

## Molecular and Genetic Epidemiology

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### Other Faculty Members

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### Major Scientific Interests of the Group

Our laboratory is interested in genetics and genomics of human autoimmune rheumatic diseases such as ANCA-associated vasculitis, systemic lupus erythematosus, rheumatoid arthritis and systemic sclerosis. We are taking both genome-wide and candidate gene approaches to find genomic variations associated with development of the rheumatic diseases, as well as those associated with their serious clinical manifestations such as interstitial lung disease. These studies will eventually lead to understanding the pathogenesis of the intractable diseases, identification of molecular targets and biomarkers.

### Projects for Regular Students in Doctoral or Master's Programs

- 1) Identification of genomic variations associated with autoimmune rheumatic diseases
- 2) Biologic and bioinformatic analyses of the variations associated with autoimmune rheumatic diseases

### Study Programs for Short Stay Students (one week – one trimester)

Genome database (tutorial), SNP typing (laboratory).

### Selected Publications

- 1) Namba N, Kawasaki A, Sada K-e, Hirano F, Kobayashi S, Yamada H, Furukawa H, Shimada K, Hashimoto A, Matsui T, Nagasaka K, et al. Association of *MUC5B* promoter polymorphism with interstitial lung disease in myeloperoxidase - antineutrophil cytoplasmic antibody - associated vasculitis. *Ann Rheum Dis* 2019; doi: 10.1136/annrheumdis-2018-214263.
- 2) Juge P-A, Lee JS, Ebstein E, Furukawa H, Dobrinskikh E, Gazal S, Kannengiesser C, Ottaviani S, Oka S, Tohma S, Tsuchiya N, et al. *MUC5B* promoter variant and rheumatoid arthritis with interstitial lung disease. *N Engl J Med* 2018; 379:2209-19.
- 3) Terao C, Kawaguchi T, Dieude P, Varga J, Kuwana M, Hudson H, Kawaguchi Y, Matucci-Cerinic M, Ohmura K, Riemekasten G, Kawasaki A, et al. Transethnic meta-analysis identifies *GSDMA* and *PRDMI* as susceptibility genes to systemic sclerosis. *Ann Rheum Dis* 2017;76:1150-8.
- 4) Kawasaki A, Hasebe N, Hidaka M, Hirano F, Sada K-e, Kobayashi S, Yamada H, Furukawa H, Yamagata K, Sumida T, Miyasaka N, et al. Protective role of *HLA-DRB1\*13:02* against microscopic polyangiitis and MPO-ANCA positive vasculitides in a Japanese population: a case-control study. *PLoS One* 2016;11:e0154393.
- 5) Furukawa H, Oka S, Shimada K, Rheumatoid Arthritis associated Interstitial Lung Disease (RA-ILD) Study Consortium, Tsuchiya N, Tohma S. *HLA-A\*31:01* and methotrexate-induced interstitial lung disease in Japanese rheumatoid arthritis patients: a multi-drug hypersensitivity marker? *Ann Rheum Dis* 2013;72:153-5.
- 6) Furukawa H, Oka S, Shimada K, Sugii S, Ohashi J, Matsui T, Ikenaka T, Nakayama H, Hashimoto A, Takaoka H,

Arinuma Y, et al. Association of human leukocyte antigen with interstitial lung disease in rheumatoid arthritis: A protective role for shared epitope. *PLoS One* 2012;7: e33133.

- 7) **Kawasaki A, Furukawa H**, Kondo Y, Ito S, Hayashi T, Kusaoi M, Matsumoto I, Tohma S, Takasaki Y, Hashimoto H, Sumida T, et al. *TLR7* single-nucleotide polymorphisms in the 3' untranslated region and intron 2 independently contribute to systemic lupus erythematosus in Japanese women: a case-control association study. *Arthritis Res Ther* 2011;13:R41.
- 8) **Kawasaki A, Kyogoku C, Ohashi J, Miyashita R, Hikami K**, Kusaoi M, **Tokunaga K**, Takasaki Y, Hashimoto H, Behrens TW, **Tsuchiya N**. Association of *IRF5* polymorphisms with systemic lupus erythematosus in a Japanese population. Support for a crucial role of intron 1 polymorphisms *Arthritis Rheum* 2008;58: 826–34.
- 9) **Kyogoku C**, Dijstelbloem HM, **Tsuchiya N, Hatta Y, Kato H, Yamaguchi A**, Fukazawa T, Jansen MD, Hashimoto H, van de Winkel JGJ, Kallenberg CGM, et al. Fc $\gamma$  receptor gene polymorphisms in Japanese patients with systemic lupus erythematosus: Contribution of *FCGR2B* to genetic susceptibility. *Arthritis Rheum* 2002;46:1242-54.
- 10) **Tsuchiya N**, Husby G, Williams RCJr, Stieglitz H, Lipsky PE, Inman RD. Autoantibodies to HLA-B27 sequence cross-react with the hypothetical sequence of arthritis-associated *Shigella* plasmid. *J Clin Invest* 1990;86:1193-203.