10th Global Network Forum

on Infection and Immunity

Host-pathogen interaction in respiratory infectious diseases

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Host-pathogen interaction in respiratory infectious diseases

- Friday 2 - Saturday 3 February 2024, Chiba, Japan

- Organized by
  Joint Usage / Medical Mycology Research Center (MMRC),
  Chiba University

- Organizing Committee
  - Kazutoshi Shibuya (Toho University)
  - Yoshitsugu Miyazaki (National Institute of Infectious Diseases)
  - Hiroji Chibana (Chiba University)
  - Yoshiyuki Goto (Chiba University)
  - Naruhiko Ishiwada (Chiba University)
  - Shinobu Saijo (Chiba University)
  - Hiroki Takahashi (Chiba University)
  - Akira Watanabe (Chiba University)
  - Takashi Yaguchi (Chiba University)
  - Mitsutoshi Yoneyama (Chiba University)

Acknowledgements

We would like to offer very special thanks to the following organizations for their generous educational grants.
Their financial support makes this Forum possible.

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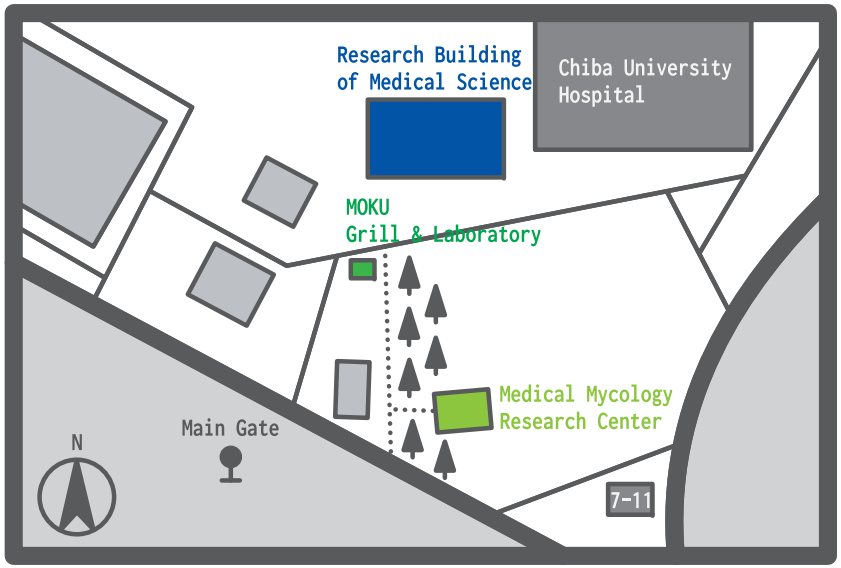
Poster Session

■ 13:30 - 15:50 Friday 2 February 2024

■ Lecture Room 2, 3rd Floor,
Research Building of Medical Science, Chiba University



■ PROGRAMME

All sessions will take place in the Lecture Room 2
unless otherwise stated.

13:00 - 13:30 Reception and Poster Setup
13:30 - 14:40 Presentation of ODD-numbered Group
14:40 - 15:50 Presentation of EVEN-numbered Group
Please be sure to remove your poster by 16:10.
16:30 - 18:00 Welcome Reception and Poster Award Ceremony
MOKU - Grill & Laboratory
All Poster Presenters are encouraged to attend.

P-01 TRBP regulates RLR-mediated antiviral innate immune signal

Koji Onomoto [1○], Monami Sakai [1], Miyu Watanabe [1], Tomoko Takahashi [2], Kumiko Ui-Tei [3], Mitsutoshi Yoneyama [1]

1 Division of Molecular Immunology, Medical Mycology Research Center, Chiba University
2 Graduate School of Science and Engineering, Saitama University
3 Graduate School of Science, The University of Tokyo

P-02 Biomarker VAP2 for vascular inflammation in serum of severe patients with COVID-19 in Chiba University Hospital

Kazuo Suzuki [1○], Seiichiro Sakao [2], Shota Murata [3], Haruna Asano [3], Toshihiko Yoshida [3], Kazuyuki Matsushita [3], Shunsuke Furuta [4], Ken-Ichi Hanaki [5], Takashi Miki [6], Hidetoshi Igari [7]

1 Division of Co-creative Research in Disaster Therapeutics, Research Institute of Disaster Medicine, Chiba University
2 Department of Respirology, Graduate School of Medicine, Chiba University
3 Department of Laboratory Medicine, Chiba University Hospital
4 Department of Allergy and Clinical Immunology, Graduate School of Medicine, Chiba University
5 Management Department of Biosafety, National Institute of Infectious Diseases
6 Department of Medical Physiology, Graduate School of Medicine, Chiba University
7 Department of Infection Control, Chiba University Hospital

P-03 Anti-*staphylococcus aureus* compound was found in genus *Nocardia*

Yu Lu [1○], Yosuke Seto [2], Yasumasa Hara [2], Akiko Takaya [2], Hiroki Takahashi [1]

1 Division of Bio-resources, Medical Mycology Research Center, Chiba University
2 Department of Natural Products Chemistry, Graduate School of Medical and Pharmaceutical Sciences, Chiba University

P-04 Structural analysis of pentacyclic triterpene glycosides as a quorum quencher of *Staphylococcus aureus*

Aki Shibata [1○], Junpei Yamaguchi [1], Mariko Kitajima [2], Hayato Ishikawa [2], Yuumi Matsuoka [3], Akiko Takaya [1]

