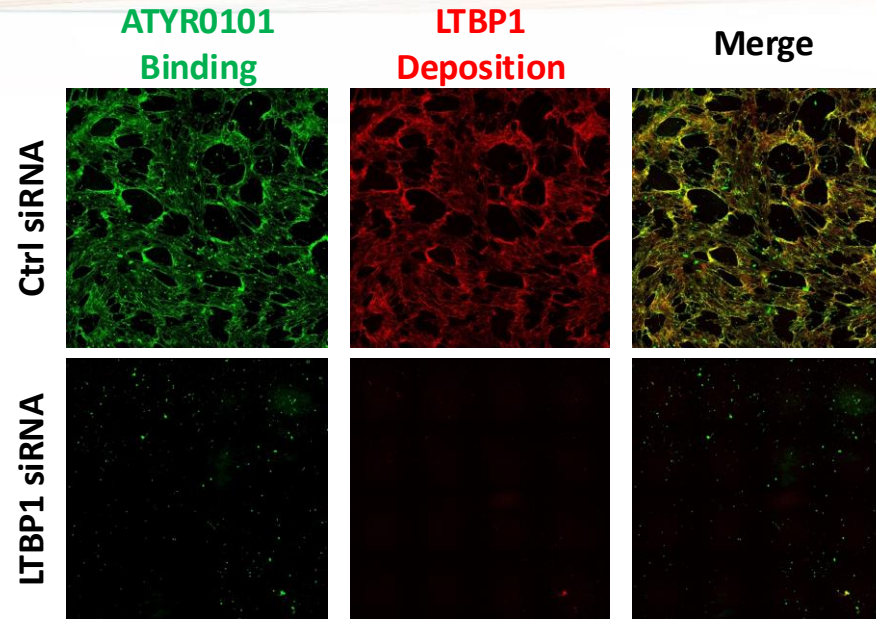
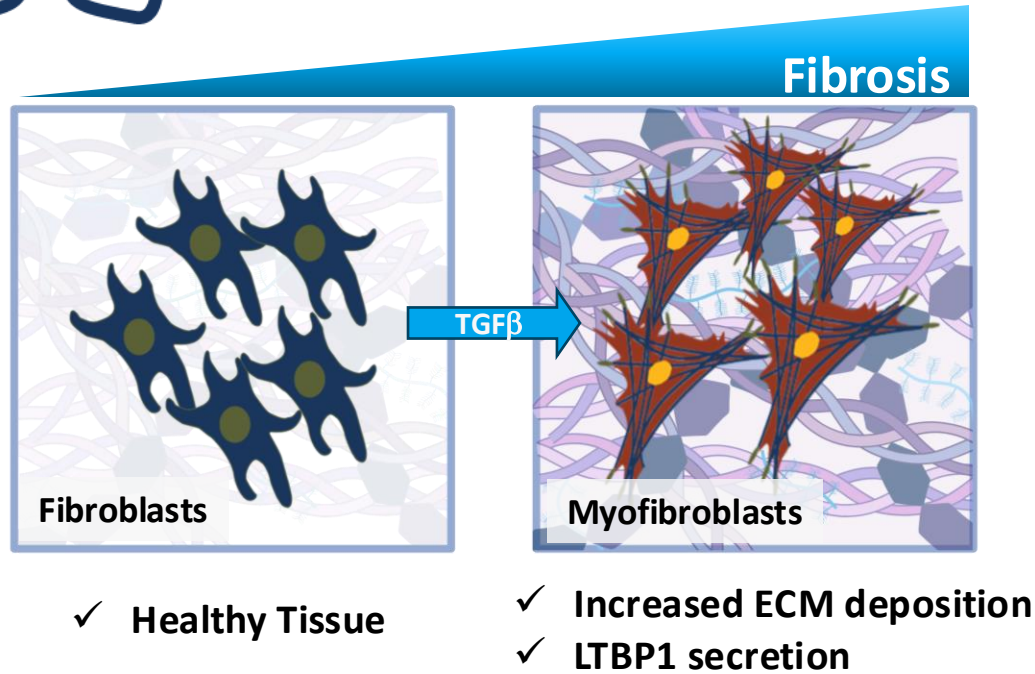
- DARS fragment is **naturally occurring & released from macrophages** under inflammatory conditions
- Latent TGF β Binding Protein 1 (**LTBP1**) has been identified as the **binding partner** for ATYR0101

