Pulmonary fibrosis inhibited by pentraxin-2/SAP in research study

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Promedior, Inc., a clinical stage biotechnology company developing novel therapies to treat fibrotic and inflammatory diseases, announced today the publication of collaborative research in the *International Journal of Biochemistry and Cell Biology* entitled, "TGF-beta driven lung fibrosis is macrophage dependent and blocked by Serum amyloid P." The research showed that human Pentraxin-2 (PTX-2), also called human Serum amyloid P (SAP), potently inhibits all undesirable pro-fibrotic pathologies driven by TGFβ1 and represents a novel therapeutic approach for the treatment of diseases that involve lung fibrosis, including idiopathic pulmonary fibrosis (IPF). This research validates that PTX-2/SAP can have therapeutic effects even in conditions driven by TGFβ1 growth factor, and builds on the body of research showing the unique role of PTX-2/SAP in activating the body's natural ability to resolve tissue damage in disease processes that cause fibrosis and inflammation.

In this study, researchers examined the effects of PTX-2/SAP in the lung specific TGFβ1 transgenic mouse model, since many of the pathogenic mechanisms observed in lung fibrosis can be stimulated by the growth factor TGFβ1. Highlights of the results from this study validating the potential therapeutic effects of PTX-2/SAP in pulmonary fibrosis included:

- PTX-2/SAP inhibited all of the pathologies driven by TGFβ1 including apoptosis, airway inflammation, pulmonary fibrocyte

and M2 macrophage accumulation and collagen deposition, without affecting the levels of TGFβ1 in the lung;

- An abbreviated therapeutic dose schedule was equally efficacious and demonstrated a sustained durability of effect following cessation of drug dosing, suggesting that intermittent dosing may be feasible in human patients;

- PTX-2/SAP levels were reduced in the serum of IPF patients when compared to closely matched healthy control subjects and the levels of SAP in IPF patient serum directly correlated with lung function;

- PTX-2/SAP directly inhibited M2 macrophage differentiation of monocytes obtained from IPF patients, suggesting that IPF patient monocytes would be responsive to PTX-2 therapy.

The findings regarding the effects of PTX-2/SAP in the lung specific TGFβ1 transgenic mouse model expand on previous preclinical studies, in which Promedior investigators determined that PTX-2/SAP potently inhibited lung fibrosis in both acute bleomycin-induced pulmonary fibrosis models and chronic asthma models through an inhibition of pulmonary fibrocyte and pro-fibrotic (M2) macrophage activation and accumulation, associated with increased macrophage production of the regulatory cytokine IL-10.

"Our research clearly shows the beneficial anti-fibrotic effects of Pentraxin-2 in TGFβ1-induced lung disease," said lead author Erica L. Herzog, M.D., Ph.D., Assistant Professor of Medicine (Pulmonary), Yale School of Medicine. "These findings highlight the potential of Pentraxin-2 to be a potent and durable inhibitor at a pivotal point in the disease pathway of progressive pulmonary fibrotic diseases."

Based on this research and other clinical and preclinical studies, Promedior is developing a pipeline of drugs based upon recombinant forms of PTX-2/SAP for the treatment and prevention of fibrotic and inflammatory diseases. The company is conducting human clinical studies to evaluate Pentraxin-2 therapeutics for a number of fibrotic diseases, including IPF and post-surgical scarring in glaucoma patients.

"These new findings further support our confidence in Pentraxin-2 as a novel therapeutic for many severe and chronic inflammatory and fibrotic diseases, including IPF," said Mark L. Lupher, Jr., Ph.D., Chief Scientific Officer, Promedior. "By showing that PTX-2/SAP has dominant therapeutic effects even downstream of TGFβ1 pathways through the ability to inhibit pathologic fibrocytes and macrophages and promote regulatory macrophage function, these results further confirm that Pentraxin-2 regulates fundamental mechanisms of the innate immune system, opening an exciting new approach to treat inflammatory and fibrotic diseases."

Provided by Yates Public Relations

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