Program

International Academy for Advanced Oncology

IAAO 2025

The Forefront of Cancer Biology and Drug Discovery

2025 August 1 (Fri) 13:00 – 19:00
August 2 (Sat) 9:00 – 15:00
@ Toranomon Hills Forum

C-FINDs
CHUGAI FOUNDATION
FOR INNOVATIVE DRUG DISCOVERY SCIENCE

The Forefront of Cancer Biology and Drug Discovery

DAY 1: Friday, August 1, 2025 13:00 – 19:00 On-site in Tokyo

Opening Remarks

13:00 **Motoo Ueno**, President, Chugai Foundation for Innovative Drug Discovery Science (C-FINDs)

Introduction

13:05 **Bruce A. Chabner, MD**, Professor, Harvard Medical School, USA

1. Special Lecture

13:10 **The Genetic Code and Secreted Proteins**
Speaker: **Gary Ruvkun, PhD**, Professor, Harvard Medical School, USA
Chair: **Bruce A. Chabner, MD**, Professor, Harvard Medical School, USA

14:10 **Break**

2. Cancer Plasticity and Senescence

14:25 **Retrotransposable Elements and Human Endogenous Retroviruses: New Targets for Cancer Intervention and Treating Chronic Inflammation**
Speaker: **Laszlo Radvanyi, PhD**, Professor, University of Toronto, Canada
Chair: **Chikashi Ishioka, MD, PhD**, Director, JR Sendai Hospital, Japan

15:05 **Tumor-Promoting Secretome from Senescent CAFs in the Steatotic Liver Tumor Microenvironment**
Speaker**: Naoko Ohtani, MD, PhD**, Professor, Osaka Metropolitan University, Japan
Chair: **Chikashi Ishioka, MD, PhD**, Director, JR Sendai Hospital, Japan

15:45 **Break**

3. Initiatives Targeting Tumor Drivers and Drug Resistance

16:00 **Targeting the Cell Cycle in Cancer Therapy**
Speaker: **Marcos Malumbres, PhD**, ICREA Research Professor, Vall d'Hebron Institute of Oncology, Spain
Chair: **Josep Tabernero, MD, PhD**, Director, Vall d'Hebron Institute of Oncology, Spain

16:40 **An Omics Approach to Drug Discovery**
Speaker: **Liron Bar-Peled, PhD**, Associate Professor, Harvard Medical School, USA
Chair: **Josep Tabernero, MD, PhD**, Director, Vall d'Hebron Institute of Oncology, Spain

17:20 **In Search of Precision Medicine for Brain Metastases: From Bench to Bedside (and Back to Bench)**
Speaker: **Priscilla Brastianos, MD**, Associate Professor, Harvard Medical School, USA
Chair: **Masakazu Toi, MD, PhD**, Director, Tokyo Metropolitan Komagome Hospital, Japan

18:00 **Overcoming Resistance to FGFR Inhibition in FGFR2-Rearranged Cholangiocarcinoma**
Speaker: **Lipika Goyal, MD**, Associate Professor, Stanford Cancer Center, USA
Chair: **Masakazu Toi, MD, PhD**, Director, Tokyo Metropolitan Komagome Hospital, Japan

18:40 **Announcement (C-FINDs)**

19:00 **Networking Dinner**

DAY 2: Saturday, August 2, 2025 9:00 – 15:00 On-site in Tokyo

4. Early Detection and Diagnosis

9:00 **2025: The Digital Pathology Odyssey Continues**
Speaker: **Inti Zlobec, PhD**, Professor, University of Bern, Switzerland
Chair: **Hitoshi Nakagama, MD, D.M.Sc**, President, The Japan Agency for Medical Research and Development, Japan

9:40 **Redefining Early Cancer Detection: Novel CRISPR Tools Meet Next-Generation Biospecimens**
Speaker: **Cesar M. Castro, MD**, Associate Professor, Harvard Medical School, USA
Chair: **Hitoshi Nakagama, MD, D.M.Sc**, President, The Japan Agency for Medical Research and Development, Japan

10:20 **Data–Driven Integration of Histopathology and Genomics for Precision Oncology**
Speaker: **Shumpei Ishikawa, MD, PhD**, Professor, The University of Tokyo, Japan
Chair: **Hitoshi Nakagama, MD, D.M.Sc**, President, The Japan Agency for Medical Research and Development, Japan

11:00 **Break**

5. Novel Approaches in Cancer Immunotherapy

11:10 **Developing CAR-T Cell Therapy to Eradicate Oncogene-Driven Drug Tolerant Persister Cells**
Speaker: **David Barbie, MD,** Jane Rodgers Chair, Dana-Farber Cancer Institute, USA
Chair: **Hiroyoshi Nishikawa, MD, PhD,** Professor, Kyoto University, Japan

11:50 **Engineered and Adjuvant Enhancements of CAR-T Cell Effector Functions**
Speaker: **Avery Posey, PhD**, Assistant Professor, University of Pennsylvania, USA
Chair: **Hiroyoshi Nishikawa, MD, PhD,** Professor, Kyoto University, Japan

12:30 **Lunch/ Advisory Board Meeting**

6. Breakthrough Technology Session: Innovative Drug Discovery Technologies

13:20 **Dendritic-T Cell Crosstalk in Shaping Immunotherapy Responses**
Speaker: **Rony Dahan, PhD,** The Rina Gudinski Career Development Chair, Weizmann Institute of Science, Israel
Chair: **Kiyohiko Hatake, MD, PhD,** Professor, Akasaka Sanno Medical Center, Japan

14:00 **Shaping the Future of Cancer Care: Chugai's Cutting-Edge Technologies**
Speaker: **Tomoyuki Igawa, PhD,** Associate Vice President, Chugai Pharmaceutical Co., Ltd.
Chair: **Kiyohiko Hatake, MD, PhD,** Professor, Akasaka Sanno Medical Center, Japan

Closing Remarks

14:40 **Hiroyuki Mano, MD, PhD**, President, National Cancer Center, Japan

Official language: English
Dress code: Business Casual

Next Forum Information

IAAO 2026

Day 1: Friday July 31
Day 2: Saturday August 1
Venue: Toranomon Hills Forum

Opening Remarks

Motoo Ueno

President, Chugai Foundation for Innovative Drug Discovery Science (C-FINDs)

As president of C-FINDs, I am very pleased to host the International Academy for Advanced Oncology, IAAO. I would like to express my sincere gratitude to all of the distinguished guests, experts, and investigators attending this forum from overseas and Japan.

IAAO is a major C-FINDs event that reflects three guiding principles: "Top-level science", “Development of young researchers", and "Global perspective”. We are pleased to welcome you to this forum, IAAO 2025, organized by C-FINDs.

