【Grant-in-Aid for Scientific Research (S)】

Broad Section I

Title of Project：Role of ILC2 in idiopathic interstitial pneumonia

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Research Project Number：18H05286　Researcher Number：90468489
Keyword：Respiratory medicine

【Purpose and Background of the Research】

Idiopathic interstitial pneumonias (IIPs) are a set of diseases that are characterized by progressive deposition of collagen in the pulmonary alveolar interstitium. It has been reported that type 2 immune responses are inappropriately upregulated in the lungs of IIPs patients. However, the etiology of the disease is not fully understood. Group2 innate lymphoid cells (ILC2), which we discovered in 2010 produce large amounts of type 2 cytokines in response to IL-33. IL-33-activated ILC2 have been reported to exacerbate IIPs in the bleomycin-induced mouse model of pulmonary fibrosis. In this project, we will investigate the role of ILC2 in pulmonary fibrosis and verify the pathology of IIPs.

【Research Methods】

The mouse model of bleomycin-induced fibrosis is the most common model used to study IIPs. However, this is a model of acute fibrosis that occurs in 2 weeks and is resolved spontaneously after several weeks. To understand the chronic fibrosis that characterizes idiopathic pulmonary fibrosis (IPF), we have established a new mouse strain which lacks several systems for inhibition of ILC2 and develops pulmonary fibrosis. Unlike conventional models, the fibrosis in this strain occurs spontaneously and worsens in an age-dependent manner. In this project, we will investigate the pathogenic mechanism of IPF by single cell RNA-Sequence analysis, thorough the use of samples from this mouse model of fibrosis and from IPF patients.

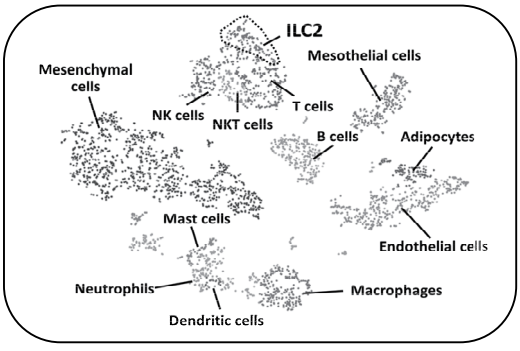

Fig. 1 Single cell RNA-Sequence

【Expected Research Achievements and Scientific Significance】

Find a candidate factors that could be a target for new therapy for IIPs.

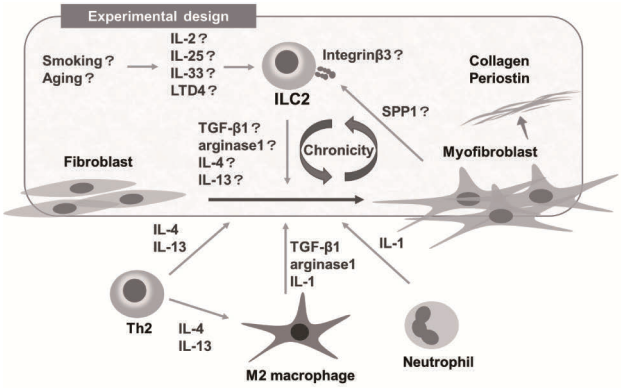

Fig. 2 ILC2 and pulmonary fibrosis

【Publications Relevant to the Project】

・Koga S, Hozumi K, Hirano KI, Yazawa M, Terooatea T. Peripheral PDGFRalpha(+)gp38(+) mesenchymal cells support the differentiation of fetal liver-derived ILC2.　(2018)

・Moro K, Kabata H, Tanabe M, Koga S, Takeno N, Mochizuki M, Fukunaga K, Asano K, Betsuyaku T, Koyasu S. Interferon and IL-27 antagonize the function of group 2 innate lymphoid cells and type 2 innate immune responses. Nat Immunol, 17(1): 76-86 (2016)

・Moro K, Yamada T, Tanabe M, Takeuchi T, Ikawa T, Kawamoto H, Furusawa J, Ohtani M, Fujii H, Koyasu S. Innate production of T(H)2 cytokines by adipose tissue-associated c-Kit(+)Sca-1(+) lymphoid cells. Nature, 463(7280): 540-544 (2010)

【Term of Project】

FY2018-2022

【Budget Allocation】

148,200 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.ims.riken.jp/labo/56/index.html