1 Department of Natural Products Chemistry, Graduate School of Medical and Pharmaceutical Sciences, Chiba University
2 Laboratory of Middle Molecular Chemistry, Graduate School of Pharmaceutical Sciences, Chiba University
3 Immunology Frontier Research Center (IFReC), Osaka University

P-05 Loss of hemolytic properties in *Streptococcus pyogenes* due to a single nucleotide mutation in the *sagD* gene

Misako Ohkusu [1○], Takeshi Shimizu [2], Naruhiko Ishiwada [1]

1 Department of Infectious Diseases, Medical Mycology Research Center, Chiba University

2 Department of Molecular infectiology, Graduate School of Medicine, Chiba University

P-06 A critical role of the periplasm in copper homeostasis in Gram-negative bacteria

Jun-ichi Ishihara [1○], Tomohiro Mekubo [2], Chikako Kusaka [2], Suguru Kondo [2], Ryotaro Oiko [3], Kensuke Igarashi [4], Hirofumi Aiba [5], Shu Ishikawa [6], Naotake Ogasawara [2], Taku Oshima [3], Hiroki Takahashi [1]

1 Division of Bio-resources, Medical Mycology Research Center, Chiba University

2 Graduate School of Science and Technology, Nara Institute of Science and Technology

3 Graduate School of Engineering, Toyama Prefectural University

4 Bioproduction Research Institute, National Institute of Advanced Industrial Science and Technology (AIST)

5 Graduate School of Pharmaceutical Sciences, Nagoya University

6 Graduate School of Science, Kobe University

P-07 The unique phenotype of carbapenem-tolerant *Klebsiella*

Natsuki Yamanaka [1○], Hiroki Takahashi [2], Akiko Takaya [1]

1 Department of Natural Products Chemistry, Graduate School of Medical and Pharmaceutical Sciences, Chiba University

2 Division of Bio-resources, Medical Mycology Research Center, Chiba University

P-08 A novel mechanism that enhances general stress responses of enterohemorrhagic *Escherichia coli*

Takeshi Shimizu [1○], Shin Suzuki [1], Takashi Hamabata [2]

1 Department of Molecular Infectiology, Graduate School of Medicine, Chiba University

2 Department of Infectious Diseases, Research Institute, National Center for Global Health and Medicine

P-09 Monitoring changes in bacteria under antimicrobial exposure with ciprofloxacin with florescent moieties

Hina Saito [1○], Ayaka Okabe [2], Nemoto Tetsuhiro [2], Akiko Takaya [1]

1 Department of Natural Products Chemistry, Graduate School of Medical and Pharmaceutical Sciences, Chiba University

2 Department of Pharmaceutical Chemistry, Graduate School of Pharmaceutical Sciences, Chiba University

P-10 Analysis of ClpP activation and antibacterial activity of Koetjapic acid derived from *Sandricum indicum*

Takumi Segawa [1○], Keisuke Sugimoto [1], Junpei Yamaguchi [1], Yasumasa Hara [2], Takahito Kuribara [3], Tetsuhiro Nemoto [3], Akiko Takaya [1]

1 Department of Natural Products Chemistry, Graduate School of Medical and Pharmaceutical Sciences, Chiba University

2 Faculty of Agriculture, Kagawa University

3 Department of Pharmaceutical Chemistry, Graduate School of Pharmaceutical Sciences, Chiba University

P-11 Assessment of the exposome of patients with hypersensitivity pneumonitis and the effects of environmental interventions

Sho Shimada [1○], Shiro Sonoda [1], Masaru Ito [1], Naoki Kagi [2], Tsukasa Okamoto [1,3], Yasunari Miyazaki [1]

1 Department of Respiratory Medicine, Tokyo Medical and Dental University

2 Department of Architecture and Building Engineering, Tokyo Institute of Technology

3 Department of Pulmonary Immunotherapeutics, Tokyo Medical and Dental University

P-12 Effectiveness of isavuconazole in invasive Aspergillosis complicated with lung and brain abscess during hematopoietic stem cell transplantation in pediatric patient with myelodysplastic syndrome

Naruhiko Ishiwada [1○], Hajime Nemoto [2], Moeko Hino [2], Takahiro Aoki [2], Yoshiharu Yamashita [2], Tomoko Okunushi [2], Koo Nagasawa [2], Akira Watanabe [3], Shingo Yamazaki [4], Hiromichi Hamada [2]

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3 Division of Clinical Research, Medical Mycology Research Center, Chiba University

4 Division of Pharmacy, Chiba University Hospital

P-13 Research on the role of CARD9 deficiency in the pathogenesis of dematiaceous fungal infection

Ruijun Zhang [1,2,3○], Wu Weiwei [3], Wang Xiaowen [3], Li Ruoyu [3]

1 Division of Molecular Immunology, Medical Mycology Research Center, Chiba University

2 Department of Dermatology, Shanxi Bethune Hospital

3 Department of Dermatology, Peking University First Hospital, Research Center for Medical Mycology

P-14 Mutations in complex components involved in mRNA polyadenylation and factors involved in its folding affect 5-FC susceptibility in *Aspergillus fumigatus*

Teppei Arai [1○], Hiroki Takahashi [2], Hidetaka Majima [1], Akira Watanabe [1]

1 Division of Clinical Research, Medical Mycology Research Center, Chiba University

2 Division of Bio-resources, Medical Mycology Research Center, Chiba University

P-15 Dysfunction of Cyp51A can lead to high susceptibility to triazoles in *Aspergillus fumigatus*

Hidetaka Majima [1○], Teppei Arai [1], Katsuhiko Kamei [2,3], Akira Watanabe [1]

