

## Medicine and Rheumatology

### 1. Staffs and Students (April, 2010)

Professor	Nobuyuki MIYASAKA Masayoshi HARIGAI	
Associate Professor	Hitoshi KOHSAKA, Ryuji KOIKE, Kazuki TAKADA	Tetsuo KUBOTA, Toshihiro NANKI,
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Assistant Professor	Shinya HIRATA, Akito TAKAMURA, Kaori WATANABE	Fumitaka MIZOGUCHI Michi TANAKA,
Visiting Lecturer	Rieko TSUBATA, Yoshiki NONOMURA, Kenji NAGASAKA, Peter Y. Shane, Toru KINO	Hiroyuki HAGIYAMA, Yukiko KOMANO, Jun OGAWA, Sae OCHI,
Research Nurse	Shoko KAWASE	
Graduate Student	Kayoko KANEKO, Yoshishige MIYABE*, Hisanori HASEGAWA*, Naoki KIMURA*, Hayato YAMAZAKI, (*GCOE QAISS)	Ryoko SAKAI, Shin FUKUDA*, Tadashi HOSOYA*, Akiko SUZUKI*,
Research Student	Chie MIYABE	
Resident physician	Humio HIRANO, Shoko KASAI, Mari KIHARA, Yoko NAKAZATO, Kenchi TAKENAKA, Natsuka UMEZAWA, Waka YOKOYAMA	Sunao KANDA, Hiroshi KAWANO, Yusuke MATSUO, Tetsuya SAITO, Tomoko TAKIZAWA, Akio YAMAMOTO,
Research worker	Hiroshi TAKAHASHI	
Office administrator	Rie FUJIME, Momoko MITSUISHI	Kaori KONNO,
Technical Staff	Aya SATO, Eri YOSHIMOTO	Sayaka ONO,

### 2. Purpose of Education

We have provided medical students and graduates with the opportunity to obtain the ability to identify important clinical problems and to solve them by clinical reasoning through their active participation into the diagnosis and management of various rheumatic diseases.

### 3. Research Subjects

Following studies have been extensively carried out in our laboratory with various biochemical, immunological, molecular biological and statistical techniques:

- 1) Development of new therapeutics for the treatment of rheumatoid arthritis using cell cycle regulators.
- 2) Investigation of mechanism and development of new therapeutics for the treatment of polymyositis.
- 3) The pathological role of chemokines/chemokine receptors in autoimmune diseases, including rheumatoid arthritis and polymyositis, for understanding their mechanisms and development of new therapeutics.
- 4) Investigation of role of BAFF/BLyS and Toll-like receptor in SLE.
- 5) Establishment of evidence-based treatment of rheumatic diseases by implementing several cohort studies.

#### 4. Clinical Services

We have provided care to a large number of patients with diverse rheumatic diseases with 25,687 clinic visits and 267 hospital admissions in 2010. We have aimed to practice evidence-based medicine and to provide care that is in accordance with the global standard. We have contributed to the development of potential new drugs and treatments through participation into industry- as well as investigator-initiated clinical trials for chemical and biological agents. We have also contributed to the refinement of the care of rheumatoid arthritis patients through the conduct of various pharmacovigilance studies.

