WELCOME MESSAGE

On behalf of the organizers, it is our great pleasure to welcome you to The International Symposium on Advanced Immunology 2026 (also known as the 15th International Symposium of IFReC). This symposium is co-hosted by ©Senri Life Science Foundation and Immunology Frontier Research Center (WPI-IFReC), The University of Osaka.

World-leading scientists will gather at this two-day symposium to present lectures highlighting recent achievements in basic research in microbiology and immunology. On the first day, Professor Shimon Sakaguchi of IFReC, a 2025 Nobel Laureate, will deliver a lecture. In addition to well-established scientists, promising early-career researchers have also been selected as speakers, particularly for the second day of the symposium.

This scientific meeting provides a platform for researchers and students from a wide range of disciplines. We hope that the active participation of university researchers, researchers from industry, and clinical scientists will foster new interactions and promote future collaborations.

We would like to express our sincere gratitude to all participants, and we hope that this symposium will offer a valuable opportunity to exchange ideas and expertise, thereby contributing to the further advancement of microbiology, immunology, and the life sciences.

We wish you a rewarding and intellectually stimulating time at the symposium.

Symposium Organizers

Shizuo Akira, MD/PhD

Kiyoshi Takeda, MD/PhD

Schedule on February 5

9:45 am - Registration

10:30 - 10:40	**Opening remarks by Shizuo Akira** (President of the Senri Life Science Foundation)
10:40 - 11:20	**Tadamitsu Kishimoto (The University of Osaka, Japan)** 'Interleukin 6; from its discovery to clinical application Past, Present and Future'
11:20 - 12:00	**James Di Santo (Institut Pasteur, France)** 'A T cell-centric View of Human Innate Lymphoid Cell Differentiation'
12:00 - 13:30	**Group Photo & Lunch**
13:30 - 14:10	**Kenneth Murphy (Washington University in St. Louis, USA)** 'Dendritic cell diversity in directing discrete immune modules'
14:10 - 14:50	**Miriam Merad (Icahn School of Medicine at Mount Sinai, USA)** 'Macrophages: "Master regulators of inflammation control"'
14:50 - 15:10	**Break**
15:10 - 15:50	**Diane Mathis (Harvard University, USA)** 'Meningeal Treg control of brain health and degeneration'
15:50 - 16:30	**Shimon Sakaguchi (The University of Osaka, Japan)** 'Treatment of immunological diseases by converting disease-mediating T cells into Tregs'
16:40 -	**Reception party at "Senri Room" on the 6th floor**

Notice

- ✓ All the sessions are conducted in English.
- ✓ All the participants are required to wear name tags at the symposium site.
- ✓ Eating, photo and video shooting are prohibited in the conference room.

Schedule on February 6

9:15 am - Registration

10:00 - 10:40	**Christophe Benoist (Harvard University, USA)** 'Immgen T'
10:40 - 11:05	**Shunsuke Mori (The University of Osaka, Japan)** 'Discrimination of Self and Neoself Antigens by T Cells in Immune Homeostasis'
11:05 - 11:30	**Kazuki Nagashima (Harvard University, USA)** 'Mapping the T cell repertoire to a model system of the human gut microbiome'
11:30 - 11:55	**Caterina Faliti (Emory University, USA)** 'Mapping B Cell Tolerance Breakdown in Lymph Nodes of Lupus Patients'
11:30 - 13:30	**Lunch**
13:30 - 13:55	**Ryuya Edahiro (The University of Osaka, Japan)** 'Integrative projection of multi-layer omics data into the single-cell immune landscape'
13:55 - 14:20	**Akiko Oguchi (RIKEN/ Kyoto University, Japan)** 'Mapping RNA dynamics in immunity in single cells and space'
14:20 - 14:45	**Hiutung Chu (University of California San Diego, USA)** 'Inflammation shapes bacterial evolution and host immunity'
14:45 - 15:05	**Break**
15:05 - 15:45	**Fiona Powrie (The University of Oxford, UK)** 'Gut Reactions: Immune regulatory pathways in the intestine'
15:45 - 16:25	**Kiyoshi Takeda (The University of Osaka, Japan)** 'Identification of microbiota-derived metabolite and T cell subset implicated in the pathogenesis of Crohn's disease'
16:25 - 16:35	**Closing remarks by Kiyoshi Takeda** (Director of IFReC)