1 Division of Clinical Research, Medical Mycology Research Center, Chiba University

2 Division of Infection Control and Prevention, Medical Mycology Research Center, Chiba University

3 Department of Infectious Disease, Japanese Red Cross Ishinomaki Hospital

P-16 Rapid formation of huge phagosomes with peripheral neutrophils phagocytosing *Aspergillus fumigatus*

Hidetaka Majima [1○], Kazuo Suzuki [2,3,4], Kaoru Kato [5], Shota Murata [6], Hayato Koshikawa [7], Hiroki Takahashi [1], Fuyu Ito [8], Ryota Hirose [9], Toru Utsunomiya [9], Hyangok Jeon [10], Kazuko Uno [4], Ken-ichi Hanaki [3], Toshinori Nakayama [11], Takashi Miki [2,7], Akira Watanabe [1,2]

1 Medical Mycology Research Center, Chiba University

2 Research Institute of Disaster Medicine, Chiba University

3 National Institute of Infectious Diseases

4 Louis Pasteur Center for Medical Research

5 Biomedical Research Institute, AIST

6 Clinical Research Center, Chiba University Hospital

7 Chiba University Graduate School of Medicine

8 Teikyo University

9 Shinko Seiki

10 Tomocube Inc.

11 Chiba University

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Yasunori Muraosa [1○], Ken Miyazawa [1], Shogo Takatsuka [1], Yasutaka Hoshino [1], Takashi Umeyama [1], Yoshitsugu Miyazaki [1]

1 Department of Fungal Infection, National Institute of Infectious Diseases

P-18 Real-time monitoring of mycelial growth in shake liquid culture using hyphal dispersion mutant of *Aspergillus fumigatus*

Ken Miyazawa [1○], Takashi Umeyama [1], Shogo Takatsuka [1], Yasunori Muraosa [1], Yasutaka Hoshino [1], Keietsu Abe [2], Yoshitsugu Miyazaki [1]

1 Department of Fungal Infection, National Institute of Infectious Diseases

2 Department of Agricultural Chemistry, Graduate School of Agricultural Science, Tohoku University

P-19 Research on genome diversity and evolution of the pathogenic fungus *Aspergillus fumigatus*

Masaki Nagayama [1○], Yoko Kusuya [2], Hiroki Takahashi [1]

1 Division of Bio-resources, Medical Mycology Research Center, Chiba University

2 Biological Resource Center, National Institute of Technology and Evaluation

P-20 Genomic diversity of the pathogenic fungus *Aspergillus fumigatus* in Japan

He Xiaohui [1○], Yoko Kusuya [2], Daisuke Hagiwara [3,4], Takahito Toyotome [5], Teppei Arai [6], Bian Cai [7], Masaki Nagayama [8], Saho Shibata [8], Akira Watanabe [6], Hiroki Takahashi [6]

1 Division of Bio-resources, Medical Mycology Research Center, Chiba University

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3 Department of Life and Environmental Sciences, University of Tsukuba

4 Microbiology Research Center for Sustainability (MiCS), University of Tsukuba

5 Department of Veterinary Medicine, Obihiro University of Agriculture and Veterinary Medicine

6 Division of Clinical Research, Medical Mycology Research Center, Chiba University

7 BGI, Shenzhen, China

8 Division of Bio-resources, Medical Mycology Research Center, Chiba University

P-21 Evolution of *Aspergillus fumigatus* during host infection

Saho Shibata [1○], Teppei Arai [2], Akira Watanabe [2], Daisuke Hagiwara [3,4], Hiroki Takahashi [1]

1 Division of Bio-resources, Medical Mycology Research Center, Chiba University

2 Division of Clinical Research, Medical Mycology Research Center, Chiba University

3 Department of Life and Environmental Sciences, University of Tsukuba

4 Microbiology Research Center for Sustainability (MiCS), University of Tsukuba

P-22 Antifungal susceptibilities of clinical isolates of *Scedosporium apiospermum* in Japan

Naoto Maruguchi [1○], Hidetaka Majima [1], Teppei Arai [1], Akira Watanabe [1]
1 Division of Clinical Research, Medical Mycology Research Center, Chiba University

P-23 Profile of antimicrobial susceptibility of *Prototheca bovis* isolated from milk samples in Tokachi district, Japan

Sofia Marisel Rivelli Zea [1○], Takahito Toyotome [1]
1 Department of Veterinary Medicine, Obihiro University of Agriculture and Veterinary Medicine

P-24 *Candida albicans* induces fucosylation of intestinal epithelial cells

Daichi Mori [1○], Yoshiyuki Goto [1]
1 Division of Molecular Immunology, Medical Mycology Research Center, Chiba University

P-25 Evaluation of Antifungal Selective Toxicity Using *Candida glabrata ERG25* and Human *SC4MOL* Knock-In Strains

Keiko Nakano [1○], Michiyo Sato-Okamoto [1], Azusa Takahashi-Nakaguchi [1], Kaname Sasamoto [1], Masashi Yamaguchi [1], Hiroji Chibana [1]
1 Division of Molecular Biology, Medical Mycology Research Center, Chiba University

P-26 *Candida glabrata* genes regulating phagosome maturation in macrophages

Zhao Fujiang [1○], Azusa-Takahashi Nakaguchi [1], Michiyo Sato-Okamoto [1], Hiroji Chibana [1]
1 Division of Molecular Biology, Medical Mycology Research Center, Chiba University

P-27 Lung resident memory Th2 cells induce multinucleated giant cells that can engulf live cryptococcal cells without opsonization

Keigo Ueno [1○], Yoshitsugu Miyazaki [1]
1 Department of Fungal Infection, National Institute of Infectious Diseases

P-28 The C-type lectin receptors Dectin-1/Dectin-2 and the cytokine IL-17 are critical for protection against the fungal pathogen *Sporothrix brasiliensis*

Fabio Seiti Yamada Yoshikawa [1○], Sandro Rogerio de Almeida [2], Shinobu Saijo [1]
1 Division of Molecular Immunology, Medical Mycology Research Center, Chiba University
2 Department of Clinical and Toxicological Analysis, Faculty of Pharmaceutical Sciences, University of São Paulo

P-29 LAMP Assay for Specific and Sensitive Detection of *Madurella* spp.

