

be sufficient for a thorough and accurate determination of the T cell cytokine profiles. Additionally, recent advances in the imaging technologies allow us to observe the cytokine-producing cells *in vivo* (Kamanaka *et al.*, 2006). Thus, combining traditional technologies with the modern and novel technologies will lead to the better understanding of T cell responses in the intestine.

Acknowledgements

This work was supported by grants from the Ministry of Education, Science, Sports, and Culture of Japan; the Ministry of Health and Welfare of Japan; the Global Center of Excellence (COE) program on Center of Education and Research for the Advanced Genome-based Medicine; and Yakult Bio-Science Foundation.

References

- Asseman, C. and Powrie, F. (1998). Interleukin 10 is a growth factor for a population of regulatory T cells. *Gut* **42**, 157–158.
- Beagley, K. W., Eldridge, J. H., Kiyono, H., Everson, M. P., Koopman, W. J., Honjo, T. and McGhee, J. R. (1988). Recombinant murine IL-5 induces high rate IgA synthesis in cycling IgA-positive Peyer's patch B cells. *J. Immunol.* **141**, 2035–2042.
- Beagley, K. W., Eldridge, J. H., Lee, F., Kiyono, H., Everson, M. P., Koopman, W. J., Hirano, T., Kishimoto, T. and McGhee, J. R. (1989). Interleukins and IgA synthesis. Human and murine interleukin 6 induce high rate IgA secretion in IgA-committed B cells. *J. Exp. Med.* **169**, 2133–2148.
- Betelli, E., Carrier, Y., Gao, W., Korn, T., Strom, T. B., Oukka, M., Weiner, H. L. and Kuchroo, V. K. (2006). Reciprocal developmental pathways for the generation of pathogenic effector TH17 and regulatory T cells. *Nature* **441**, 235–238.
- Chen, W., Jin, W., Hardegen, N., Lei, K. J., Li, L., Marinos, N., McGrady, G. and Wahl, S. M. (2003). Conversion of peripheral CD4⁺CD25⁻ naive T cells to CD4⁺CD25⁺ regulatory T cells by TGFβ induction of transcription factor Foxp3. *J. Exp. Med.* **198**, 1875–1886.
- Coffman, R. L., Shrader, B., Carty, J., Mosmann, T. R. and Bond, M. W. (1987). A mouse T cell product that preferentially enhances IgA production. I. Biologic characterization. *J. Immunol.* **139**, 3685–3690.
- Czerkinsky, C., Andersson, G., Ekre, H. P., Nilsson, L. A., Klareskog, L. and Ouchterlony, O. (1988). Reverse ELISPOT assay for clonal analysis of cytokine production. I. Enumeration of gamma-interferon-secreting cells. *J. Immunol. Methods* **110**, 29–36.
- Groux, H., O'Garra, A., Bigler, M., Rouleau, M., Antonenko, S., de Vries, J. E. and Roncarolo, M. G. (1997). A CD4⁺ T-cell subset inhibits antigen-specific T-cell responses and prevents colitis. *Nature* **389**, 737–742.
- Hand, T. and Belkaid, Y. (2010). Microbial control of regulatory and effector T cell responses in the gut. *Curr. Opin. Immunol.* **22**, 63–72.
- Harriman, G. R., Kunimoto, D. Y., Elliott, J. F., Paetkau, V. and Strober, W. (1988). The role of IL-5 in IgA B cell differentiation. *J. Immunol.* **140**, 3033–3039.
- Harrington, L. E., Hatton, R. D., Mangan, P. R., Turner, H., Murphy, T. L., Murphy, K. M. and Weaver, C. T. (2005). Interleukin 17-producing CD4⁺ effector T cells develop via a lineage distinct from the T helper type 1 and 2 lineages. *Nat. Immunol.* **6**, 1123–1132.
- Kamanaka, M., Kim, S. T., Wan, Y. Y., Sutterwala, F. S., Lara-Tejero, M., Galan, J. E., Harhaj, E. and Flavell, R. A. (2006). Expression of interleukin-10 in intestinal lymphocytes detected by an interleukin-10 reporter knockin tiger mouse. *Immunity* **25**, 941–952.

- Kiyono, H., Kunisawa, J., McGhee, J. R. and Mestecky, J. (2008). The mucosal immune system. In: *Fundamental Immunology* (W. E. Paul, ed.), pp. 983–1030. Lippincott-Raven, Philadelphia.
- Kunisawa, J., Nochi, T. and Kiyono, H. (2008). Immunological commonalities and distinctions between airway and digestive immunity. *Trends Immunol.* **29**, 505–513.
- Littman, D.R. and Rudensky, A.Y. (2010). Th17 and regulatory T cells in mediating and restraining inflammation. *Cell* **140**, 845–858.
- Mosmann, T. R. and Coffman, R. L. (1989). Th1 and Th2 cells: different patterns of lymphokine secretion lead to different functional properties. *Annu. Rev. Immunol.* **7**, 145–173.
- Sakaguchi, S., Yamaguchi, T., Nomura, T. and Ono, M. (2008). Regulatory T cells and immune tolerance. *Cell* **133**, 775–787.
- Seder, R. A. and Paul, W. E. (1994). Acquisition of lymphokine-producing phenotype by CD4+ T cells. *Annu. Rev. Immunol.* **12**, 635–673.
- Street, N. E. and Mosmann, T. R. (1991). Functional diversity of T lymphocytes due to secretion of different cytokine patterns. *FASEB J.* **5**, 171–177.
- Stumhofer, J. S., Silver, J. S., Laurence, A., Porrett, P. M., Harris, T. H., Turka, L. A., Ernst, M., Saris, C. J., O’Shea, J. J. and Hunter, C. A. (2007). Interleukins 27 and 6 induce STAT3-mediated T cell production of interleukin 10. *Nat. Immunol.* **8**, 1363–1371.
- Weaver, C. T., Hatton, R. D., Mangan, P. R. and Harrington, L. E. (2007). IL-17 family cytokines and the expanding diversity of effector T cell lineages. *Annu. Rev. Immunol.* **25**, 821–852.
- Zhou, L., Ivanov, I. I., Spolski, R., Min, R., Shenderov, K., Egawa, T., Levy, D. E., Leonard, W. J. and Littman, D. R. (2007). IL-6 programs Th17 cell differentiation by promoting sequential engagement of the IL-21 and IL-23 pathways. *Nat. Immunol.* **8**, 967–974.