Organizers

- The Senri Life Science Foundation, Osaka, Japan
- Immunology Frontier Research Center (WPI-IFReC), The University of Osaka

Interleukin6; from its discovery to clinical application
Past, Present and Future

Tadamitsu Kishimoto

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Interleukin6 (IL-6), promptly and transiently produced in response to infections and tissue injuries, contributes to host defense through the stimulation of acute phase responses, hematopoiesis, and immune reactions. Although its expression is strictly controlled by transcriptional and posttranscriptional mechanisms, dysregulated continual synthesis of IL-6 plays a pathological effect on chronic inflammation, autoimmunity, and Cytokine release syndrome (CRS). CRS is a life-threatening complication induced by systemic inflammatory responses to infections including bacteria as well as SARS-CoV2 and CAR-T cell therapy. Patients diagnosed with CRS from sepsis, acute respiratory distress syndrome (ARDS), or burns showed common manifestations: strikingly elevated levels of the four proinflammatory cytokines interleukin (IL)-6, IL-8, monocyte chemotactic protein-1 (MCP-1), and IL-10 and the coagulation cascade activator, plasminogen activator inhibitor-1 (PAI-1).

Endothelial IL-6 trans-signaling promoted vascular damage and inflammatory responses via hypoxia-inducible factor-1α (HIF1α)-induced glycolysis. Using pharmacological inhibitors targeting HIF1α activity or mice with the genetic ablation of gp130 in the endothelium, we found that inhibition of IL6R (IL-6 receptor)-HIF1α signaling in endothelial cells protected against vascular injury caused by septic damage and provided survival benefit in a mouse model of sepsis. In human, the department of acute clinical medicine at Osaka University applied anti-IL-6R antibody to the treatment of severe sepsis patients and at present rescued 8 patients. As mentioned, anti-IL-6R antibody could rescue various diseases induced by overproduction of IL-6.

A T cell-centric View of Human Innate Lymphoid Cell Differentiation

James P. Di Santo

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Despite the similarities between Th cells and innate lymphoid cells (ILC) with respect to development, differentiation, plasticity potential and memory formation, our understanding of the regulatory mechanisms that orchestrate the generation of these cells remains incomplete. This is especially pronounced in human ILC biology, where much of the current literature is based on clinical observation and less often validated through hypothesis-driven experimentation. Generating basic knowledge in this area is essential in order to better understand the biological roles of human ILC during immune responses and to establish the key determinants of their protective immunity. Here, we test the hypothesis that rules controlling human Th differentiation also guide maturation of human ILC from their committed circulating precursors. Using a multi-signal framework, we identify key checkpoints in human ILC differentiation and assess how modification of these pathways affects mature ILC function. Discoveries made herein should facilitate the creation of autologous or off-the-shelf 'designer' ILCs with new specificities and defined, stable properties that may find translational applications for the treatment of human disease.

Dendritic cell diversity in directing discrete immune modules

Ken Murphy

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St. Louis, Missouri, USA.

Dendritic cells (DCs) are essential regulators of innate and adaptive immune responses, acting as sentinels for pathogens and directing the activation of appropriate immune modules. Early work recognized their profound capacity for driving T cell expansion, but the precise delineation of their precise mechanisms was complicated by their rarity and phenotypic overlap with other mononuclear phagocytes. Our studies over the last several years leveraged transcriptional analysis and other genetic tools to help define the underlying developmental and functional components of DC lineages, by identifying clonogenic progenitors for the two major subsets, cDC1 and cDC2, characterized by discrete transcriptional identities and specialized functions. Our studies have focused most intensely on the transcriptional circuitry governing subset specification and diversification. A cascade of action of the transcriptional regulators NFIL3, ZEB2, ID2, BATF3, and C/EBPs cooperatively regulate the complex interplay between the several IRF8 enhancers to control the specification and commitment of progenitors to the cDC1 lineage. The cDC1 lineage specializes in priming the cytotoxic T lymphocyte (CTL) responses, acting as the obligate cell type in vivo in natural settings for cross-presentation (XP) of viral and tumor antigens. We identified the key component WDFY4, which is strictly required for cDC1 XP and subsequent tumor rejection, and continue to investigate the cellular mechanisms in controlling a vesicular antigen processing pathway. Parallel studies explored cDC2 development (e.g., KLF4- and Notch2-dependent), which contribute to distinct type 2 and 3 immune modules. Remaining gaps include how DCs regulate the divergence of memory vs. effector progenitors and the expansion of effectors through co-inhibitory and co-stimulatory pathways. Better understanding of these processes could provide additional targets for enhance anti-tumor therapies, particularly by modulating the cDC1 pathway, which is critically required for effective anti-tumor immunity and success in checkpoint blockade therapies.