This year’s theme, “The Forefront of Cancer Biology and Drug Discovery,” reflects our strong belief in the importance of integrating basic research with translational science. From the molecular mechanisms of tumorigenesis to the design and evaluation of novel therapies, this conference aims to stimulate cross-disciplinary insights and inspire future breakthroughs.

We are deeply honored by the presence of outstanding speakers from around the world. In addition, this year we are privileged to welcome Dr. Gary Ruvkun, recipient of the 2024 Nobel Prize in Physiology or Medicine, whose pioneering discovery of microRNAs has significantly advanced our understanding of gene regulation and human biology.

I wish to express our profound gratitude to the members of the advisory board for their expert contributions in shaping the program: Dr. Chabner, Dr. Mano, Dr. Hatake, Dr. Ishioka, Dr. Kitagawa, Dr. Miyazono, Dr. Nakagama, Dr. Nishikawa, Dr. Ohtani, Dr. Tabernero, and Dr. Toi. Their unwavering dedication and expert input were indispensable. Thanks to their efforts, we are able to present a comprehensive agenda that captures both depth and breadth across the field.

In closing, I would like to thank all the participants again. C-FINDs’ sincere wish is that the IAAO forum becomes an important venue for the exchange of information that advances the fight against cancer and, concurrently, empowers patients to deal with their treatment proactively and with hope. I do hope that this two-day event will be a highly informative and fruitful time for everyone.

Session 1

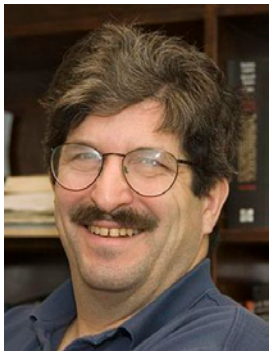
Special Lecture

The Genetic Code and Secreted Proteins

Speaker: Gary Ruvkun, PhD (Professor, Harvard Medical School, USA)

IAAO2025

Title: The Genetic Code and Secreted Proteins



Speaker

Gary Ruvkun, PhD

Professor of Genetics, Harvard Medical School
Department of Molecular Biology, Massachusetts General Hospital, USA

Chair

Bruce A. Chabner, MD

Professor of Medicine, Harvard Medical School
Clinical Director, Emeritus, MGH Cancer Center, Massachusetts General Hospital, USA

Gary Ruvkun, PhD

Research Summary

Dr. Gary Ruvkun, a professor of genetics at Harvard Medical School and investigator at Massachusetts General Hospital, is renowned for his pioneering work in gene regulation via microRNAs (miRNAs). In 1993, he elucidated how the lin-4 miRNA suppresses its target gene lin-14 by binding directly to its mRNA, revealing a novel mechanism of post-transcriptional gene regulation. Subsequently, in 2000, his lab discovered the let-7 miRNA, demonstrating its evolutionary conservation across species, including humans, thereby establishing the universality of miRNA-mediated regulation. Beyond miRNAs, Ruvkun's research has delved into insulin-like signaling pathways in *C. elegans*, uncovering conserved hormonal signals that influence metabolism and aging, with implications for human health. His work has significantly advanced our understanding of genetic regulation, development, and longevity.

Professional Experience/Awards

Dr. Gary Ruvkun earned his AB in biophysics from the University of California, Berkeley, in 1973, and his PhD in biophysics from Harvard University in 1982, where he studied under Frederick Ausubel. Following postdoctoral research with Robert Horvitz at MIT and Walter Gilbert at Harvard, he joined the faculty at Harvard Medical

School in 1985. Currently, he serves as a professor of genetics at Harvard and an investigator in the Department of Molecular Biology at Massachusetts General Hospital.

Dr. Ruvkun's groundbreaking research has been recognized with numerous prestigious awards. In 2008, he received the Albert Lasker Award for Basic Medical Research, the Benjamin Franklin Medal, and the Canada Gairdner International Award. The following year, he was honored with the Louisa Gross Horwitz Prize and elected to both the National Academy of Sciences and the American Academy of Arts and Sciences. His contributions to aging research were acknowledged with the Dan David Prize in 2011. In 2014, he was awarded the Wolf Prize in Medicine, and in 2015, the Breakthrough Prize in Life Sciences. Most recently, in 2024, Dr. Ruvkun was co-awarded the Nobel Prize in Physiology or Medicine for his discovery of microRNAs and their role in post-transcriptional gene regulation.

Beyond his research, Dr. Ruvkun is involved in astrobiology initiatives, notably the Search for Extraterrestrial Genomes project, which aims to detect DNA- or RNA-based life on other planets using advanced sequencing techniques.

Education

AB	1973	University of California, Berkeley, USA
PhD	1982	Harvard University, USA

Abstract of the lecture

The research in my lab has focused on microRNAs, siRNAs, as well as the insulin receptor kinase pathway and aging. The work has been driven by intensive genetic analyses of these pathways. The genes that emerge from such genetics are often very unfamiliar to us but often studied in depth in fungi or plants or bacteria. Such genetics has now thrust us into the genetic code. The genetic code is taught today as a puzzle solved brilliantly by the founders of molecular biology a half century ago. But as genome sequences emerged 30 years later, it was revealed that organisms across the Tree of Life have a signficantly abridged subset of tRNAs from the expected 61 tRNAs. *C. elegans* is missing 16 of the 61 tRNAs, all encoding different amino acids. *S. cerevisiae* is missing 19 tRNAs. *E. coli* is missing 22 tRNAs. The codons that correspond to these missing tRNAs are used at high frequency, but they are recognized by tRNAs with their anticodon loops RNA edited: for example, adenosine 34 in the anticodon loop is deaminated to inosine. Another 11 *C. elegans* tRNAs modify a U at position 34 of the anticodon to enable a distinct class of wobble base pairing. This wobble base pairing is central to 17 of the 48 *C. elegans* tRNAs, 1/3 of the codon recognition on ribosomes. Secreted proteins initiate translation just like every other mRNA on cytoplasmic ribosomes, but as their first 30 amino acids emerge from the ribosome, their secretory signal sequence is recognized by the Signal Recognition Particle and translational elongation is paused until the ribosome binds the Sec61 translocon at the endoplasmic reticulum and the translated polypeptide translocates across the ER membrane. We have detected *C. elegans* open reading frames with the longest runs of these codons that demand tRNA editing to be translated. We are also testing whether mutations in the genes that mediate tRNA modifications strongly affect protein secretion, especially of genes that use a high number of such forbidden codons. We are also developing a modified BLASTP analysis that does not treat all synonymous codons equally, as BLASTP current does. We want to explore whether particular runs of codons that have previously been viewed as synonymous are in fact selected for use in highly conserved nucleotide sequences of secreted proteins. Receptor kinases such as ALK are secreted proteins as are so many growth factors and their receptors in the pharma industry, so this work may be germane to the pharma research enterprise.

