GLOBAL COE
Center of Excellence
AT CHIBA UNIVERSITY
Global Center for Education and Research in Immune System Regulation and Treatment

# News Letter

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● Chiba University Global COE Program

## Global Center for Education and Research in Immune System Regulation and Treatment

CONTENTS

Dr. Tomoaki Tanaka (Department of Clinical Cell Biology and Medicine) and Dr. Shinichiro Motohashi (Department of Medical Immunology) both involved in this program, received the Chiba Medical Society Award (2011). Dr. Motohashi's research also received the 16th Inohana Alumni Award.

Tomoaki Tanaka

Lecturer, Dept. of Clinical Cell Biology and Medicine

# "The p53 world", a wide variety of physiological functions and common pathogenesis of cancer, diabetes, and age-related disease

## ～Forefront of Molecular Biology of "Life-Aging-Disease-Death"～

While many processes in biology, for instance, temporal and spatial control of gene profile during the development of organisms, increase complexity, the aging process increases entropy and culminates in the death of animals. Recent genetic studies have indicated that the aging process is subjected to a regulatory network. It is now well appreciated that the network includes the nutrient-sensing pathways (such as insulin and AKT/mTOR signals), and transcriptional and chromatin regulation (sirtuins, etc) with profound consequences. Importantly as well, it is also evident that key molecules that regulate cellular senescence and apoptosis, such as tumor suppressor p53, are critically involved in the aging process and pathogenesis of its associated diseases such as cancer, cardiovascular disease, and metabolic disorders, a testament to the importance and crosstalk of transcriptional and epigenetic regulators in the four inevitable events in our lives (Figure 1).

Tumor suppressor p53 receives multiple forms and a diverse range of stress signals such as DNA damage and oxidative or metabolic stress, and then initiates different cellular outcomes, including cell-cycle arrest, apoptosis, and/or cellular senescence. Recently several lines of evidence have suggested that p53 pathway is linked to the reprogramming process by pluripotent factors and oncogenic signals, and p53 systematically regulates intracellular metabolic pathways to preserve anti-oxidant and bioenergetic function (Figure 2). To elucidate the p53 mechanisms, we have attempted to isolate and characterize p53 chromatin complexes *in vivo* by manipulating biochemical techniques and mass-spectrometry, and to perform genome-wide screening of RNA-seq and ChIP-seq using tumor and non-tumor cells, including senescent cells and ES/iPS cells. We found several chromatin regulators and transcriptional coactivators such as CAS/CSE1 (chromosome segregation factor), Sp110 (component of PML nuclear body protein forming a multiprotein complex), and zinc finger proteins in association with p53 chromatin complexes (Figure 3). Given that they are components of intranuclear structures and have functional domains such as the bromodomain and PHD zinc finger motif that potentially function as "reader" for histone codes in epigenetic and chromatin-mediated transcriptional regulation, p53 is a bona-fide epigenetic regulators acting as "the guardian of the genome" and "the cellular gatekeeper". Further, genome-wide analyses revealed that p53 can actively and/or repressively control cell-cycle regulators, metabolic regulators, senescence-associated secretary proteins (SASPs), and linc RNAs in cancer, senescent and ES/iPS cells. Thus, our study suggests that p53 exerts multiple functions with a complexity of crosstalk to intranuclear structure and transcriptional regulation for a wide variety of transcripts, including linc RNAs in senescent and ES/iPS cells, linking to a common mechanism of cancer, life-style-related disease, and age-related disease such as diabetes and cardiovascular disorders (Figure 4).

**Figure 1. Epigenetic Regulators and Disease**

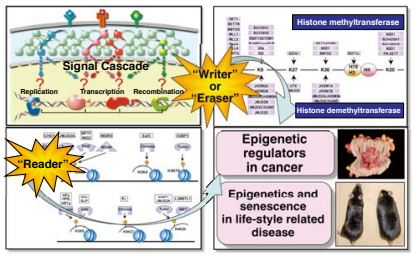



**Figure 2. Wide Variety Function of p53 and its Metabolic Role**

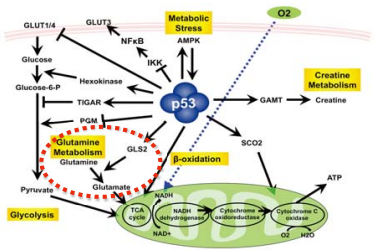



**Figure 3. Our Research Work about Tumor Suppressor p53**

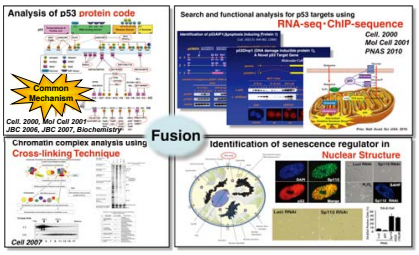
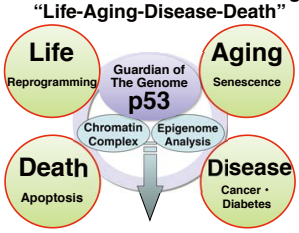



**Figure 4. Forefront of Molecular Biology of "Life-Aging-Disease-Death"**




common mechanisms of and novel therapeutic targets for cancer and life-style related disease

Shinichiro Motohashi
Associate Professor, Dept. of Medical Immunology

# NKT cell-based Immunotherapy for non-small cell lung cancer

Invariant natural killer T (iNKT) cells are activated by a specific ligand, α-Galactosylceramide (α-GalCer), in a CD1d-dependent manner, and upon activation iNKT cells modulate the function of a wide variety of other immune cells, including anti-tumor effector cells in both a direct and an indirect manner (Figure 1). Early clinical trials of iNKT cell-based immunotherapy demonstrated that the infusion of ligand-pulsed antigen presenting cells (APCs) or *in vitro* activated iNKT cells was safe and well tolerated in patients with non-small cell lung cancer (NSCLC). Intravenous injection of α-GalCer-pulsed APCs, which induces the activation of endogenous NKT cells and NKT cell-dependent responses, was well tolerated. In this clinical trial, whole PBMCs cultured with GM-CSF and IL-2 are used as antigen presenting cells (Figure 2). These APCs include DCs that can activate iNKT cells efficiently. The number of IFN-γ-producing cells in PBMCs after restimulation with α-GalCer in vitro was detected to evaluate the functional iNKT cells and NK cells that were subsequently activated by activated iNKT cells. The number of IFN-γ-producing cells was clearly elevated (good responder group) in 10 patients, while the remaining 7 patients did not show any increased IFN-γ production (poor responder group). The median survival time (MST) of the good responder group was significantly better than that of the poor responder group (Figure 3). This result suggested IFN-γ might be a valuable biological marker for predicting the clinical course in response to α-GalCer-pulsed APC administration. Two candidate biomarkers that might be associated with immune responses were also detected (Figure 4). From these results, "intravenous injection of α-GalCer-pulsed APCs for the treatment of non-small cell lung cancer" was approved by the Japanese Ministry of Health, Labour and Welfare as "Highly Advanced Medicine" (Sep. 28th, 2011). In addition, the phase I study of trans-bronchial intratumoral or intranodal α-GalCer-pulsed APC injection was initiated in patients with advanced NSCLC to activate iNKT cells in the tumor microenvironment more efficiently. Further investigation to clarify the mechanisms of iNKT cell-mediated anti-tumor immunity is in progress. It would be advantageous to identify biomarkers that may predict the clinical outcome before the treatment, and select subgroup(s) of patients who will most likely have a significant clinical benefit in any or a specific type of iNKT cell-based immunotherapy.

