

Immunotherapeutics

1. Staffs and Students (April, 2009)

Professor	Mari KANNAGI	
Associate Professor	Takao MASUDA	
Assistant Professor	Atsuhiko HASEGAWA	
Postdoctoral Position	Yukiko SHIMIZU	
Graduate Student	Takaya HAYASHI,	Ayako TAKAMORI,
	Nursarat AHMED,	Yuki IWASAKI,
	Shuichi, KINPARA,	Masashi MIYANO,
	Yotaro TAMAI,	Na Zeng
Research Student	Takuya TAKAHASHI	

2. Purpose of Education

Our research area is in between clinical and basic science, involving immunology, microbiology, and molecular biology. We participate in education for undergraduate medical students in basic immunology and a part of clinical immunology. For graduate students, we provide opportunity to research mechanisms of infectious disease and develop immunological therapeutics.

Viral infection causes various diseases including immunodeficiency, malignancy, autoimmunity, and inflammation. Human immunodeficiency virus (HIV) causes acquired immunodeficiency syndrome (AIDS), Human T-cell leukemia virus type-I (HTLV-I) causes adult T-cell leukemia (ATL) and various chronic inflammatory autoimmune-like diseases, and severe acute respiratory syndrome corona virus (SARS-CoV) causes SARS resembling acute respiratory distress syndrome. To understand mechanisms of these diseases, investigation on host immunity is indispensable. Immune responses are usually protective but sometimes harmful for the host, and are important determinants for disease manifestation. The goal of research in our department is elucidation of the role of host immunity in the diseases and development of effective immunotherapy. We also investigate intracellular mechanisms of viral replication to target direct molecules for therapy.

3. Research Subjects

1. Analysis of immunological risks for ATL development in HTLV-I-carriers.
2. Development of anti-tumor vaccine using experimental animal model system for ATL.
3. Immunological and molecular mechanism of HTLV-1 induced tumorigenesis.
4. Molecular mechanism of HIV replication especially related to HIV-1 integrase.
5. Experiments based on gene therapy to suppress HIV-1 replication.
6. Immunological suppressive mechanisms on HIV-1 replication.
7. Molecular mechanisms of SARS-CoV-induced fatal inflammatory responses.

4. Clinical Services

5. Publications

Original article

1. Nishitsuji, H., Hayashi, T., Takahashi, T., Miyano, Kannagi, M. & Masuda, T. Augmentation of reverse transcription by integrase through an interaction with host factor, SIP1/Gemin2 is critical for HIV-1 infection. *PLOS One* 4 (11): e7825, 2009.
2. Obitsu, S., Ahmed, N., Nishitsuji, H., Hasegawa, A., Nakahama, K., Morita, Nishigaki, K., Hayashi, T., Masuda, T., & Kannagi, M. Potential enhancement of osteoclastogenesis by severe acute respiratory syndrome coronavirus 3a/X1 protein. *Archiv. Virol* 154, 1457-1464, 2009.
3. Takatsuka, N., Hasegawa, A., Takamori, A., Shimizu, Y., Kato, H., Ohashi, T., Amagasa, T., Masuda, T., & Kannagi, M. Induction of IL-10- and IFN-g -producing T-cell responses by autoreactive T-cells expressing human T-cell leukemia virus type I Tax. *Int. Immunol.* 21, 1089-1100, 2009.
4. Shimizu Y, Takamori A, Utsunomiya A, Kurimura M, Yamano Y, Hishizawa M, Hasegawa A, Kondo F, Kurihara K, Harashima N, Watanabe T, Okamura J, Masuda T, Kannagi M. Impaired Tax-specific T-cell responses with insufficient control of HTLV-1 in a subgroup of individuals at asymptomatic and smoldering stages. *Cancer Sci*, 100: 481-9, 2009

5. Kinpara S, Hasegawa A, Utsunomiya A, Nishitsuji H, Furukawa H, Masuda T, Kannagi M. Stromal cell-mediated suppression of human T-cell leukemia virus type 1 expression in vitro and in vivo by type I interferon. *J Virol*, 83: 5101-8, 2009
6. Hasegawa A, Liu H, Ling B, Borda JT, Alvarez X, Sugimoto C, Vinet-Oliphant H, Kim WK, Williams KC, Ribeiro RM, Lackner AA, Veazey RS, Kuroda MJ. The level of monocyte turnover predicts disease progression in the macaque model of AIDS. *Blood*. 114: 2917-25, 2009.

International Scientific Meetings

1. Nishitsuji H, Kannagi M, Masuda T. Augmentation of reverse transcriptase (RT) activity by HIV-1 integrates through interaction with a host factor, Gemin2, is critical for HIV-1 infectivity. The 4th GERMAN-JAPANESE AIDS SYMPOSIUM. Mar. 2009, Vochem, Germany.
2. Kannagi M, Kinpara S, Hasegawa A, Utsunomiya A, Nishitsuji H, and Masuda T. Suppression of HTLV-1 expression by stromal cells in vitro and in vivo through type-I interferon responses. The 14th International Conference on Human Retrovirology. Jul. 2009, Salvador, Brazil.
3. Hasegawa A, Shimizu Y, Takamori A, Takatsuka N, Utsunomiya A, Tanosaki R, Choi I, Uike N, Okamura J, and Kannagi M. Functional evaluation of monocyte-derived dendritic cells from patients with chronic type of adult T cell leukemia. The 14th International Conference on Human Retrovirology. Jul. 2009, Salvador, Brazil.0