【Grant-in-Aid for Scientific Research (S)】
Biological Sciences (Medicine, Dentistry, and Pharmacy)

Title of Project : Generation and Maintenance of Pathogenic Immunological Memory and its Regulation

Toshinori Nakayama
(Chiba University, Graduate School of Medicine, Professor)

Research Project Number : 26221305 Researcher Number : 50237468
Research Area : Basic Medicine, Immunology
Keyword : Immunological memory, Allergy and immune-related disorder

【Purpose and Background of the Research】

The main interest of our research is the role of transcription factors that control differentiation and maintenance of memory Th1/Th2/Th17 cells and regulation of airway inflammation (asthma). "Immunological Memory" is a crucial subject to be understood in the Immunology field. We have recently proposed a "Pathogenic Th population disease induction model" in the pathogenesis of inflammatory diseases (Fig. 1). The aims of this study are to establish this concept by analyzing the role of Polycomb and Trithorax molecules in disease, to clarify the environmental factors that control the pathogenicity of memory Th cells, and to propose new strategies in the development of treatment of inflammatory diseases.

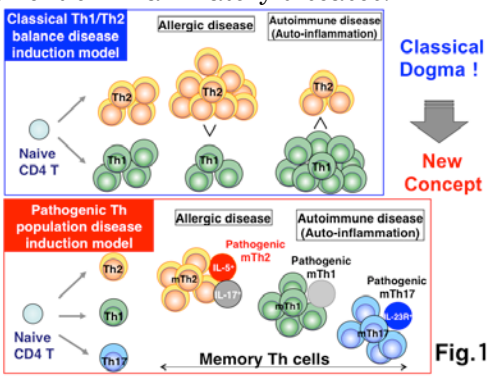

Fig.1

【Research Methods】

To identify the mechanisms regulating "Pathogenic memory Th2 cells" that induce allergic airway inflammation, we will conduct epigenetic analysis using ChIP-Seq. and RNA-Seq. We will also examine the polyps of patients with chronic sinus inflammation, while identifying the mechanism of induction of pathogenic Th2 cells in humans (e.g. by IL-33) (Fig. 2).

We will conduct epigenetic analysis on the role of EZH2 and Menin in the expression of cytokines in memory Th1, Th2, and Th17 cells.

We will analyze inducible lymphoid tissues in the lung and identify functional molecules regulating the generation and maintenance of memory Th2 cells using histological analysis with a multiphoton microscope.

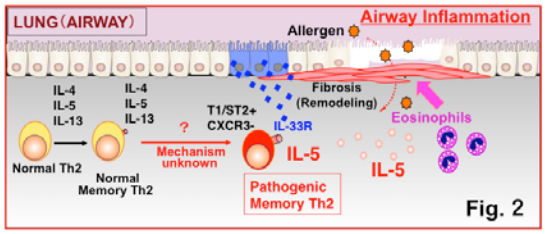

Fig. 2

【Expected Research Achievements and Scientific Significance】

Our approach to clarify the nature of "Immunological Memory" at both the molecular and chromatin levels and to prove the hypothesis that immune related disorders are induced by "Pathogenic memory Th cells" is scientifically significant. We focus on human immunology and examine inflamed tissues taken from patients. New treatment strategies in inflammatory diseases will be proposed. This study may also contribute to the development of safer and more effective vaccines. Thus, the impact of this study to society will be substantial.

【Publications Relevant to the Project】

- Endo, Y., Nakayama, T. et al., Pathogenic memory type Th2 cells in allergic inflammation. ***Trends Immunol.*** 35(2): 69-78 (2014).
- Tumes, D. J., Nakayama, T. et al., The polycomb protein Ezh2 regulates differentiation and plasticity of CD4$^+$ T helper type 1 and type 2 cells. ***Immunity*** 39(5): 819-832 (2013).
- Kuwahara, M., Nakayama, T. et al., The transcription factor Sox4 is a downstream target of signaling by the cytokine TGF-β and suppresses T_H2 differentiation. ***Nat. Immunol.*** 13:778-786 (2012).

【Term of Project】 FY2014-2018

【Budget Allocation】 150,000 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.m.chiba-u.ac.jp/class/meneki/english/