Figure 1

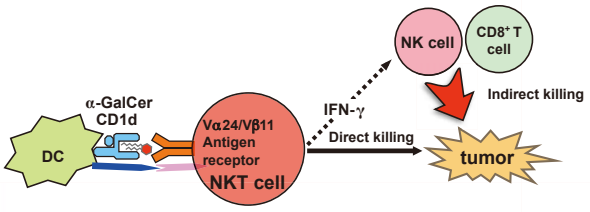



Figure 2

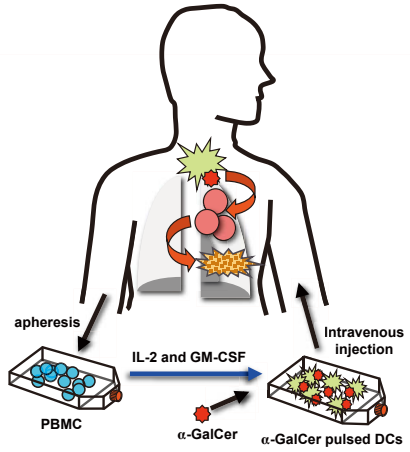



Figure 3

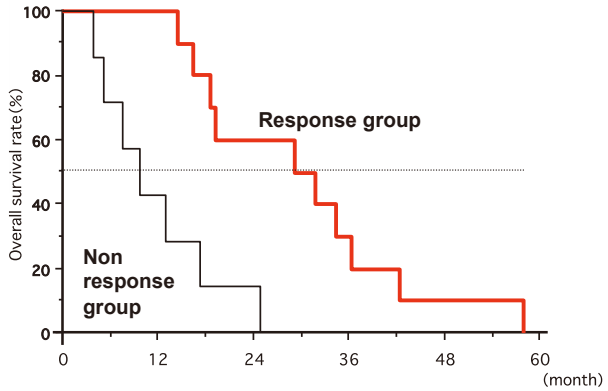
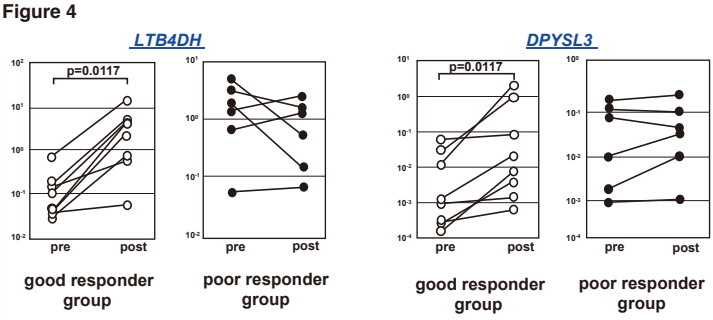



Figure 4



# Annual Best Research Award 2011

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 Annual Best Research Award 2011 went to Dr. Masayuki Miyagi (G-COE-RA) and Dr. Yusuke Endo who is now a G-COE Fellow.

Masayuki Miyagi

G-COE Research Assistant
Dept. of Orthopaedic Surgery

## The pathomechanism of chronic diskogenic low back pain

Low back pain is one of the most common and important medical problems. Intervertebral disk (IVD) pathology is thought to be a significant contributor to low back pain. However, its pathophysiology remains incompletely understood. Shinohara first reported the presence of nerve fibers in the deep layers of IVDs in diskogenic low back pain patients. Further investigations have found high levels of inflammatory mediators in degenerated human IVDs. The results of these studies suggest that the presence of sensory nerve fibers in IVDs and the persistent production of inflammatory mediators in degenerated IVDs may lead to diskogenic low back pain.

However, the pathomechanism of "chronic" diskogenic low back pain was not absolutely clear. We compared in rats the behavior of the sensory nervous system (neuropeptides in dorsal root ganglion (DRGs) and glia in the spinal dorsal horn) and inflammatory mediators (nerve growth factor: NGF, TNF-alpha, IL-6) in experimentally injured IVDs over the first eight weeks following experimental IVD injury. In this study, inflammatory mediator levels in injured IVDs were significantly higher than control levels for four days but by the end of second week no longer significantly differed from control levels (Figure 1). On the other hand, the up-regulation of neuropeptides in DRG neurons and the microglia and astrocytes in the spinal dorsal horn remained significantly higher in the injured group than in the non-injured group for the entire eight weeks studied (Figure 2). Thus, in this lumbar IVD injury model, local inflammation calmed down to normal levels within two weeks, but activation of the sensory nervous system continued for at least eight weeks. ***(Miyagi M, et al., Spine 2011 in press)***

There are two limitations to this study. First, there are some differences in the findings between animal models such as the IVD injury model and human specimens. When considering diskogenic low back pain, not only injury but also mechanical stress such as dynamic compression may be an important factor in human degenerated IVDs. Now, we are proceeding with a new project to investigate in a newly developed IVD dynamic compression model (Figure 3). Second, the evaluation of low back pain behavior is a limitation of most basic research animal models. We previously reported the gait changes using the CatWalk system (Figure 4) in a rat model of lumbar myofascial inflammation and suggested that we may be able to apply this system to the evaluation of low back pain behavior in rats. ***(Miyagi M, et al., Spine, 36(21):1760-4, 2011.)*** Now we are proceeding with a new project to investigate the low back pain behavior using the CatWalk system in a rat model of the IVD injury model.

**Figure 1. The production of inflammatory mediators in IVDs**

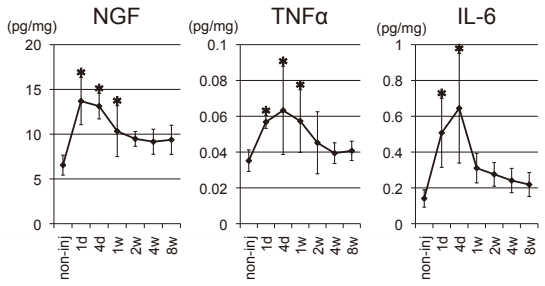



**Figure 2. Immunohistochemistry**

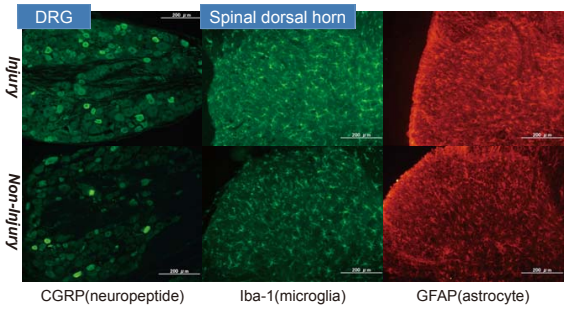



**Figure 3. IVD injury or/and dynamic compression model**

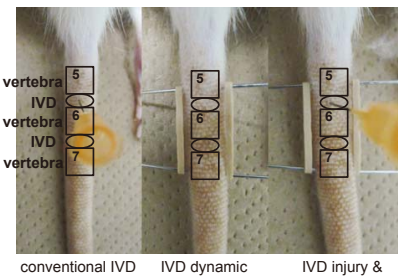
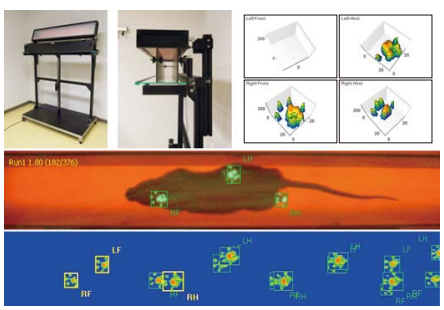
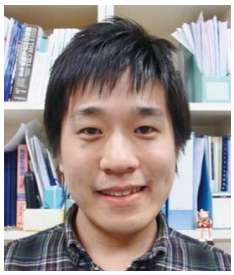



**Figure 4. CatWalk gait analysis system**



# Annual Best Research Award 2011

Dr. Endo also received the Dean's Excellent Record Award, Graduate School of Medical and Pharmaceutical Sciences, Chiba University.