#### 5. Publications

##### Original Article

1. Hashimoto J, Garner P, van der Heijde D, Miyasaka N, Yamamoto K, Kawai S, Takeuchi T, Yoshikawa H, Nishimoto N. Humanized anti-interleukin-6-receptor antibody (tocilizumab) monotherapy is more effective in slowing radiographic progression in patients with rheumatoid arthritis at high baseline risk for structural damage evaluated with levels of biomarkers, radiography, and BMI: data from the SAMURAI study. *Mod Rheumatol* (in press)
2. Ikeda T, Hirata S, Fukushima S, Matsunaga Y, Ito T, Uchino M, Nishimura Y, Senju S. Dual effects of TRAIL to suppress autoimmunity: the inhibition of Th1 cells and the promotion of regulatory T cells. *J Immunol* 185(9): 5259-5267, 2010
3. Illei, G.G., Shirota Y, Yarboro CH, Daruwalla J, Tackey E, Takada K, Fleisher T, Balow JE, Lipsky PE. Tocilizumab in systemic lupus erythematosus: data on safety, preliminary efficacy, and impact on circulating plasma cells from an open-label phase I dosage-escalation study. *Arthritis Rheum*, 62(2): 542-52, 2010
4. Kaneko K, Nanki T, Hosoya T, Mizoguchi F, Miyasaka N. Etanercept-induced necrotizing crescentic glomerulonephritis in two patients with rheumatoid arthritis. *Mod Rheumatol* 20(6):632, 2010
5. Katsumata Y, Harigai M, Kawaguchi Y, Fukasawa C, Soejima M, Kanno T, Nishimura K, Yamada T, Yamanaka H, Hara M. Diagnostic reliability of magnetic resonance imaging for central nervous system syndromes in systemic lupus erythematosus: a prospective cohort study. *BMC Musculoskelet Disord*. 2010 Jan 23;11:13.
6. Kohsaka H. Current insights in polymyositis and dermatomyositis *Clin Exp Neuroimmunol* 1(1), 22-32, 2010
7. Koike R, Tanaka M, Komano Y, Sakai F, Sugiyama H, Nanki T, Ide H, Jodo S, Katayama K, Matsushima H, Miwa Y, Morita K, Nakashima H, Nakamura H, Natsumeda M, Sato Y, Semba S, Tateishi M, Miyasaka N, Harigai M. Tacrolimus-induced pulmonary injury in rheumatoid arthritis patients. *Pulmonary Pharmacology and Therapeutics*. In press
8. Miyabe C, Mitsuhashi Y, Saito M, Tsuboi R, A novel mutation in the ATP2A2 gene in a Japanese Darier's disease patient with extremely hyperkeratotic lesions *J Dermatol* (in press)
9. Miyabe Y, Murata Y, Baba Y, Ito E, Nagasaka K. Successful treatment of cyclosporine A-resistant cytophagic histiocytic panniculitis with tacrolimus: A case report. *Mod Rheumatol* (in press)
10. Mizoguchi F, Izu Y, Hayata T, Hemmi H, Nakashima K, Nakamura T, Kato S, Miyasaka N, Ezura Y, Noda M. Osteoclast-specific Dicer gene deficiency suppresses osteoclastic bone resorption. *J Cell Biochem* 109(5):866-875, 2010
11. Nakashioya H, Nakano K, Watanabe N, Miyasaka N, Matsushita S, Kohsaka H. Therapeutic effect of D1-like dopamine receptor antagonist on collagen- induced arthritis of mice. *Mod Rheumatol* (in press)
12. Nonomura Y, Miyabe Y, Tanaka M, Tsubata R, Nanki T, Harigai M, Miyasaka N. Prominent splenic microcalcifications in a patient with systemic lupus erythematosus complicated with antiphospholipid syndrome. *J Clin Rheumatol* (inpress)
13. Okiyama N, Kitajima T, Ito Y, Yokozeki H, Miyasaka N, Kohsaka H. Addition of the collagen binding domain of fibronectin potentiates the biochemical availability of hepatocyte growth factor for cutaneous wound healing *J Dermatol Sci* (in press)
14. Sakai R, Komano Y, Tanaka M, Nanki T, Koike R, Nakajima A, Atsumi T, Yasuda S, Tanaka Y, Saito K, Tohma S, Fujii T, Ihata A, Tamura N, Kawakami A, Sugihara T, Ito S, Miyasaka N, Harigai M, for the REAL Study Group. The REAL database reveals no significant risk of serious infection during treatment with a methotrexate dose of more than 8 mg/week in patients with rheumatoid arthritis. *Mod Rheumatol* (in press)
15. Sato A, Watanabe K, Kaneko K, Murakami Y, Ishido M, Miyasaka N, Nanki T. The effect of synthetic retinoid, Am80, on T helper cell development and antibody production in murine collagen-induced arthritis. *Mod Rheumatol* 20(3):244, 2010
16. Seki I, Suzuki M, Miyasaka N, Kohsaka H. Expression of CD45 isoforms correlates with differential proliferative responses of peripheral CD4+ and CD8+ T cells. *Immunol Lett* 129(1), 39-46, 2010

17. Senju S, Hirata S, Motomura Y, Fukuma D, Matsunaga Y, Fukushima S, Matsuyoshi H, Nishimura Y. Pluripotent stem cells as source of dendritic cells for immune therapy. *Int J Hematol.* 91(3): 392-400, 2010
18. Sugihara T, Okiyama N, Suzuki M, Kohyama K, Matsumoto Y, Miyasaka M, Kohsaka H. Definitive engagement of cytotoxic CD8 T cells in C-protein induced myositis, a murine model of polymyositis. *Arthritis Rheum* 62(10), 3088-3092, 2010
19. Takenaka, K., K. Takada, D. Kobayashi, M. Moriguchi, M. Harigai, N. Miyasaka. A case of IgG4-related disease with features of Mikulicz's disease, and retroperitoneal fibrosis and lymphadenopathy mimicking Castleman's disease. *Mod Rheumatol.* 2011 Jan 18. [Epub ahead of print]
20. Tanaka Y, Takeuchi T, Mimori T, Saito K, Nawata M, Kameda H, Nojima T, Miyasaka N, Koike T; RRR Study investigators. Discontinuation of infliximab after attaining low disease activity in patients with rheumatoid arthritis: RRR (remission induction by Remicade in RA) study. *Ann Rheum Dis* 69(7):1286-1291, 2010
21. Toyomoto M, Ishido S, Miyasaka M, Sugimoto H, Kohsaka H. Anti-arthritic effect of E3 ubiquitin ligase, c-MIR, expression in the joints. *Int Immunol* (in press).
22. Yamazaki H, Nanki T, Miyasaka N, Harigai M. Methotrexate and trimethoprim-sulfamethoxazole use for PCP prophylaxis. *J Rheumatol* (inpress)
23. Watanabe K, Penfold MET, Matsuda A, Ohyanagi N, Kaneko K, Miyabe Y, Matsumoto K, Schall TJ, Miyasaka N, Nanki T. Pathogenic role of CXCR7 in rheumatoid arthritis. *Arthritis Rheum* 62(11):3211, 2010