



# News Letter

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● Chiba University Global COE Program  
**Global Center for Education  
and Research in Immune  
System Regulation and  
Treatment**

## C O N T E N T S

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Drs. Koji Tokoyoda, Atsushi Onodera,  
Kotaro Suzuki, Ayako Inamine and  
Kaoru Ito
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# Research Highlights

Dr. Koji Tokoyoda, Assistant Professor, Dept. of Immunology, who was also Independent Research Associate of the G-COE Program last academic year, recently won two notable awards, **the 2010 Robert Koch Postdoctoral Awards for Young Scientists** and **the 2010 JSI (Japanese Society for Immunology) 5th Young Investigator Awards** for his work regarding the generation and maintenance of the immunological memory. Following is a brief introduction to his work.



**Koji Tokoyoda**  
Assistant Professor, Dept. of Immunology

## Life-style of memory helper T cells in immune memory

“Immunity” defends our body from infection of bacteria and virus and also, by memorizing the antigen information, more quickly and strongly removes the re-invaded pathogen. The ability to memorize the information has been a key factor in the development of vaccines. Studies on vaccine began about 200 years ago. It is well-known that immune memory system used by vaccine is constructed by memory lymphocytes in the body. However, it had been unclear how memory lymphocytes are maintained in the body.

Memory lymphocytes are categorized into memory plasma cells which produce functional antibodies, memory cytotoxic T cells which survey infected cells, and memory helper T cells which control the generation and maintenance of the other memory lymphocytes. Our previous studies had shown that memory plasma cells are maintained on CXCL12-expressing stromal cells of the bone marrow (Tokoyoda et al., *Immunity*, 20: 707-718, 2004). Moreover, we recently reported that memory helper T cells who play a central role in immune memory are also maintained in the bone marrow and reside on IL-7-expressing stromal cells but not CXCL12-expressing cells (Tokoyoda et al., *Immunity*, 30: 721-730, 2009, Figure 1 and 2). BM memory helper T cells are long-lived, functional *in vitro* and *in vivo*, and resting (Figure 3). These findings indicated that memory plasma cell and memory helper T cell reside on a distinct stromal cell, respectively, and rest there with high function. We suggested that the specified microenvironment for memory lymphocytes like for example CXCL12- and IL-7-expressing stromal cells are called “niche”, and these memory lymphocytes are like stem cells who rest there with high function, and multi-potency (Tokoyoda et al., *Nat. Rev. Immunol.*, 10: 193-200, 2010).

This concept may change the goal of vaccination, because it is not only for making a lot of antibodies but for maintaining memory lymphocytes in their niches. Namely, by monitoring memory lymphocytes in their niches, vaccination can be further improved. In addition, a bad memory in the case of chronic autoimmune diseases and allergy may also take advantage of similar mechanisms to a good memory like infection and vaccination. Our short-time goal is to clarify the role of memory helper T cells in immune memory, especially when the former antigen re-invades, namely in the secondary immune response, contributing the understanding of the systemic immune system (Figure 4).

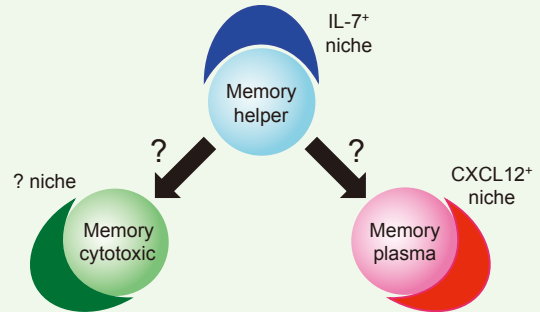


Figure 1. Memory lymphocytes are maintained on their distinct niches

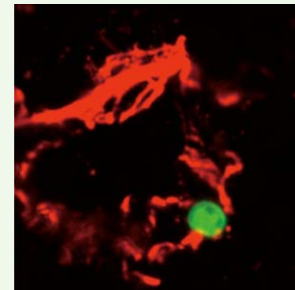


Figure 2. Memory helper T cells (green) reside on stromal cells (red)

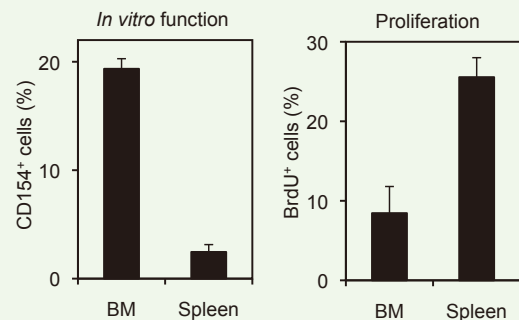


Figure 3. BM memory CD4 T cells are resting with high responsiveness

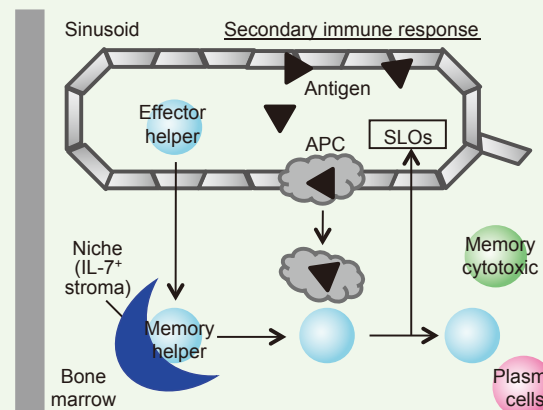


Figure 4. Systemic mechanisms in immune memory and secondary immune response. APC: antigen-presenting cells, SLO: secondary lymphoid organs

# Research Highlights

## Annual Best Research Award 2010

This award is given to Ph.D. students in the G-COE relevant fields whose research is recognized as most outstanding through the year. The winner for the Annual Best Research Award 2010 went to Dr. Atsushi Onodera, who is now G-COE Independent Research Associate. His award-winning research is shown below.



**Atsushi Onodera**  
G-COE Independent Research Associate  
Dept. of Immunology

### Regulation of Th2 cell differentiation and function by polycomb and trithorax complex

The number of allergy sufferers is increasing each year in Japan. However, no curative therapeutic strategies have been developed. We have focused on the role of CD4-positive helper T (Th) cells, which play a role of conductor in immune responses and are subdivided into at least three populations—Th1, Th2, and Th17, based on their cytokine production profile (Figure 1). Th cells typically balance each other and regulate protective immune responses. However, if the balance shifts towards a type2 bias, allergic diseases can develop. Th2 cells regulate the production of antibodies and the recruitment of eosinophils through secretion of interleukin (IL)-4, IL-5, and IL-13, so-called Th2 cytokines. According to these observations, Th2 cells are thought to be central players in the allergic response. We hypothesized that the control of Th2 cell differentiation and function results in the inhibition of allergic responses. Therefore, we have investigated the molecular mechanism involved in the induction of Th2 cell differentiation and the maintenance of Th2 cell identity. As a result, we found that the epigenetic regulation of transcription factor GATA3 and Th2 cytokine expression are critical for Th2 cell differentiation. Epigenetic regulation of gene expression is an acquired regulatory mechanism of gene expression. Epigenetics is becoming a key concept to understanding cell differentiation and gene regulation. Polycomb (PcG) and trithorax (TrxG) complex are known to be involved in the epigenetic regulation of their target genes (Figure 2). PcG and TrxG were originally identified in *Drosophila*. They play crucial roles in cancer formation and stem cell maintenance in humans. In contrast, their roles in the immune system are poorly understood. We performed further analysis of epigenetic regulation of Th2 differentiation with a focus on PcG and TrxG. Recently, we found the Th2-specific displacement of PcG by TrxG at the upstream region of the GATA3 gene, a transcription factor essential for Th2 cell differentiation (Figure 3). After Th2 cell differentiation, the recruitment of TrxG complex was required for the maintenance of GATA3 expression, because increased GATA3 expression was not maintained in the absence of Menin, a critical molecule for DNA binding in the TrxG complex (Figure 4). This study was published in the *Journal of Experimental Medicine* (*J Exp Med.* 2010; 207: 2493-506). Now, we are proceeding with a new project to identify genome-wide PcG and TrxG target genes using a next generation ChIP-seq technology. Finally, we hope to find new strategies for the treatment of allergic disorders by defining the molecular mechanisms that underlie the diseases.

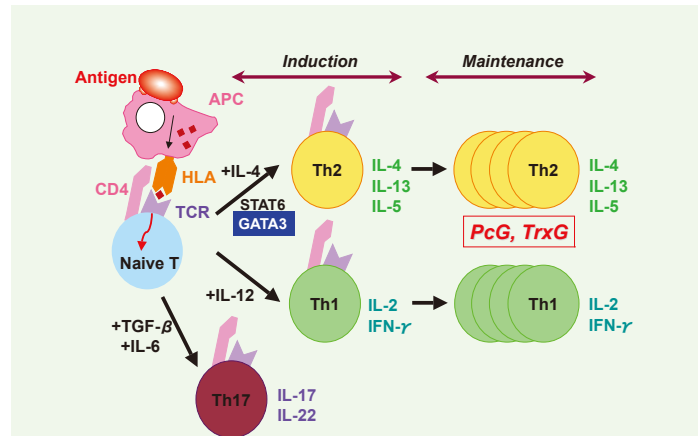


Figure 1. Induction and maintenance of helper T cell subsets

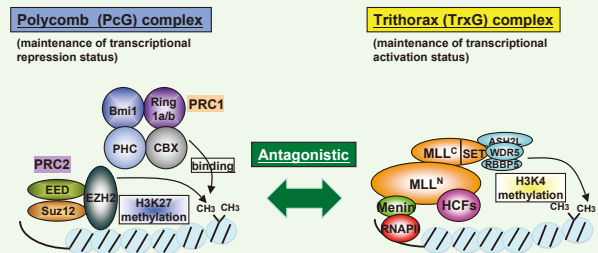


Figure 2. Polycomb and trithorax complex

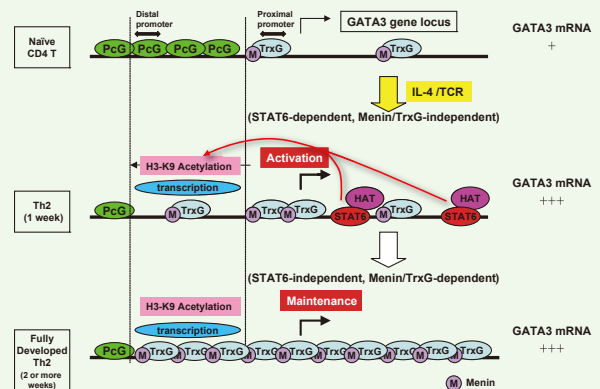


Figure 3. Displacement of PcG by TrxG at the GATA3 gene locus

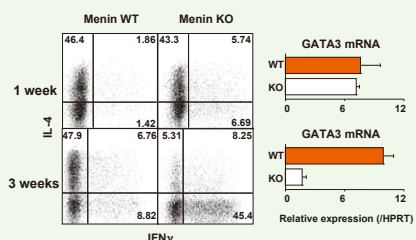


Figure 4. Menin-deficient Th2 cells failed to maintain GATA3 expression and the ability to produce IL-4

## Mast cell research progresses!



**Kotaro Suzuki**  
G-COE Independent Research Associate  
Dept. of Molecular Genetics

### Role of STATs in Mast Cells

Many cytokines transmit their signals through the activation of the member of signal transducers and activators of transcription (STATs). There are seven STAT proteins, STAT1, STAT2, STAT3, STAT4, STAT5a, STAT5b, and STAT6. A variety of physiological roles of STAT proteins has been clarified not only in T cells and B cells but also in mast cells. In this letter, I show the roles of STAT proteins in murine mast cells.