Session 2

Cancer Plasticity and Senescence

2-1. Retrotransposable Elements and Human Endogenous Retroviruses: New Targets for Cancer Intervention and Treating Chronic Inflammation

Speaker: Laszlo Radvanyi, PhD (Professor, University of Toronto, Canada)

2-2. Tumor-Promoting Secretome from Senescent CAFs in the Steatotic Liver Tumor Microenvironment

Speaker: Naoko Ohtani, MD, PhD (Professor, Osaka Metropolitan University, Japan)

Title: Retrotransposable Elements and Human Endogenous Retroviruses: New Targets for Cancer Intervention and Treating Chronic Inflammation

Laszlo Radvanyi, PhD

Professor, Department of Immunology, University of Toronto
Visiting Scientist, Princess Margaret Cancer Centre, Toronto, Ontario, Canada

Speaker

Chikashi Ishioka, MD, PhD

Professor Emeritus, Tohoku University, Japan
Director, JR Sendai Hospital, Japan

Chair

Laszlo Radvanyi, PhD

Research Summary

Dr. Laszlo Radvanyi's research focuses on the role of non-coding genomic elements—such as retrotransposable elements (LINE-1, SINE/Alu), human satellite repeats (HSAT), and human endogenous retroviruses (HERVs) in cancer initiation and progression. His lab investigates how these elements, when reactivated in cancer, modulate immune responses through innate inflammation, particularly during early tumor development. Additionally, his team explores how these transcripts are disseminated via extracellular vesicles, contributing to systemic inflammation and immune dysfunction in cancer and aging. They also aim to harness tumor-specific expressions of these elements as novel antigens for mRNA vaccine-based cancer immunotherapies and T-cell therapies.

Professional Experience/Awards

Dr. Laszlo Radvanyi is Hungarian in origin. He is a cancer immunologist that has held research and leadership positions across academia and industry. He was most recently the President and Scientific Director of the Ontario Institute for Cancer Research (OICR) from 2018-2025. He is currently a Professor in the Department of Immunology

at the University of Toronto and a Visiting Scientist at the Princess Margaret Cancer Center in Toronto, Ontario. He is also the national Independent Chair of Digital Health and Discovery Platform (DHDP), a national Canadian government funded initiative to develop AI-based precision medicine across Canada in a centralized and accessible network. He earned his PhD in Clinical Biochemistry and Immunology from the University of Toronto in 1996. Following his doctorate, he completed a postdoctoral fellowship at Harvard Medical School's Joslin Diabetes Center. Dr. Radvanyi's career has encompassed significant roles in both academia and the pharmaceutical industry. He served as a Senior Scientist at Sanofi Pasteur, co-leading a team focused on cancer vaccine antigen discovery. Subsequently, he spent a decade (2004-2014) at the University of Texas MD Anderson Cancer Center as a Professor in the Department of Melanoma Medical Oncology. There, he established a GMP-grade T-cell therapy manufacturing program for metastatic melanoma and conducted research on tumor-infiltrating lymphocytes (TILs), earning the Department of Cancer Medicine 1st Place Faculty Research Award in 2011. In the biotech sector, Dr. Radvanyi was the founding Chief Scientific Officer of Iovance Biotherapeutics (2014-2015), the first biotech company pioneering the development of commercial TIL therapies for cancer patients. Afterwards, he held the position of Senior Vice President and Global Head of the Immuno-Oncology Translational Innovation Platform at EMD Serono (Merck KGaA), where he revitalized the company's immuno-oncology research pipeline and established key academic partnerships before joining OICR in 2018. Throughout his career, Dr. Radvanyi has received numerous accolades, including the Becton Dickinson Award for Best Research Presentation from the Canadian Society for Immunology and multiple fellowships from esteemed organizations such as the Natural Sciences and Engineering Research Council of Canada (NSERC) and the Cancer Research Institute (CRI). More recently, he was the recipient of the Order of the Knights Cross from the Republic of Hungary for his achievements and leadership in the biomedical sciences.

Education

PhD 1996 University of Toronto, Canada

Abstract of the Lecture

We are at the cusp of a revolution in understanding the role of “non-coding” elements or the so-called “dark genome” in human health. These elements, comprising the remnants of ancient retroviral infections during human evolution passed on through the germline, as well as peri-centromeric satellite repeat elements (HSAT) and other repetitive sequences, comprise up to 70% of our genome. These regions contain active retrotransposable elements such as LINE-1 and SINE/Alu elements as well as human endogenous retroviruses (HERVs) such as HERV-K that are usually turned on and regulate gene expression, tissue specification and early differentiation during embryonic development. However, these retroelements are strictly shut down by DNA methylation and other epigenetic regulatory mechanisms after a critical fetal implantation stage during pregnancy. Certain transposed elements, such as HERV LTRs can remain active regulating the transcription of several critical coding genes into and during adult life, but essentially almost all retroelements are shut off by strict negative regulatory epigenetic control mechanisms. Recently, it has now become apparent that during aging and induction of pathophysiological conditions, including cancer, autoimmune disease, and neurodegenerative disease, these negative epigenetic regulatory mechanisms become defective allowing both RNA transcripts and expressed protein ORFs of LINE-1, SINE/Alu, HERV-K and HSAT to be expressed in diseased tissues. Moreover, the primitive viral-like nature of these retroelement

sequences can trigger innate immune sensing pathways that drive chronic innate inflammation mediated by type I IFNs, their associated pro-inflammatory cytokines, and NFκB. If left unchecked, this persistent retroelement activation and ensuing chronic inflammation can contribute to cancer progression and exacerbate autoimmune and neurodegenerative diseases. The term “non-coding” for these regions is also becoming a misnomer since more and more elements in these genomic regions are found to be transcribed and translated into active proteins regulating cell signaling or induce the expression of ORFs that can be antigens recognized by the immune system.

This talk will introduce the components of this active “dark genome” and present new insights from work in our lab on how these retroelements play role in cancer initiation and immune modulation, particularly by their systemic dissemination in extracellular vesicles (EVs) facilitating chronic inflammation during cancer initiation and progression. Data on the potential of expressed ORFs from LINE-1 and HERV-K to be potential new tumor antigens for immunotherapy will also be presented. Lastly, we will present some provocative data on how existing drugs can be repurposed to target the activity of retrotransposable elements in modulating inflammation and preventing cancer development.