Macrophages: "Master regulators of inflammation control"

Miriam Merad

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Macrophages are central regulators of inflammation and tissue homeostasis, yet their distinct roles in health and disease are only beginning to be fully appreciated. In this talk, I will discuss two major macrophage functions that can be harnessed therapeutically to influence the outcome of major human diseases. I will first discuss tissue-resident macrophages, which are long-lived cells that act as guardians of tissue integrity. These cells support organ homeostasis by maintaining stem cell niches, sustaining neuronal and vascular function, and tuning inflammatory responses to injury. In contrast, monocyte-derived macrophages are recruited during tissue injury and play a dominant role in pathogenic inflammation, contributing to chronic inflammatory diseases and driving cancer progression. I will highlight how targeting monocyte-derived macrophages can significantly impact cancer progression.

I will then discuss how aging is associated with a profound shift in macrophage balance. Aging is characterized by the attrition and dysfunction of resident tissue macrophages, together with expanded myelopoiesis and accumulation of inflammatory macrophages within tissues. This age-associated myeloid inflammation creates a permissive environment for tumor initiation and progression. I will present evidence that myeloid-driven inflammation is a key contributor to cancer progression with age, and that therapeutic blockade of inflammatory pathways can limit disease progression in mice and human. Together, these findings highlight macrophages as central orchestrators of inflammation across the lifespan and suggest that targeting age-associated myeloid inflammation represents a promising strategy for cancer prevention and intervention.

Meningeal Treg control of brain health and degeneration

Diane Mathis

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Distinct populations of Foxp3+CD4+ regulatory T cells (Tregs) have by now been found in a number of non-lymphoid tissues, e.g. visceral adipose tissue, skeletal muscle, the skin, the brain/meninges and the heart. These "tissue Tregs" populations are distinct from those circulating through lymphoid organs in their transcriptomes, T-cell-receptor repertoires and growth/survival factor dependencies. Beyond their immunologic functions in controlling local responses to pathogens, they exert a variety of non-immunologic roles in ensuring tissue homeostasis – for example, regulating local and systemic metabolism, supervising tissue repair and regeneration, and controlling nociceptive processing. To illustrate these points, I will discuss the unique Treg compartment in the dural meninges that encases the brain, focusing primarily on its role in safeguarding brain homeostasis but also introducing new results on their impact on the development of Alzheimer's Disease in mouse models.

Treatment of immunological diseases by converting disease-mediating T cells into Tregs

Shimon Sakaguchi[1,2], R. Kawakami[2], M. Arai1, and N. Mikami[1]