#### STAT5a

IL-3 is known to be an inducer of proliferation and survival of murine mast cells. STAT5a plays critical roles in these IL-3-mediated functions (1). Figure 1 shows that IL-3-mediated proliferation of bone marrow-derived mast cells (BMMCs) is severely impaired in STAT5a-deficient mice. And STAT5a is also essential for mast cell survival through upregulation of *bcl-x(L)* (1).

#### STAT6

The IL-4-STAT6 pathway induces mast cell apoptosis (2,3) and inhibits TNF- $\alpha$  production through the induction of tristetraprolin which regulates mRNA rapid degradation (4). Figure 2 shows that IL-4 inhibits IgE-induced neutrophil recruitment into the peritoneal cavity through a STAT6-dependent mechanism (4).

#### STAT4

Given that previous studies have shown that STAT4 is expressed in limited cell types, including NK cells and Th1 cells. We recently found that STAT4 is expressed in BMMCs and activated by IFN- $\beta$  but not IL-12 or IL-23 (5). Figure 3 shows that IFN- $\beta$ -induced expression of monocyte chemoattractant protein-1 (MCP-1), a chemokine that preferentially attracts monocyte/macrophage, was severely impaired in STAT4<sup>-/-</sup> BMMCs as compared with WT BMMCs. These results suggest that STAT4 is essential for IFN- $\beta$ -induced MCP-1 expression in BMMCs (5). Because mast cells are distributed in almost all tissues, our results suggest that mast cells may be involved in the enhancement of the antiviral responses initiated by pDC by producing MCP-1 in response to type I IFNs-STAT4 signals (Figure 4).

#### References

- 1) Ikeda K et al. Stat5a is essential for the proliferation and survival of murine mast cells. *Int. Natl. Allergy and Immunol.* 137 S1: 45, 2005.
- 2) Suzuki K et al. Proteolytic processing of Stat6 signaling in mast cells as a negative regulatory mechanism. *J. Exp. Med.* 196: 27, 2002.
- 3) Nakajima H et al. Lineage-specific negative regulation of STAT-

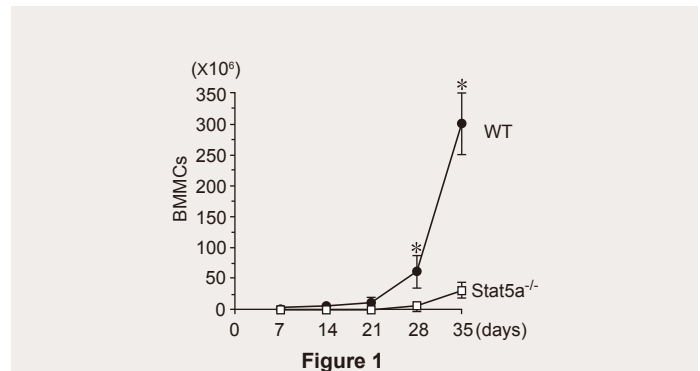


Figure 1

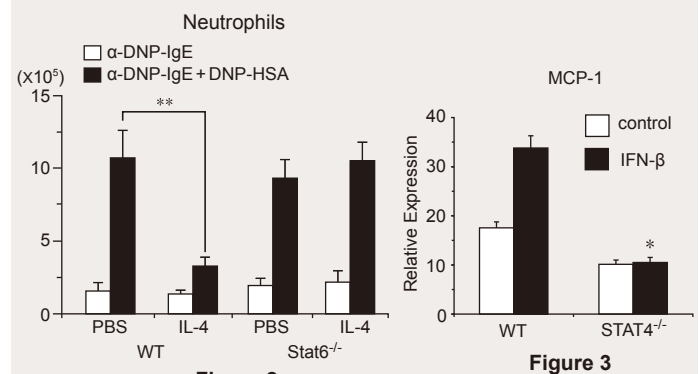


Figure 2

Figure 3

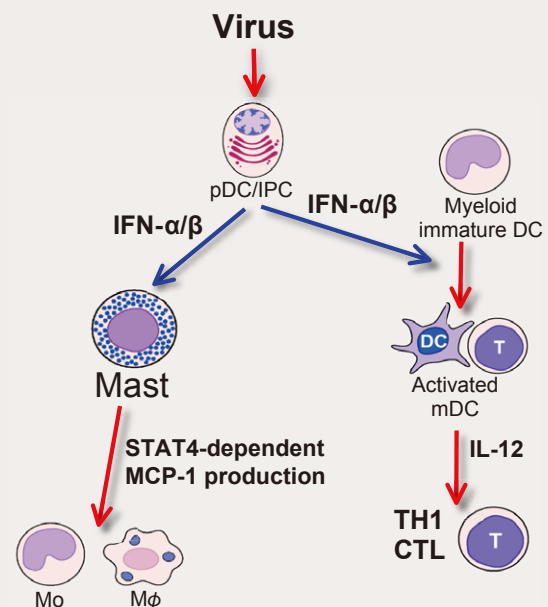


Figure 4

mediated signaling by proteolytic processing. *Cytokine & Growth Factor Reviews.* 14: 375, 2003.

- 4) Suzuki K et al. IL-4-Stat6 signaling induces tristetraprolin expression and inhibits TNF- $\alpha$  production in mast cells. *J. Exp. Med.* 197: 1717, 2003.

- 5) Iida K et al. STAT4 is required for IFN- $\beta$ -induced MCP-1 expression in mast cells. Submitted.

## TR in allergy



**Ayako Inamine**  
G-COE Fellow  
Dept. of Otorhinolaryngology

### A new Immunotherapeutic approach to Japanese cedar pollen allergy

Japanese cedar pollinosis, caused by the pollen of the Japanese cedar tree, is the most common seasonal allergic disease in Japan. In recent years, our country has experienced an increase in the prevalence of allergic rhinitis. A variety of medications has been administered to improve symptoms. Anti-histamines, anti-leukotrienes and intranasal steroids are most widely prescribed to relieve sneezing, nasal discharge and nasal obstruction. These drugs reduce symptoms, but do not treat the underlying disease and have a high risk of associated some adverse events.

Antigen-specific immunotherapy is effective for changing the natural course of allergic diseases, preventing the development of other allergic diseases, and reducing new allergic sensitization, particularly taken over a long period. However, conventional administration by the subcutaneous route is associated with a risk, albeit low, of anaphylactic shock and the inconvenience of frequent visits to a physician.

A recent review of randomized controlled studies of sublingual immunotherapy (SLIT) for allergic rhinitis suggests that this approach has the benefit of allowing treatment to be carried out in the home environment and has been found to be safety and effective treatment strategy as an alternative route of administration. However, clinical improvement is limited and development of an effective and safe adjuvant for SLIT is needed (Figure 1).

We are attempting to elucidate clinical biomarkers correlated with clinical symptoms in preparation for a future double-blind, placebo-controlled study of SLIT, with a focus on the mechanism of inhibition against allergic responses.

Lactobacillus are cultures of potentially beneficial bacteria of healthy gut microflora that are reported to be effective in treatment of various allergic diseases as immunomodulators. Heat-killed Lactobacillus influenced the maturation of DCs induced by uptake of antigen, but the patterns differed significantly among strains. KW3110 strongly induced expression of CCR-7 and PD-L2 in mature DCs (Figure 2). In OVA-sensitized mice, sublingual administration of low doses of KW3110 decreased IgE production and nasal symptoms induced by nasal OVA provocation (Figure 3). Thus, we have demonstrated that sublingual administration by KW3110 is of clinical interest as a new oral mucosal immunotherapy for allergic rhinitis. A clinical study in patients with Japanese cedar pollinosis is in progress to examine this hypothesis and may yield further information on the potential of Lactobacillus (Figure 4).

We hope to find new developmental strategies for SLIT by defining the regulatory mechanisms of allergic disease, and also to investigate

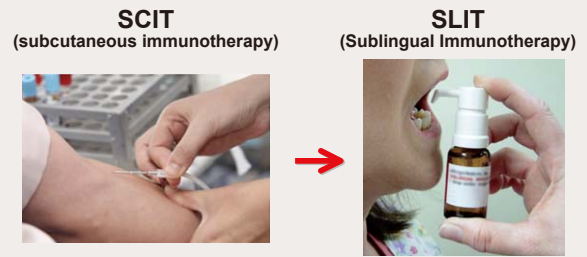


Figure 1. Allergen specific immunotherapy

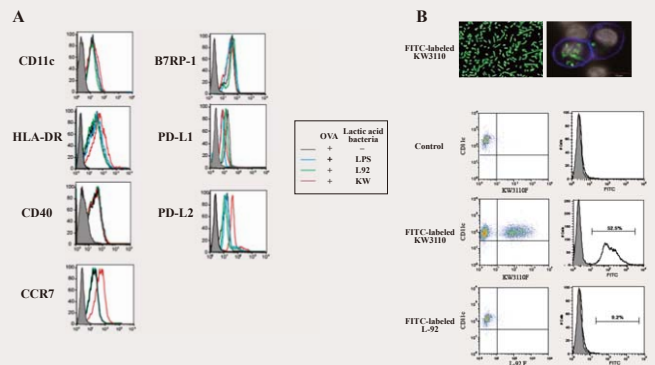


Figure 2. Characteristics of immature DCs and DCs matured using OVA together with LPS, L-92 or KW3110 strains

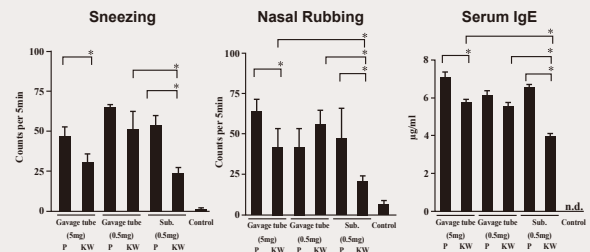


Figure 3. Influence of intragastric administration via a gavage tube or sublingual administration of lactic acid bacteria on nasal symptoms and serum IgE

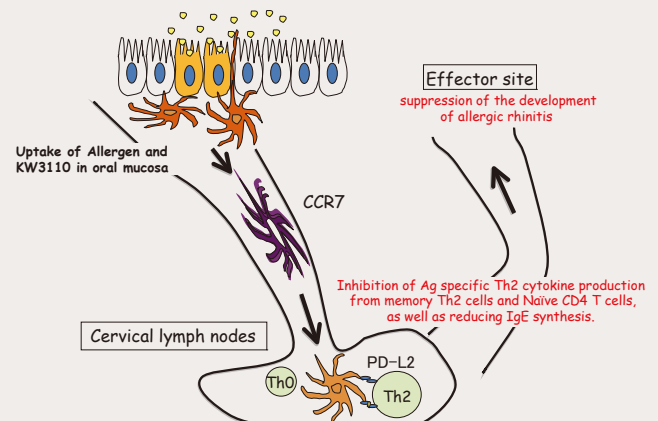


Figure 4. KW3110 is clinical interest as a new oral adjuvant immunotherapy for allergic rhinitis

IgE+ B cell memory with a view to developing new treatments for allergic disease. These strategies would provide a new target for allergic immunotherapy.