References

1. Ruzanov P, Evdokimova V, ..., **Radvanyi L,** ..., Stein LD, Sorensen PH. Oncogenic ETS fusions promote DNA damage and proinflammatory responses via expression and dissemination of pericentromeric RNAs in extracellular vesicles. *J Clin Inv* 2024; Mar 26: e169470
2. Strum S, Evdokimova V, **Radvanyi L**, Spreafico, A. Extracellular vesicles and their applications in tumor diagnostics and immunotherapy. *Cells* 2024; 13: 2031.
3. Evdokimova V, Gassmann H, Burdach SEG, **Radvanyi L**. Current State of Immunotherapy and Mechanisms of Immune Evasion in Ewing Sarcoma and Osteosarcoma. *Cancers* 2022; 15: 272-292
4. Wang-Johanning F, **Radvanyi L**, …, Hunt KK, Johanning GL. Human endogenous retrovirus K triggers an antigen-specific immune response in breast cancer patients. *Cancer Res* 2008; 68: 5869-5877
5. Li M, **Radvanyi L**, …, Johanning GL, Wang-Johanning F. Down-regulation of human endogenous retrovirus type K (HERV-K) viral env RNA in pancreatic cancer cells decreases cell proliferation and tumor growth. *Clin Can Res* 2017; 23: 5892-5911

Title: Tumor-Promoting Secretome from Senescent CAFs in the Steatotic Liver Tumor Microenvironment

Naoko Ohtani, MD, PhD

Professor of Department of Pathophysiology, Osaka Metropolitan University, Graduate School of Medicine, Japan

Speaker

Chikashi Ishioka, MD, PhD

Professor Emeritus, Tohoku University, Japan
Director, JR Sendai Hospital, Japan

Chair

Naoko Ohtani, MD, PhD

Research Summary

Professor Naoko Ohtani's research centers on the tumor microenvironment, particularly in the context of obesity-associated liver cancer, where cellular senescence and gut microbiota play key roles. Her team discovered that deoxycholic acid—a metabolite produced by gut bacteria in obese individuals—induces a senescence-associated secretory phenotype (SASP) in cancer-associated fibroblasts (CAFs) within tumors, thereby promoting cancer progression. They aim to uncover the molecular mechanisms by which various gut microbial metabolites and components contribute to liver diseases, including hepatocellular carcinoma, using advanced techniques such as single-cell analysis.

Professional Experience/Awards

Professor Naoko Ohtani has served as a Professor in the Department of Pathophysiology at Osaka Metropolitan University's Graduate School of Medicine since April 2022. She earned her Doctor of Medicine degree from Kyoto Prefectural University of Medicine.

Her research spans pathological biochemistry, experimental pathology, tumor biology, and gut microbiota, with a particular focus on the tumor microenvironment and cellular senescence.

Professor Ohtani has played key roles in numerous scientific societies, including serving on the boards of the Japanese Cancer Association, the Japanese Society for Cancer Immunology, and the Japanese Society for Molecular Biology. She has also contributed to the organization of international conferences, such as the AACR-JCA Joint Conference.

Her achievements have been recognized through prestigious awards, including the Woman Scientist Award from the Japanese Cancer Association in 2017 for her outstanding contributions to cancer research, and the Women Immunology Researcher Award from the Japanese Society for Immunology in 2024 for her work elucidating mechanisms of anti-tumor immune suppression associated with SASP factors.

Throughout her career, Professor Ohtani has demonstrated a strong commitment to advancing medical science, particularly cancer research, through innovative investigation and active engagement with the global scientific community.

Education

MD	1988	Kyoto Prefectural University of Medicine, Japan
PhD	1995	Kyoto Prefectural University of Medicine, Japan

Abstract of the lecture

Metabolic dysfunction-associated steatotic liver disease (MASLD) and steatohepatitis (MASH) are increasingly recognized as major backgrounds of hepatocellular carcinoma (HCC). We previously reported that hepatic stellate cells (HSCs) exposed to the gut microbial metabolite deoxycholic acid (DCA) acquire a senescence-associated secretory phenotype (SASP), characterized by secretion of inflammatory cytokines, chemokines, and proteases. Obesity-associated hepatic translocation of lipoteichoic acid (LTA), a Gram-positive bacterial component, further amplifies this phenotype via Toll-like receptor 2, creating a positive feedback loop. IL-1β, a key SASP factor from senescent HSCs, plays a pivotal role in HCC development. In a MASH-associated HCC mouse model, IL-33 was highly expressed in senescent HSCs in tumor regions in an IL-1β-dependent manner. IL-33-deficient mice developed significantly fewer tumors, highlighting its oncogenic role. We also identified a novel mechanism of SASP factor release: LTA activates gasdermin D, forming membrane pores that release IL-33. The released IL-33 promotes HCC progression by activating ST2-positive regulatory T cells, which suppress antitumor immunity. In human MASH-HCC samples, senescent HSCs exhibited both IL-33 overexpression and gasdermin D N-terminal accumulation, suggesting a conserved mechanism in humans. In this study, we further characterized senescent HSCs as cancer-associated fibroblasts (CAFs) using Flex single-cell transcriptome analysis of human HCC tissues. HSCs with higher expression of senescence markers produced more secreted proteins. We identified SASP factors from these senescent HSCs that correlated with poor prognosis, indicating their potential as biomarkers for steatotic HCC progression.

References

1. Yoshimoto S, Loo TM, ..., Hara E, **Ohtani N**. Obesity-induced gut microbial metabolite promotes liver cancer through senescence secretome. *Nature* 2013; 499: 97-101
2. Loo TM, Kamachi F, ..., Hara E, **Ohtani N**. Gut Microbiota Promotes Obesity-Associated Liver Cancer through PGE2-Mediated Suppression of Antitumor Immunity. *Cancer Discov* 2017; 7: 522-538
3. Yamagishi R, Kamachi F, ..., Hara E, **Ohtani N**. Gasdermin D-mediated release of IL-33 from senescent hepatic stellate cells promotes obesity-associated hepatocellular carcinoma. *Science Immunol* 2022; 7: eabl7209

Session 3

Initiatives Targeting Tumor Drivers and Drug Resistance

3-1. Targeting the Cell Cycle in Cancer Therapy

Speaker: Marcos Malumbres, PhD
(ICREA Research Professor, Vall d'Hebron Institute of Oncology, Spain)

3-2. An Omics Approach to Drug Discovery

Speaker: Liron Bar-Peled, PhD (Associate Professor, Harvard Medical School, USA)

3-3. In Search of Precision Medicine for Brain Metastases: From Bench to Bedside (and Back to Bench)

Speaker: Priscilla Brastianos, MD
(Associate Professor, Harvard Medical School, USA)

3-4. Overcoming Resistance to FGFR Inhibition in FGFR2-Rearranged Cholangiocarcinoma

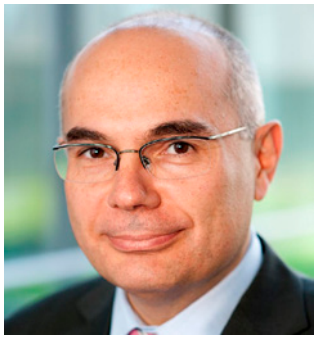
Speaker: Lipika Goyal, MD (Associate Professor, Stanford Cancer Center, USA)

Title: Targeting the Cell Cycle in Cancer Therapy

Speaker

Marcos Malumbres, PhD

ICREA Research Professor, Director, Systems Oncology Program, and Group leader, Cancer Cell Cycle group, Vall d'Hebron Institute of Oncology (VHIO), Spain



Chair

Josep Tabernero, MD, PhD

Director, Vall d'Hebron Institute of Oncology (VHIO), Spain
Head of the Medical Oncology Department at the Vall d'Hebron University Hospital, Spain

Marcos Malumbres, PhD

Research summary

Dr. Marcos Malumbres leads the Cancer Cell Cycle group at the Vall d'Hebron Institute of Oncology (VHIO), focusing on the molecular mechanisms governing cell proliferation and differentiation, particularly in cancer. His research has significantly contributed to the development of CDK4/6 inhibitors for metastatic breast cancer treatment. Currently, his lab investigates resistance mechanisms to these inhibitors and explores novel therapeutic strategies for aggressive cancers by combining molecular and functional studies with patient-derived models for advanced personalized cancer therapies.

