European Respiratory Society
Annual Congress 2012

Abstract Number: 1093

Publication Number: P3148

Abstract Group: 1.5. Diffuse Parenchymal Lung Disease

Keyword 1: Anti-inflammatory **Keyword 2:** No keyword **Keyword 3:** No keyword

Title: The JAK3 inhibitor CP-690550 is a potent anti-fibrosis agent in a murine model of pulmonary fibrosis induced by bleomycin

Mr. Beixian 7838 Zhou zbeixian@126.com , Ms. Zhiping 7839 Fu apple9507@126.com , Dr. Yansheng 7840 Wang wangyansheng1999@126.com and Prof. Dr Jun 7841 Xu xufeili@vip.163.com MD . [1] The State Key Lab of Respiratory Disease, Guangzhou Medical University, Guangzhou, China, 510120 .

Body: Rationale: We previously suggested that JAK3, a cytoplasmic tyrosine kinase involved in receptor signaling for cytokines storm, is a molecular determinant in exacerbated innate immune inflammation. A selective JAK3 inhibitor can alleviate immunopathologic injury. Dose it has a potential for treating the lung fibrosis associated with autoimmunity? In the present study, CP-690550, a novel inhibitor of JAK3, was subjected to examination of its effects on lung fibrosis in a murine model of Bleomycin(BLM)-induced pulmonary inflammation. Methods&Results: Flow cytometry for typing bronchoalveolar lavage fluid (BAL) cells showed much higher level of T cells containing high frequencies of CD3+CD8+ and NKT+ cells in the BLM-challenged mice than control, but no significant changes were detected in the mice with CP-690550 treatment(15 mg/kg/d for two weeks) or JAK3-/- mice where pathology displayed attenuation of the lung fibrosis, corresponding to significantly increased survival rates(38.5% of BLM-challenged mice v.s.100% of the mice treated with CP-690550 or 84.6% of JAK3-/- mice following BLM challenge, $P<0.01$).Cytokines profiling by liquid-Chip demonstrated significantly elevated levels of IP-10, IFN-γ and reduced TGF-β1 secretion following BLM challenge in the lung homogenates and blood of the JAK3-/- or reduction of TGF-β1 in the blood of JAK3+/+ mice with CP-690550 treatment, compared to the JAK3+/+ mice. Conclusion: These results suggest that CP-690550 treatment has the capacity to counter immune inflammation-associated lung fibrosis through modulation of cytotoxic T cells-mediated autoimmune inflammation as well as inhibition of production of fibrostic cytokines.