Phenotypic Characterization of Bleomycin-Induced Pulmonary Fibrosis Model in Mice

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Abstract

Idiopathic pulmonary fibrosis (IPF) is a progressive and ultimately fatal disease that causes scarring and thickening of the lung tissue leading to respiratory failure. Despite the approval of Pirfenidone and Nintedanib in multiple countries for the treatment of IPF, lung fibrosis remains a major unmet medical need. Bleomycin-induced pulmonary fibrosis is a useful pre-clinical model in several species, most prevalently rodent models, to evaluate potential prophylactic and therapeutic drugs for IPF. Correlation between in-life lung parameters and histopathology has been well demonstrated using standard-of-care drugs in our studies. Lung injury was further analyzed by cellular phenotyping, gene expression and cytokine profiling. These biological analyses demonstrate that this model is a relevant model to evaluate anti-fibrotic agents.

Creation of Customized, Client-Specific Study Designs in Mouse Model for IPF

- **Study animals**: C57BL/6 (aged 6-8 weeks)
- **Fibrosis induction**: Clinical grade Bleomycin-instilled via oralpharyngeal route or osmotic pump
- **Option of test article administration**: PO, IP, IV, IM, SC, inhalation and osmotic pumps
- **Treatment regimen**: Therapeutic or Prophylactic

Standard Readouts

- Body weight
- Survival
- Lung weight
- Leukocyte count in bronchoalveolar lavage (BAL)

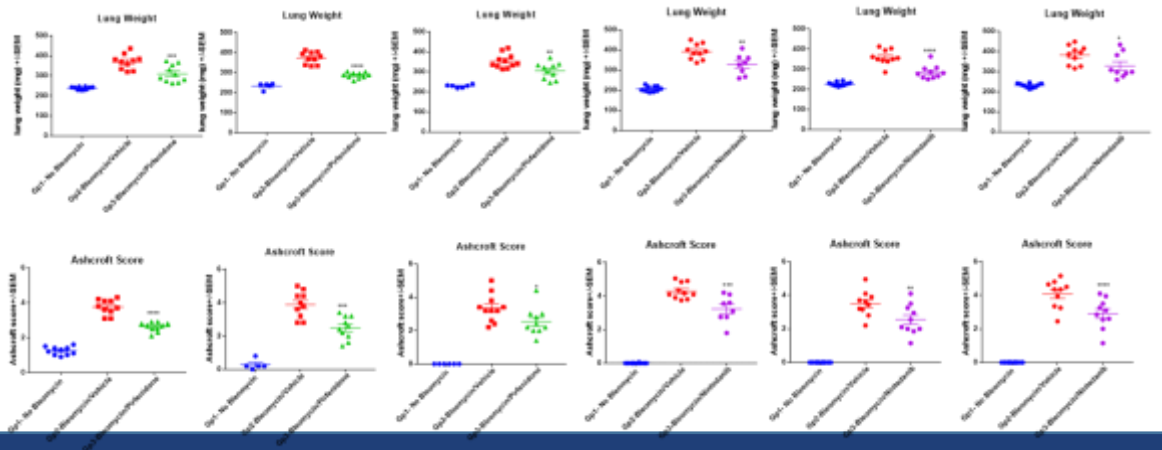
Fibrotic Characterization

- Lung hydroxyproline
- Serum/BAL soluble mediators
- Lung Fibropanel™ Gene expression
- Lung histology, Immunohistochemistry and Digital Pathology
- Phenotyping by FACS Analysis

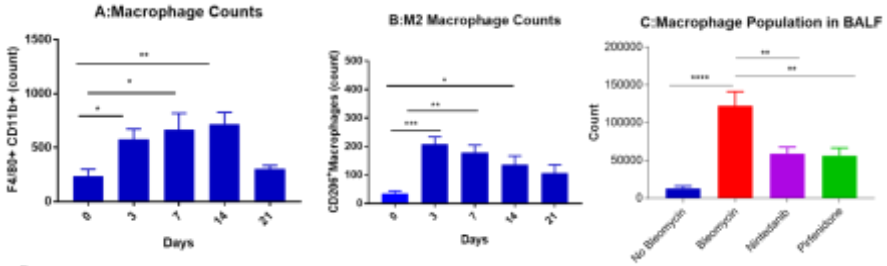
Lung Function Measurements

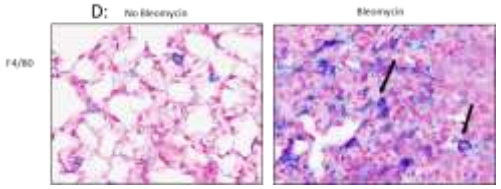
- flexiVent™
- Hypoxia related parameters
- Whole-body plethysmography

Reproducibility and Consistency of Bleomycin Induced IPF Model with Standard of Care



Macrophage Infiltration in Lung Tissue and Bronchoalveolar Lavage Fluid (BALF)

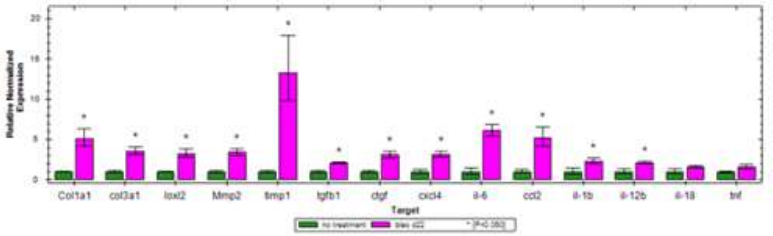




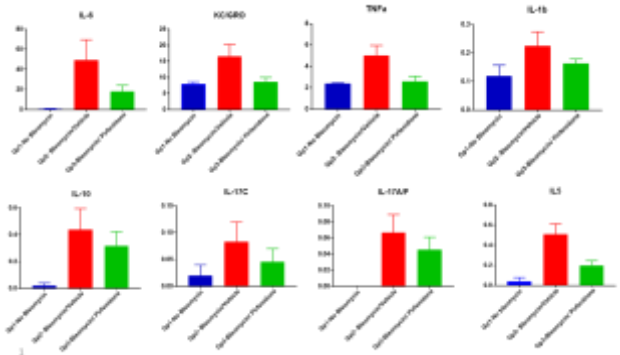
Bleomycin induced macrophage infiltration into lung tissue by Flow Cytometry (A, B), IHC (D)

Macrophage population in BALF (C)

Fibropanel™ Gene Expression Analysis



Pro-inflammatory Cytokine Analysis in BALF



Summary & Conclusions

Evaluation of new drugs, either small molecule or biologics requires robust and reliable pre-clinical animal models. Aragen Bioscience offers customized and high quality pre-clinical animal models with ex vivo readouts to support your anti-fibrosis drug development. The model described above has also been established in client-provided transgenic animals as well as in rats. Our expert and experienced staff provide scientific input and support for all project stages. Visit our website at www.aragen.com and have Aragen become your partner for characterization and development of new drugs for this important medical need.

The data shown are from various client research studies. We would like to thank our clients for their support and their permission to present these data.