[1]Immunology Frontier Research Center, The University of Osaka

[2]Institute for Life and Medical Sciences, Kyoto University

Regulatory T cells (Tregs), specifically expressing the transcription factor FoxP3 in the nucleus, CD25 and CTLA-4 on the cell surface, are actively engaged in the maintenance of immunological self-tolerance and homeostasis. There are numerous demonstrations mainly from animal models that self-tolerance can be reinstated and autoimmune disease be treated by expanding endogenous natural Tregs (nTregs) or generating Tregs from Tconvs (induced Tregs: iTregs). An outstanding issue for Treg-based therapy of immunological diseases is then how to expand or generate antigen-specific Tregs for disease-specific treatment. Our attempts for this aim have been to convert antigen-specific Tconvs, especially disease-mediating effector/memory-type T cells, into functionally stable FoxP3+ Tregs. We have recently shown that inhibition of CDK8/19, a serine threonine kinase involved in a T-cell signaling pathway, is able to evoke Foxp3 expression in Tconv cells including effector/memory T cells even under in vivo and in vitro conditions abundant in proinflammatory cytokines. In addition, in the course of in vitro generation of iTregs from antigen-specific naive or effector/memory Tconvs, deprivation of CD28 co-stimulatory signal is able to establish Treg-specific epigenetic changes, especially Treg-specific CpG demethylation, at enhancer regions of Treg-signature genes including FoxP3, CD25, and CTLA-4. These findings in mice have enabled in vitro generation of functionally stable iTregs from peripheral blood Tconvs in autoimmune disease patients by a combination of a newly developed CDK8/19 inhibitor and CD28 signal deprivation, and by repeating this iTreg induction process. It will be discussed how iTregs akin to nTregs in function and stability can be generated from the peripheral blood of autoimmune disease patients and how they can be instrumental in treating autoimmune and other inflammatory diseases.

Immgen T

David Zemmour and **Christophe Benoist**

The immgen T consortium

Department of Immunology, Harvard Medical School, Boston, MA, USA

A group of 42 labs collaborated, under the auspices of the "immgen T" program, to perform a systematic exploration of the diversity of T lymphocytes in the mouse. The goal was to probe comparatively and uniformly T cells in all possible organ locations and immunological challenges. Spanning 853 samples across 97 experiments, single-cell analyses jointly determined gene and protein expression as well as αβTCR composition. The results bring forth a number of striking observations: unexpected relationships between T cells under different conditions, unrecognized non-canonical T cells, and unforeseen facets of the diversity, selection and organismal distribution of the TCR repertoire. The data make one revise relationships between immunological function, gene programs, and cell types/states. Most importantly, the breadth of the data harmonizes T cell diversity overall, and provides an integrated framework into which all T cells can be integrated, either by computational processing that maps transcriptome datasets into the immgen T framework, or with flow cytometry panels that map directly onto the immgen T framework. We will discuss these discoveries, as well as the community tools that enable public use of the framework.

Discrimination of Self and Neoself Antigens by T Cells in Immune Homeostasis

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The discrimination of self- and nonself-antigens by T cells is the fundamental concept of immunology. However, this concept alone does not allow us to understand the mechanism of autoimmunity, in which the immune response is elicited against self-antigens. In particular, it remains unclear why different self-antigens are targeted in different autoimmune diseases, such as type I diabetes, systemic lupus erythematosus (SLE) and multiple sclerosis. The invariant chain is a non-polymorphic molecule that associates with newly synthesized MHC-II molecules at the endoplasmic reticulum and transports the MHC-II to lysosomal compartments, where it acquires peptide antigens. At low levels of invariant chain expression, normal peptide antigen presentation by MHC-II is severely impaired and unusual self-antigens, termed neoself-antigens, are presented on MHC-II. When neoself-antigen presentation was induced by deletion of the invariant chain in adult mice, neoself-reactive T cells were clonally expanded, leading to the development of a lupus-like systemic autoimmune disease. When neoself-reactive CD4+ T cells were transferred into congenitally invariant chain-deleted mice, they showed autoantibody production, indicating that neoself-reactive T cells play a pathogenic role. In SLE patients, approximately 10% of the TCR repertoire of clonally expanded CD4+ T cells is reactive to neoself-antigens, suggesting that neoself-antigens are the primary target of autoreactive T cells in SLE. Further analyses of neoself-reactive TCRs from lupus patients revealed that neoself-reactive TCRs recognize specific self-antigens presented on MHC-II in the absence of invariant chain. Epstein-Barr virus reactivation was involved in the presentation of neoself-antigens through downregulation of the invariant chain. Our results showed that self-antigens can be further subdivided into classical self-peptide antigens and neoself-antigens depending on the level of the invariant chain. Since T cells are not tolerant to neoself-antigens, presentation of neoself-antigens on MHC-II caused by abnormal antigen presentation activates neoself-reactive T cells to induce autoimmunity. Our findings shed light on the underlying causes of autoimmune diseases.