Professional experience

Dr. Marcos Malumbres earned his biology degree from the Universidad de Navarra and completed his PhD in Molecular Biology at the Universidad de León in 1993. He pursued postdoctoral research at New York University Medical Center, focusing on oncogenes and cell cycle control. In 1998, he joined Mariano Barbacid's lab at the Spanish National Cancer Research Centre (CNIO) in Madrid. He became a Staff

Scientist at the Spanish National Research Council (CSIC) and was appointed senior group leader at CNIO in 2004, leading the Cell Division and Cancer Group until 2022.

In 2023, Dr. Malumbres joined VHIO as the head of the Cancer Cell Cycle Group and ICREA Research Professor. He also serves as External Associated Faculty at IRB Barcelona and has been a visiting professor at Dana-Farber Cancer Institute, Harvard University, since 2019.
Dr. Malumbres has authored over 200 international publications, contributing significantly to understanding cell cycle regulators and their implications in cancer therapy. His work has been pivotal in the development of CDK4/6 inhibitors for metastatic breast cancer, as well as exploring multiple cell cycle-targeted therapies in several tumor types. His accolades include election to the European Molecular Biology Organization (EMBO) in 2016 and the Gold Medal from the Spanish Association Against Cancer (AECC) in 2019. He has served on various scientific advisory boards, including European TRANSCAN, Worldwide Cancer Research, and advisory boards in several national and international institutions and scientific journals.

Abstract of the lecture

Unscheduled cell proliferation is one of the main hallmarks of tumor cells. Many of the components of the cell machinery that transduce extracellular and intracellular cues into cell proliferation decisions are altered in cancer, resulting in aberrant cell division cycles. Accordingly, targeting cell cycle enzymes is considered an attractive strategy with applications in multiple, if not all, tumor types. Among these enzymes, cyclins-dependent kinases (CDKs), considered the engine of the cell cycle, have been deeply explored. Inhibiting CDK4, and its closely related family member CDK6, has become the standard-of-care in advanced or high-risk estrogen receptor (ER)-positive, HER2-negative breast cancer, along endocrine therapy, due to the critical role of CDK4-cyclin D complexes in triggering cell cycle progression downstream of ER. Yet, CDK4/6 inhibitors are not efficient in other tumor types, and most advanced ER+ breast cancers relapse after these treatments (Álvarez-Fernández & Malumbres, 2020). What is next after CDK4/6 therapies is not clear, especially given the multiple mechanisms of resistance, as well as the complexity of the functional role of other CDKs and related enzymes (Malumbres & Barbacid, 2009). Unfortunately, it is still unclear how most oncogenic aberrations hijack cell proliferation and what are the critical biomarkers and targets for personalized cell cycle therapies in cancer patients.

We will discuss what are the most immediate therapeutic opportunities for preventing cell cycle progression after resistance to CDK4/6 inhibitors in breast cancer patients, and to what extent these ideas can be applied to other tumor types such as gynecological malignancies, as well as other aggressive scenarios such as MYC-high or Retinoblastoma protein (RB1)-null tumors. Finally, we will consider what we are learning from hereditary cell cycle defects, such as mosaic variegated aneuploidy (MVA; Malumbres & Villarroya-Beltri, 2024), a syndrome with dramatic cellular and clinical consequences caused by mutations in cell cycle regulators.

References

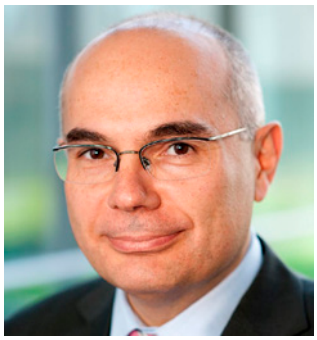
1. Álvarez-Fernández M, **Malumbres M**. Mechanisms of Sensitivity and Resistance to CDK4/6 Inhibition. *Cancer Cell* 2020; 37:514-529.
2. **Malumbres M**, Barbacid M. Cell cycle, CDKs and cancer: a changing paradigm. *Nat Rev Cancer* 2009; 9:153-66.
3. **Malumbres M**, Villarroya-Beltri C. Mosaic variegated aneuploidy in development, ageing and cancer. *Nat Rev Genet* 2024; 25: 864-878.

Title: An Omics Approach to Drug Discovery

Speaker

Liron Bar-Peled, PhD

Eileen and Jim Rullo Endowed Chair for Cancer Research
Associate Professor of Medicine, Massachusetts General Hospital Cancer Center, Harvard Medical School, USA



Chair

Josep Tabernero, MD, PhD

Director, Vall d'Hebron Institute of Oncology (VHIO), Spain
Head of the Medical Oncology Department at the Vall d'Hebron University Hospital, Spain

Liron Bar-Peled, PhD

Research summary

Dr. Liron Bar-Peled's research focuses on how cancer cells adapt to oxidative stress by activating the NRF2/KEAP1 pathway, which regulates antioxidant responses. His lab employs chemical proteomics to uncover how NRF2 fosters a redox environment that protects critical proteins from reactive oxygen species (ROS), thereby supporting cancer cell proliferation. By identifying ROS-sensitive proteins and mapping their druggability, his team aims to develop small-molecule inhibitors targeting these vulnerabilities, offering new therapeutic strategies for cancers with deregulated redox control, such as non-small cell lung cancer and ovarian cancer.

Professional experience

Dr. Liron Bar-Peled is an Associate Professor of Medicine at Harvard Medical School and a principal investigator at the Massachusetts General Hospital Cancer Center. He earned his B.Sc. in Biochemistry from the University of Georgia in 2004 and completed his PhD in Biology at the Massachusetts Institute of Technology, where he studied amino acid sensing in the mTORC1 pathway under Dr. David Sabatini. His doctoral work was recognized with the 2014 Science & SciLifeLab Prize for Young Scientists.