ATYR0101 Therapeutic Molecule

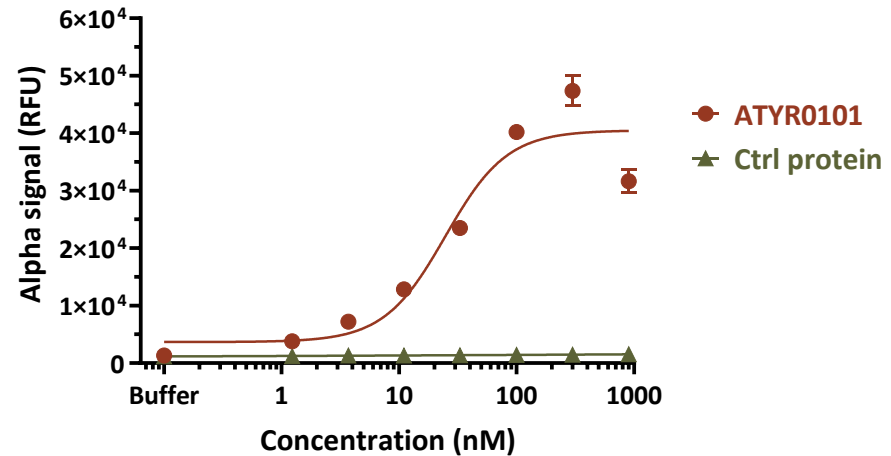


- **ATYR0101 is a fusion protein** derived from a proprietary extracellular domain of DARS (aspartyl-tRNA synthetase)
- Addition of an Fc improves circulating half-life

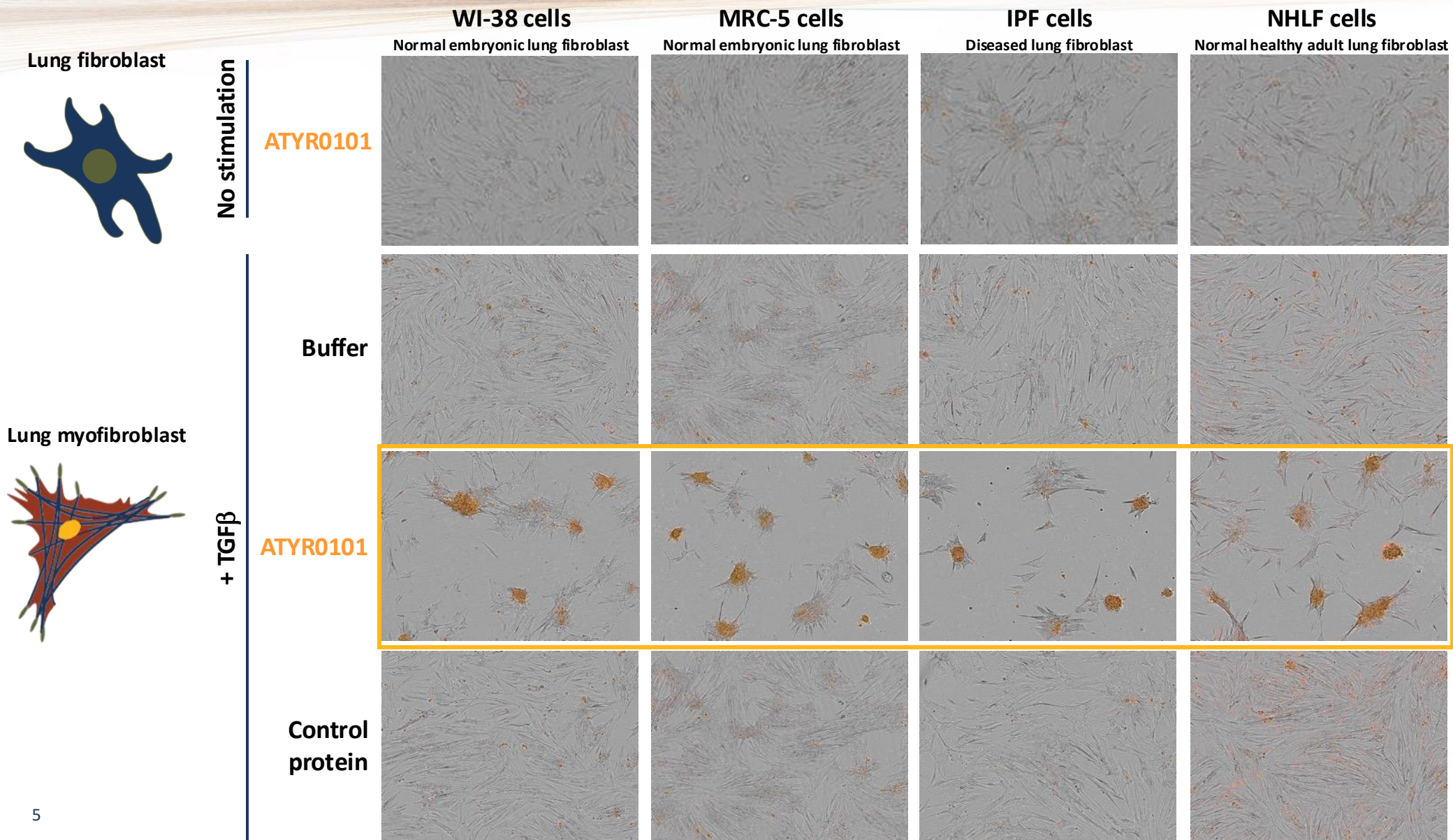
ATYR0101 Binds to Myofibroblast Extracellular Matrix Via LTBP1