Mapping the T cell repertoire to a model system of the human gut microbiome

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Certain bacterial strains from the microbiome induce a potent, antigen-specific T cell response. Previous reports have profiled strains from the gut microbiome under artificial conditions of mono-colonization. While this approach can identify strains that have a potential to modulate immune cell function, it does not reveal how a strain behaves in the physiological context of a complex community. Here, we colonize germ-free mice with a complex defined community (>100 bacterial strains) and profile T cell responses to each strain individually. Unexpectedly, the pattern of T cell responses suggests that many T cells in the gut repertoire recognize multiple bacterial strains from the community. We constructed T cell hybridomas from 92 T cell receptor (TCR) clonotypes; by screening every strain in the community against each hybridoma, we find that nearly all the bacteria-specific TCRs exhibit a one-to-many TCR-to-strain relationship, including 13 abundant TCR clonotypes that are polyspecific for 18 Firmicutes in the community. We discover that the 13 TCRs share a single target: a conserved substrate-binding protein (SBP) from an ABC transport system. Treg and Th17 cells specific for the SBP are abundant in community-colonized and SPF mice. Our work reveals that T cell recognition of Firmicutes is focused on a widely conserved cell-surface antigen, opening the door to new therapeutic strategies in which colonist-specific immune responses are rationally altered or redirected.

Mapping B Cell Tolerance Breakdown in Lymph Nodes of Lupus Patients

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Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease driven by abnormal B and T cell reactivity against self-antigens, leading to persistent autoantibody production and tissue damage. Despite advances in understanding, the mechanisms underlying immune tolerance breakdown and the contributions of specific immune cell subsets remain poorly defined, largely due to limited access to human lymphoid tissues.

Central and peripheral tolerance checkpoints normally eliminate or silence autoreactive cells. Our previous work demonstrated that 9G4 autoreactivity in SLE arises from defects in naïve B cell tolerance and extrafollicular (EF) differentiation, as well as from dysregulated germinal center (GC) activity. GCs are sites where T helper cells guide B cell selection and affinity maturation; in SLE, aberrant GC activity fosters self-reactivity. However, the mechanisms controlling autoreactive cell selection, localization, and release into circulation remain unclear.

Lymph node fine needle aspirates (LN-FNAs) now enable minimally invasive sampling of tissue-resident immune cells, allowing detailed analysis of their origins, phenotypes, and trafficking. This approach is particularly relevant in the context of emerging therapies such as CAR-T cells that target autoreactive B cells. LN-FNAs permit direct monitoring of GC activity and B cell differentiation in vivo.

We profiled LN-resident immune cells from 50 SLE patients and 50 matched healthy controls using advanced serological and cellular tools. Paired blood immunophenotyping provided complementary insights into circulating B cell subsets and antibody specificities. High-dimensional 43-color flow cytometry identified major B cell populations and antigen-specific cells using tetramerized probes.

Our findings reveal hyperactive lymph node immunity in SLE, characterized by plasma cell expansion, GC activation, and loss of tolerance. Characterization of VH4-34 B cell autoreactivity highlighted a major contribution of tissue B cell compartments and defective tolerance checkpoints in lupus donors. These cells recognized multiple self-antigens within their antibody repertoire, defining key mechanisms underlying tolerance loss and disease pathogenesis.

Integrative projection of multi-layer omics data into the single-cell immune landscape