**Kaoru Ito**  
G-COE Fellow  
Dept. of Cardiovascular Science and Medicine

### Cardiac Mast Cells and Macropages Play Crucial Roles in the Genesis of Atrial Fibrillation in Angiotensin II-infused Mouse Hearts

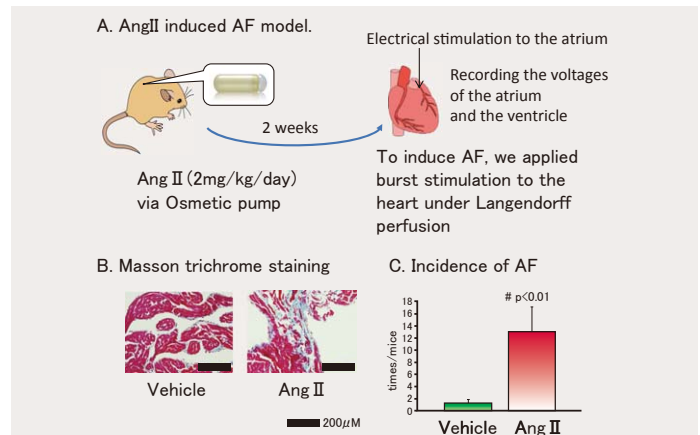
Atrial fibrillation (AF) is the most common arrhythmia encountered in clinical practice, and worsens heart failure and causes stroke, contributing to increased morbidity and mortality. Although the pathophysiology of AF remains incompletely understood, clinical and experimental studies have suggested that inflammation underlies a susceptible AF substrate.

To elucidate how inflammation is linked to the development of structural remodeling as a susceptible AF substrate in stressed hearts, we first administered angiotensin II (Ang II) (2mg/kg/day) subcutaneously via an osmotic mini-pump for 14 days. (Figure 1A) After AngII infusion, we applied electrical stimulation to the hearts under Langendorff perfusion, and found that AF was induced more frequently in Ang II-infused mice than in vehicle-infused control mice. (Figure 1C) Masson trichrome staining revealed that Ang II-infusion promoted atrial fibrosis. (Figure 1B) In addition, toluidine blue staining and immunostaining using anti-Mac3 antibody revealed that the atrium was infiltrated by mast cells (Figure 2A) and macrophages (Figure 2B) in Ang II-infused mice.

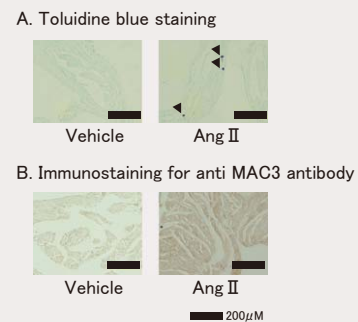
First, to elucidate the role of mast cells in the pathogenesis of AF, we administered cromolyn, which is a mast cell stabilizer and abrogates mast cell degranulation. In Ang II infused mice hearts, cromolyn treatment didn't change the number of mast cells in the atria (Figure 3A), but reduced macrophage infiltration into the atria. (Figure 3B) As a result, the atrial structural remodeling (Figure 3C) and AF inducibility (Figure 3D) in Ang II-infused mice were suppressed by cromolyn.

Next, to elucidate the role of macrophages, we used an expressing vector encoding a dominant-negative human MCP-1 with deletion of N-terminal amino acids (7ND) to inhibit macrophage recruitment. In Ang II infused mouse hearts, 7ND injection didn't suppress mast cell infiltration into the atria (Figure 4A), but inhibited macrophage accumulation in the atria (Figure 4B), resulting in reduced atrial fibrosis (Figure 4C) and decreased AF inducibility. (Figure 4D)

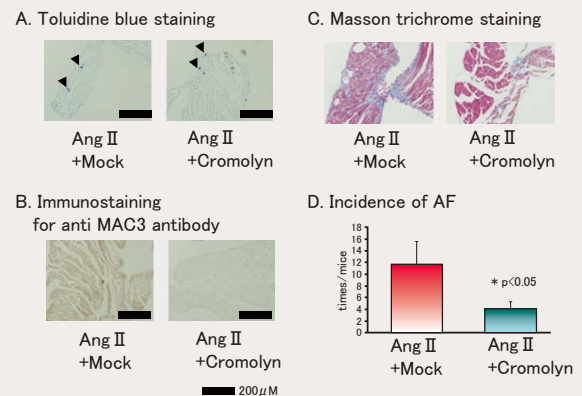
These results suggest that an inflammatory cascade involving mast cells and macrophages contributes to the pathogenesis of AF in Ang II-infused mouse hearts. This study highlights a potential application of stabilization of the mast cell-macrophage cascade to achieve upstream prevention of AF in stressed hearts.



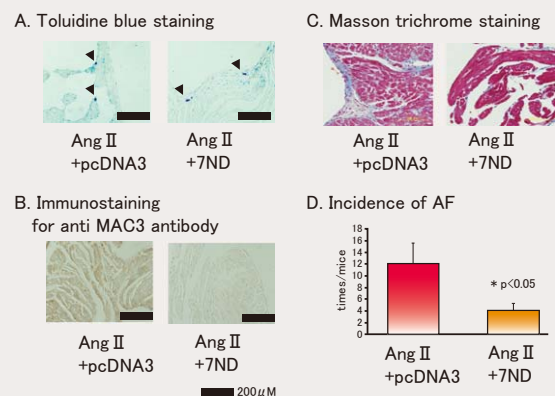
**Figure 1. Ang II induced AF model**



**Figure 2. The numbers of mast cells and macrophages were increased in the atria of Ang II-infused mice hearts.**



**Figure 3. Cromolyn treatment suppressed AF inducibility in Ang II-infused mice.**



**Figure 4. 7ND treatment decreased AF inducibility in Ang II-infused mice.**

## Inauguration of Two New Programs

### 1. Presentation seminar Intermediate/Advanced

Presentation seminar Intermediate/Advanced, new subjects for graduate students, was introduced into the curriculum. All lectures and practices were given in English, by expert native English speakers. The seminars focus on scientific presentations in English, and students intensively learned and practiced not only the basics necessary for presentations but also techniques for improving these presentations, such as how to respond to a difficult situation in a question and answer period, effective body language and so on. The results of a questionnaire given to the students in both Intermediate and Advanced courses showed a high level of satisfaction with the lectures. Followings is a summary of the seminar (Advanced) and feedback from students (excerpts from the questionnaire).

#### General Instruction Objective (GIO) :

In this course, you will learn how to deliver an effective and memorable English presentation. Not only will you learn about the structure of a presentation, but you will also obtain the essential techniques and elegant language skills to achieve your presentation goals. In addition, you will participate in the course both as a presenter and as an audience member, giving you the opportunity to practice asking and responding to questions smoothly.

#### Content and Specific Behavioral Objectives (SBO) Summary :

◆Date: August 2-5, 2010

[No.1]

#### Subject: The Opening and Body

You will learn language and techniques for introducing yourself, stating the purpose and the outline, beginning your presentation, and moving on to your next point.

[No.2]

#### Subject: The Closing and Q&A Session

You will learn language and techniques for closing and summarizing, and inviting and answering questions in a Q&A.

[No.3]

#### Subject: Making Your Presentation Special

This lesson focuses on ways to make your presentation more memorable and effective using visuals and giving examples.

[No.4]

#### Subject: Introducing Your University and Studies

This lesson focuses on presentations to introduce yourself, your school, faculty and/or department, stating the organizational structure and your responsibilities and obligations.



[No.5]

#### Subject: Explaining Charts and Figures

Today's lesson will give you the tools you need to explain and refer to numbers, charts and data, and help your audience to follow them.

[No.6]

#### Subject: Making a Proposal

This lesson focuses on techniques used in making effective proposal presentations explaining a work plan, schedule and budget.

[No.7]

#### Subject: Putting it All Together

Today's "role play" focused lesson gives you the opportunity to use what you have learned throughout the course to make presentations.

[No.8]

#### Subject: Final Presentation

This is the lesson in which you will deliver a presentation on a topic of your choice. Your classmates will participate as the audience, asking you questions in your Q&A and, afterwards, providing positive and constructive feedback on your performance.

#### Comments from students

•I learned how to deliver a presentation for the first time and learned a lot from the lectures. We studied 90 min×2 lessons for a fourth straight day, which was much harder than I had expected, and I felt we were short of time in preparing for the final presentation. Due to small-group (15 or so students) guidance, I got better acquainted with other G-COE RAs. (Name plates and changing seating worked very well!!) If there is another opportunity like this next year, I will surely take it again. I hope all graduate students can take the seminar since it is very useful.

•I appreciate leaning the lessons with G-COE RAs in a friendly atmosphere. My hope is that it will have more practical content specifically for scientific presentations.

### 2. Clinical Oncology

A new subject of study, Special lectures of Clinical Oncology, was initiated in our graduate school.

All the lectures are given in English, by core members of the G-COE program.

#### General Instruction Objective (GIO) :

Malignant diseases are manifested by the dysregulation and malfunction of the immune system. In these special lectures, the mechanisms of immune cell regulation and cancer will be introduced. Through the lectures, students will get a good motivation to start their medical research.

#### Content and Specific Behavioral Objectives (SBO) Summary :

◆Date: August 9-10, 2010

[No.1] Lecturer: Nakayama Toshinori

#### Subject: Anti-tumor immunity mediated by memory T cells

Understanding the mechanisms on anti-tumor immunity mediated by memory Th1/Th2 cells.

[No.2] Lecturer: Tokuhiisa Takeshi

#### Subject: Germinal center and B cell lymphoma-genesis

Germinal centers (GCs) are a complex cellular microenvironment that directs generation of high affinity memory B cells. We discuss molecular mechanisms of the B cell lymphoma-genesis in GCs.

[No.3] Lecturer: Matsue Hiroyuki

#### Subject: Dendritic Cells and Tumor

In this lecture, I will review roles of dendritic cells (DC) in the process of tumor formation especially in the context of "Cancer-Immunosurveillance" (Burnet) and the new concept "Cancer-Immunoediting"(Schreiber), and I will focus on discussing DC-based cancer immunotherapies: Their past, present and future.