Following his PhD, Dr. Bar-Peled conducted postdoctoral research as a Damon Runyon Fellow in Dr. Benjamin Cravatt's lab at The Scripps Research Institute. There, he utilized chemical proteomics to map reactive cysteine residues, identifying new druggable components within the NRF2 antioxidant response pathway. In 2019, he established his own laboratory at Massachusetts General Hospital, focusing on the intersection of cancer metabolism, redox biology, and chemical biology.

Dr. Bar-Peled's innovative work has earned him several prestigious awards, including the AACR-MPM Transformative Cancer Research Award, the Damon Runyon-Rachleff Innovation Award, the Melanoma Research Foundation Young Investigator Award, the Harold M. Weintraub Graduate Student Award, and the 2023 Krantz Quantum Award. In 2023, he was named a Pew-Stewart Scholar for Cancer Research, recognizing his efforts to develop therapies targeting proteins previously considered "undruggable" in ovarian cancer.

Dr. Bar-Peled continues to advance the field of cancer research by integrating chemical proteomics with genomic screening to identify novel therapeutic targets, particularly in cancers with altered redox states. In 2020 he co-founded Scorpion Therapuetics which was partially acquired for their lead program in 2025 by Eli Lily. His work not only deepens the understanding of cancer biology but also paves the way for the development of targeted treatments for patients with limited options.

Education

BS	2004	University of Georgia, USA
PhD	2013	Massachusetts Institute of Technology, USA

Abstract of the lecture

Cysteine-focused chemical proteomic platforms have accelerated the clinical development of covalent inhibitors of a wide-range of targets in cancer. However, how different oncogenic contexts influence cysteine targeting remains unknown. To address this question, we have developed *DrugMap*, an atlas of cysteine ligandability compiled across 416 cancer cell lines. We unexpectedly find that cysteine ligandability varies across cancer cell lines, and we attribute this to differences in cellular redox states, protein conformational changes, and genetic mutations. Leveraging these findings, we identify actionable cysteines in NFκB1 and SOX10 and develop corresponding covalent ligands that block the activity of these transcription factors. We demonstrate that the NFκB1 probe blocks DNA binding, whereas the SOX10 ligand increases SOX10-SOX10 interactions and disrupts melanoma transcriptional signaling. Our findings reveal heterogeneity in cysteine ligandability across cancers, pinpoint cell-intrinsic features driving cysteine targeting, and illustrate the use of covalent probes to disrupt oncogenic transcription factor activity.

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Title: In Search of Precision Medicine for Brain Metastases: From Bench to Bedside (and back to Bench)

Speaker

Priscilla Brastianos, MD

Associate Professor of Medicine
Director, Central Nervous System Metastasis Center
Massachusetts General Hospital
Harvard Medical School, USA

Chair

Masakazu Toi, MD, PhD

Director, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, Japan

Priscilla Brastianos, MD

Research Summary

Dr. Brastianos' research focuses on elucidating the molecular mechanisms driving primary and metastatic brain tumors. Her work emphasizes the characterization of tumor and immune microenvironments to accelerate the development of novel therapeutic approaches for brain tumors. Her laboratory has identified clinically actionable genetic alterations in various brain tumors, including meningiomas, craniopharyngiomas, glioneuronal tumors, and brain metastases. These discoveries have led to the initiation of national multicenter clinical trials aimed at evaluating novel therapies for primary and metastatic brain tumors, which are already transforming patient care.

Professional Experience/Awards

Dr. Priscilla Brastianos earned her BSc in biochemistry and chemistry from the University of British Columbia, graduating as class valedictorian and receiving multiple

awards, including the Science Scholar Award and the Canadian Society for Chemistry Prize. She completed her medical degree and internal medicine residency at Johns Hopkins School of Medicine, where she was honored with the Johns Hopkins Medical Student Award for Excellence in Research and the national Leah J. Dickstein, MD, award for leadership and scholarship. Subsequently, she pursued fellowship training in hematology/oncology and neuro-oncology at the Dana-Farber Cancer Institute and Massachusetts General Hospital, during which she received several accolades, such as the ASCO Young Investigator Award and a Susan G. Komen Postdoctoral Fellowship Award. Currently, Dr. Brastianos serves as the Director of the Central Nervous System Metastasis Center at Massachusetts General Hospital and leads an R01-funded laboratory. Her pioneering research has led to the identification of novel therapeutic targets in brain tumors, notably discovering activating BRAF mutations in papillary craniopharyngiomas, which has opened avenues for targeted therapies. Her work has also demonstrated that brain metastases harbor distinct genetic drivers compared to primary tumors, influencing treatment strategies.

Dr. Brastianos has been recognized with several prestigious awards, including the Damon Runyon Clinical Investigator Award, a Breast Cancer Research Foundation Award, a Susan G. Komen Career Catalyst Award, a 'NextGen Star' Award by the American Association for Cancer Research, the American Brain Tumor Association Joel Gringas Award, a Rising Innovator Award from the American Association for Cancer Research, and the Society of Neuro-Oncology Mid-Career Exemplary Physician Award. Her commitment to advancing neuro-oncology is further exemplified by her role in leading national, biomarker-driven clinical trials and her dedication to mentoring the next generation of scientists. She currently serves as the national co-chair of the Neuro-Oncology Committee of the Alliance for Clinical Trials in Oncology, the National Cancer Institute-sponsored cooperative group committee.

Education

MD 2006 Johns Hopkins School of Medicine
Internal Medicine Residency
2006-2009 Johns Hopkins Hospital
Medical Oncology and Neuro-Oncology Fellowship
2009-2012 Dana-Farber Cancer Institute/Massachusetts General Hospital, Harvard Medical School
Postdoctoral fellow
2010-2012 Dana-Farber Cancer Institute, Broad Institute and Massachusetts General Hospital

Abstract of the lecture

Central nervous system (CNS) metastases are a common and devastating complication of cancer. Historically patients with brain metastases have been excluded from genomic studies and therapeutic trials. Much of our work has focused on understanding the genomic landscape of brain metastases, with the goal of identifying actionable alterations and using those insights to inform new therapeutic strategies. By comparing brain metastases to matched extracranial sites across tumor types, we found that brain metastases frequently harbor clinically actionable mutations not detected elsewhere in the body. These findings challenge the assumption that profiling extracranial disease is sufficient, and they highlight the potential need to study intracranial lesions directly when clinically feasible, especially when making treatment decisions for patients with CNS metastases. This work laid the groundwork for a new approach to clinical trial design for patients with brain metastases. We developed prospective trials specifically for patients with brain metastases, integrating molecular profiling and selecting therapies based on alterations found in brain lesions with CNS-

penetrant drugs and built in real-time genomic data to drive treatment selection. These trials not only broaden access for patients historically excluded from clinical trials but also generate data that is directly relevant to intracranial metastases. We have also been investigating mechanisms of resistance in the CNS and studying how the CNS microenvironment evolves during therapy. Altogether, this work reflects a translational pipeline, from identifying the genomic divergence of brain metastases, to designing trials that meet the specific needs of this patient population. By bringing the biology of brain metastases to the center of drug development efforts, we hope to open up new therapeutic possibilities for patients who urgently need better options.