Yusuke Endo
G-COE Fellow
Dept. of Immunology

## Identification of pathogenic memory Th2 cells, which are required for allergic inflammation and clarification of molecular mechanisms controlling IL-5 production in memory Th2 cells.

Approximately 30% of the Japanese population suffers from allergic disease. However, only symptomatic therapies are presently available, and no curative therapeutic strategies have been developed. We are trying to clarify the underlying molecular mechanisms of allergic disease, focusing on the role of CD4-positive helper T (Th) cells. Effector Th cells are subdivided into at least three distinct subsets (Th1, Th2, and Th17 cells) according to their cytokine production profiles (Figure 1). Among them, Th2 cells produce IL-4, IL-5, and IL-13 (so-called Th2 cytokines) and are thought to play a critical role in allergic disease.

After antigen clearance, some of the effector Th cells are maintained as memory Th cells for long periods in vivo through the contraction phase (Figure 2). Memory Th cells play an important role in 'immunological memory' that is central in immune responses, and they are involved in a wide variety of diseases. Memory Th cells displayed higher heterogeneity as compared to effector Th cells and are subdivided into several subpopulations according to the expression of cell surface molecules, cytokine production, and expression of transcription factors even in the same Th subsets. However, functional difference of each subpopulation in memory Th cells remains to be analyzed in detail. Therefore, this study is an important subject that needs to be further analyzed to understand the development of disease including allergic disorders.

Recently, we found that memory Th2 cells expressed CXCR3, a well-known marker for Th1 cells, and were subdivided into four distinct subpopulations according to the expression of CD62L and CXCR3. IL-5-producing cells were predominantly detected in the CD62L$^{lo}$CXCR3$^{lo}$ population in memory Th2 cells (Figure 3) and this population played a critical role in the memory Th2-dependent allergic airway inflammation. Furthermore, T-box transcription factor, *Eomesodermin* (Eomes) was up-regulated in memory Th2 cells and suppressed GATA3-dependent IL-5 production, which resulted in reduced airway inflammation (Figure 4). This study was published in the November issue of Immunity (Endo et al., *Immunity* 35, 733).

In this study, we have identified pathogenic memory Th2 cells and clarified molecular mechanisms, which are required for the induction of memory Th2-dependent eosinophilic airway inflammation. We will apply this study to human memory CD4 T cells for the treatment of allergic disorders.

**Figure 1. Differentiation and function of helper T cell (Th) subsets**

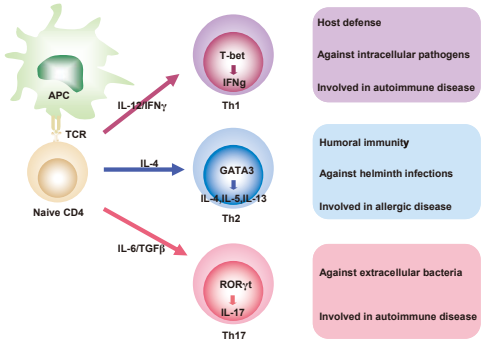



**Figure 2. Overview of memory Th cell generation**

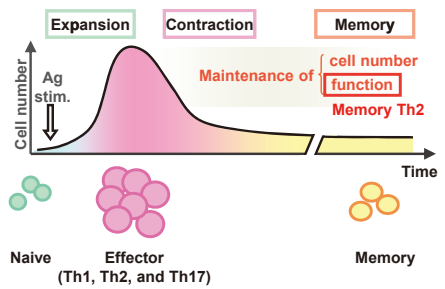



**Figure 3. The CD62L$^{lo}$CXCR3$^{lo}$ population of memory Th2 cells selectively produces IL-5**

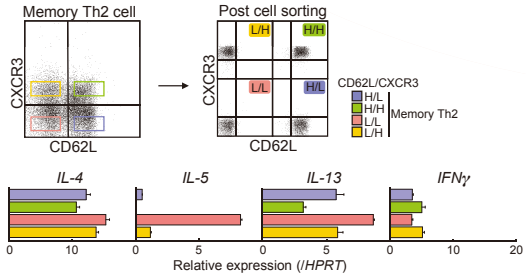
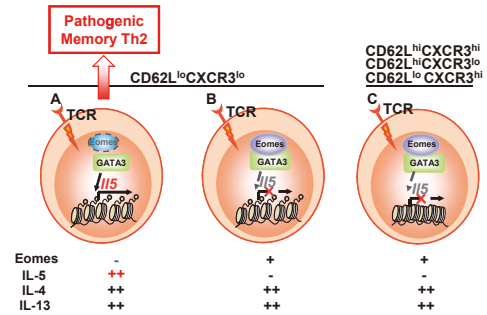



**Figure 4. Identification of pathogenic memory Th2 cell and mechanisms controlling IL-5 production**



Dr. Kenta Shinoda, who is now a G-COE Fellow, was awarded the Dean's Excellent Record Award, Graduate School of Medical and Pharmaceutical Sciences, Chiba University, at the graduation ceremony. His research is shown below.

Kenta Shinoda
G-COE Fellow
Dept. of Immunology

# Role of CD69 for the generation of memory T helper lymphocytes

Immunity is said to have a memory for most invading agents encountered before, because a second encounter with the same agent prompts a rapid and vigorous response. Memory T helper (Th) lymphocytes play an essential role in immunological memory. In their absence, the generation of long-lived plasma cells and the maintenance and secondary expansion of memory cytotoxic T cells are impaired. Despite their eminent importance for the regulation of immune reactions and immunological memory, little is known about the molecular mechanisms of the generation and maintenance of memory Th cells.

After antigen recognition, naive Th cells activate and expand into a large pool of effector Th cells in secondary lymphoid organs, such as spleen and lymph nodes. Most of the effector Th cells die during a phase of contraction; however, a small proportion survive and differentiate into memory Th cells in body. To date, we have showed that effector Th cells relocated to the bone marrow (BM) after their activation in secondary lymphoid organs, and were maintained as memory Th cells in the BM. In addition, memory Th cells persist as resting in the BM, next to IL-7-secreting stromal cells, suggesting that IL-7 is the prime survival signal for these memory cells. Upon challenge with the antigen, they could efficiently induce the production of high-affinity antibodies by B lymphocytes. Taken together, these results suggest that effector Th cells relocate to the BM and maintain on a survival niche for a long period. However, mechanisms involved in this process remain unknown.

In the steady states, resting memory Th cells mostly express CD69 (Figure 1), which is well-known as an early activation marker of lymphocytes. We focused on CD69 and examined to clarify the role of CD69 in memory Th cells. We enumerated memory Th cells in CD69-deficient mice. Although CD69 does not appear to be required for the development of effector Th cells, the number of antigen-specific memory Th cells in CD69-deficient mice dramatically decreased compared to wild-type mice (Figure 2). In addition, CD69-deficient Th cells failed to induce an efficient production of high-affinity antibodies in vivo (Figure 3). In the way of generation of memory Th cells, we show that CD69 regulates the homing of effector Th cells to BM as an adhesion molecule. These data suggest that CD69 plays a crucial role in the generation of memory Th cells and that the relocation of effector Th cells to the bone marrow is essential for generation of memory Th cells (Figure 4). In the case of allergy or autoimmune diseases, we think there are similar mechanisms underlying the generation and maintenance of harmful memory Th cells. We will clarify the mechanisms involved in the maintenance of harmful memory Th cells in chronic diseases.