[No.4] Lecturer: Okamoto Yoshitaka

#### Subject: Current situation and treatment of head and neck cancer

The management of advanced head and neck cancer has generally involved the combined-modalities of chemotherapy, radiation therapy and surgery. However, the prognosis still remains poor. The development of new treatment strategies to improve the prognosis and QOL of patients will be discussed.

[No.5] Lecturer: Tanzawa Hideki

#### Subject: The mechanism of resistance to chemotherapy and radiotherapy of cancer

This lecture will lead to understand and explain the mechanism of resistance to chemotherapy and radiotherapy of cancer, and the practical method of translational research.

[No.6] Lecturer: Akutsu Yasunori, Matsubara Hisahiro

#### Subject: Translational research for esophageal cancer

Esophageal cancer is still the worst malignant disease, and its prognosis is miserable. First, clinical diagnosis and treatments will be reviewed, and second, translational research for esophageal cancer will be presented.

[No.7] Lecturer: Motohashi Shinichiro

#### Subject: NKT cell-based immunotherapy for cancer

In this lecture, the progress to date in the clinical studies of NKT cell-based immunotherapy for cancer is reviewed and the role of NKT cells in immunotherapy highlighted.

[No.8] Lecturer: Kamada Tadashi

#### Subject: Carbon ion radiotherapy for malignant disease

Carbon ion radiotherapy (CIRT) is a unique radiotherapy, which possesses well localized, and superior depth dose distribution in addition to uniform, less repairable radiobiological effects. In this lecture, the up to date results of carbon ion radiotherapy in various cancers at the National institute of Radiological sciences will be discussed.

### NIRS-Chiba University G-COE Joint Symposium on Carbon-Ion Therapy and Immunotherapy

January 15, 2010  
Auditorium, Research Building for Charged Particle Therapy 2F  
National Institute of Radiological Sciences (NIRS)

The NIRS-Chiba University G-COE Joint Symposium on Carbon-Ion Therapy and Immunotherapy was held on January 15. The program was designed for encouraging much discussion on basic and clinical research results toward future development of novel less-invasive therapeutic strategies, searching for common ground between carbon ion therapy and the immunological mechanism from what has been known until now. Dr. Ken-ichiro Seino (Institute of Medical Science St. Marianna University School of Medicine) presented a keynote lecture on tumor immunity from the basics to a future vision including the potential of regenerative immunotherapy by using iPS cells, in an easy-to-understand manner. For a special lecture, Dr. Kazuhiro Kakimi (Dept. of Immunotherapeutics (Medinet), Graduate School of Medicine, the University of Tokyo) presented results of clinical trials of immunotherapy and also explained the problems of current immunotherapy including the basic research results, in terms of creating immunosuppressive environment. His talk was very suggestive enough to provide an important direction toward a breakthrough to the current immunotherapy, which does not sufficiently meet many patients' expectations.

Much heated and fruitful discussion was generated by the 97 participants in this symposium, which was concluded with great success. We would like to strengthen our partnership with the National Institute of Radiological Sciences in order to develop less invasive cancer therapy with fewer side effects, combining carbon ion therapy with immunotherapy.

Shinichiro Motohashi



### The 1st Chiba-Uppsala Academia Joint Workshop “Inflammation/Immunity and Cancer”

February 19, 2010, the 1st Auditorium  
Chiba University Hospital 3F



“The 1st Chiba-Uppsala Academia Joint Workshop” was held on February 19, 2010 at the 1st Auditorium at Chiba University Hospital. This was the first project on the academic and research collaboration agreed on in 2008 between Uppsala University in Sweden and Chiba University. This workshop was also one of events to celebrate the 60th anniversary of Chiba University.

Dr. Claesson-Welsh from Uppsala University and Dr. Yokote from Chiba University organized this project and invited five leading researchers, including Dr. Welsh herself, from Uppsala University. The workshop began with the opening remarks by Dr. Kohno, director of University Hospital. The focus of this workshop was on “Inflammation/Immunity and Cancer”, and the workshop was divided into four different topics. The first session was on “Inflammatory Regulation.” At first, Dr. Heyman made a presentation on regulation of antibody responses. Dr. Nakajima, Department of Molecular Genetics, then spoke about the role of IL-17 in asthma. The last presentation of the first session was on the characterization of p53 associated proteins by proteomic approach by Dr. Tanaka (Department of Clinical Cell Biology and Medicine).

The second session was on “Inflammatory Diseases.” Dr. Kämpe, Dr. Takemoto (Department of Clinical Cell Biology and Medicine), and Professor Suzuki (Department of Immunology, G-COE coordinator) made presentations on autoimmune polyendocrine syndrome, R3h-domain containing like, and ANCA-associated vasculitis. Because these presentations concerned different organs, we had an opportunity to learn a wide range of recent results in inflammatory disease.

The third session was on “Angiogenesis and Vascular Inflammation.” Drs. Welsh, Dimberg and Minamino (Department of Cardiovascular Science and Medicine) made their presentations about VEGF,  $\alpha$ B-crystallin, and vessel formation of cardiovascular disease, respectively.

The fourth session was on “Immunity and Cancer.” Drs. Essand, Yoshitomi (Department of General Surgery and Molecular Diagnosis) and Iwama (Department of Cellular and Molecular Medicine) made presentations on T cells and viruses in cancer therapy, revealing the molecular mechanisms underlying the pancreatic cancer by proteomic and conventional approach, and on regulation of normal and cancer stem cell self-renewal by the polycomb complexes. Lively discussions took place throughout the workshop, and it was very interesting to experience the different approaches the Swedish researchers made to the study.

We greatly appreciate the more than 70 participants who came to this workshop. We were also happy to be able to further discuss joint research projects. This workshop was a great opportunity for us to build the first step of our relationship with Uppsala University. We have decided to hold a joint workshop every other year, hopefully next time at Uppsala University.

Masaki Fujimoto  
Chiba-Uppsala Academia Joint Workshop Office



# Chiba University G-COE Joint Workshop with Uppsala Faculty

February 20, 2010, 1st Lecture Hall, Main Building 1F  
Faculty of Medicine, Chiba University



The Chiba University G-COE Joint Workshop with Uppsala Faculty was held on Saturday, February 20, in cooperation with Uppsala University in Sweden. This was the third workshop in "Presentation and Discussion by G-COE-RA". Five faculty members from Uppsala University, who were invited for the first project on the academic and research collaboration, joined the workshop as discussion leaders. They brought a new and more global perspective to the workshop, encouraging stimulating discussions. The atmosphere closely paralleled that of making a presentation overseas. Each successive workshop has increased the desired results. The comments below were made by the Uppsala faculty team.



It was a great honor to participate as a discussion leader in the Chiba University Global COE Joint workshop with Uppsala Faculty, and a delight to listen to the PhD students presenting their work.

I was very much impressed by the clarity of the presentations and the pure excellence of the science. The work presented was creative and novel, of a high international level, and brought many new ideas that I will try to incorporate into my research at Uppsala University. Importantly, this workshop provided an opportunity for the PhD-students to practice giving a lecture to an international audience. Without exception, they performed superbly. Congratulations to Dr. Nakayama and Dr. Suzuki for organizing this successful program.

—By Anna Dimberg



My main impression of the G-COE workshop held on Feb 20, 2010 was that of very high ambition. Clearly, the PhD students had prepared excellently for their talks, which were held in English. Many presentations were on challenging translational project, often in the absolute forefront in their fields. Most of the talks were also very well planned to be within time, which is essential for an event like this. It was sometimes a challenge for the PhD students to respond to questions from the audience. It is vital to constantly improve the skills in communication in English, for all of who do not have English as our first language. I would like to encourage the PhD students to continue to practice to present in English and for their fellow students in the audience to ask questions in English. This will ensure success when participating in international exchange of all kinds. My best wishes to all the PhD students: Good luck with your research!

—By Lena Claesson-Welsh



The presentations of the research projects by the graduate students were generally very well performed. It was obvious that a lot of effort had been taken in preparing excellent powerpoint presentations with

high quality pictures. The oral presentations had been well rehearsed and were easy to understand. The students also kept the allotted time very well, much appreciated by the chairmen. The scientific quality of the projects was excellent. An area where some improvement could be made is to train the students in understanding spoken scientific English in a stressful situation, since some of the young investigators had problems answering the questions they got after their presentations. Usually, this was just a matter of not understanding the English, because when they were asked in Japanese they could reply adequately. Thus, my overall comment is that the programme is very impressive in the quality both of the students and of their scientific achievements. To reach excellence in an international setting, it is recommended that the ability of the students to communicate in spoken English is improved.

—By Birgitta Heyman



On the 20th of February 2010, 3rd year PhD students presented their scientific work at a joint workshop at Chiba University together with representatives from the Uppsala University. First of all, the day as such

must be regarded as a success. It was a pleasure to listen to and discuss the science presented at the workshop. The overall level of the presentations was very high, which was reflected by the fact that much of the presented work had already been accepted in or submitted to renowned medical journals. I would like, in particular point out the presentations on the development and role of CD4 T cells, which I regard as highly innovative and in the scientific front line.

Credits also to Dr. Nakayama and Dr. Suzuki for a well-organized day.

Finally, I would like to thank everyone involved for making the stay in Chiba such a pleasant experience.

—By Magnus Essand



# Advanced Medicine Progress Seminar

by Seeds Grant Competition Winners 2009

Co-organized by Chiba University COE start-up program

February 23, 2010, Library Hall 3F, Library of Health Sciences, Chiba University



We held a seed grant competition for advanced medicine for the purpose of seed exploitation, acceleration of Translational Research (TR) and enhancing young researchers' motivation to do clinical study, at Chiba University. We have been supporting eight selected excellent study proposals in providing research grants and regular discussions, in order to accelerate the realization of TR. An open seminar took place on February 23, 2010 to report progress in these studies.

Each of the studies is aimed at developing diagnostic biomarkers, or novel therapeutic agents and treatments targeting various diseases including neurodegenerative diseases, nasal allergy and prostate cancer. From the reports at the seminar, we recognized that the stage of research varied greatly among the studies, however, energetic efforts have been made to promote them toward realizing TR. The support offered by this event has led to acceleration in TR, thus we will cooperatively strive for patients to have effective diagnosis or remedies as soon as possible.

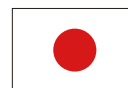
Shinichiro Motohashi, Program leader, Seeds Grant Competition

## NZ-RIKEN-CHIBA Joint Workshop

# “Recent advances in immune regulation and immunotherapy”

June 14, 2010, Research Center for Allergy and Immunology (RCAI)

June 16, 2010, Library Hall 3F, Library of Health Sciences, Chiba University



The NZ-RIKEN-CHIBA Joint Workshop “Recent advances in immune regulation and immunotherapy” was held in cooperation with the RIKEN Research Center for Allergy and Immunology (RCAI), the Ministry of Research, Science & Technology, New Zealand, and The G-COE program. This event was launched by the Ministry's proposal for continuous exchange of research and personnel among researchers from New Zealand, this G-COE program and others, involved in immunological and clinical studies. This time seven researchers in New Zealand visited Japan to introduce and discuss ongoing research studies with domestic researchers with a view to seeking collaboration in the future.

