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学位論文の題名	Effect of Japanese cedar specific immunotherapy on allergen-specific TH2 cells in peripheral blood (スギ特異的免疫療法が末梢血中の抗原特異的ヘルパーT 細胞に 与える影響) Annals of Allergy, Asthma & Immunology. Vol. 110 : P.380-385,2013

2 Allergen-specific immunotherapy is the only method that can modify the course of allergic diseases.<sup>1</sup> However, how subcutaneous immunotherapy (SCIT) improves allergic rhinitis is 3 not fully understood.<sup>2,3</sup> The involvement of a shift from  $T_H 2$  to  $T_H 1$  responses in peripheral 4 blood in pollen SCIT has been contentious,<sup>4</sup> partly because of difficulties analyzing 5 antigen-specific  $T_{\rm H}$  cells.<sup>5</sup> We aimed to use recent technical advances<sup>6–8</sup> to establish a more 6 7 direct and simple method to analyze antigen-specific T<sub>H</sub> cells and to clarify the involvement of a  $T_H 2/T_H 1$  shift in peripheral blood in pollen specific immunotherapy. After short-term 8 (6-hour) antigen stimulation, antigen-specific T<sub>H</sub> cells in peripheral blood of Japanese 9 10 children and young adults with Japanese cedar pollinosis undergoing SCIT were analyzed by multicolor flow cytometry for the presence of the activation marker CD154 and intracellular 11 cytokines. Twenty-eight patients aged between 5 and 22 years were enrolled in the study; 22 12 had started SCIT after enrolling in the study (SCIT group), and the remaining 6 were 13 planning to start SCIT in the next off-season (control group). The number of Japanese cedar-14specific interleukin (IL) 5–, IL-4–, IFN- $\gamma$ –, IL-17A–, IL-10– and tumor necrosis factor  $\alpha$ – 15 producing T<sub>H</sub> cells without antigen-driven cell proliferation was determined. The seasonal 16 increase in the number of Japanese cedar-specific IL-5- and IL-4-producing T<sub>H</sub> cells seen 17 18 in the control group was suppressed in the SCIT group (P < .005 and P < .001, respectively). We report a powerful method for the analysis of antigen-specific T<sub>H</sub> cells in peripheral 19blood. This method will contribute to our understanding of immune mechanisms of 20 21 immunotherapy and help us develop more sophisticated allergen specific immunotherapy.

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## 23 **References**

- Frew AJ. Allergen immunotherapy. J Allergy Clin Immunol. 2010;125(suppl 2):S306–
   S313.
- Shamji MH, Durham SR. Mechanisms of immunotherapy to aeroallergens. Clin Exp
   Allergy. 2011;41:1235–1246.
- 3. Akdis CA, Akdis M. Mechanisms of allergen-specific immunotherapy. J Allergy Clin
   Immunol. 2011;127:18–27.
- 4. Wachholz PA, Nouri-Aria KT, Wilson DR, et al. Grass pollen immunotherapy for
   hayfever is associated with increases in local nasal but not peripheral Th1:Th2 cytokine
   ratios. Immunology. 2002;105:56–62.
- 5. Thiel A, Scheffold A, Radbruch A. Antigen-specific cytometry: new tools arrived! Clin
  Immunol. 2004;111:155–161.
- 6. Frentsch M, Arbach O, Kirchhoff D, et al. Direct access to CD4+ T cells specific for
  defined antigens according to CD154 expression. Nat Med. 2005;11:1118–1124.
- 37 7. Perfetto SP, Chattopadhyay PK, Roederer M. Seventeen-colour flow cytometry:
- unravelling the immune system. Nat Rev Immunol. 2004;4:648–655.
- 8. Prussin C, Yin Y, Upadhyaya B. T(H)2 heterogeneity: Does function follow form? J
  Allergy Clin Immunol. 2010;126:1094–1098.

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