Isato Yoshioka [1○], Yugo Mori [1], Ahmed Hassan Fahal [2], Emmanuel Edwar Siddig [2], Satoshi Kaneko [3], Takashi Yaguchi [1]
1 Management Unit of Microbiological Resources, Medical Mycology Research Center, Chiba University
2 Mycetoma Research Centre, University of Khartoum
3 Department of Eco-epidemiology, Institute of Tropical Medicine (NEKKEN), Nagasaki University

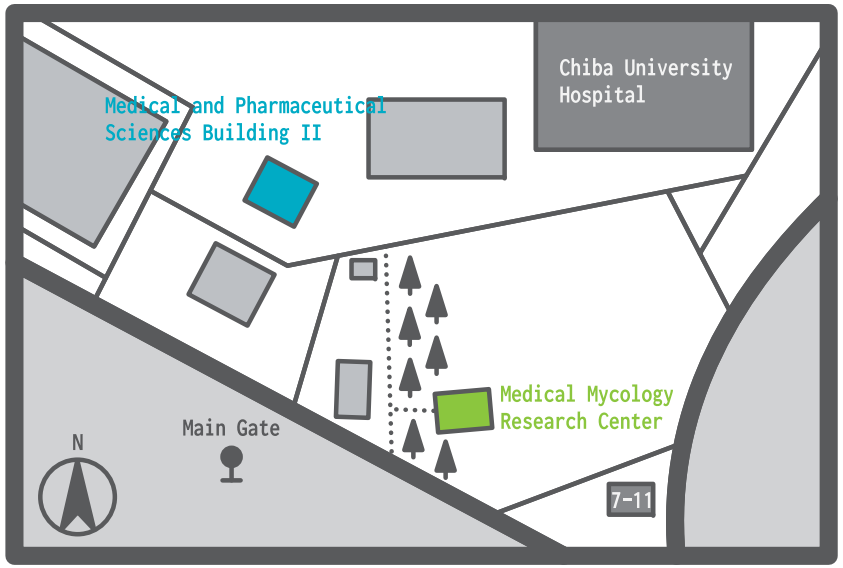
P-30 Revelation of the mechanism underlying drug resistance of *Trichophyton* strains

Yugo Mori [1○], Isato Yoshioka [1], Sayaka Ban [1], Takashi Yaguchi [1]
1 Management Unit of Microbiological Resources, Medical Mycology Research Center, Chiba University

Workshop Session

■ 09:20 - 16:25 Saturday 3 February 2024

■ Main Conference Room, 1st Basement Floor,
Medical and Pharmaceutical Sciences Building II,
Chiba University



■ PROGRAMME

09:00 - 09:20 Reception
09:20 - 09:25 Opening Remarks : Kazutoshi Shibuya
09:25 - 11:15 Workshop Session Part I
11:15 - 12:15 Lunch Break
12:15 - 14:45 Workshop Session Part II
14:45 - 15:00 Coffee Break
15:00 - 16:20 Workshop Session Part III
16:20 - 16:25 Closing Remarks

Workshop Session Part I

■ Chairperson : Hiroki Takahashi

09:25 - 10:05 ONLINE
Mda5/MAVS Signaling: Going non-viral or not?
Joshua J. Obar, PhD

10:05 - 10:45
How *Aspergillus fumigatus* protects itself when producing gliotoxin
Gustavo H. Goldman, PhD

10:45 - 11:15
Genomic diversity of the pathogenic fungus *Aspergillus fumigatus* in Japan reveals the complex genomic basis of azole resistance
Hiroki Takahashi, PhD

Workshop Session Part II

■ Chairperson : Akira Watanabe

12:15 - 12:45
A Study of Host Response in post-Influenza *Aspergillus* superinfection
Shogo Takatsuka, PhD

12:45 - 13:25
Allergic pneumonia due to bacteria and fungi
~ Hypersensitivity pneumonitis ~
Yasunari Miyazaki, MD PhD

13:25 - 14:05
Pathological tissue inflammatory memories shape the intractable pathology of chronic lung inflammation
Kiyoshi Hirahara, MD PhD

14:05 - 14:45
Gut microbiome - keystone modifier of infectious immunity and opportunities for therapy
Hein Min Tun, PhD BVSc MSc

Workshop Session Part III

■ Chairperson : Mitsutoshi Yoneyama

15:00 - 15:40 ONLINE
Autophagy and host defense against mycobacteria
Eun-Kyeong Jo, MD PhD

15:40 - 16:20 ONLINE
MTr1 inhibition as a novel approach to tackle influenza viruses
Hiroki Kato, PhD

Mda5/MAVS Signaling: Going non-viral or not?

