

# Genetic Regulation

## 1. Staffs and Students (in 2010)

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	Yusuke SAITO,	Tomonori KANAZAWA,
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## 2. Purpose of Education

Genetic factors, i.e. structural and/or functional diversity of human genome, are more or less involved in the etiology and pathogenesis of human diseases. Main objective of Genetic Regulation is to identify the gene mutations or polymorphisms and to decipher the molecular mechanisms involved in the etiology and pathogenesis of intractable diseases, in order to develop new strategies for diagnosis, treatment and/or prevention of the diseases. Current research is focused on the cardiovascular diseases (e.g. idiopathic cardiomyopathy, idiopathic arrhythmia, and coronary heart disease), autoimmune diseases (e.g. Burger disease, Behcet disease, rheumatoid arthritis, and chronic thromboembolic pulmonary hypertension) and infectious diseases (e.g. HIV/AIDS). In addition, genome diversity in immune-related genes is investigated from the view-point of primate evolution.

## 3. Research Subjects

- 1) Identification and functional analysis of disease-related genes for cardiovascular diseases
- 2) Identification and functional analysis of disease-related genes for autoimmune diseases
- 3) Identification and functional analysis of disease-related genes for infectious diseases
- 4) Structural, functional and evolutionary analyses of MHC and immune-related genes in vaccination

## 4. Publications

### Original Article

1. Matuda S, Arimura T, Kimura A, Takekura H, Ohta S, Nakano K. A novel protein found in the I bands of myofibrils is produced by alternative splicing of the DLST gene. *Biochim Biophys Acta*. 2010; 1800(1): 31-39.
2. Arimura T, Sato R, Machida N, Bando H, Zhang DY, Morimoto S, Tanaka R, Yamane Y, Bonne G, Kimura A. Improvement of left ventricular dysfunction and of survival prognosis of dilated cardiomyopathy by administration of calcium sensitizer SCH00013 in a mouse model. *J Am Coll Cardiol*. 2010; 55(14): 1503-1505.
3. #Neely1 GG, #Kuba K, #Cammarato A, Isobe K, Amann S, Zhang L, Murata M, Elmen L, Gupta V, Arora S, Sarangi R, Dan D, Fujisawa S, Usami T, Xia CP, Keene AC, Alayari NA, Yamakawa H, Elling U, Berger C, Novatchkova M, Koglgruber R, Fukuda K, Nishina H, Isobe M, Pospisilik JA, Imai Y, Pfeufer A, Hicks A, Pramstaller PP, Subramaniam S, Kimura A, Ocorr K, Bodmer R, Penninger JM. A global in vivo Drosophila RNAi screen identifies NOT3 as a conserved regulator of heart function. *Cell*. 2010; 141(1): 142-153. (#; equal contribution)
4. Takahashi M, Kimura A. HLA and CTLA4 polymorphisms may confer a synergistic risk in the susceptibility to Graves' disease. *J Hum Genet*. 2010; 55(5): 323-326.
5. #Wichukchinda N, #Nakajima T, Saipradit N, Nakayama EE, Ohtani H, Rojanawiwat A, Pathipvanich P, Ariyoshi K, Sawanpanyalert P, Shioda T, Kimura A. TIM1 haplotype may control the disease progression to AIDS in a HIV-1-infected female cohort in Thailand. *AIDS*. 2010; 24(11): 1625-1631. (#; equal contribution)
6. Itaya S, Nakajima T, Kaur G, Terunuma H, Ohtani H, Mehra N, Kimura A. No evidence of an association between the APOBEC3B deletion polymorphism and susceptibility to HIV infection and AIDS in Japanese and Indian

- populations. *J Infect Dis.* 2010; 202(5): 815-816.
7. An J, Nakajima T, Kuba K, Kimura A. Losartan inhibits LPS-induced inflammatory signaling by PPAR-gamma-dependent mechanism in human THP-1 macrophage. *Hypertension Res.* 2010; 33(8): 831-835.
  8. #Choi JO, #You CW, Nah JC, Park JR, Lee BS, Choi BY, Cho BY, Lee SC, Park SW, Kimura A, Park JE. Long-term outcome of four Korean families with hypertrophic cardiomyopathy caused by four different mutations. *Clin Cardiol.* 2010; 33(7): 430-438. (#; equal contribution)
  9. Hitomi N, Kubo T, Kitaoka H, Hirota T, Hamada T, Hoshikawa E, Hayato K, Okawa M, Kimura A, Doi YL. A frameshift deletion mutation in the cardiac myosin-binding protein C gene was associated with dilated phase of hypertrophic cardiomyopathy and dilated cardiomyopathy. *J Cardiol.* 2010; 56(2): 189-196.
  10. Naruse TK, Chen Z, Yanagida R, Yamashita T, Saito Y, Mori K, Akari H, Yasutomi Y, Miyazawa M, Matano T, Kimura A. Diversity of MHC class I genes in Burmese-origin rhesus macaque. *Immunogenetics.* 2010; 62(9): 601-611.
  11. Sugimoto C, Watanabe S, Naruse T, Kajiwara E, Shiino T, Umamo N, Ueda K, Sato H, Ohgimoto S, Hirsh V, Villinger F, Ansari AA, Kimura A, Miyazawa M, Suzuki Y, Yamamoto N, Nagai Y, Mori K. Protection of macaques with diverse MHC genotypes against a heterologous SIV by vaccination with a deglycosylated live-attenuated SIV. *PLoS ONE.* 2010; 5(7): e11678.
  12. Chen Z, Nakajima T, Tanabe N, Hinohara K, Sakao S, Kasahara Y, Tatsumi K, Inoue Y, Kimura A. Susceptibility to chronic thromboembolic pulmonary hypertension may be conferred by miR-759 via its targeted interaction with polymorphic fibrinogen alpha gene. *Hum Genet.* 2010; 128(4): 443-452.
  13. Purevjav E, Varela J, Morgado M, Kearney DL, Li H, Taylor MD, Arimura T, Moncman CL, McKenna W, Labeit S, Vatta M, Bowles NE, Kimura A, Boriek AM, Towbin JA. Nebulette mutations are associated with dilated cardiomyopathy and endocardial fibroelastosis. *J Am Coll Cardiol.* 2010; 56(18): 1493-1502.
  14. Shichi D, Arimura T, Ishikawa T, Kimura A. Heart-specific small subunit of myosin light chain phosphatase activates Rho-associated kinase and regulates phosphorylation of myosin phosphatase target subunit 1. *J Biol Chem.* 2010; 285(44): 33680-33690.
  15. Li Z, Ai T, Samani K, Xi Y, Tzeng HP, Xie M, Taylor MD, Wu S, Ge S, Dong JW, Cheng J, Ackerman MJ, Kimura A, Sinagra G, Brunelli L, Faulkner G, Vatta M. A ZASP missense mutation, S196L, leads to cytoskeletal and electrical abnormalities in a mouse model of cardiomyopathy. *Circulation Arrhythm Electrophysiol.* 2010; 3(6): 646-656.

#### Review Article

1. Kimura A. Molecular basis of hereditary cardiomyopathy: abnormalities in calcium sensitivity, stretch response, stress response and beyond. *J Hum Genet.* 2010; 55(2): 81-90.

#### Book Chapter

1. Nakajima T, Kimura A. Comparative genomics: insight into human health and disease. In *The HLA Complex in Biology and Medicine: a resource book.* (Mehra N, ed), pp566-588, Jaypee Brothers Medical Publishers Ltd., New Delhi, 2010.