**Figure 1. Memory Th cells (red) reside on stromal cells (blue) and express CD69 (green)**

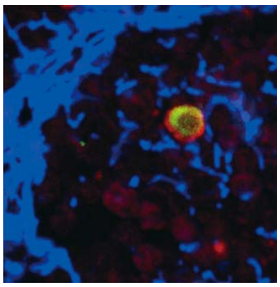


**Figure 2. CD69 is required for the generation of antigen-specific memory Th cells**

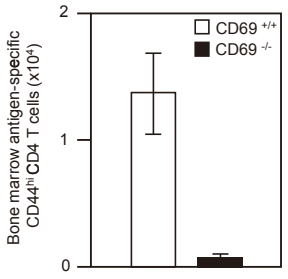



**Figure 3. CD69-deficient Th cells fail to provide efficient help for B cells**

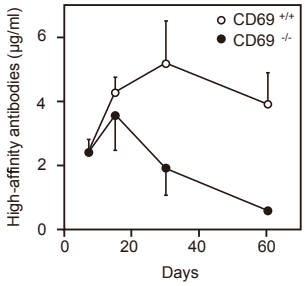
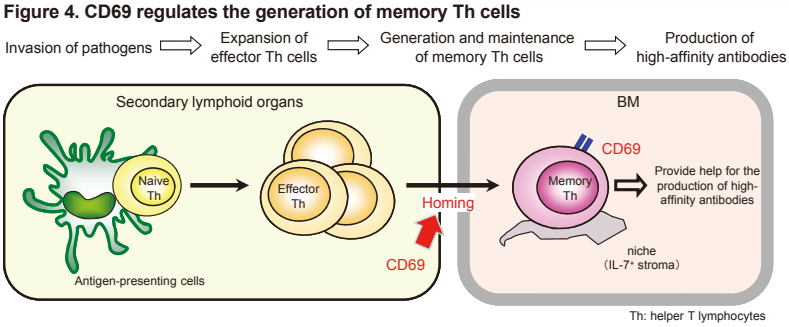



**Figure 4. CD69 regulates the generation of memory Th cells**



# Reports of Study Abroad

Eight young researchers involved in this program contributed reports of study abroad. Let's hear their experience and advice.

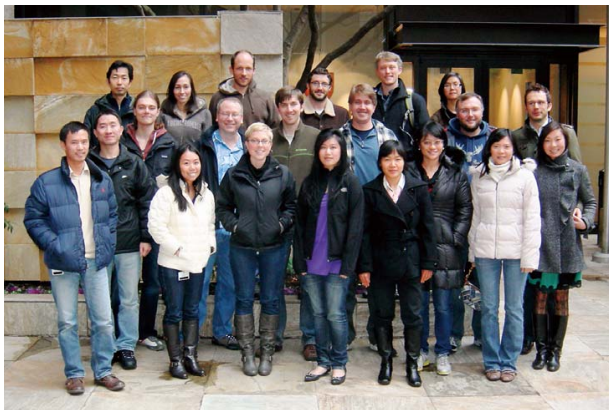
## *TSLP in Allergic Diseases*

**Masayuki Kitajima**
Immunology Program
Benaroya Research Institute at Virginia Mason
(from October 2008)

With collaborators and graduate students, we reported that enhanced Th2 differentiation and allergen-induced airway inflammation in Zfp35-deficient mice (Kitajima *et al*, J Immunol, 2009) and memory Th2 cells induce antitumor immunity by activating NK cells (Kitajima *et al*, Cancer Res, 2011). With strong hope in international collaboration cultivated in the research activities I have begun research activities as a fellow researcher in unison with the idea of Global COE program. After a year and half as G-COE fellow, now I am a postdoctoral fellow in the same laboratory (that of Dr. Steven Ziegler).

The cytokine thymic stromal lymphopoietin (TSLP) has been implicated in the development and progression of allergic inflammation in both humans and mice. We reported that TSLP enhances the function of Th2 cells as a result of studying as a G-COE fellow (Kitajima *et al*, Eur J Immunol, 2011). Thus, the novel function of TSLP suggests that TSLP is involved in homeostasis of Th2 cells in allergic inflammation directly. Next, I am investigating TSLP-activated DCs, which have not been extensively investigated. In this study, using CCL17-eGFP transgenic mouse-derived FLT3L-induced bone marrow DC subsets ($CD11b^{High}$ DC, $CD24^{High}$ DC, and pDC), we found that CCL17-eGFP-expressing DCs induced by TSLP were part of $CD11b^{High}$ DCs. And the GFP-positive DCs had a high level of costimulatory molecules and MHCII expression compared to the GFP-negative DCs, and they had increased Th2 differentiation *in vitro*. Taken together, these results may indicate identification of TSLP-targeted DCs and establishment of the DC assay system, and suggest that it has a potential for providing new information on the role of TSLP-activated DCs in allergic inflammation.

In research activities that keep evolving with the globalization, learning the research form of real overseas research laboratories is sure to become a provision of the postgraduate who conducts research activities of Japan in the future. Moreover, I am convinced that the process of piling discussion and study results with a worldwide researcher has touched off the growth of the postgraduate who has the connection with the fellow researcher's own growth.



With members of the laboratory
Masayuki Kitajima (first from left in top raw), Steven F. Ziegler (third from left in middle raw)

## *Study at University of Wisconsin-Madison*

**Jiro Terada**
Dept. of Respirology, Graduate School of Medicine, Chiba University
[ Dept. of Comparative, University of Wisconsin Madison
(from April 2009 to March 2011) ]

I'd like to express my appreciation of the opportunity to have worked as a G-COE-RA. I'll briefly present my research life from 2005 to 2011.

My PhD study started after I had worked as a respiratory physician for five years. The goal of my research was to study basic science in respiratory medicine. The first half of my PhD research was respiratory neuro-regulation using physiological methods under professors Fukuda and Kuwaki in Dept. of Autonomic Physiology, while the second half was cell-cell communication using pancreas cell-line with molecular technique. After the completion of my PhD study, I went to the University of Wisconsin Madison with my sons and wife. I worked there for two years under Gordon Mitchell who is well known in the study of respiratory neuroplasticity. My research projects were 1) Diaphragm long-term facilitation during sleep in unanesthetized rats and 2) Respiratory neuroplasticity for respiratory failure in spinally injured rats. Madison is a beautiful and safe capital city of the state of Wisconsin in the midwestern U.S. It was more difficult at first to understand the culture and English than I expected. But thanks to my boss, colleagues and friends in Japan, I've finished my projects there. Now I think I had great and irreplaceable experience with my family. So I think it would be good challenge for young researchers to do some research in foreign countries. Again, I was deeply grateful to everyone who encourages my research life in Chiba and Madison, especially the members of the G-COE program.

With members of the laboratory
Jiro Terada (second from right in front raw), Gordon Mitchell (third from right in middle raw)

## *A research project report: from University of Michigan*

**Yuumi Nakamura**
Department of Pathology, University of Michigan
(from May 2009)

I had finished a graduate degree, and then worked as G-COE research fellow at Chiba University in 2009. During that period, my research project was focused on the role of the NLRP3-inflammasome in mast cells. After that, to investigate this more deeply, I started to work as a research fellow in Dr. Gabriel Nunez's lab at the University of Michigan. I'm now using a "human disease-associated Nlrp3 mutant knock-in mouse" that is a very powerful tool for analyzing the role of Nlrp3-inflammasome *in vivo*. Recently, many studies have suggested the activation of the NLRP3 inflammasome is involved in a variety of metabolic diseases including obesity, atherosclerosis and type 2 diabetes. I believe our current project in this field may have the potential to lead to better treatment for inflammasome-associated diseases.