The joint workshop was held on Monday, June 14, at RCAI. The meeting covered issues on “Immune activation and regulation”, “Infection, autoimmune, allergy and vaccine” and “Immunotherapy”, providing an opportunity for scientists from both countries to learn the latest developments in their respective fields. On Wednesday, June 16, another meeting for presentation and discussion with the researchers from New Zealand took place at Chiba University. Following the welcome address by Dr. Haruaki Nakaya, Dean, Graduate School of Medicine, and greetings from Dr. John Fraser, Head School of Medical Sciences, University of Auckland, the six New Zealand researchers presented their studies such as ‘Strategies to enhance CD8+ T cell responses to vaccination’, related investigations on bacterial infection stimulating CD8+ T cells in lymph node for responses to vaccination and so on, to our faculty and graduate students. In the afternoon, after a site visit to the Center for Advanced Medicine, they made individual visit to laboratories for further discussions. We expect progress in this exchange, with the possibility for increasing the collaboration we found in this workshop.



John Fraser

### Researchers from New Zealand

**Anne Camille La Flamme**, Senior Lecturer, Victoria University of Wellington

**Rod Dunbar**, Associate Professor, University of Auckland

**Gavin F Painter**, Principal Scientist, Team Leader, Industrial Research Ltd

**Gib Bogle**, Senior Research Fellow, Auckland Bioengineering Institute

**Ian F. Hermans**, Doctor, Malaghan Institute of Medical Research, Wellington

**John Fraser**, Head, School of Medical Sciences, University of Auckland

**Sarah Hook**, Associate Professor, School of Pharmacy, University of Otago



at the Chiba University Inohana Library



at the RIKEN Research Center for Allergy and Immunology

## The 6th Global COE Workshop

# Presentation and Discussion by G-COE-RA

June 26, 2010, 1st Lecture Hall, Main Building 1F  
Faculty of Medicine, Chiba University

The 6th Global COE Workshop that was the fourth workshop in “Presentation and Discussion by G-COE-RA” took place on June 26. This year 36 graduate students selected as G-COE-RA, increasing the number of the RAs by 10 from the 2009 academic year, including the 26 RAs newly selected. They presented their experimental plan and results in English in this workshop. Two advisory professors, in addition to the student’s mentors, evaluated each presentation. For many of them it was their first time to make a presentation in English, however the results were very impressive and exceeded expectations. Better preparation may have resulted from hearing about this event from friends and senior staff. Some RAs selected this year again joined sessions as RA discussers to be actively involved in the discussions. They actually led each discussion period, thereby showing their ability to communicate in English. The workshop ended fruitfully, being upgraded to a higher level.



## RCAI International Summer Program 2010 Co-organized by the G-COE Program

*Date: August 17-27, 2010 (Lecture course)*

*August 30-September 26, 2010 (Internship course)*

*Place: RIKEN Research Center for Allergy and Immunology (RCAI)*



The RCAI International Summer Program (RISP) 2010 took place at the RIKEN Research Center for Allergy and Immunology (RCAI), August 17-27, jointly organized by RCAI and the G-COE Program, targeting graduate students and postdoctoral fellows overseas. This fifth Summer Program had 44 participants from 10 countries including 24 women, selected from among 141 applicants worldwide. In the early part of lecture course, besides oral and poster presentations, participants attended intensive lectures on the basic concepts to leading-edge study of immunology by 14 distinguished researchers invited from home and abroad. Later in the program, June 22-27, the participants attended the 14th International Congress of Immunology held at Kobe. In this summer program, all the participants were going to make poster presentations at the ICI, however more than 10 of them were selected to make oral presentations, reflecting the high level of their research. RISP invites promising young researchers from all over the world, who become better acquainted and deepen their mutual exchange; this can be an invaluable asset for building a network for advancing research. Three of the participants stayed on at RCAI for a 1-month internship. The overall results of the questionnaire given to participants showed a high level of satisfaction with this program: 100% answered “yes” to the question, “Would you encourage your colleagues to attend the RCAI Summer Program?”

## Regulation of Immune Disorders

August 20, 2010

The 1st Auditorium, Chiba University Hospital 3F

The 4th Chiba University Global COE symposium was held on August 20, 2010 in the auditorium at Chiba University Hospital. The symposium focused on “Regulation of Immune Disorders” by the invited speakers, who presented big topics in their current researches in the form of educational lectures for RA students.

The plenary lecture by Dr. Anjana Rao (Department of Pathology, Harvard Medical School; Immune Disease Institute and Program in Cellular and Molecular Medicine, Children’s Hospital Boston) entitled “Leukemia-associated mutations in TET2 diminish catalytic activity” was exciting for all attendees including RA graduate students. After her lecture, **gene expression and regulation** in epigenetics study were discussed in the talks of “transcriptional regulation of CD4/CD8 lineage choice”, “STAT6-mediated displacement of Polycomb by the Trithorax complex establishes long-term maintenance of GATA3 expression in Th2 cells” presented by Dr. Toshinori Nakayama, and “Unexpected role for the polycomb gene Bmi1 in lymphoid commitment”. In the second session on **NKT cells and mucosal immunity**, Dr. Mitchell Kronenberg (La Jolla Institute for Allergy and Immunology) described “Recognition of microbial and environmental antigens by invariant natural killer T cells”, followed by presentations on “Antigen-specific memory CD4 T cells selectively expanded by NKT cell activation *in vivo*” and “Omitting felony by switching fate: Lineage conversion of CD4 Th cells to CD8 CTLs”, which were highlighted in the current NKT study. Next, Dr. Takeshi Tokuhiya focused on **memory cells** in his talk entitled “Roles for Bcl6 in differentiation of germinal center B cells” followed by lectures on “Differentiation and function of follicular helper CD4 T cells (T<sub>FH</sub>)” and “Protective and pathogenic immunological memory”. **Regulation of allergic disorders** was also discussed with RA students. Finally, **translational researches** on “NKT cell-based immunotherapy for cancer: Nasal submucosal administration of antigen- presenting cells may induce effective anti-tumor immune responses” and “Approach to clinical trial of synthetic immunoglobulin treatment fovasculitis” were discussed.

Thus, all attendees were able to engage in discussions with prominent investigators from all over the world and learn about their current research activities. These discussions with symposium speakers are sure to show attendees how to engage in high level research in immunology.

—By Kazuo Suzuki



Anjana Rao  
LIAI, Harvard Medical School  
(Plenary Lecture)



I could learn the latest and broad immunological knowledge at the 4th G-COE symposium. In particular, the seminar of Dr. Andreas who is one of authorities on immunological memory was very impressive and beneficial for advancing my research. In addition, it was very useful for me, as a respiratory physician, to learn about the roles of TSLP and CD8<sup>+</sup>T cells in the pathogenesis of bronchial asthma. Contents of this symposium considered the pathogenesis of allergic diseases and were very useful for both medical researchers and clinicians. It was my great pleasure to attend this symposium.

Jun Ikari, G-COE-RA, Dept. of Developmental Genetics



I obtained a great deal of information from several immunology specialists at the 4th Chiba University Global COE Symposium. Through attending this symposium, I learned of a wide variety of recent findings from basic research to clinical findings. Discussions with foreign researchers at the symposium will be remarkably helpful for the development of their research fields. I think that Chiba University Global COE Symposiums will greatly activate immunology research.

Yuuki Obata, G-COE-RA, Dept. of Molecular Cell Biology

## The 7th Chiba University G-COE Workshop

August 21, 2010

The 7th Chiba University Global COE Workshop was held on August 21, in the form of a discussion tour. Drs Rao, Crotty, Ziegler, Kronenberg, Cheroutre and Radbruch who were invited speakers in the symposium held the previous day, participated in this workshop. Each of them visited several laboratories involved with this G-COE Program in turn, in order to have discussions with young researchers and graduate students. It was so productive that a lot of significant comments and suggestions were provided for examining the direction of their future research.

## Chiba University G-COE

## Retreat 2010

September 4 and 5, 2010, Seimei-no-Mori Resort

The Chiba University G-COE Retreat 2010 was held on September 4 and 5 at the Seimei-no-mori Resort. Sixty graduate students and PI researchers involved in this G-COE program participated and had the opportunity for in-depth discussion at a quiet place. The program consisted of two special lectures, 8 oral presentations, 8 poster presentations, and 36 one-minute presentations. On the first day, Dr. Keiji Tanaka, Director of The Tokyo Metropolitan Institute of Medical Science, gave a special lecture in which he explained not only the latest studies on but also a history of proteasome. It gave us a great insight into future research. The next day, for a special lecture, Dr. Takeshi Tokuhisa, Chiba Univer-



Keiji Tanaka  
Director,  
The Tokyo Metropolitan  
Institute of Medical  
Science



Takeshi Tokuhisa  
Professor,  
Dept. of Developmental  
Genetics

sity, gave a talk about a required ability for mentor. This talk had a great impact on our students and young researchers. In the presentations by G-COE Independent Research Associates and G-COE Fellows, topics touched on a variety of subjects and we had discussions on each topic, which were very meaningful for new developments in our research. In the poster presentations held in a congenial atmosphere, each poster was discussed profoundly. Dr. Yuusuke Endo (G-COE-RA) got the best poster award. We believe that this program provided mutual understanding between students and principal investigators.

Hiroshi Nakajima  
Director, G-COE Retreat



The G-COE Retreat 2010 was held at Seimei-no-mori Resort on September 4-5. This is my second time participating in this retreat. In the magnificent and relaxed surroundings, the retreat gave us a chance to discuss a number of issues, deepen mutual understanding, and I have spent two enriched days. Different from last year, most of the RAs gave self-introduction, showing their personality and interests and so on to participants. From this, we could get clear impressions of the young researchers. In the poster presentation held in the evening, presenters were requested to give oral presentation in 5 min. Dr. Motohashi played as a time-keeper using his iPhone. The presentation became interesting because his iPhone's bell ringing. It's difficult for me to explain my presentation in 5 min. I received valuable advice from participants. In the special lecture, I think I got a hint from Prof. Tanaka's talk about the treasure for him. Prof. Tokuhisa gave a talk about developing a mature personality according research based on his experience. For me, as an international student, I was also deeply impressed by his lectures, especially about what he learned and felt during overseas study. For the international student benefiting from the G-COE program such as me, it's so lucky to have a chance to hear the wonderful lectures given by famous professors. This experience became a treasure for me. I really appreciated having such opportunity.

Wu Shuang, G-COE-RA, Dept. of Medicine and Clinical Oncology



It was very useful for me to make a presentation of my research at the Chiba University G-COE Retreat 2010. I received a lot of advice after my presentation, which has been of great help for my future study. At night, I got acquainted with many researchers and discussed a wide range of issues, including some not familiar to me. This helped me expand my knowledge. This program increased my motivation and was very a fruitful experience for me. I think the beauties of nature in the Seimei-no-mori Resort helped us to relax and communicate with each other. I appreciate the opportunity to join the retreat.