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Multi-omics molecular quantitative trait locus (mol-QTL) analyses elucidate biological mechanisms of human diseases, while current mol-QTL catalogues are mostly at bulk resolution and centered on Europeans. Here, we constructed immune single-cell atlas with multi-layer omics from 235 Japanese persons, including patients with coronavirus disease 2019 (COVID-19) and healthy individuals. The dataset consists of single-cell transcriptomics from >1.5 million peripheral blood mononuclear cells, host genetics, plasma proteomics, and gut metagenomics. We mapped the germline genetic effects on gene expression within immune cell types and across cell states. We elucidated cell type and context-specific HLA and genome-wide associations with T/B cell receptor repertoires (e.g., COVID-19 and HLA class I interactions in CD8+ T cells). Colocalization utilizing dynamic genetic regulation of gene expression provided better understandings of genome-wide association signals. Differential gene and protein expression analyses revealed cell type and context-specific effects of polygenic risk scores for COVID-19 hospitalization. Leveraging whole-genome sequencing and SNP genotyping, we projected various somatic mutations such as mosaic chromosomal alterations (mCAs), loss of the Y chromosome (LOY), and mitochondrial DNA heteroplasmy into single-cell resolution, which were highly cell type-specific. We identified immune features specific to somatically mutated cells (e.g., monocyte-specific accumulation of LOY). In-vitro analysis of clonally expanded mCAs in a COVID-19 patient using single-cell B cell receptor showed no reactivity against SARS-CoV-2 antigens. Single-cell technology resolved associations between disease-related gut bacteria and peripheral immune cells abundance. Thus, immune cells were dynamically regulated in a cell state-dependent manner characterized by multi-omics profiles. Our study shows a value of multi-omics anchored by single-cells to interpret biological phenomena at fine resolution.

Mapping RNA dynamics in immunity in single cells and space

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Precise regulation of gene expression is fundamental to immune cell function, yet standard scRNA-seq provides only a limited view of RNA regulation. We have developed single-cell transcriptomic strategies that enable high-resolution analysis of RNA regulation at transcription start site and isoform levels. These approaches extend immune transcriptomics beyond gene-level expression, allowing a more detailed characterization of immune cells and molecular heterogeneity.

Building on this foundation, we are developing a next-generation spatial RNA sequencing platform designed to overcome the 3′ -end bias inherent to most existing spatial methods. By achieving gene-body–wide coverage while preserving spatial information, this approach enables accurate analysis of transcript structures and isoform diversity within tissues. Although applications to immune systems are still emerging, this technology allows spatially resolved interrogation of transcription initiation, RNA structure, and isoform usage in complex tissue contexts. Together, these technologies provide a framework for mapping RNA dynamics in immunity across single cells and space, offering new insights into immune cell organization and the regulatory programs underlying immune-mediated diseases.

Inflammation shapes bacterial evolution and host immunity

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Chiba University-UCSD Center for Mucosal Immunology, Allergy and Vaccines (cMAV)

Chronic inflammation profoundly alters host-microbe interactions, yet its impact on the evolutionary trajectories of resident bacteria remains poorly understood. While inflammatory diseases such as inflammatory bowel disease (IBD) are associated with extensive shifts in the composition of the microbial community, whether inflammation drives genetic adaptation within persisting bacterial lineages, and how such evolution influences host immunity, is unclear. Here, we integrate longitudinal human metagenomics, experimental evolution under oxidative stress, and gnotobiotic mouse models of colitis to examine how inflammatory environments shape bacterial evolution in the gut. In IBD patients, we identify recurrent inflammation-associated allele frequency shifts enriched in bacterial stress-response, iron-handling, and capsule-associated pathways. Using Bacteroides fragilis as a tractable model, experimental evolution reveals convergent genetic changes that enhance resistance to inflammatory stress but are also associated with increased immunogenicity, including elevated pro-inflammatory responses, Th17 polarization, and worsened colitis severity in vivo. Long-read sequencing of a longitudinally sampled Crohn's disease patient further reveals inflammation-linked selective sweeps and a mobile genetic element encoding iron acquisition functions that dominates during active disease and is lost in remission. Together, these findings support a model in which inflammation not only reshapes microbial ecology but also drives within-host bacterial evolution with functional consequences for immune responses, potentially further exacerbating inflammatory disease states.

Gut Reactions: Immune regulatory pathways in the intestine

Fiona Powrie

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The gastrointestinal tract is home to trillions of commensal bacteria that play an important role in nutrition, immune system development and host defence. In inflammatory bowel disease, a chronic debilitating disease of the gastrointestinal tract, there is a breakdown in the healthy dialogue between the host and its microbial residents resulting in chronic inflammation in the bowel. Utilising model systems, I will discuss pathways of regulatory T cell adaptation in the intestine and the role of tissue niches and microbiota derived signals in determining the balance between tolerance and inflammation. Our results highlight the importance of spatial cues for healthy host microbial cross-talk. Further understanding of these pathways may provide new approaches to tackle chronic inflammatory diseases.