At Dr. Nunez's home
(from left, Gabriel Nunez, Nakamura's family)

## *Crucial role of CD8αα for T cell memory survival*

**Ryo Shinnakasu**
Division of Developmental Immunology
La Jolla Institute for Allergy & Immunology
(from May 2009)

A hallmark of immune T cell memory is that repeated infections with a pathogen are met with more rapid and enhanced protective immunity against that organism. Effector memory T cells (EM) are located in various tissues and have a heightened and immediate effector function. By contrast, central memory T cells (CM) reside within lymphoid tissues and require proliferation and differentiation to become effector cells.

On the other hand, allergy responses are caused by an abnormal immunoresponse to antigens that are non-pathogen originally. Memory T cells are known to affect these allergy responses.

When I belonged to Chiba University I performed my basic researches about generation of EM and CM for the development of the allergic prevention and cure by the immune system.

Currently, I belong to the laboratory of Dr. Hilde Cheroutre at the La Jolla Institute for Allergy & Immunology. It becomes clear from our past study gradually that CD8αα serve as key components for maintain the intraepithelial lymphocytes which is a kind of effector memory T cells and now I am performing the analysis from a molecule level about the function mechanism of CD8αα.

I have had a lot of precious experience since I started research in U.S. 2 years ago. I want to make the most of these experiences for my future research in Japan and I want to tell students what I felt through research life in U.S for about the differences of how to lead and the way of thinking for research in comparison to Japan.

With members of the laboratory
Ryo Shinnakasu (third from left), Hilde Cheroutre (third from right)

With members of the laboratory
Haruhiro Toko (fifth from left), Mark Sussman (center in back raw)

## *Heart Institute in San Diego State University*

**Haruhiro Toko**
Department of Biology
San Diego State University
(from February 2010)

I belonged in Cardiovascular Science and Medicine, Chiba University Graduate School of Medicine. From Feb., 2010, I have studied at Heart Institute in San Diego State University (P.I. Mark Sussman). In this lab., almost all researchers study about the role of kinases such as Akt and Pim1, or the role of cardiac progenitor cells in the pathological heart.

Before coming here, I studied about the molecular mechanisms of how some gene mutations induce dilated cardiomyopathy. I clarified that a kinase, CaMKII, is an important factor to induce cardiac dysfunction in dilated cardiomyopathy. From the results, I was interested in the role of kinases in the heart diseases. Kinases / phosphatases regulate crucial aspects of growth and survival through phosphorylation / dephosphorylation of target substrates. Many reports involved in my study demonstrated that processes of cardiac hypertrophy, myocardial infarction, and heart failure are dictated in part by which kinases / phosphatases are involved and also by the intensity and duration of specific enzymatic activities. While research has identified numerous critical regulatory kinases and phosphatases in the myocardium, the intracellular mechanism for temporal regulation of signaling duration and intensity remains obscure. I would like to clarify the mechanism, so I decided to come here. Now, I have focused on an enzyme, which regulates phosphorylated kinases / phosphatases, and have examined the role of the enzyme in the physiological and pathological heart.

## *My professional and cultural experiences in the United States*

**Jun Ikari**
Pulmonary, Critical Care, Sleep and Allergy Medicine, Department of Internal Medicine, University of Nebraska Medical Center
(from April 2011)

I have researched at The University of Nebraska Medical Center since April 2011 under the supervision of Professor Stephen I. Rennard who is one of the leading authorities on chronic obstructive pulmonary disease (COPD) around the world.

In Japan, I researched on 'A role of PHF11 in activated B cells'. Polymorphism of the PHF11 is highly associated with high serum IgE levels and clinical severity of asthma. We found exogenous murine Phf11 in activated B cells augments frequencies of class switch recombination to IgE and generation of IgE-secreting long-lived plasma cells.

In the United States, I am evaluating the altered repair function of lung fibroblast that contributes to the development of COPD. Also I am exploring the therapeutic approach to restore the repair function in COPD. As for my advice for studying abroad, I recommend cultivating the ability to research independently, because the autonomy of the individual is valued in the United States. I also think it is important to improve discussion skills in English, because researchers are requested to actively join discussions at a meeting. The experience of communicating in English at the G-COE conferences and the laboratory meetings at the Department of Developmental Genetics has been really great help for me professionally.

I live in the city of Omaha, Nebraska. Omaha is a very quiet, safe and serene place to live. I enjoy watching sports, sharing meals with friends at my home and travelling. I can feel America's dynamism through the vast extent of land and diverse cultures. I want to grow as a person and a researcher utilizing these experiences. I'm deeply grateful that my position here will afford me that opportunity.

With members of the laboratory
Jun Ikari (second from right), Stephen I Rennard (second from left)

## *How solve the drug lag and how improve Translational Research*

**Masaya Koshizaka**
Duke Clinical Research Institute, Duke University
(from July 2011)

Since 2007, I engaged in improving the management of the clinical trials scientifically and ethically at the Chiba University Clinical Research Center. It is necessary to have the objective data center for clinical trials. I involved in setting up and operating the data center, in order to manage large clinical data properly.

Japan lags behind the other countries in clinical trials.

It is told that it takes more time and money to do clinical trials in Japan than the other Asian countries. It is one reason of the drug lag, the delay of domestic introduction of overseas innovative medicine.

It is necessary to clear up the drug lag, in order to use new drugs for Japanese patients as soon as possible. Thus we have to participate in the global clinical trials. For this goal, I participate in the actual global clinical trials of cardiovascular diseases and diabetes, as a researcher at Duke Clinical Research Institute (DCRI), the top level research institute.

DCRI is in North Carolina, which has nature and enough resources of study. In DCRI there are many research fellows, who came from Australia, Brazil, Canada, China, Denmark, Holland, Italy, and Taiwan.

I could learn not only clinical trials, but also western communication and culture.

After going back to Japan, I would like to improve Japanese clinical researches.

IN DCRI I also participate in the Biomarker project in order to learn about Translational Research (TR). I would like to contribute to TR of Chiba University in the future, too.

At the home of Dr. John H. Alexander (Koshizaka's mentor)
(From left, Koshizaka's family, Alexander's family, and Hideki Hanaoka)

## *A report of studying abroad at Haverd Medical School*

**Kaoru Ito**
Department of Genetics, Harvard Medical School
(from April 2011)

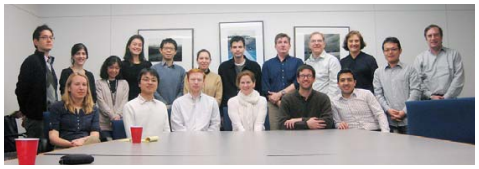
I did the research about heart failure and its pathophysiology in Chiba University. Since the mechanisms of heart failure are diversified, I studied a molecular biological approach. At the same time, I got interested in the genetic approach. Next generation sequencer (NGS) and the new methods which can be performed in NGS might increase my interest in genetics. And I thought it was a good idea to pursue the pathophysiology of heart failure by investigating cardiomyopathy which is an extreme model of genetic heart failure. So I asked my boss and my superiors where the best lab was to study cardiomyopathy by genetic approach and I got valuable advices. Fortunately, now I work for the lab which is famous for cardiomyopathy.

Our research subjects are familial heart diseases, the large cohort study regarding cardiac hypertrophy and mouse models of heart failure. Now I am engaged in the first and second ones. Because we deal with huge data of genome, RNAseq and ChIPseq and so on, our lab members are divided into two groups, a dry group which is engaged in the computer work and a wet group which is engaged in small animal experiments. Because I am curious about the new technique, I also do some work which is related with a small animal experiment though I am in a dry group.

