

Department of Immunology

1. Staffs and Students (April, 2009)

Professor	Takeshi Tsubata, M.D., Ph.D.	
Associate Professor	Takahiro Adachi, Ph.D.	
Junior Associate Professor	Makoto Tsuiji, Ph.D.	
Assistant Professor	Kozo Watanabe, Ph.D.	
Assistant Professor	Yusuke Kishi, Ph.D.	Naoko Matsubara, Ph.D.
	Man Rong Yong, Ph.D.	
Technician	Koji Hayashizaki,	
Secretary	Hiroko Takahashi,	Junko Shinya
Graduate Student	T.D.C.P.Gunasekara,	Xu Miduo,
	Yasuro Sakamaki,	Chiaki Takaku,
	Mai Tanaka,	Weng Dong,
	Yoshiyuki Sudo,	Yuki Takanohashi,
	Ami Hashimoto	

2. Purpose of Education

The immune system is essential for host protection against pathogens and cancer cells, and its ability to protect host is augmented by vaccination and previous infection. In contrast, abnormal immune responses are involved in pathogenesis of autoimmune diseases and allergy. Faculty members of the Department of Immunology are coordinating the lecture course of immunology and instructing graduate students to conduct their research projects on immunology for elucidating how the normal immune system respond to pathogens but not self-antigens or environmental antigens, how this discrimination is disrupted in allergy and autoimmune diseases, and how vaccination augments immune responses. Some of the research projects are aiming at developing new strategies for augmenting infection immunity and for controlling abnormal immune responses.

3. Research Subjects

- 1) Elucidation of the roles of membrane-bound lectins and their glycan ligands in normal and abnormal immune responses of B lymphocytes.
- 2) Elucidation of the roles of unfolded protein response molecules in B lymphocyte immune responses.
- 3) Elucidation of the regulatory mechanisms for self-reactive B lymphocytes and their defect in autoimmune diseases.
- 4) Chemical biology of B lymphocyte immune responses
- 5) Generation of novel strategies for host protection against pathogens and treatment of autoimmune diseases.

5. Publications

[Original Article]

1. Watanabe, K. and Tsubata, T. (2009): Autophagy connects antigen receptor signaling to costimulatory signaling in B lymphocytes. *Autophagy*. 5: 108-110.
2. Toda, M., Hisano, R., Yurugi, H., Akita, K., Maruyama, K., Inoue, M., Adachi, T., Tsubata, T. and Nakada, H. (2009): Ligation of tumor-produced mucins to CD22 dramatically impairs splenic marginal zone B cells. *Biochem J.* 417:673-683.
3. Hou, R., Ohtsuiji, M., Ohtsuiji, N., Zhang, L., Adachi, T., Hirose, S. and Tsubata, T. (2009): The centromeric interval of chromosome 4 derived from C57BL/6 mice accelerates type 1 diabetes in NOD.CD72^b congenic mice. *Biochem. Biophys. Res. Comm.* 380: 193-197.
4. Yanaba, K., Bouaziz, J.-D., Matsushita, T., Tsubata, T., and Tedder, T. F. (2009): The development and function of regulatory B cells expressing IL-10 requires antigen receptor diversity and TLR signals. *J. Immunol.* 182: 7459-7472.
5. Abdu-Allah, H. H. M., Watanabe, K., Hayashizaki, K., Iwayama, Y., Takematsu, H., Kozutsumi, Y., Tsubata, T., Ishida, H. and Kiso, M (2009): Synthesis of biotinylated sialoside to probe CD22-ligand interactions. *Tetrahedron Lett.* 50: 4488-4491.
6. Engels, N., König, L. M., Heemann, C., Lutz, J., Tsubata, T., Griep, S., Scharader, V. and Wienands, J. (2009): Recruitment of the cytoplasmic adaptor Grb2 to surface IgG and IgE provides antigen receptor-intrinsic costimulation to class-switched B cells. *Nature Immunol.* 10: 1018-25.

7. Abdu-Allah, H. H. M., Watanabe, K., Hayashizaki, K., Takaku, C., Tamanaka, T., Takematsu, H., Kozutsumi, Y., Tsubata, T., Ishida, H. and Kiso, M. (2009): Potent small molecule mouse CD22 inhibitors: exploring the interaction of the residue at C-2 of sialic acid scaffold. *Bioorg Med. Chem. Lett.* 19:5573-75.
8. Kishi, Y., Tsubata, T. (2010): Apoptosis of marginal zone B-cells in unimmunized mice. *J Med Dent Sci.* 56: 49-54.
9. Man, RY., Ondera, T., Komatsu, E., Tsubata, T. (2010): Augmented B lymphocyte response to antigen in the absence of antigen-induced B lymphocyte signaling in an IgG-transgenic mouse line. *Plos one.* 5:8815.
10. Ishiura, N., Nakashima, H., Watanabe, R., Kuwano, Y., Adachi, T., Takahashi, Y., Tsubata, T., Okochi, H., Tamaki, K., Tedder, TF., Fujimoto M.(2010): Differential phosphorylation of functional tyrosines in CD19 modulates B lymphocyte activation. *Eur J Immunol.* 40: 1192-1204.
11. Kishi, Y., Aiba, Y., Higuchi, T., Furukawa, K., Tokuhisa, T., Takemori, T. and Tsubata, T. (2010): Augmented antibody response with premature germinal center regression in CD40L-transgenic mice. *J Immunol.* 185: 211-219.
12. Bolduc, A., Long, E., Stapler, D., Cascalho, M., Tsubata, T., Koni, P. A. and Shimoda, M. (2010): Constitutive CD40L expression on B cells prematurely terminates germinal center response and leads to augmented plasma cell production in T cell areas. *J Immunol.* 185: 220-230.