ATYR0101 Directly Binds LTBP1

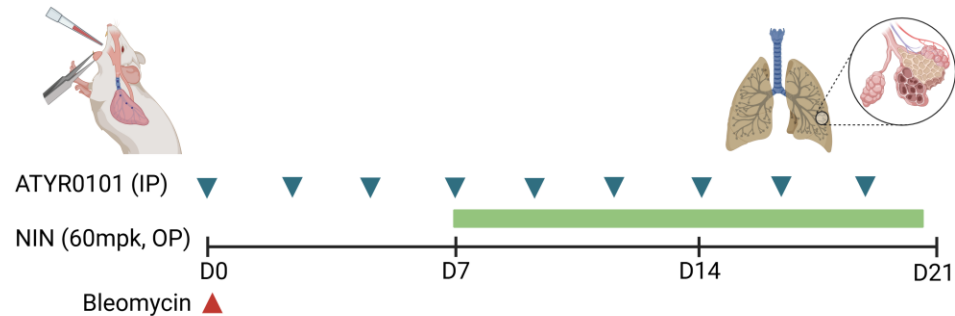


ATYR0101 Induces Apoptosis in Lung Myofibroblasts

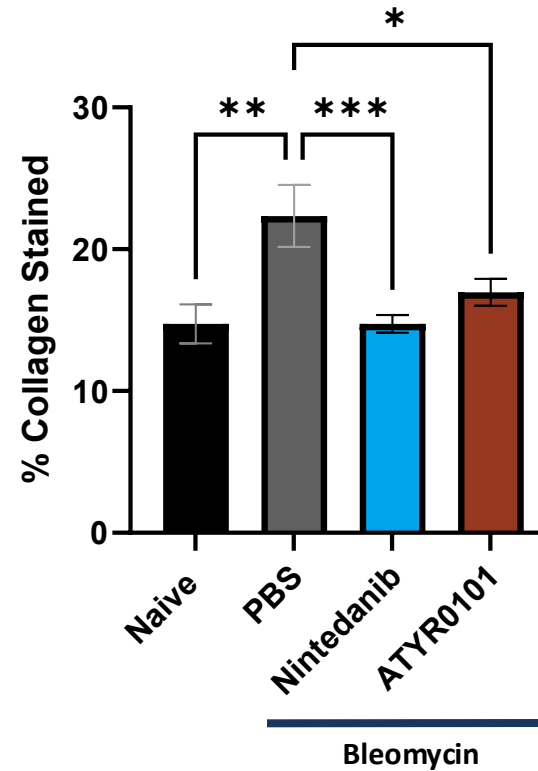


ATYR0101 Reduces Histologic Fibrosis Measures in Bleomycin-induced Lung Fibrosis

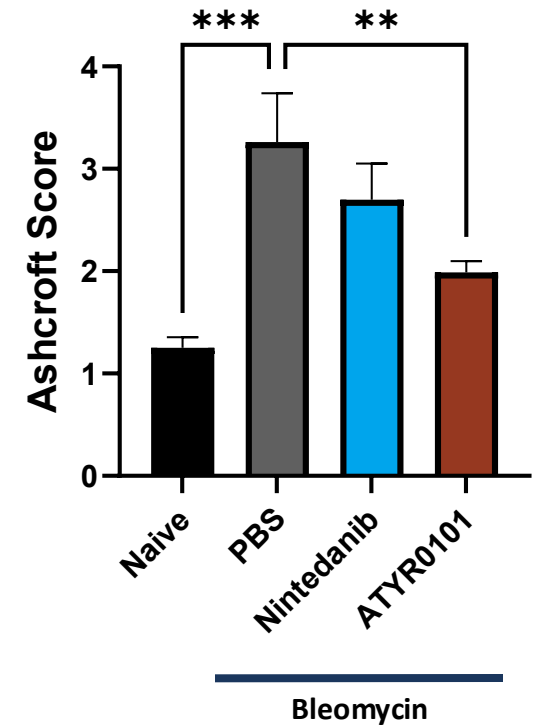