In our lab, when we conduct experiments which are concerned with NGS, what I need to do is just to prepare the samples because our research assistants and technicians do the other experiments.

I thought that division of labor improves the efficiency. But I make an effort to watch the experiment because I am a beginner in the field. Our lab uses human samples mainly and we can get human samples easier than we do so in Japan, not only blood samples for DNA extraction but also fresh organ samples for RNA extraction. In addition, a lot of collaborations with other institutes are being made and many labs provide their ideas to advance the research. I was surprised at the systematic and effective research environment.

Finally, just before I went to the US to study abroad, the biggest earthquake we have ever experienced hit Japan. So being in anguish over whether I should leave Japan or not, I came to Boston. Now I still think about it. But I believe that I must do what I should do in the US and I will find a way to give something back to Japan after returing to my country.



With members of the laboratory
Kaoru Ito (first from left in top raw), Jonathan.G.Seidman (Professor, first from right in top raw), Cristine.E.Seidman (Professor, third from right in top raw)

The 8th Global COE Workshop

February 19, 2011

# Presentation and Discussion by G-COE-RA

*1st Lecture Hall, Main Building 1F, Faculty of Medicine, Chiba University*

The 8th Global COE Workshop that was the fifth workshop in "Presentation and Discussion by G-COE-RA" took place on February 19. Thirty-three G-COE-RAs presented the progress of each research. Some of them talked coolly about the results in an assuming tone, and some kept on talking with much enthusiasm that might be brought from passion to their own research studies, or other might have got nervous for their first experience of presentation in English. The audiences were drawn into their presentations that were full of each RA's characteristics and charm, while also being impressed with the research quality on which each RA is working. Most of the presentations were assertive and sophisticate. Students took English Presentation Seminar, which was introduced at the Graduate School of Medicine and Pharmaceutical Science last summer; we believe it has contributed a lot for their improvement. The participants enjoyed discussions through a barrage of questions made by the students in the Q and A periods. This workshop was very active and fruitful. We have seen the RA grow by increasing experience in presentation and discussion in this manner, and realized the significance and evident progress of the workshop as well as the Global COE Program.

March 8, 2011

# Advanced Medicine Progress Seminar by Seeds Grant Competition Winners 2010

*The 3rd Auditorium, Chiba University Hospital 3F*

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 March 8, 2011 to report progress in these studies.

Each of the studies is aimed at developing tumor markers, diagnostic drug for tumor localization, or novel therapeutic agents and treatments targeting various diseases including neurodegenerative diseases and malignant tumors. 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. Two studies we make a continuing support were reported the steady progress compared to last year. We will continue to support by holding this seed grant competition until we will establish a clear trend to promote the research for diagnostic or therapeutic development generated from Chiba University starting from this in-house seed exploitation.

Shinichiro Motohashi
Program Leader,
Seeds Grant Competition

March 29, 2011

# Inaugural Joint Scientific Meeting – Medical University of Vienna and Chiba University –

*Conference Room, Main Building 2F, Faculty of Medicine, Chiba University*

Inaugural Joint Scientific Meeting –Medical University of Vienna (MUV) and Chiba University– was held on March 29, 2011. This was the first event on the academic and research collaboration activities agreed on in 2010 between Medical University of Vienna in Austria and Chiba University. The symposium program was designed by the Chiba University Graduate School of Medicine and Chiba University Hospital in order to encourage the medical research activities between both universities, with supports by Chiba University G-COE program and the Health and Labor Science Research programs for Translational Research.

The symposium began with the opening remarks by Dr. Yoichi Kohno, director of University Hospital. The focus of this workshop was on "The LDL receptor to immature cell diseases". At first, Dr. Hideaki Bujo, Graduate School of Medicine (Chaired by Dr. Takashi Miki, Graduate School of Medicine) made a presentation on the LDL receptor family study overview. Dr. Chiaki Nakaseko, Graduate School of Medicine and University Hospital (Chaired by Dr. Atsushi Iwama, Graduate School of Medicine), then spoke about the prognostic impact of serum soluble LR11 on acute leukemia. The last presentation was on the adipocyte-based gene therapy for interactive serum protein deficiencies by Dr. Masayuki Kuroda, Chiba University Hospital (Chaired by Dr. Koutaro Yokote, Graduate School of Medicine). The symposium finished with the closing remarks by Dr. Haruaki Nakaya, dean of Graduate School of Medicine.

The symposium was much productive with the enthusiastic discussion by many participants for the future collaborative research projects. The joint meeting will be next held at MUV.

Hideaki Bujo
Joint Program Chiba University Office

Message with Selected Slides

Dear President Dr. Saito, dear Colleagues!
I deeply regret that unfortunate events bringing sadness to many Japanese people preclude my participation in this Inaugural Joint Scientific Meeting of our Universities.
My thoughts and hopes are with all of you.
I wish you and your colleagues a successful meeting now, and a rapid recovery from the dire consequences of the powers of nature.
Hoping that we will be able to meet soon,
With best regards,

Wolfgang J. Schneider

MEDICAL UNIVERSITY OF VIENNA

The 9th Global COE Workshop

# Presentation and Discussion by G-COE-RA

*1st Lecture Hall, Main Building 1F, Faculty of Medicine, Chiba University*

June 4, 2011

The 9th Global COE Workshop that was the sixth workshop in "Presentation and Discussion by G-COE-RA" was held on Saturday, June 4. This year 33 graduate students selected as G-COE-RAs, including the 17 RAs newly selected. The RA has been widely recruited from the related research field of this program, thus the increasing number of departments has been involved in this program every year. In particular, in the Graduate School of Pharmaceutical Sciences, the number of the RAs has doubled from last year to 10 and consequently three departments have newly involved. New RAs made a presentation on their experimental plan, and the RAs selected again this year on research results and progresses additionally in English. In the Q and A periods, each RA was pelted with questions. To respond them smoothly actually requires higher English communicative ability. We are sure that the RAs will further improve the ability making use of program designed for that purpose, including a video of the presentation and Presentation Seminar for scientific seminar in English, in addition to experience in the workshop. Besides the student's mentors, two advisory professors evaluated each presentation. The increasing number of advisory professors newly involved could be a sign for fulfillment and progress of this program.

# IMSUT/RCAST - Chiba University Global COE Joint Retreat 2011

## "Toward new era in the basic and clinical immunology"

*Date: September 17-18, 2011*
*Place: Oiso Prince Hotel*

**Toshio Suda**
Professor
Department of Cell Differentiation,
Keio University School of Medicine

IMSUT/RCAST - Chiba University Global COE Joint Retreat was held for the first time in cooperation with The IMSUT (Institute of Medical Science, The University of Tokyo) & RCAST (Research Center for Advanced Science and Technology, The University of Tokyo) Global COE Program "Center of Education and Research for the Advanced Genome-Based Medicine: For personalized medicine and the control of worldwide infectious diseases". One-hundred and ten graduate students and researchers from the both G-COE programs gathered and studied together for two days, developing new interaction and stimulating active discussion. Dr. Toshio Suda, Professor of Keio University, gave a keynote lecture entitled "Stem Cells and Cancer Stem Cells". The program was organized by the program committee in which members are Drs. Taishin Akiyama and Jun Kunisawa from the IMSUT and Dr. Hiroshi Nakajima from Chiba University. The followings are reports from some participants.

At the poster session, Soichi Tofukuji, G-COE-RA, Department of Immunology, Graduate School of Medicine, Chiba University, received the Best Poster Award.