Identification of microbiota-derived metabolite and T cell subset implicated in the pathogenesis of Crohn's disease

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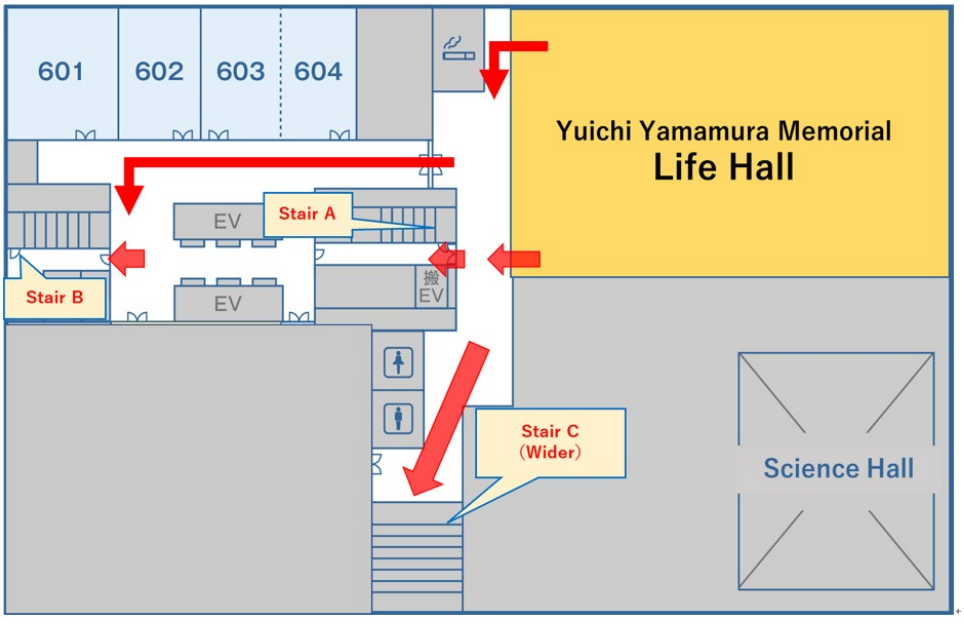
The intestine represents a unique tissue environment harboring a complex community of microbiota. Under healthy conditions, intestinal immune cell activity is tightly regulated to prevent inappropriate inflammatory responses against commensal microorganisms. Dysregulated interactions between the intestinal microbiota and host immunity contribute to the development of inflammatory bowel diseases (IBD), including Crohn's disease and ulcerative colitis. Within the intestine, microbiota are spatially segregated from host cells by the barrier function of intestinal epithelial cells, yet they influence host physiology through the production of metabolites in the intestinal lumen.