Tomozumi Takatani, G-COE-RA, Dept. of Pediatrics



Poster presentation by Mr Endo,  
the best poster award winner



# Development and Maintenance of Immune Memory

December 4, 2010

Sapia Hall, Tokyo Station Conference, Tokyo

The G-COE Program held the 5th Chiba University Global COE Symposium at Tokyo, on Saturday, December 4, co-organized by IMSUT & RCAST G-COE Program, The University of Tokyo. This fifth symposium, entitled “Development and Maintenance of Immune Memory”, featured topics relating to immunological memory. Since the regular annual meeting of the Japanese Society for Immunology did not take place this year, with the idea of being a substitute for that, the symposium was held the next day after the general meeting of the Japanese Society for Immunology took place at Tokyo. This time, the theme was confined to immunological memory, though, more than 150 participants got together, which may suggest that immunological research in this area is receiving more attention. A total of 21 talks including one given by an invited researcher from the U.S. were presented in the symposium, starting with a session on Memory CD4 T cells and ending with one on Memory B/Plasma cells. All lectures were given in English including a question and answer period, dealing with the latest findings in the field where studies are progressing rapidly. The symposium was very fruitful with lively and stimulating discussion on each talk. At the end, Dr. Tasuku Honjo, Kyoto University, logically and energetically presented the latest studies on the mechanism of class switch recombination in the plenary lecture, and many participants were very impressed not only with the research results he demonstrated but also his attitude to ward doing research. I believe this symposium will lead to progress in the research of immunological memory in the future.

–Takeshi Tokuhisa, Symposium Director

## Participating as a speaker

Having felt relieved because my PhD thesis defense was finished, I had a big job to round off the year, English presentation in the 5th G-COE Symposium on December 4. I attended this symposium with a bit different tension because it was held at the Tokyo station conference, and there was a large audience, though I have given English presentations in G-COE-RA workshop several times in the past. I managed to finish the presentation, but in the question period... I muttered, “I couldn’t understand the meaning of the question well” in the mind. I got into a panic and answered in English, but in an incomplete sentence. However, thanks to this experience, I recognized again the difficulty of answering questions in English, and of telling correctly people in other fields in English. I kept in mind that I’d speak better next time.

I had a lot of fun to attend this symposium because ‘immunological memory’, which is closely related to my research, was the main theme and there were a lot of interesting presentations. I was really excited to hear the presentations by various speakers from the young to leading figure’s professors. It was valuable to participate and talk in this symposium, including my failure.

Yusuke Endo  
G-COE-RA, Dept. of Immunology



Tasuku Honjo, Kyoto University  
(Plenary Lecture)





# TOPICS

## Robert Koch Postdoctoral Awards for Young Scientists

Dr. Koji Tokoyoda, Assistant Professor, Dept. of Immunology

In cooperation with the German Societies of Hygiene and Microbiology, Immunology and Virology, the Robert Koch Foundation in Germany annually presents postdoctoral awards to outstanding work by young scientists. This year Dr. Koji Tokoyoda, Assistant Professor, Dept. of Immunology received the award for immunology for his work on the generation and maintenance of the immunological memory. Dr. Tokoyoda attended the award ceremony held in Berlin on November 12 to be honored with the other winners for the Robert Koch Award and the Robert Koch Gold Medal, along with receiving a diploma and prize money. He is the first Japanese scientist to win this award. The award-winning study is reported on page 2 of this newsletter.



At the award ceremony Dr. Koji Tokoyoda (left), Prof. Jörg Hacker, Präsident der Deutschen Akademie der Naturforscher Leopoldina (right)

## Best poster award at the International ISSX Ms Mio Watanabe, second-year student of master course, Laboratory of Pharmacology and Toxicology, Graduate School of Medical and Pharmaceutical Sciences

Ms Mio Watanabe, second-year student of master course, Graduate School of Medical and Pharmaceutical Sciences, won the best poster award of International ISSX (International Society for the Study of Xenobiotics) Meeting held in Istanbul in September. She studied drug metabolism using humanized CYP3A mouse constructed with human artificial chromosome. The title of her poster was Humanized CYP3A Mice: (2) Functional Expression of Human CYP3A Isoforms in CYP3A-HAC Mice and Inhibition of CYP3A via Mechanism-Based Inactivation.

## A jointly developed New Influenza Simple Test Kit won Minister of Science and Technology Policy Award in recognition for industry-academia-government collaboration performance

This simple test kit for detection of new Influenza H1N1 won the Minister of Science and Technology Policy Award in June. The kit was jointly developed by the National Center for Global Health and Medicine, Mizuho Medy Co.,Ltd., Chiba University Hospital, University of Miyazaki Hospital and Dr. Kazuo Suzuki, Professor, (Dept. of Immunology, Graduate School of Medicine, Chiba University). Without any special devices, this kit enables to give a diagnosis in clinical practice and contributes to the people's health and medical care cost containment.



## A related article on H5N1 influenza appeared in the Medical Tribune

Dr. Thuy T. B. Phung (Researcher, National Hospital of Pediatrics, Hanoi, Vietnam)  
Dr. Kazuo Suzuki, Professor, Dept. of Immunology

This study conducted by Dr. Thuy T. B. Phung, who visited Chiba University Graduate school of Medical and Pharmacology Sciences under the JSPS RONPAKU (Dissertation PhD) Program, was reported as a topic in "the 14th International Congress of Immunology" section of Medical Tribune. The title of her research project was "Key cytokines/chemokines in acute respiratory distress syndrome with avian influenza (H5N1) infection in Vietnamese children".



Almost biweekly pace!

For our graduate students, top-ranked world researchers gave lectures including recent findings of their studies. The seminar has been held a total of 23 times after the last report in vol.2.

**G-COEセミナー**

平成21年12月9日(火)  
17:00~18:00  
大カンファレンスルーム

**‘Sex and B Cells’**

**Dr. Philippa Marrack**  
千葉大学客員教授  
Distinguished Professor, University of Colorado  
Investigator, Howard Hughes Medical Institute at Denver  
Professor, Integrated Department of Immunology,  
University of Colorado Denver and National Jewish Health

主催: グローバルCOEプログラム  
共催: 千葉バイオサイエンス研究会  
連絡先: 千葉大学大学院医学研究科 免疫発生学  
中 山 道 義 (TEL:226-2195 内線5504)  
橋 本 和 男 (TEL:226-2195 内線70365)

**G-COE セミナー**

平成22年1月15日(金)  
千葉大学医学部本館2F  
大カンファレンスルーム  
13:30~14:15

**“Biologic therapies in vasculitis”**

**Dr. David Jayne**  
Visiting Professor, Chiba University  
Professor Cambridge University  
Addenbrookes Hospital, UK

主催: グローバルCOEプログラム  
共催: 千葉バイオサイエンス研究会  
連絡先: 千葉大学大学院医学研究科 免疫発生学  
中 山 道 義 (TEL:226-2195 内線5504)  
橋 本 和 男 (TEL:226-2195 内線70365)

**G-COE セミナー**

平成22年1月15日(金)  
千葉大学医学部本館2F  
大カンファレンスルーム  
14:15~15:00

**“ANCA associated vasculitis and anti-GBM disease in China”**

**Dr. Ming-hui Zhao**  
Visiting Professor, Chiba University  
Professor Peking University  
First Hospital, Beijing, China

主催: グローバルCOEプログラム  
共催: 千葉バイオサイエンス研究会  
連絡先: 千葉大学大学院医学研究科 免疫発生学  
中 山 道 義 (TEL:226-2195 内線5504)  
橋 本 和 男 (TEL:226-2195 内線70365)

**G-COEセミナー**

平成22年2月18日(木)  
17:00~18:00  
大カンファレンスルーム

タンパク質シトルリン化酵素PAD4の  
構造と機能

**Dr. 山田 道之**  
横浜市立大学名誉教授

主催: グローバルCOEプログラム  
共催: 千葉バイオサイエンス研究会  
連絡先: 中山道義 (千葉大学大学院医学研究科 免疫発生学)  
TEL:043-226-2195 内線5505

**G-COEセミナー**

平成22年3月29日(月)  
17:00~18:00  
第1講義室

**CCR2 and Treg/Th17 Imbalance  
in Kawasaki Disease**

**Dr. Seema Ahuja**  
Professor,  
Dept. of Medicine, Texas Health Science Center  
San Antonio, Texas, USA.

主催: グローバルCOEプログラム  
共催: 千葉バイオサイエンス研究会  
連絡先: 中山道義 (千葉大学大学院医学研究科 免疫発生学)  
TEL:043-226-2195 内線5501

**G-COEセミナー**

予測医学 : システム生物学の臨床応用  
Predictive medicine : an application of systems biology

**矢野浩二郎先生**  
AstraZeneca Senior Research Fellow  
In Systems Biology, Department of Physiology,  
Development and Neuroscience, University of Cambridge

平成22年4月6日(火) 18:00~19:00  
千葉大学医学部本館1F 第2講義室

主催: グローバルCOEプログラム  
共催: 千葉バイオサイエンス研究会  
連絡先: 中山道義 (千葉大学大学院医学研究科 免疫発生学)  
TEL:043-226-2195 内線5501

**G-COEセミナー**

リン酸化プロテオミクスの最前線

**石濱 泰 先生**  
慶應義塾大学先端生命科学研究所  
准教授

平成22年4月8日(水) 17:00~18:00  
千葉大学医学部本館1F 第2講義室

主催: グローバルCOEプログラム  
共催: 千葉バイオサイエンス研究会  
連絡先: 中山道義 (千葉大学大学院医学研究科 免疫発生学)  
TEL:043-226-2195 内線5501

**G-COEセミナー**

Recognition of microbial components by  
Nod2: The role in the innate immunity  
and Crohn's disease

**Dr. Koichi Kobayashi**  
Department of Cancer Immunology & AIDS  
Dana-Farber Cancer Institute  
Assistant Professor of Pathology  
Harvard Medical School

平成22年4月15日(水) 17:00~18:00  
千葉大学医学部本館2F スカララホール

主催: グローバルCOEプログラム  
共催: 千葉バイオサイエンス研究会  
連絡先: 中山道義 (千葉大学大学院医学研究科 免疫発生学)  
TEL:043-226-2195 内線5490

**G-COEセミナー**

平成22年4月15日(木)  
17:00~18:00  
第2講義室

多彩な生理・病理現象を制御する新たな鍵分子  
として認知されつつある生体膜脂質代謝酵素,  
ジアシルグリセロールキナーゼ

**坂根 郁夫先生**  
千葉大学大学院 理学研究科  
基礎理学専攻 化学コース  
生体機能化学研究室 教授

主催: グローバルCOEプログラム  
共催: 千葉バイオサイエンス研究会  
連絡先: 中山道義 (千葉大学大学院医学研究科 免疫発生学)  
TEL:043-226-2195 内線5501