Joshua J. Obar, PhD
Associate Professor
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Geisel School of Medicine at Dartmouth, Department of Microbiology & Immunology, 1 Medical Center Drive, Lebanon NH 03756 USA

Biography :

Josh received his Bachelor of Arts degree from Ohio Wesleyan University in 2001. He received his Ph.D. from Dartmouth College in Microbiology & Immunology in 2006 conducting his thesis work with Dr. Edward Usherwood. From 2006-2010 he conducted his post-doctoral work in Dr. Leo Lefrancois' laboratory at the University of Connecticut Health Center. In 2010 he started his own laboratory at Montana State University as an Assistant Professor, where he developed his interest in fungal biology and long-standing collaboration with Dr. Robert Cramer. In 2015, his laboratory moved to Dartmouth College, where he was promoted to Associate Professor in 2018 continuing to focus on respiratory fungal pathogens.

Abstract :

MDA5 is a cytosolic pattern-recognition receptor (PRR) that initiates interferon (IFN) responses upon its binding to double-stranded RNA (dsRNA) and its subsequent interaction with the signaling adaptor protein MAVS. Recently, our group demonstrated that MDA5 is essential for host resistance against *Aspergillus fumigatus* across a range of fungal strains. While fungal dsRNA was sufficient for activating MDA5 signaling in some *Aspergillus fumigatus* strains, it was not universal. We found that only fungal RNA from mycovirus infected strains was capable of activating MDA5. Moreover, mycovirus infection increased fungal sensitivity to the antifungal killing activity of leukocyte and dampened type 2 immunity and fungal allergic airway disease. In conclusion, our research begins to address the trans-kingdom interaction of pathogen in regulating the antifungal immune response in mammals.

How *Aspergillus fumigatus* protects itself when producing gliotoxin

Gustavo H. Goldman, PhD
Professor
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Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo

Biography :

PhD in Molecular Biology at the University of Gent, Belgium in 1993. Postdoctoral fellow at the UMDNJ, 1993-1994. Assistant, Associate, and full Professor at the Universidade de São Paulo (1994 to current days). Visiting professor at Vanderbilt University, USA, and universidade do Minho and Nova de Lisboa, Portugal. Member of the American Academy of Microbiology and Brazilian Academy of Sciences. Recipient of the Moselio Schaechter from ASM and Hans Fischer Senior Professor at the Technical University of Munich, Germany.

Abstract :

Gliotoxin (GT) is the best studied *A. fumigatus* mycotoxin with known toxic effects that impair human immune cell function. GT is also highly toxic to *A. fumigatus* and this fungus has evolved self-protection mechanisms that include (i) GT efflux pump GliA, (ii) GT neutralising enzyme GliT, and (iii) negative regulation of GT biosynthesis by GtmA. We identified a transcription factor, RglT, important for *A. fumigatus* oxidative stress resistance, GT biosynthesis and self-protection, and virulence. RglT regulates the expression of several *gli* genes of the GT biosynthetic gene cluster, including *gliT*, by directly binding to their respective promoter regions. RglT is the main regulator of GliT and this GT protection mechanism also occurs in the non-GT producing fungus *A. nidulans*.

Funding: FAPESP, Brazil and NIAID-NIH, USA

Genomic diversity of the pathogenic fungus *Aspergillus fumigatus* in Japan reveals the complex genomic basis of azole resistance

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Medical Mycology Research Center, Chiba University, Japan

Biography :

■ Education :

B.A. 2002 The Undergraduate School of Chemical Science and Technology, Kyoto University

Ph.D. 2009 Information Science, Nara Institute Science and Technology

■ Career :

2009 – 2012 Assistant Professor, Information Science, Nara Institute Science and Technology

2012 – present Associate Professor, Medical Mycology Research Center, Chiba University

Abstract :

Aspergillus fumigatus is a pathogenic fungus with a global distribution. Although azole-resistant TR-mutants (TR34 and TR46) are widely distributed, only a few TR-mutants have been isolated in Japan. The emergence of azole-resistant *A. fumigatus* (ARAf) other than the TR-mutants is a problem in Japan. Additionally, the genetic diversity of *A. fumigatus* strains in Japan remains relatively unknown. In this study, we analyzed the genome sequences of 171 strains from Japan as well as the antifungal susceptibility of these strains. We found that 22 strains were highly tolerant to itraconazole. Next, we conducted a population analysis of 876 strains by combining the available genomic data for strains isolated worldwide, which were grouped in six clades. We observed the geographic characteristics of clades such as Clade 2 where the strains from Japan were over-represented. Finally, using 640 strains from Clades 1, 2, and 4, the genomic loci associated with azole resistance were detected on the basis of a genome-wide association study and a ridge regression analysis. Thus, we revealed the complexity of the genomic mechanism underlying the emergence of ARAf strains other than the TR-mutants as well as the genomic diversity of *A. fumigatus* in Japan.

A Study of Host Response in post-Influenza *Aspergillus* superinfection

Shogo Takatsuka, PhD

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Department of Fungal Infection,
National Institute of Infectious Diseases, Japan

Biography :

■ Work Experience

Studying the technique of antibody production by DNA immunization under Dr. Chiba Joe during doctoral program (2008-2011). Assistant Professor at the Research Institute for Biomedical Sciences, Tokyo University of Science (2011-2015). Engaged in research on memory B cells under Dr. Daisuke Kitamura. Research scientist (2016-2018), Senior researcher (2019-present), at the Department of fungal infection, National Institute of Infectious Diseases. Engaged in research on host immunity in Aspergillosis.