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Title: Overcoming Resistance to FGFR Inhibition in FGFR2-Rearranged Cholangiocarcinoma

Lipika Goyal, MD

Associate Professor of Medicine, Director of Gastrointestinal Oncology, Stanford Cancer Center, USA

Speaker

Masakazu Toi, MD, PhD

Director, Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital, Japan

Chair

Lipika Goyal, MD

Research Summary

Dr. Lipika Goyal specializes in gastrointestinal oncology, with a particular emphasis on hepatocellular carcinoma and cholangiocarcinoma. Her research investigates mechanisms of drug resistance, especially concerning fibroblast growth factor receptor (FGFR) mutations, and aims to enhance the efficacy of targeted therapies. She has contributed to the development of futibatinib for cholangiocarcinoma treatment and leads studies on tumor-immune interactions to improve immunotherapy outcomes. Dr. Goyal's work also encompasses gender representation in clinical trial authorship and the integration of complementary practices like mudras in medicine.

Professional Experience/Awards

Dr. Lipika Goyal serves as the Director of the Gastrointestinal Oncology Program at the Stanford Cancer Institute and holds the position of Associate Professor of Medicine (Oncology) at Stanford University. She earned her medical degree from Harvard Medical School in 2007, completed her internal medicine residency at Brigham and Women's Hospital in 2010, and pursued a fellowship in Hematology and Oncology at Dana-Farber Cancer Institute, concluding in 2013.

Throughout her career, Dr. Goyal has been recognized for her significant contributions to cancer research. In 2023, she was honored as the American Cancer Society's Researcher of the Year, acknowledging her advancements in understanding FGFR-related drug resistance and her efforts to improve therapeutic strategies for biliary tract cancers.

Additionally, Dr. Goyal received an Innovation Award from the Stanford Cancer Institute in October 2023. This award supports her collaborative research aimed at elucidating the mechanisms of lymph node metastatic tolerance in high-risk resectable cholangiocarcinoma. The study focuses on characterizing immune cells at tumor sites and in lymph nodes to identify changes that enable tumor persistence, with the goal of developing strategies to enhance immunotherapy effectiveness.

Dr. Goyal's dedication to patient care, research, and education continues to impact the field of oncology, particularly in advancing treatments for challenging gastrointestinal malignancies.

Education

BA	2001	University of Pennsylvania, USA
MD	2007	Harvard Medical School, USA

Abstract of the lecture

The discovery of FGFR2 fusions and rearrangements as actionable drivers in intrahepatic cholangiocarcinoma has marked a significant therapeutic milestone. FGFR inhibitors, including futibatinib and pemigatinib, were among the first therapies approved for this disease. These agents have demonstrated objective response rates of 36–42% and median durations of response ranging from 7 to 9 months—offering a meaningful advance over standard chemotherapy in the second-line setting.

However, the clinical benefit of FGFR inhibitors is ultimately limited by the development of resistance. Through collaborative, multi-institutional efforts, we have begun to unravel key mechanisms underlying therapeutic failure, including the emergence of secondary mutations in the FGFR2 kinase domain and the activation of bypass signaling pathways.

This talk will provide an overview of the clinical impact of FGFR inhibition in cholangiocarcinoma, highlight emerging insights into mechanisms of acquired resistance, and discuss promising strategies—including next-generation FGFR inhibitors—designed to delay or overcome resistance. These advances underscore the importance of integrating molecular understanding with drug development to extend the duration and depth of response for patients with FGFR2-driven cholangiocarcinoma.

Session 4

Early Detection and Diagnosis

4-1. 2025: The Digital Pathology Odyssey Continues

Speaker: Inti Zlobec, PhD (Professor, University of Bern, Switzerland)

4-2. Redefining Early Cancer Detection: Novel CRISPR Tools Meet Next-Generation Biospecimens

Speaker: Cesar M. Castro, MD (Associate Professor, Harvard Medical School, USA)

4-3. Data–Driven Integration of Histopathology and Genomics for Precision Oncology

Speaker: Shumpei Ishikawa, MD, PhD (Professor, The University of Tokyo, Japan)

Title: 2025: The Digital Pathology Odyssey Continues

Inti Zlobec, PhD

Professor, Digital Pathology, University of Bern
Institute of Tissue Medicine and Pathology (ITMP)
Switzerland

Speaker

Hitoshi Nakagama, MD, D.M.Sc

President, The Japan Agency for Medical Research and Development (AMED), Japan

Chair

Inti Zlobec, PhD

Research summary

Dr. Inti Zlobec serves as the Head of Digital Pathology at the Institute of Tissue Medicine and Pathology, University of Bern. Her research focuses on translational applications of artificial intelligence (AI) and machine learning to analyze pathology images and spatial tissue data. The primary goal is to discover and validate novel prognostic and predictive biomarkers for colorectal cancer patients. Her interdisciplinary team integrates digital pathology with computational tools to enhance cancer diagnostics and personalized treatment strategies.

Professional Experience/Awards

Dr. Inti Zlobec earned her PhD in Experimental Pathology from McGill University in 2007. She completed a postdoctoral fellowship at the University Hospital Basel, focusing on tissue-based colorectal cancer research utilizing biostatistical models. In 2010, she achieved habilitation and shortly afterwrads joined the University of Bern's Institute of Pathology, where she established and led the Translational Research Unit (TRU) and later the Tissue Bank Bern (TBB). She was appointed Associate Professor in 2014 and became Professor of Digital Pathology in April 2022.

Professor Zlobec is actively involved in several professional organizations. She is a member of the Executive Team at the Center for Artificial Intelligence in Medicine (CAIM) at the University of Bern, Co-Founder and President of the Swiss Consortium

for Digital Pathology (SDiPath),Chair of the European Society of Pathology's Working Group on Digital & Computational Pathology, and on the Board of the European Society of Digital and Intgerative Pathology (ESDIP).

Her contributions to the field are reflected in her impressive academic metrics, including a Discipline H-index (D-index) of 76 in Medicine, with over 19,945 citations. Her most cited works focus on the Immunoscore for colon cancer classification and tumor budding in gastrointestinal cancers.

Professor Zlobec also advocates for diversity and mentorship in AI and medicine and promotes both through CAIM's Diversity in AI in Medicine (DAIM) working group.