**G-COEセミナー**

自己反応性T細胞の生体内イメージング  
Intravital imaging of autoantigen specific T cells in the CNS

**川上 直人先生**  
Max Planck Institute of Neurobiology,  
Department of Neuroimmunology

平成22年5月18日(火) 17:00~18:00  
千葉大学医学部本館2F 大カンファレンスルーム

主催: グローバルCOEプログラム  
共催: 千葉バイオサイエンス研究会  
連絡先: 中山道義 (千葉大学大学院医学研究科 免疫発生学)  
TEL:043-226-2195 内線5501

**G-COEセミナー**

上皮細胞間/バリア形成機構と  
生体内ホメオスタシス

**月田 早智子先生**  
大阪大学大学院生命機能研究科  
医学系研究科  
教授

平成22年5月7日(月) 17:00~18:00  
千葉大学医学部本館1F 第2講義室

主催: グローバルCOEプログラム  
共催: 千葉バイオサイエンス研究会  
連絡先: 中山道義 (千葉大学大学院医学研究科 免疫発生学)  
TEL:043-226-2195 内線5501

**G-COEセミナー**

平成22年7月7日(水) 18:00~19:00  
医学部本館1階 第3講義室

リンパ球の機能制御と病態形成における  
サイトカインシグナル調節因子SOCS1の役割

**小林隆志先生**  
慶應義塾大学医学部総合医学研究センター  
特別研究准教授

主催: グローバルCOEプログラム  
共催: 千葉バイオサイエンス研究会  
連絡先: 中山道義 (千葉大学大学院医学研究科 免疫発生学)  
TEL:043-226-2195 内線5501

**G-COEセミナー**

平成22年7月15日(木) 17:00~18:00  
大カンファレンスルーム

ウイルス感染に応答した自然免疫誘導のメカニズム  
Virus-induced activation of innate immune system

**米山 光俊先生**  
千葉大学高度医学研究センター 免疫発生学研究室  
免疫学技術開発機構が担うTANAM2産生細胞の免疫応答

主催: グローバルCOEプログラム  
共催: 千葉バイオサイエンス研究会  
連絡先: 中山道義 (千葉大学大学院医学研究科 免疫発生学)  
TEL:043-226-2195 内線5501

**G-COEセミナー**

平成22年8月31日(火) 17:00~18:00  
大カンファレンスルーム

Epithelial cells initiate TH2 immunity  
during allergy and worm infection

**Dr.DeBroski Herbert**  
Assistant Professor,  
Division of Immunobiology,  
Cincinnati Children's Research Foundation

主催: グローバルCOEプログラム  
共催: 千葉バイオサイエンス研究会  
連絡先: 中山道義 (千葉大学大学院医学研究科 免疫発生学)  
TEL:043-226-2195 内線5501

**G-COEセミナー**

平成22年9月2日(木) 17:30~18:30  
千葉大学医学部本館2F 大カンファレンスルーム

TSLP enhances the function of helper type2 cells

**Dr. Masayuki Kitajima**  
Postdoctoral Fellow  
Immunology Program,  
Benaroya Research Institute at Virginia Mason

主催: グローバルCOEプログラム  
共催: 千葉バイオサイエンス研究会  
連絡先: 中山道義 (千葉大学大学院医学研究科 免疫発生学)  
TEL:043-226-2195 内線5501

**G-COEセミナー**

自然免疫系による腸管免疫制御

**竹田 潔 先生**  
大阪大学医学系研究科・免疫制御学  
教授

平成22年9月17日(金) 17:00~18:00  
千葉大学医学部本館2F 大カンファレンスルーム

主催: グローバルCOEプログラム  
共催: 千葉バイオサイエンス研究会  
連絡先: 中山道義 (千葉大学大学院医学研究科 免疫発生学)  
TEL:043-226-2195 内線5501

**G-COEセミナー**

異種細胞間接着形成における  
ネクチンの機能と作用機構

**高井 義美 先生**  
神戸大学医学部  
医学部長

平成22年10月8日(金) 17:00~18:00  
千葉大学医学部本館2F 大カンファレンスルーム

主催: 千葉大学グローバルCOEプログラム  
共催: 千葉バイオサイエンス研究会  
連絡先: 中山道義 (千葉大学大学院医学研究科 免疫発生学)  
TEL:043-226-2195 内線5501

**G-COEセミナー**

リンパ球動態制御のメカニズムとその破綻

**木梨達雄先生**  
関西医科大学 教授

平成22年10月15日(金) 13:30~14:30  
千葉大学医学部本館2F 大カンファレンスルーム

主催: 千葉大学グローバルCOEプログラム  
共催: 千葉バイオサイエンス研究会  
連絡先: 中山道義 (千葉大学大学院医学研究科 免疫発生学)  
TEL:043-226-2195 内線5501

**G-COEセミナー**

ガス分子による代謝システム制御機構  
の系統的探索と医学応用

**末松 誠 先生**  
慶應義塾大学医学部医科学教室 教授  
医学部長

平成22年10月28日(木) 17:30~18:30  
千葉大学医学部本館1F 第1講義室

主催: 千葉大学グローバルCOEプログラム  
共催: 千葉バイオサイエンス研究会  
連絡先: 中山道義 (千葉大学大学院医学研究科 免疫発生学)  
TEL:043-226-2195 内線5501



**G-COEセミナー**

平成22年11月1日(月)  
12:00-13:00  
医学部本館2階  
大カナルスルーム

**Role of Schnurri 3  
in effector T cell differentiation**

**Dr. Makio Iwashima**  
Associate Professor  
Department of  
Microbiology and Immunology  
Stritch School of Medicine  
Loyola University Chicago, USA

主催：千葉大学グローバルCOEプログラム  
共催：千葉大学医学部附属病院  
連絡先：中山道 (千葉大学医学部附属病院 免疫学講座)  
TEL: 043-226-2185 内線5001

**G-COEセミナー**

Lessons from mouse models of  
anaphylaxis

**Dr. Fred Finkelman**  
McDonald Professor of Medicine and Professor of Pediatrics  
University of Cincinnati College of Medicine

平成22年11月29日(月) 18:00~19:00  
千葉大学医学部附属病院3階 第1講堂

主催：千葉大学グローバルCOEプログラム  
共催：千葉大学医学部附属病院  
連絡先：中山道 (千葉大学医学部附属病院 免疫学講座)  
TEL: 043-226-2185 内線5001

**G-COEセミナー**

臓器移植時におけるウイルス感染

**荒木幸一 先生**  
Emory Vaccine Center  
Department of Microbiology and Immunology  
Emory University School of Medicine

平成22年12月6日(月) 17:00~19:00  
千葉大学医学部本館2F 大カナルスルーム

主催：千葉大学グローバルCOEプログラム  
共催：千葉大学医学部附属病院  
連絡先：中山道 (千葉大学医学部附属病院 免疫学講座)  
TEL: 043-226-2185 内線5001

**G-COEセミナー**

Cryopyrin and diseases  
in man and mouse

**Dr. Hal Hoffman**  
Associate Professor of Pediatrics and Medicine  
at the University of California, San Diego, CA.

平成22年12月9日(木) 18:00~19:00  
千葉大学医学部本館2F 大カナルスルーム

主催：千葉大学グローバルCOEプログラム  
共催：千葉大学医学部附属病院  
連絡先：中山道 (千葉大学医学部附属病院 免疫学講座)  
TEL: 043-226-2185 内線5001

## Allergy Clinical Conference

**Go beyond the borders**

In the conference researchers from Dept. of Allergy and Clinical Immunology, Dept. of Pediatrics, Dept. of Otorhinolaryngology and Dept. of Dermatology discuss allergic diseases across disciplines.

**第5回アレルギー臨床カンファレンス**

アレルギー疾患に関する臨床医、研究者、大学院生、研修医、医学士を対象に、下記の通り、第5回アレルギー臨床カンファレンスを開催いたします。

本カンファレンスは、アレルギー疾患の診断に関する最新知見の発表と議論を活性化するため、グローバルCOE主催で年一回、開催しています。

皆さんの積極的な参加をお待ちしています。\*参加は無料です。

● 日 時：平成22年3月10日(水) 18:00より  
● 会 場：千葉大学医学部附属病院 第1講堂

- 「好酸球増多性疾患」  
1) 診断提示  
アレルギー-膠原病内科 小林芳久先生、川島寛先生、中込大樹先生  
2) 好酸球増多性疾患の鑑別診断  
アレルギー-膠原病内科 高松 宏昌先生
- 「好酸球性副鼻腔炎という概念」  
アレルギー-耳鼻咽喉科 山本 隆三先生  
千葉芳実病院 耳鼻咽喉科 山本 隆三先生
- 「発熱、肝障害、全身の紅斑を認めた1例」  
皮膚科 外川 八美先生  
皮膚科 山本 隆三先生
- 「アレルギー疾患の病態における遺伝的多型の影響」  
皮膚科 山本 隆三先生

【主催】 グローバルCOEプログラム

問い合わせ先：中山道 (千葉大学医学部附属病院 免疫学講座)  
千葉大学医学部附属病院 免疫学講座  
TEL: 043-226-2185 FAX: 043-226-2186

**第6回アレルギー臨床カンファレンス**

アレルギー疾患に関する臨床医、研究者、大学院生、研修医、医学士を対象に、下記の通り、第6回アレルギー臨床カンファレンスを開催いたします。

本カンファレンスは、アレルギー疾患の診断に関する最新知見の発表と議論を活性化するため、グローバルCOE主催で年一回、開催しています。

皆さんの積極的な参加をお待ちしています。\*参加は無料です。

● 日 時：平成22年7月23日(金) 18:00より  
● 会 場：千葉大学医学部附属病院 第1講堂

- 「生体腎臓移植に足質に腫瘍を認めた1例」  
皮膚科 及川 真希子先生
- 「腫瘍に誘発したSLEの一例」  
～腫瘍およびSLE発症の免疫学的メカニズムについて～  
アレルギー-膠原病内科 アレルギー-膠原病内科 加藤 ちえ子先生
- 「気管支喘息におけるキナーゼファミリーの役割」  
小児科 岸上 祐三郎先生  
耳鼻咽喉科 山本 隆三先生
- 「舌下免疫療法の新法」  
耳鼻咽喉科 山本 隆三先生

【主催】 グローバルCOEプログラム

問い合わせ先：中山道 (千葉大学医学部附属病院 免疫学講座)  
千葉大学医学部附属病院 免疫学講座  
TEL: 043-226-2185 FAX: 043-226-2186

**第7回アレルギー臨床カンファレンス**

アレルギー疾患に関する臨床医、研究者、大学院生、研修医、医学士を対象に、下記の通り、第7回アレルギー臨床カンファレンスを開催いたします。

本カンファレンスは、アレルギー疾患の診断に関する最新知見の発表と議論を活性化するため、グローバルCOE主催で年一回、開催しています。

皆さんの積極的な参加をお待ちしています。\*参加は無料です。

● 日 時：平成22年12月15日(水) 18:00より  
● 会 場：千葉大学医学部附属病院 第2講堂

- スナック物産に対する舌下免疫療法の最新知見  
耳鼻咽喉科 山口俊哉先生
- 肺炎も包から作製する3次元培養疫学～その意義と今後の応用～  
皮膚科 藤田 慶明先生
- 多発結核/皮膚病態に併発した自己抗体の意義  
～間質性肺炎が先行した結核性肺炎の一例を交えて～  
アレルギー-膠原病内科 アレルギー-膠原病内科 藤田千晶先生
- 学習期まで寛解傾向がみられない「難治アレルギー疾患」に対する  
急速経口免疫療法  
小児科 山本 隆三先生

【主催】 グローバルCOEプログラム

問い合わせ先：中山道 (千葉大学医学部附属病院 免疫学講座)  
千葉大学医学部附属病院 免疫学講座  
TEL: 043-226-2185 FAX: 043-226-2186

## Basic Science Joint Meeting (BSJM)

This seminar has been held every week coordinated by graduate students working group.