Mouse Bleomycin Model



% Collagen in Total Lung Area

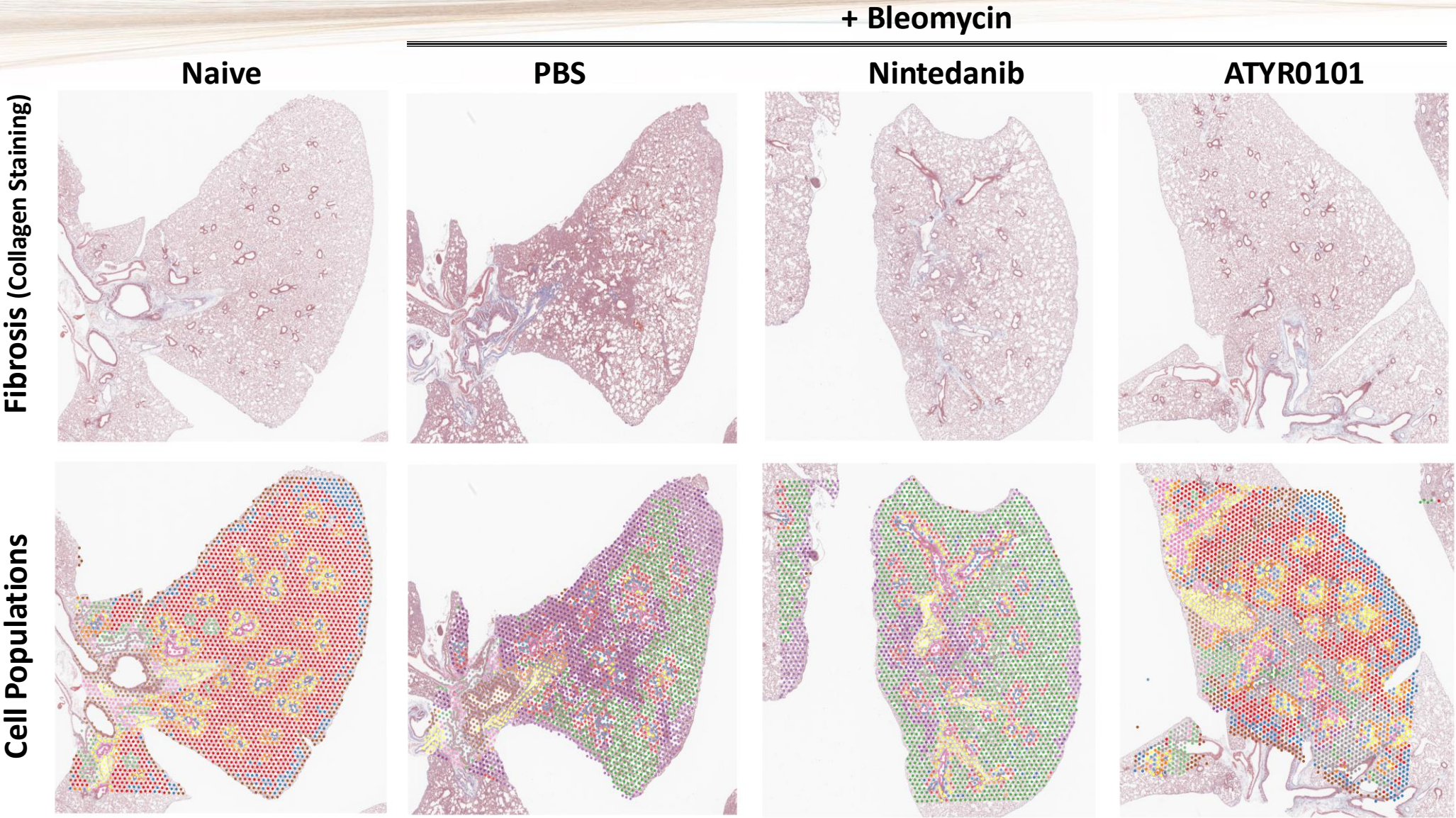


Ashcroft Score (Lung Fibrosis)

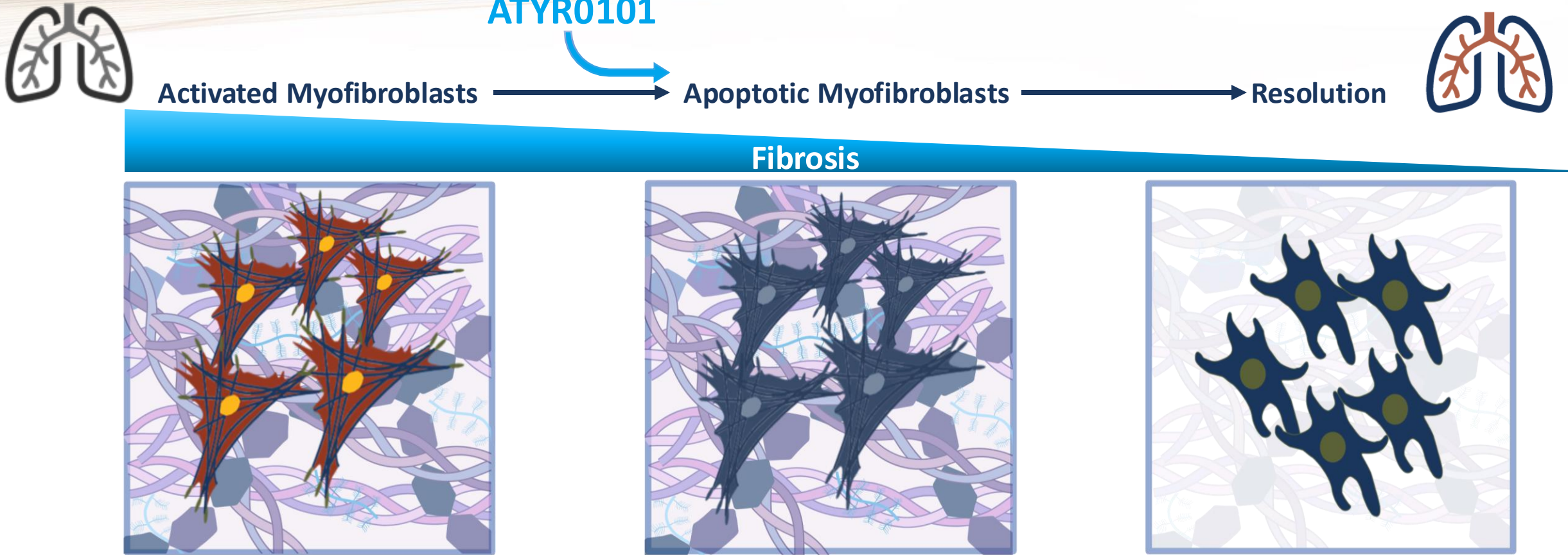


- The degree of collagen & fibrosis was significantly lower in ATYR0101 treatment groups as compared to the PBS control group

ATYR0101 Treatment In Lung Fibrosis Model Results in Unique Anti-Fibrotic Effects



Evasion of Myofibroblast Apoptosis is a Hallmark of Fibrotic Diseases



ATYR0101 has the potential to **reverse established fibrosis** by clearing pathogenic myofibroblasts