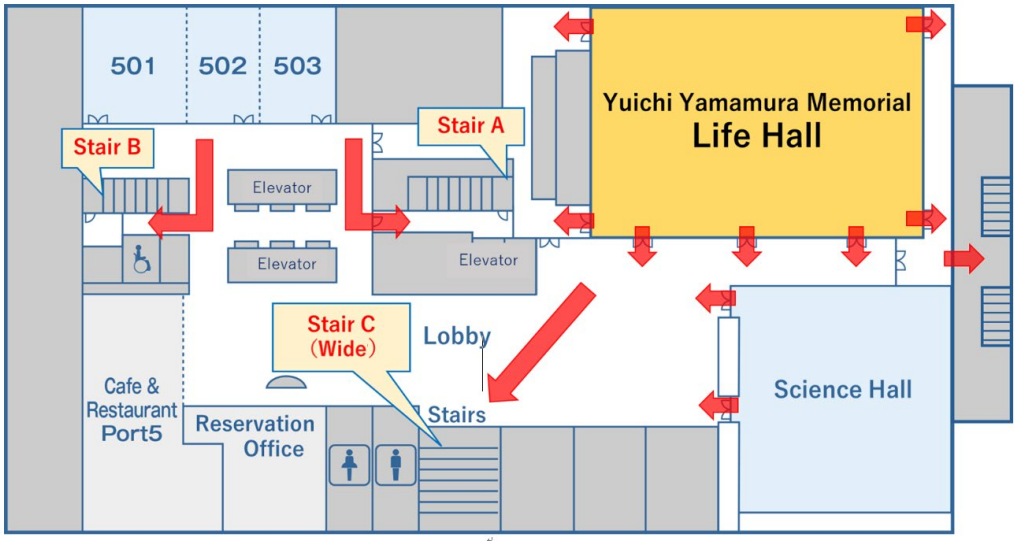
We investigated the role of microbiota-derived metabolites in the pathogenesis of IBD. We identified lysophosphatidylserine, a metabolite elevated in the intestinal lumen of Crohn's disease patients, who exhibited an increased abundance of bacteria carrying the phospholipase A gene. Using murine colitis models, we demonstrated that lysophosphatidylserine exacerbates intestinal inflammation through aberrant activation of Th1 cells. Furthermore, deep profiling of human intestinal T cells revealed a pathogenic subset of $CD4^+$ tissue-resident memory T (Trm) cells enriched in the intestine of Crohn's disease patients. Single-cell multiomic analysis of intestinal $CD4^+$ T cells further identified transcription factors that characterize this Crohn's disease–specific Trm population.

Collectively, our findings highlight both microbiota-derived metabolites and a pathogenic subset of $CD4^+$ Trm cells as key contributors to the pathogenesis of Crohn's disease.

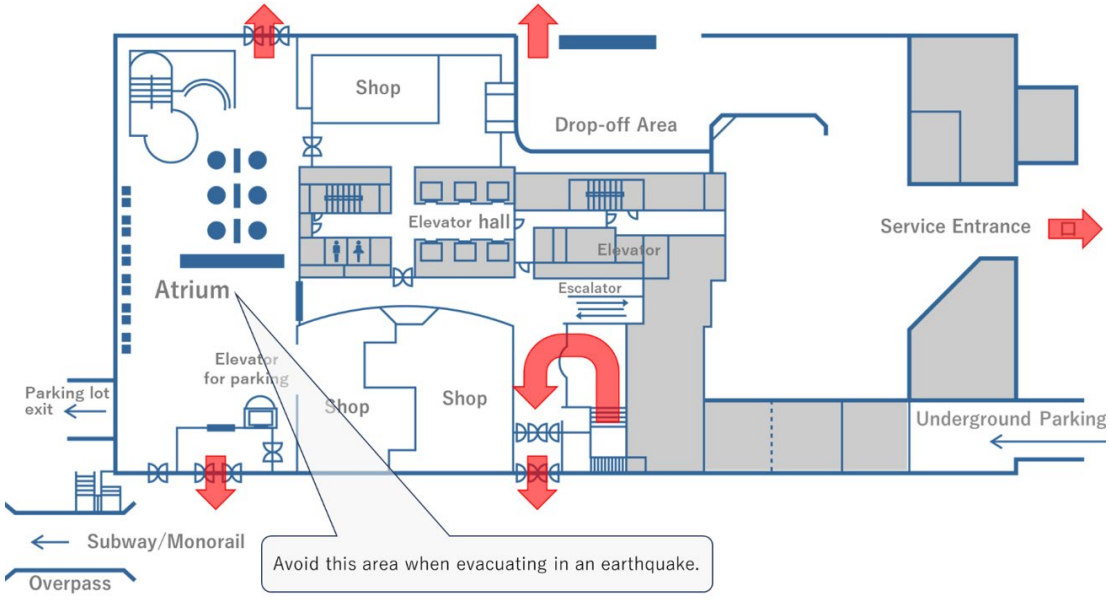
Evacuation routes on the 6th floor



Evacuation routes on the 5th floor



Evacuation routes on the 1st floor



- Announcements will be made in an emergency. We will provide guidance if evacuation becomes necessary. Please remain where you are, stay calm, and await instructions from the staff.
- During evacuation, please exit using the routes indicated by the red arrows.
- Do not use the elevators.