The journal *Proceedings of the National Academy of Sciences U.S.A. (PNAS)* reports in its July 29th issue a study by the group of Erwin Wagner demonstrating that over-expression of the AP-1 transcription factor Fra-2 in mice results in pulmonary fibrosis. This work unravels an unexpected profibrogenic function of the Fra-2 protein and suggests that Fra-2/AP-1 has to be considered a contributing pathogenic factor of pulmonary fibrosis in humans.

Pulmonary fibrosis is the often fatal end stage condition of various lung diseases. To date, the molecular pathways leading to fibrosis are only incompletely understood and effective therapies are not available. In their recent report published in PNAS, Erwin Wagner’s team provide novel insights into the pathogenesis of fibroproliferative diseases by generating transgenic mice which over-express the AP-1 transcription factor Fra-2. Unexpectedly, ectopic expression of Fra-2 in various tissues resulted in spontaneous development of fibrosis of the lung, skin and liver as well as premature mortality. The pulmonary phenotype was characterized by vascular remodeling and obliteration of pulmonary arteries, inflammation and release of various cytokines and chemokines also implicated in the human disease. Moreover, the relevance of these findings is further highlighted by the fact that Fra-2 was found to be strongly expressed in human samples of idiopathic and autoimmune-mediated pulmonary fibrosis. These findings identify Fra-2 expression as a novel profibrogenic factor and suggest that targeting Fra-2 may be a promising approach to treat fibroproliferative diseases.

**Reference:**