■ Education

Department of Biological Science and Technology, Tokyo University of Science. (2011)

Abstract :

In recent years, *Aspergillus*-mediated infections have become the most common cause of death among fungal diseases. In particular, post-Influenza *Aspergillus* superinfection often results in severe disease and death, even in healthy individuals without compromised immunity. In this study, we established a model of influenza-associated pulmonary aspergillosis (IAPA) in mice and analyzed the number of *Aspergillus* in the lungs after infection and their survival rates. The results showed that the number of *Aspergillus* in the lung after infection was significantly higher than that in the group infected with *Aspergillus* infection alone. The survival rate of IAPA group decreased to about 40% by day 9 after *Aspergillus* superinfection. In addition, β-D glucan levels in the lungs were elevated due to the lack of clearance of *Aspergillus*. To artificially reproduce the elevated β-D glucan concentration in the lungs, lower respiratory administration of β-D glucan after influenza virus infection induced a severe IAPA-like inflammatory response. A mechanism for this rapid increase in inflammatory response was suggested to be the production of large amounts of IL-6 by alveolar macrophages in response to β-D glucan. These results may contribute to our understanding of the pathogenesis of IAPA.

Allergic pneumonia due to bacteria and fungi ~ Hypersensitivity pneumonitis ~

Yasunari Miyazaki, MD PhD

Professor

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Department of Respiratory Medicine,
Tokyo Medical and Dental University Hospital, Japan

Biography :

March 1990 Graduated from Tokyo Medical and Dental University
June 1990 Tokyo Medical and Dental University Hospital Internal Medicine Resident
July 1991 Kudanzaka Hospital Internal Medicine
October 1993 Tokyo Medical and Dental University Hospital Internal Medicine
October 1996 Tokyo Metropolitan Bokutoh Hospital Internal Medicine
July 1998 Director of Internal Medicine, Asama General Hospital
December 2001 The University of Utah Post-Doc Researcher
October 2009 associate professor, Tokyo Medical and Dental University Sleep Medicine
August 2012 Professor, Tokyo Medical and Dental University Health Center
May 2018 Professor Department of Respiratory Medicine, Tokyo Medical and Dental University

Abstract :

Hypersensitivity pneumonitis is allergic pneumonia and is classified as an interstitial lung disease. There are over 300 causative antigens, including bacteria and fungi, but it is not an infectious disease.

Up until now, there were no diagnostic standards because it was difficult to identify the causative antigen. However, with the accumulation of clinical trials and improvements in diagnostic measures, provisional diagnostic standards and treatment guidelines have been announced in Europe, the United States, and Japan.

This disease is classified into non-fibrotic and fibrotic, and fibrotic hypersensitivity pneumonitis has a poor prognosis. Summer-type hypersensitivity pneumonitis accounts for 80% of non-fibrotic hypersensitivity pneumonitis and is caused by *Trichosporon asahii*. There have been almost no reports only in Japan. This fungus breeds during the rainy season, so symptoms occur from summer to autumn. Among fibrotic hypersensitivity pneumonitis, bird-related hypersensitivity pneumonitis is the most common at 60%, followed by summer-type hypersensitivity pneumonitis, which comes in second at around 15%, which is lower than the proportion of non-fibrotic hypersensitivity pneumonitis.

Although *Trichosporon asahii* antibody titers can be measured, it is difficult to measure antibodies for other fungi. The causative fungus will likely be identified through an investigation of the residential environment. In therapy, it is essential to remove antigens from the environment, so there is a need for antigen identification. Today we will provide an overview of hypersensitivity pneumonitis caused by other bacteria and fungi, including our efforts to identify antigens.

Pathological tissue inflammatory memories shape the intractable pathology of chronic lung inflammation

Kiyoshi Hirahara, MD PhD

Professor

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Department of Immunology,
Graduate School of Medicine, Chiba University, Japan

Biography :

Dr. Hirahara graduated from Niigata University school of Medicine in 2001. He was engaged in clinical practice as a physician, specifically in respiratory medicine for more than three years and he started a Ph.D. course supervised by Professor Toshinori Nakayama in the Department of Immunology at Chiba University in 2004. From 2009 to 2013, he worked as a postdoctoral fellow with Dr. John J. O'Shea at the MIIB of the US NIAMS, NIH. In 2013, he joined the Department of Immunology at Chiba University as a faculty member. In 2022, he was appointed professor in Department of Immunology at Chiba University. Dr. Hirahara is now mainly carrying out research on the "tissue inflammatory memories" in the lung. Dr. Hirahara received the 10th Young Investigator Award (Japanese Society for Immunology, Japan, 2015) and 2017 Seymour and Vivian Milstein Young Investigator Award (International Cytokine & Interferon Society, 2017).

Abstract :

Severe type 2 inflammation cause tissue damage in the patients with intractable allergic diseases. Ex-inflamed tissues store "tissue inflammatory memories", which consists of tissue resident memory T (TRM) cells and ectopic lymphoid tissues such as inducible bronchus associated lymphoid tissue (iBALT). The storage of the pathological tissue inflammatory memories causes chronic inflammation. An integrated understanding of the mechanisms underlying the induction of tissue inflammatory memories is required for the establishment of next-generation therapies for intractable allergic diseases. In this seminar, I will focus on chronic airway inflammation. I will introduce our recent research progress regarding the heterogeneity of memory-type pathogenic TRM cells; that is, the IL-5-producing memory-type Tpath2 subset is critical for the recruitment and differentiation of eosinophils in the allergic airway inflammation, while Amphiregulin-producing Tpath2 cells are critical for the induction of fibrotic changes. In the case of chronic allergic conjunctivitis, we recently identified CGRP-expressing Tpath2 cells that induce severe itching. In order to develop new therapeutic strategies for intractable allergic diseases, it will become increasingly important to understand the precise features of Tpath cells.

