Application of MSD on the lung cancer associated idiopathic pulmonary fibrosis

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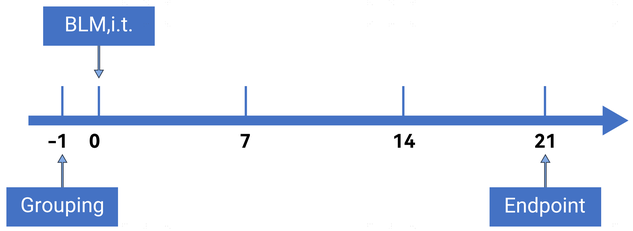
Abstract #107

Introduction

Idiopathic pulmonary fibrosis (IPF) is a progressive and irreversible chronic disease that kill ten thousand of people in China every year. The risk of IPF is highly correlated with smoke, air pollution, dust, virus infection and aging. Average survival period of patients diagnosed as IPF is around 2.8 years which is less than several types of cancers, therefore, IPF is also thought to be a lung cancer-like disease. In the past few decades, many animal models were created to mimic human IPF, however, induction materials, animal species and strain differences, sex, physiology structure and progress of disease make the choice of IPF animal models selection more difficult. In addition, lack of strong evidence of cytokines biomarker detection hampered the discovery of anti-IPF drugs. Meso Scale Discovery (MSD) instrument is an efficient tool to high throughput analyze the lowest level of several cytokines and other biomarkers in the same time and was used to detect the bleomycin (BLM) induced mouse lung fibrosis in this study.

Experimental design

Animal: C57BL/6 mouse
Bleomycin injection: intratracheal, 0.8 mg/kg
Experimental period: 3 Weeks
Positive control: Pirfenidone



Results

• Bodyweight

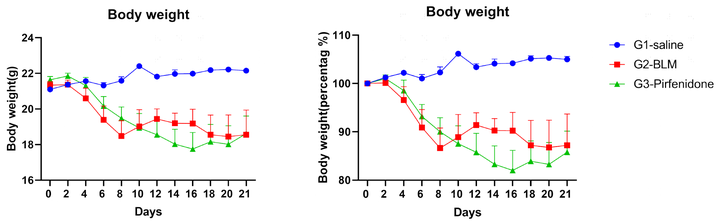


Fig. 1. Severe reduction of bodyweight is the typical symptom for BLM induced IPF models, although pirfenidone is a clinical drug used to cure IPF, the loss of bodyweight in pirfenidone treated group is similar to that of BLM group.

• Survival rate

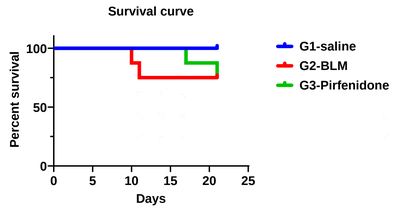


Fig 2. Pirfenidone significantly prolonged the survival period of BLM induced IPF mice.

• Lung weight and Lung ratio

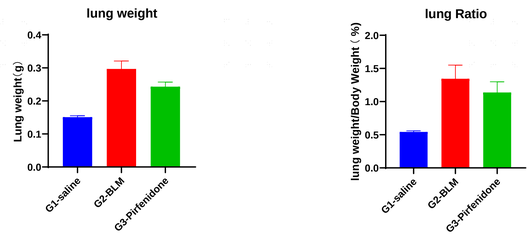


Fig 3. BLM caused a significant increase of lung weight and ratio and improved by Pirfenidone.

• HE and Masson staining

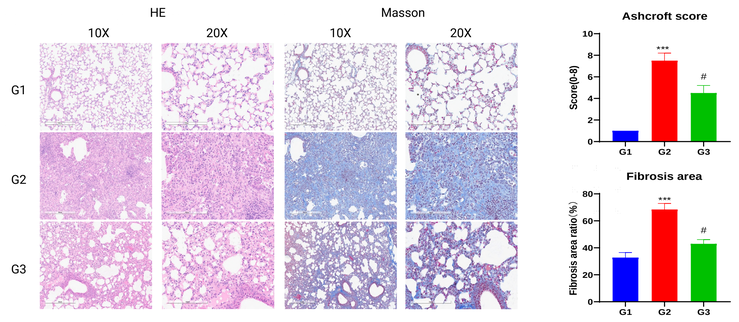


Fig 4. The pathology examination of BLM induced IPF indicated a increase of Ashcroft score and fibrosis area and pirfenidone reduced both of the Ashcroft score and fibrosis area after 21 days treatment.

• Soluble hydroxyproline

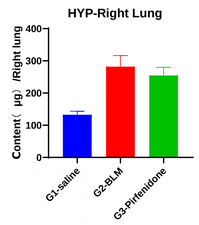
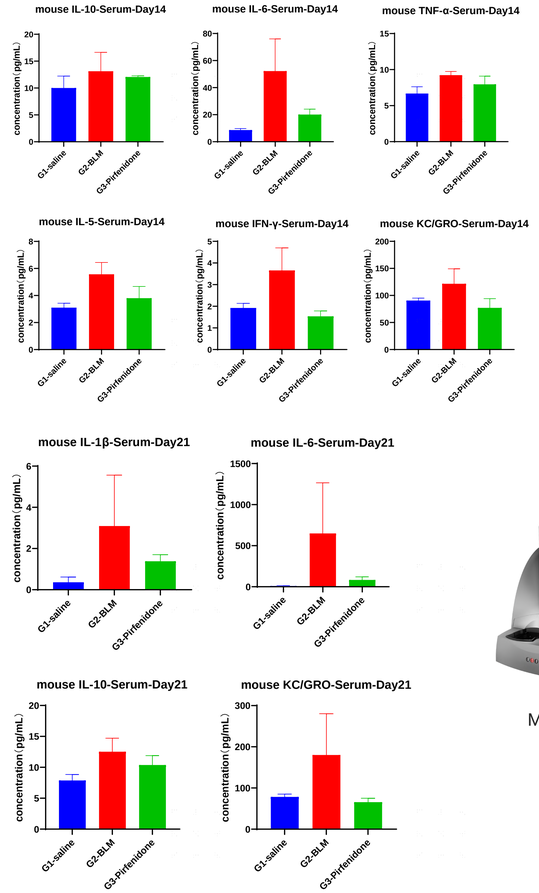


Fig 5. Soluble hydroxyproline is significantly increased in the right lungs of BLM-induced IPF and not affected by pirfenidone treatment.

• Cytokines determination using MSD



MSD S600

Fig 6. MSD detection in this study depicted a similar results of multiple cytokines levels including keratinocyte chemoattractant (KC)/human growthregulated oncogene (GRO) chemokine that in human IPF using only 30 ul serum samples.

Conclusion

In summary, the MSD detection and pathological evaluation proved that male and female mice treated with 0.8 mg/kg BLM through intratracheal injection is a suitable mouse model for the development of anti-IPF dugs. Using MSD detection, several mouse cytokines were measured simultaneously and showed that IFN-γ, IL-5, TNF-α, and IL-10 and other cytokines were increased in the IPF mouse model and were recovered after pirfenidone treatment at day 14 which mimics the cytokines profile in IPF patients.

Acknowledgement

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