- |   |  |  |
|---|--|--|
| <p><b>25. November 27, 2009</b><br/>Nobuya Yoshida, Graduate Student, Dept. of Developmental Genetics</p> <p><b>26. January 22, 2010</b><br/>Chiaki Iwamura, Assistant Professor, Dept. of Immunology</p> <p><b>27. February 12, 2010</b><br/>Hiroaki Takatori, Assistant Professor, Dept. of Molecular Genetics</p> <p><b>28. April 2, 2010</b><br/>Tetsuichiro Saito, Professor, Dept. of Developmental Biology</p> <p><b>29. April 9, 2010</b><br/>Satoru Miyagi, Assistant Professor, Dept. of Cellular and Molecular Medicine</p> <p><b>30. April 16, 2010</b><br/>Saki Kawashima, G-COE RA, Dept. of Molecular Genetics</p> <p><b>31. April 23, 2010</b><br/>Atsushi Onodera, Assistant Professor, Dept. of Immunology</p> <p><b>32. May 7, 2010</b><br/>Haruko Takano, Post Doctoral Fellow, Biomedical Research Center</p> <p><b>33. May 14, 2010</b><br/>Akio Matsumoto, Associate Professor, Dept. of Pharmacology</p> <p><b>34. May 21, 2010</b><br/>Ryuichi Sugamata, Assistant Professor, Dept. of Immunology</p> <p><b>35. May 28, 2010</b><br/>Naohiko Seki, Associate Professor, Dept. of Functional Genomics</p> | <p><b>36. June 4, 2010</b><br/>Toshinao Oyama, Post Doctoral Fellow, Dept. of Molecular and Tumor Pathology</p> <p><b>37. June 11, 2010</b><br/>Asuka Morita, Graduate Student, Dept. of Autonomic Physiology</p> <p><b>38. June 18, 2010</b><br/>Shinichiro Motohashi, Associate Professor, Dept. of Medical Immunology</p> <p><b>39. June 25, 2010</b><br/>Jun Ikari, G-COE RA, Dept. of Developmental Genetics</p> <p><b>40. July 2, 2010</b><br/>Tomoaki Tanaka, Assistant Professor, Dept. of Clinical Cell Biology and Medicine</p> <p><b>41. July 9, 2010</b><br/>Satoshi Fujimoto, Assistant Professor, Dept. of Developmental Biology</p> <p><b>42. July 16, 2010</b><br/>Akira Suto, Assistant Professor, Dept. of Molecular Genetics</p> <p><b>43. July 23, 2010</b><br/>Hiroyuki Hosokawa, Assistant Professor, Dept. of Immunology</p> <p><b>44. September 3, 2010</b><br/>Kenta Shinoda, G-COE RA, Dept. of Immunology</p> <p><b>45. September 10, 2010</b><br/>Makiko Kashio, Graduate Student, Dept. of Cellular and Molecular Medicine</p> <p><b>46. September 17, 2010</b><br/>Tomokazu Nagao, Lecturer, Dept. of Immunology</p> | <p><b>47. September 24, 2010</b><br/>Hiroyuki Ishikawa, Associate Professor, Dept. of Biology, Graduate School of Science</p> <p><b>48. October 1, 2010</b><br/>Hiroshi Ishii, Graduate Student, Dept. of Neurobiology</p> <p><b>49. October 8, 2010</b><br/>Masakatsu Yamashita, Head of Laboratory, Kazusa DNA Research Institute</p> <p><b>50. October 15, 2010</b><br/>Shigetoshi Horiguchi, Lecturer, Dept. of Otorhinolaryngology, Head and Neck Surgery</p> <p><b>51. October 22, 2010</b><br/>Yusuke Endo, G-COE RA, Dept. of Immunology</p> <p><b>52. November 5, 2010</b><br/>Yuko Muroyama, Assistant Professor, Dept. of Developmental Biology</p> <p><b>53. November 12, 2010</b><br/>Takashi Miki, Professor, Dept. of Medical Physiology</p> <p><b>54. November 19, 2010</b><br/>Tohru Minamino, Lecturer, Dept. of Cardiovascular Science and Medicine</p> <p><b>55. November 26, 2010</b><br/>Nobuya Yoshida, Graduate Student, Dept. of Developmental Genetics</p> <p><b>56. December 17, 2010</b><br/>Yasunori Sato, Lecturer, Chiba University Hospital Clinical Research Center</p> <p><b>57. December 24, 2010</b><br/>Naohiko Seki, Associate Professor, Dept. of Functional Genomics</p> |
|---|--|--|

# G-COE Research Assistant Members

G-  
COE

As part of graduate students education, The G-COE Program has adopted G-COE-RAs every year. These positions are competitive and selected across disciplines from among various Ph.D. students in the relevant fields. This year, 36 G-COE-RAs are studying with the special supports and guidance designed to nurture the ability to be internationally active. The accompanying photos are all of the members of G-COE-RAs in 2010, most of which were taken at the 6th Global COE Workshop held on June 26.



**Kazuhide Takeuchi**  
Dept. of Public Health



**Mei-Lan Liu**  
Dept. of Cardiovascular  
Science and Medicine

RA



**Tetsuhiro Ishikawa**  
Dept. of Orthopedic  
Surgery



**Masayuki Miyagi**  
Dept. of Orthopedic  
Surgery



**Masataka Yokoyama**  
Dept. of Cardiovascular  
Science and Medicine



**Yoshihito Kameda**  
Dept. of Cardiovascular  
Science and Medicine



**Masashi Uchida**  
Dept. of Clinical  
Pharmacology



**Tomokazu Sumida**  
Dept. of Cardiovascular  
Science and Medicine

Me



**Yohko Ogasawara**  
Dept. of Cardiovascular  
Science and Medicine



**Nijiro Nohata**  
Dept. of  
Otorhinolaryngology



**Yusuke Endo**  
Dept. of Immunology



**Kenta Shinoda**  
Dept. of Immunology



**Yukiko Watanabe**  
Dept. of Immunology



**Shu Horiuchi**  
Dept. of Immunology

mb



**Soichi Tofukuji**  
Dept. of Immunology



**Yukiko Hiramatsu**  
Dept. of Molecular  
Genetics



**Jun Ikari**  
Dept. of Developmental  
Genetics



**Jin Yuan**  
Dept. of Cellular and  
Molecular Medicine



**Seitaro Nomura**  
Dept. of Cardiovascular  
Science and Medicine



**Shuang Wu**  
Dept. of Medicine and  
Clinical Oncology

ers



**Morito Mezawa**  
Dept. of Molecular Cell  
Biology and Medicine



**Kazumasa Aoyama**  
Dept. of Molecular Cell  
Biology



**Yuuki Obata**  
Dept. of Molecular Cell  
Biology



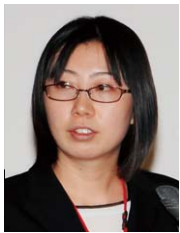
**Hiroto Kamoda**  
Dept. of Orthopedic  
Surgery



**Norimasa Ikeda**  
Dept. of Frontier Surgery



**Teruyoshi Saito**  
Dept. of Molecular and  
Tumor Pathology



**Yohko Yamaguchi**  
Dept. of Molecular  
Biology and Oncology



**Shinya Okamoto**  
Dept. of Biochemistry



**Ayumi Yamamoto**  
Dept. of Clinical Molecular  
Biology



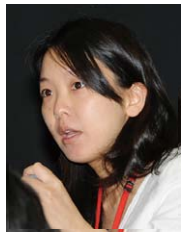
**Saki Kawashima**  
Dept. of Molecular  
Genetics



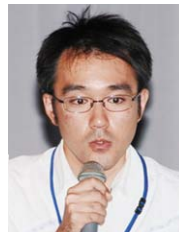
**Yukari Saito**  
Dept. of Molecular  
Genetics



**Tomozumi Takatani**  
Dept. of Pediatrics



**Junko Tanaka**  
Dept. of Pediatrics



**Hidekazu Nagano**  
Dept. of Clinical Cell  
Biology and Medicine



**Fumiya Yamaide**  
Dept. of Public Health



**Junpei Suzuki**  
Dept. of  
Pharmacogenomics

## New Members

### Core Members



**Hisahiro Matsubara**  
Professor and Chairman,  
Department of Frontier  
Surgery,  
Graduate School of  
Medicine, Chiba University



**Koutaro Yokote**  
Professor and Chairman,  
Department of Clinical Cell  
Biology and Medicine,  
Graduate School of  
Medicine, Chiba University

### G-COE Independent Research Associate

**Atsushi Onodera**  
Department of Immunology

### G-COE Fellow

**Takashi Ito**  
Department of Cardiovascular Science and Medicine

**Akane Suzuki**  
Department of Immunology

**Takafumi Mayama**  
Department of Clinical Cell Biology and Medicine

### JSPS Fellow (G-COE)

**Asami Hanazawa**  
Department of Immunology

## Upcoming Events

### The 8th Chiba University Global COE Workshop (Presentation and Discussion by G-COE-RA )

Date: February 19, 2011

Venue: The 1st Lecture Hall, Main Building 1F, Faculty of Medicine, Chiba University

### Advanced Medicine Progress Seminar by Seeds Grant Competition Winners 2010

Date: March 8, 2011

Venue: The 3rd Auditorium, Chiba University Hospital 3F

### G-COE Retreat jointly organized with IMSUT & RCAST G-COE Program and Chiba University G-COE Program (tentative)

Date: September 17-18, 2011

Venue: Naito Seminar House, Tokyo University Yamanaka-Ryou

## Editor's Note

Vol. 3 of the newsletter contains many news items. In particular, some of the research activities are featured as highlights since our young researchers have produced plenty of results in their fields. We fill our newsletter with articles on events like international conferences with numerous visitors from abroad, symposia or workshops with a view to collaboration, education for RAs to be active internationally, which including a retreat, a newly established training course for improving the ability of discussion in international settings and so on. We are delighted to report that the G-COE program has made the steady progress as a global center. Please feel free to inform us of any comments or requests you may have about the newsletter; we welcome your feedback.

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