### *Kotaro Suzuki*

*Department of Molecular Genetics, Graduate School of Medicine, Chiba University*

The Chiba University G-COE Retreat 2011 was held on September 17 and 18 at Oiso Prince Hotel. This was our 3rd Retreat and IMSUT/RCAST-Chiba University G-COE Joint Retreat. The maximum number of graduate students and PI researchers participated compared with the past 2 times of conventions. Also in the contents, almost all presentations in each field were high quality. In Poster Presentation as well as Oral Presentation, we had in-depth discussion. We believe that this program provided mutual understanding between students and PI.

### *Hiroshi Ashida*

*Division of Bacterial infection, The Institute of Medical Science, The University of Tokyo*

I attended the "IMSUT/RCAST - Chiba University Global COE Joint Retreat 2011" at Oiso. In this retreat, young scientists and graduate students, who specialize in immunology, from Chiba University and IMSUT presented recent data on oral presentations or poster sessions. Although I am unfamiliar to immunology (I am a bacteriologist), it was good opportunity to motivate myself through discussion and communicate with same generation. In particular, advises and questions from another field specialists to my research subject will provide me turning points to further execute research.

Finally, I thank retreat secretaries, executive committees, and all participants for their support and participation.

### *Ryuta Uraki*

*Division of Virology, The Institute of Medical Science, The University of Tokyo*

I am a master course's student researching the pathogenicity of influenza virus. I was so nervous because the theme of this seminar was immunology, not virology which is my major. However, in spite of my anxiety, this seminar was so attractive and exciting for me to get fruitful advice about the interesting phenomenon I have focused on from wonderful professors and seniors. Further, this seminar gave me fine chance to present my research orally in English and to communicate with researchers in other fields. I would like to make use of what I learned in this seminar to perform more creative research.

### *Tomokazu Sumida*

*Department of Cardiovascular Science and Medicine, Graduate School of Medicine, Chiba University*

The G-COE retreat was held at Oiso overlooking the blue ocean and the white beach. As this year's retreat was co-hosted by IMSUT/RCAST and Chiba University, more programs became available and it seemed there was educational consideration for training young researchers.

Many of the presentation based on the latest immunological research provided me with great learning experience, since I usually study about cardiology and do not have much opportunity to encounter basic immunological study. Learning that the immunological system was associated with so many pathophysiological conditions and also finding the possibility of its relevance with cardiovascular diseases, I developed deeper interest in medical science.

During this 2-day meeting, the communication with researchers from other universities through poster sessions and reception, encouraged and motivated me to research harder and deeper. I really appreciate having the opportunity to join this occasion.

### *Satomi Tanaka*

*Department of Cellular Molecular Medicine, Graduate School of Medicine, Chiba University*

This year's Global COE Joint Retreat was held in a hotel that faced on Oiso long beach. I felt quite nervous because I had to present our recent work in English in front of a large audience. However, we had a social gathering the night before and dressed in plain clothes, unlike an ordinary academic conference, so we were able to have a more lively discussion in a pleasant atmosphere. It was also a good chance to talk to a lot of researchers from other departments. Furthermore, I was very impressed with the lecture on normal and cancer stem cells presented by Dr. Suda. Thank you for giving me the valuable opportunity.

### *Yosuke Kurashima*

*Division of Mucosal Immunology, The Institute of Medical Science, The University of Tokyo*

I was participated in the Global COE Joint Retreat on September 17 to 18th. It was a great opportunity for me to learn recent research direction in the medical fields such as Immunology, Infection, and Cancer at once. In the keynote lecture, Prof. Suda from Keio Univ. presented the data indicating the importance of hypoxic microenvironment for the maintenance of hematopoietic stem cells in the stem cell niche. Because "Immune Cell Metabolism" is becoming one of the recent notable fields in the immunology, the experimental results indicating the importance of H1F1a for the regulation of TCA cycle in stem cell niche was very impressive for me. Last but not least, I would like to express my sincere appreciation for setting up this wonderful meeting to the organizers and administrators. I'd definitely want to participate next time, if there is a chance like this time.

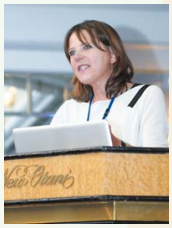
# Immune System Regulation toward Disease Control

*November 30, 2011*
*Hotel New Otani Makuhari, Chiba*










The G-COE Program held the 6th Chiba University Global COE Symposium at Makuhari, on Wednesday, November 30th, co-organized by IMSUT & RCAST G-COE Program, The University of Tokyo. This sixth symposium, entitled "Immune System Regulation toward Disease Control", focused on immune-related diseases. Since the regular annual meeting of the Japanese Society for Immunology was held for 3 days until the preceding day at the Makuhari Messe, the symposium was filled with enthusiasm. Participants listened intently to presentations and discussed topics of mutual interest heatedly. The fact that the hall was fully packed with audience suggests that we successfully lined up attractive researchers from home and abroad. A total of 15 talks were presented in symposium, starting with a session on lymphocyte development and homeostasis, followed by those on immunological memory and T lymphocyte function, and ending with one on allergy and inflammation. Personally, I was most interested in Dr. Meinrad Busslinger's presentation about a genome-wide analysis of the transcriptional regulation in B cells by ChIP-Seq and RNA-Seq. His lecture provided me with useful information to precede my study based on the same technology he used. At lunchtime, I happened to sit next to him and fortunately talked with him directly. I asked him some questions and discussed new insights into the genome-wide study. Additionally, I led the symposium as MC and made several announcements in English. I also took over the management of the symposium cooperating with G-COE office members. This was my first time to do MC work and management, so I found some points to improve at next chance. However, it was a great experience for me. I believe this symposium will transmit new information toward the rest of the world from Chiba University, and lead to progress in the research of immunological field in the future.

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

The G-COE Program held the 6th Chiba University Global COE Symposium at Makuhari in Chiba prefecture and I could learn the latest immunological knowledge. At this symposium, the seminar of Dr. Chen Dong who is one of the authorities on Th17 cell research was very impressive. Not only could I learn the most recent findings in Th17 cells from his study, but this seminar also increased my motivation for my study. Additionally, I could gain a further understanding of signaling pathway and cytokines for the immune system. Overall, this seminar was beneficial for advancing my research. Moreover, when I saw the researchers vigorously discussing on the newest topics, I persuaded myself that research in the immunological field made further progress in the near future. By using the knowledge acquired at this symposium, I would like to work hard and contribute to the development of medicine and bioscience.

I worked as a stuff member in this symposium and had the opportunities to speak with some researchers directly. However, I keenly felt the importance of English speaking ability for communication. I will make a conscious effort to study English in order to be able to communicate more smoothly when participating in the next symposium.

**Yukiko Watanabe**
G-COE-RA
Dept. of Immunology







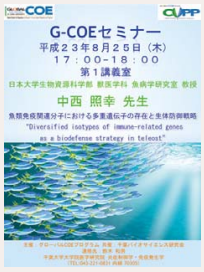
## G-COE Seminar

**Learn from the forefront**

For our graduate students, top-ranked world researchers gave lectures including recent findings of their studies.