1. Shinoda K., et al. PNAS 113(20): E2842-51 (2016)
2. Morimoto Y., et al. Immunity 49(1): 134-150.e6 (2018)
3. Ichikawa T., et al. Nat. Immunol. Nov;20(11):1469-1480. (2019)
4. Okano M., et al. Immunity (2022) 55(12):2352-2368.e7 (2022)
5. Sato Y., et al. Nat. Rev. Nephrol. Aug;19(8):525-537 (2023)

Gut microbiome — keystone modifier of infectious immunity and opportunities for therapy

Hein Min Tun, PhD BVSc MSc
Associate Professor ; Associate Director
heintun@cuhk.edu.hk

JC School of Public Health and Primary Care, The Chinese University of Hong Kong ; Microbiota I-Center (MagIC)

Biography :
Prof. Hein Tun is an Associate Professor at the JC School of Public Health and Primary Care, the Chinese University of Hong Kong (CUHK), an Associate Director at Microbiota-I Center (MagIC), and the PI of System Microbiology and Antimicrobial Resistance (SMART) Lab at Li Ka Shing Institute of Health Sciences, CUHK. In parallel, he is an Adjunct Professor at the Nanjing Medical University and an Honorary Associate Professor at the University of Hong Kong. His research interests range from studies on the mechanistic and functional roles of microbiome in health and diseases to One Health surveillance of antimicrobial-resistant bacteria and resistome. He published more than 100 original research articles in leading international journals. He serves the editorial boards of Cellular and Molecular Life Sciences and Frontiers in Microbiology. Moreover, he has received several international research awards including the Gold Medal at 2021 Inventions Geneva Evaluation Days, Canadian Institute of Health Research Fellowship and Dik Zwart Award.

Abstract :
The global recurrent threat of respiratory virus pandemics highlights the essential needs of developing alternative prophylaxis and therapeutics of respiratory virus infection. Host and environmental factors drive proper establishment of the gut microbiome and immune system especially during early life, which in turn is related to consecutive susceptibility to respiratory virus infection. Our recent studies demonstrated gut microbiota as the foundation to orchestrate immune response to COVID-19 vaccines and the persistence of those antibodies in the body. In parallel, our mechanistic studies also illustrated that early-life gut dysbiosis extensively impacted the development of innate immunity and the pathogenesis of influenza A and SARS-CoV-2 infection. Moreover, certain keystone gut bacteria species have the potentials of to modulate both innate and adaptive immunity and enhance antiviral responses.

Autophagy and host defense against mycobacteria

Eun-Kyeong Jo, MD PhD
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Department of Microbiology, College of Medicine, Chungnam National University (CNU) ; Infection Control Convergence Research Center, CNU, Korea

Biography :
Eun-Kyeong Jo, M.D., Ph.D. has been a professor at Chungnam National University since 2003. She has published ~200 scientific articles. Her discoveries focused on the mechanisms by which host autophagy impacts the activation of immune defense and revealing the new function of nuclear receptors in the context of infection and inflammation. Prof. Jo has served as a Director of Medical Research Centers for the last 16 years, which has been one of the leading groups studying infection and immunity in Korea. Furthermore, she has received several prestigious awards, including the Wunsch Medical Award in 2015 and the L'Oréal-UNESCO for Women in Science Award in Korea in 2020.

Abstract :
Autophagy is a lysosomal degradation pathway to eliminate intracellular cargos, thus maintaining homeostasis against various stresses. Additionally, autophagy serves as a crucial effector mechanism in the innate defense against intracellular bacterial infection. Over the past two decades, our focus has centered on unraveling the roles of autophagy and elucidating the mechanisms through which it activates host protective immunity against *Mycobacterium tuberculosis* infection. Key players in the activation of the autophagy pathway include signaling through the vitamin D receptor, the AMP-activated protein kinase pathway, estrogen-related receptor-α, sirtuin 3 activation, and various nuclear receptors. This presentation will introduce our previous and ongoing works for antibacterial autophagy against mycobacteria, shedding light on the manipulation of autophagy as a strategy for enhancing host defense against mycobacterial infections.

MTr1 inhibition as a novel approach to tackle influenza viruses

Hiroki Kato, PhD
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Institute of Cardiovascular Immunology,
University Hospital Bonn, University of Bonn, Germany

Biography :

Hiroki Kato is a Principal Investigator at the Institute of Cardiovascular Immunology, University of Bonn, Germany. His research focuses on uncovering the mechanisms of replication in pathogenic viruses and understanding the pathogenesis of autoimmune diseases caused by dysregulated innate immunity. After completing his Ph.D. under the supervision of Prof. Shizuo Akira at Osaka University, he worked as a Postdoc in Prof. Craig Mello's lab at the University of Massachusetts. Subsequently, he served as an Associate Professor in Prof. Takashi Fujita's lab at Kyoto University. Since 2018, he has been independently leading his own research in the current position.

Abstract :

RNA methyltransferase MTr1 catalyzes 2'-*O*-methylation of the first nucleotide (N1-2'-*O*-Me) of immature cap0 mRNA and snRNA to generate mature cap1. The physiological role of MTr1 in viral infection remains elusive.

Our results revealed that N1-2'-*O*-Me by MTr1 is required for the replication of influenza A virus (IAV). IAV and other *Orthomyxoviridae* as well as *Bunyavirales* are known to synthesize cap1 mRNA by "cap snatching" mechanism. MTr1 was also required for replication of influenza B virus (IBV), but not for that of other *Orthomyxoviridae* including influenza D virus (IDV) and Thogoto virus (THOV), and *Bunyavirales* including Rift Valley fever virus (RVFV).