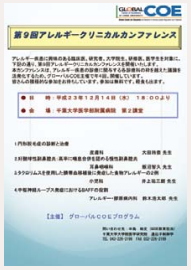





## Allergy Clinical Conference

**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 cross-disciplinarily discuss allergic diseases.


## Basic Science Joint Meeting (BSJM)

Coordinated by PhD student working group

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

**59. January 7, 2011**
Yuichi Michikawa, Senior Researcher, RadGenomics Project, Research Center for Charged Particle Therapy, National Institute of Radiological Sciences

**60. January 14, 2011**
Harukiyo Kawamura, Assistant Professor, Dept. of Medical Physiology

**61. January 21, 2011**
Kentaro Takahashi, Graduate Student, Dept. of Molecular Genetics

**62. January 28, 2011**
Chiaki Iwamura, Assistant Professor, Dept. of Immunology

**63. February 4, 2011**
Akira Matsuura, Professor, Div. of Nanoscience, Graduate School of Advanced Integration Science/Department of Biology, Faculty of Science

**64. February 18, 2011**
Shinichiro Motohashi, Associate Professor, Dept. of Medical Immunology

**65. February 25, 2011**
Ayako Inamine, G-COE Fellow, Dept. of Otolaryngology, Head and Neck Surgery

**66. April 1, 2011**
Haruko Takano, Post Doctoral Fellow, Biomedical Research Center

**67. April 8, 2011**
Mitsujirou Osawa, Lecturer, Dept. of Cellular and Molecular Medicine

**68. April 15, 2011**
Kouya Suzuki, Graduate Student, Dept. of Immunology

**69. April 22, 2011**
Junji Yamashita, Research Fellow, Dept. of Immunology

**70. May 6, 2011**
Ayako Matsumoto, JSPS Fellow, Dept. of Pharmacology/Dept. of Neurobiology

**71. May 13, 2011**
Koji Onomoto, Assistant Professor, Div. of Molecular Immunology, Medical Mycology Research Center

**72. May 20, 2011**
Hideki Hanaoka, Director/Professor, Chiba University Hospital Clinical Research Center

**73. May 27, 2011**
Jing Pan, G-COE RA, Dept. of Developmental Genetics

**74. June 4, 2011**
Hiroyuki Ishikawa, Associate Professor, Dept. of Biology, Graduate School of Science

**75. June 10, 2011**
Akio Matsumoto, Associate Professor, Dept. of Pharmacology

**76. June 17, 2011**
Masayuki Kuroda, Associate Professor, Center for Advanced Medicine

**77. June 24, 2011**
Atsushi Onodera, Assistant Professor, Dept. of Immunology

**78. July 1, 2011**
Tatsuya Sato, Assistant Professor, Dept. of Developmental Biology

**79. July 8, 2011**
Takaaki Konuma, Graduate Student, Dept. of Cellular and Molecular Medicine

**80. July 15, 2011**
Masaya Yokota, Graduate Student, Dept. of Molecular Genetics

**81. July 22, 2011**
Nobuhide Tsuruoka, Clinical Fellow, Dept. of Reproductive Medicine/Dept. of Developmental Genetics

**82. September 2, 2011**
Takeshi Murata, Associate Professor, Graduate School of Science

**83. September 9, 2011**
Tomoaki Tanaka, Lecturer, Dept. of Clinical Cell Biology and Medicine

**84. September 16, 2011**
Tohru Minamino, Lecturer, Dept. of Cardiovascular Science and Medicine

**85. October 7, 2011**
Shunsuke Nakamura, Graduate Student, Dept. of Cellular and Molecular Medicine

**86. October 14, 2011**
Arifumi Iwata, Clinical Fellow, Dept. of Molecular Genetics

**87. October 28, 2011**
Asami Hanazawa, Graduate Student, Dept. of Immunology

**88. November 4, 2011**
Motoo Kitagawa, Associate Professor, Dept. of Molecular and Tumor Pathology

**89. November 11, 2011**
Tetsuhiro Chiba, Assistant Professor, Dept. of Medicine and Clinical Oncology

**90. November 18, 2011**
Daiju Sakurai, Lecturer, Dept. of Otolaryngology, Head and Neck Surgery

**91. November 25, 2011**
Naohiko Seki, Associate Professor, Dept. of Functional Genomics

**92. December 2, 2011**
Susumu Kawamoto, Professor, Molecular Biology, Medical Mycology Research Center

**93. December 9, 2011**
Soichi Tofukuji, Graduate Student, Dept. of Immunology/Kazusa DNA Research Institute

**94. December 16, 2011**
Fumihiro Ishibashi, Graduate Student, Dept. of Immunology/Dept. of Thoracic Surgery

# New Members

## RAs Newly Selected in 2011

**Kenta Watanabe**
Department of Clinical Pharmacology

**Taiji Nakano**
Department of Pediatrics

**Satomi Tanaka**
Depertment of Cellular and Molecular Medicine

**Aika Nojima**
Department of Cardiovascular Science and Medicine

**Mani Kohno**
Department of Developmental Genetics

**Go Sasahara**
Depertment of Otorhinolaryngology, Head & Neck Surgery

**Tomohiko Makiyama**
Lab. of Chemical Pharmacology

**Jing Pan**
Department of Developmental Genetics

**Muradil Mutallip**
Depertment of Otorhinolaryngology, Head & Neck Surgery

**Jun Matsumoto**
Department of Clinical Pharmacology

**Xin Wang**
Department of Biochemistry

**Yoshiki Kaneko**
Department of Molecular Biology and Oncology

**Eriko Suwa**
Department of Geriatric Pharmacology and Therapeutics

**Kenichi Ishibashi**
Department of Molecular Cell Biology

**Hiroyuki Suzuki**
Department of Molecular Imaging and Radiotherapy

**Moeko Hino**
Department of Pediatrics

**Tadashi Shiohama**
Department of Pediatrics

## G-COE Collaborators

**Itsuko Ishii**
Associate Professor, Department of Clinical Pharmacology

**Noritaka Ariyoshi**
Associate Professor, Division of Pharmacy, Chiba University Hospital

**Koichi Ueno**
Professor, Department of Geriatric Pharmacology and Therapeutics

**Toshihiko Murayama**
Professor, Laboratory of Chemical Pharmacology

**Mitsutoshi Yoneyama**
Professor, Division of Molecular Immunology, MMRC

**Shinobu Saijo**
Associate Professor, Division of Molecular Immunology, MMRC

## G-COE Independent Research Associate

**Tumes Damon**
Department of Immunology

## G-COE Fellows

**Yusuke Endo**
Department of Immunology

**Kenta Shinoda**
Department of Immunology

**Masaya Koshizaka**
Chiba University Hospital Clinical Research Center

**Shunsuke Furuta**
Department of Molecular Genetics

# Upcoming Events

**The 10th Chiba University G-COE Workshop (Presentation and Discussion by G-COE-RA)**
Date: February 11, 2012
Venue: The 1st Lecture Hall, Main Building 1F, Faculty of Medicine, Chiba University

**CCRC 10th Anniversary and CFMRC Inauguration Symposium**
Date: March 19, 2012
Venue: The Auditorium, Medical and Pharmaceutical Science Building II 1F, Chiba University

**The 11th Chiba University G-COE Workshop (Presentation and Discussion by G-COE-RA)**
Date: June 2012

**G-COE Retreat 2012**
Date: September 8-9, 2012
Venue: Seimei-no-Mori Resort

**The University of Auckland – RCAI- Chiba University Symposium (tentative)**
Date: Autumn 2012 / Venue: New Zealand

**The 7th Chiba University G-COE Symposium**
Date: January 2013

**The 12th Chiba University G-COE Workshop (Presentation and Discussion by G-COE-RA)**
Date: February 2013

## Editor's Note

Here is vol.4 of our newsletter. There were earthquakes, tsunami and a nuclear power plant accident last year, but medical and clinical researches have steadily progressed. Seeing from vol. 1, you may recognize how the promotion of this G-COE program has contributed to provide a better environment for young researchers who aim to do medical research or develop treatments. Also events have expanded in many different directions from an international perspective. We are sure that this G-COE program will produce many young researchers capable of working on the international stage. (Kazuo Suzuki, G-COE Coordinator)

**Chiba University Global COE Program**
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