Further investigation indicated that N1-2'-*O*-Me is essential for the interaction between host capped RNA and IAV polymerase subunit PB2 to initiate cap-snatching.

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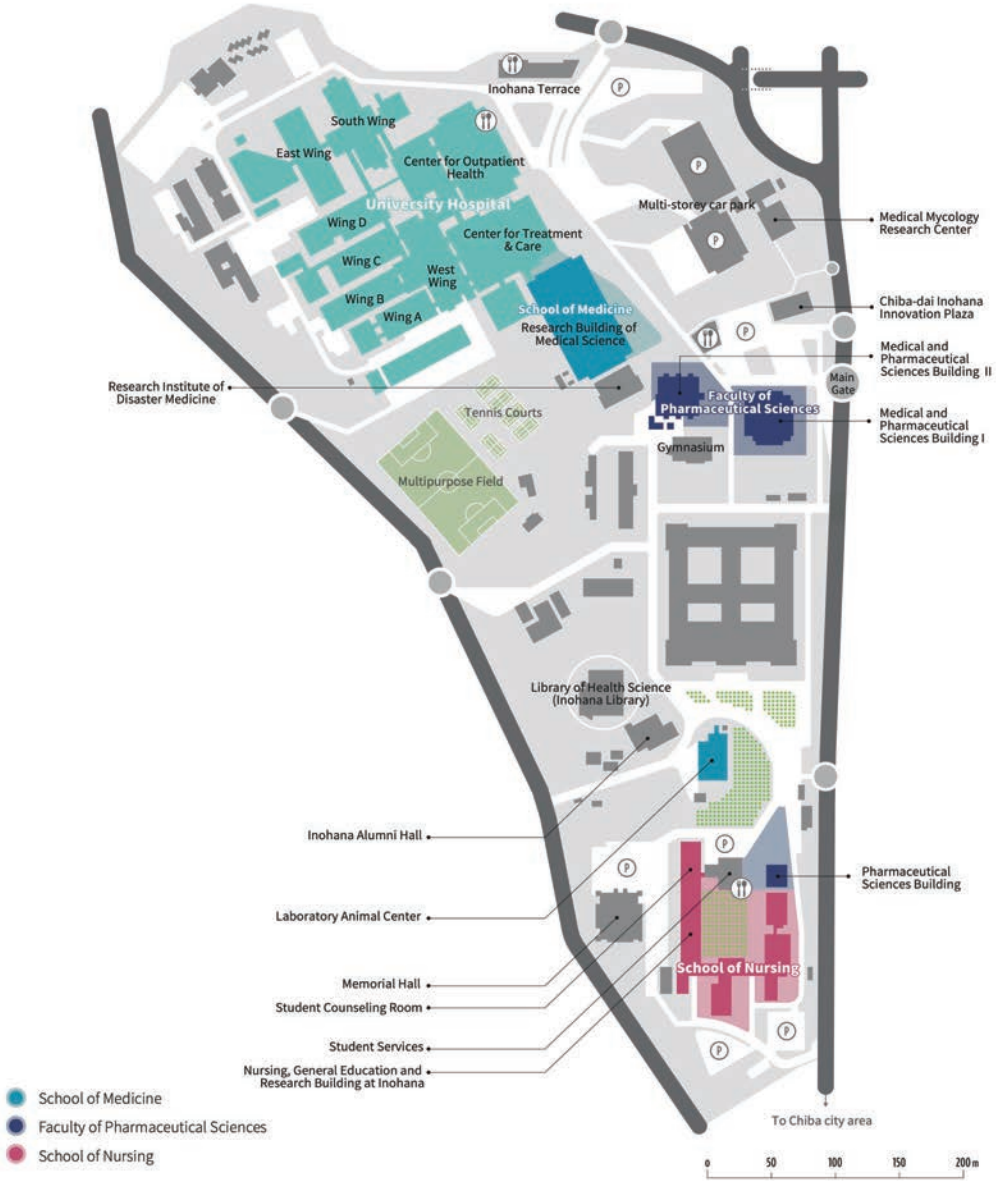

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1 min walk from **Chibadai Kangogakubu Iriguchi** or **Chibadai igakubu, Yakugakubu Iriguchi (Keisei Bus)** to the Main Gate
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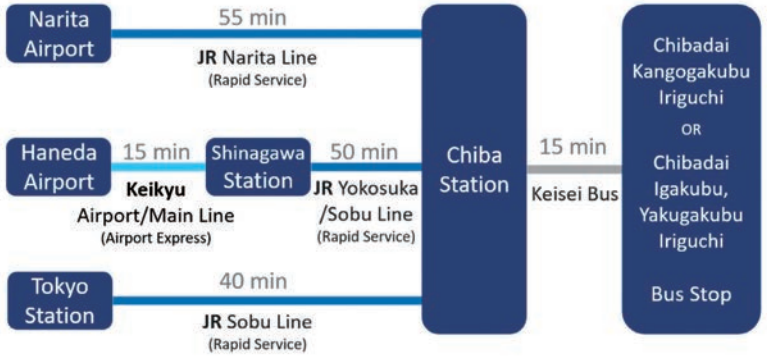
15 min by taxi from **Chiba Station (JR)** to the Main Gate

Public Transportation



The routes indicated above are examples. The most convenient route may be different depending on the day and the time.