Education

PhD 2007 McGill University, Canada

Abstract of the lecture

Pathology is going digital! On the one hand, digitization of glass slides and automated lab workflows are meant to improve efficiency and open the gateway to AI applications. On the other, pathologists are faced with interpreting images for diagnosis in a completely different way (on a monitor rather than microscope) yet still assuring the quality of their diagnoses with no change in turn-around-times. Is AI meant to help here? Generative AI and large language models (LLMs) have shown promising capabilities in delivering precise pathology diagnoses and suggesting effective treatment plans when paired with histological images and textual input. Foundational models have attracted attention for their ability to recognize complex tissue patterns and to be fine-tuned for enhanced accuracy in specific applications. With AI making headlines across the field, we would imagine that AI in pathology is ready for prime time. Is it? In today's talk, we explore the answer to this question, taking a bird's eye-view on where the community stands with the transition to digital pathology. We will then take a critical approach to the current market for AI applications and associated challenges. We will ask ourselves, which medical professionals do tissue-based AI algorithms benefit (pathologists or oncologists?), and how will pathologists and oncologists deal with the rise in increasingly complex biomarker algorithms? Indeed, pathologists seem ready to use AI tools based on hand-crafted features, leading to verifiable AI outputs, but what about those tools using end-to-end deep learning for predicting molecular aberrations, therapy response or prognosis? The computational companion diagnostic tests are starting to gain momentum, but how will pathologists trust tests whose results they cannot verify- should they? Finally, we will look at where we go from here. The technologies are at our fingertips, including spatial transcriptomics and multiplex immunofluorescence, as well as LLM and vision-language models to name a few. To wrap up, we look at where the field is going and what we can expect in the near to mid- to long-term future.

Title: Redefining Early Cancer Detection: Novel CRISPR Tools Meet Next-Generation Biospecimens

Cesar M. Castro, MD

Associate Professor of Medicine, Harvard Medical School
Director, Gynecologic Oncology Program - Mass General Hospital (MGH) Cancer Center
USA

Speaker

Hitoshi Nakagama, MD, D.M.Sc

President, The Japan Agency for Medical Research and Development (AMED), Japan

Chair

Cesar M. Castro, MD

Research summary

Dr. Cesar M. Castro, Associate Professor of Medicine at Harvard Medical School and Director of the Gynecologic Oncology Program at Massachusetts General Hospital (MGH), leads pioneering research in translational oncology. His work focuses on integrating nanotechnology, molecular imaging, and liquid biopsy techniques to enhance the detection and monitoring of solid tumors, notably gynecologic cancers. Dr. Castro's lab has developed innovative diagnostic platforms utilizing extracellular vesicle analysis, aiming to enable non-invasive, point-of-care cancer diagnostics applicable in both advanced and resource-limited settings. By combining multi-omics profiling with machine learning, his team seeks to uncover novel biomarkers and therapeutic targets, advancing personalized cancer care. Additionally, Dr. Castro is committed to mentoring emerging scientists and fostering interdisciplinary collaborations to translate scientific discoveries into clinical applications.

Professional Experience/Awards

Dr. Cesar M. Castro earned his B.A. and M.A. degrees from the University of California, Berkeley as a Regents Scholar, followed by an M.D. from the University of California, San Francisco (UCSF). He completed his Internal Medicine residency at UCSF and pursued a fellowship in adult oncology through the Dana-Farber/Mass General

Brigham Cancer Care program. During his fellowship, he obtained a Master of Medical Sciences (MMSc) in Clinical Investigation from Harvard Medical School.

At MGH, Dr. Castro serves as Director of the Gynecologic Oncology Program and the Cancer Therapy Program within the Center for Systems Biology. He also co-leads the Gynecologic Cancers Program at the Dana-Farber/Harvard Cancer Center. His research emphasizes the development of nanotechnology-based diagnostics and liquid biopsy platforms for cancer detection and monitoring. Dr. Castro has led initiatives to implement decentralized cancer diagnostics in countries such as Botswana, Uganda, and Ghana, supported by NIH funding. He is Director of the Cancer Program at the MGH Center for Systems Biology and Chair of the Mass General Brigham Phase 1 Cancer Clinical Trials Institutional Review Board.

Dr. Castro's contributions have been recognized through various awards and appointments. He is a standing member and alternate chair of the NIH Innovations in Nanotechnology and Nanosystems Study Section and serves on the steering committee for the U.S. National Cancer Institute's Liquid Biopsy Consortium. In 2025, he was elected to the American Society for Clinical Investigation. His work has received funding from the National Institutes of Health, Department of Defense, Robert Wood Johnson Foundation, American Cancer Society, and Ovarian Cancer Research Fund, among others. Additionally, he holds six awarded patents. Dr. Castro is dedicated to mentoring the next generation of scientists and clinicians, fostering interdisciplinary collaborations to advance cancer research and improve patient outcomes.

Education

MD 2005 The University of California, San Francisco School of Medicine, USA

Abstract of the lecture

Democratizing molecular testing for cancer screening, diagnostics, and monitoring in resource-constrained regions domestically and globally remains an unmet need. Complicated hardware, multi-step assays, and readouts influenced by environmental conditions challenge the widespread adoption of emerging technologies. As such, highly multidisciplinary efforts that leverage imaging, engineering, and oncology skillsets are best positioned to make inroads. The increasing worldwide prevalence of human papillomavirus-related cancers, such as cervical, head and neck, and anal cancers demands improved and reliable profiling platforms without burdening existing workflows. Other non-HPV cancers are similarly in great need of early detection and monitoring for early recurrences (e.g. minimal residual disease). Successful screening and tracking efforts that feature easy-to-operate tactics, durable reagents, and highly accurate readouts indifferent to environmental conditions can increase access to populations residing outside highly resourced medical centers. An overview of recently introduced CRISPR-inspired nanotechnology strategies that directly tackle such unmet clinical needs will be presented.

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Title: Data–Driven Integration of Histopathology and Genomics for Precision Oncology

Shumpei Ishikawa, MD, PhD

Professor, Department of Preventive Medicine at the Graduate School of Medicine, the University of Tokyo, Japan
Division Chief, Division of Pathology, Exploratory Oncology Research & Clinical Trial Center, National Cancer Center, Japan

Speaker

Hitoshi Nakagama, MD, D.M.Sc

President, The Japan Agency for Medical Research and Development (AMED), Japan

Chair

Shumpei Ishikawa, MD, PhD

Research summary

Dr. Shumpei Ishikawa, based at the Graduate School of Medicine, the University of Tokyo, leads pioneering research at the intersection of cancer genomics and pathology. His work focuses on integrating cancer histopathology with genomic data to uncover novel biomarkers and therapeutic targets, particularly in gastric cancer. His early achievement includes the publication of the first draft map of human copy number variation through international collaboration (Nature, 2006).

Currently, his research is centered on the genomics and immunogenomics of gastric carcinoma (GC). He discovered RHOA driver mutations specifically present in diffuse-type GC (Nature Genetics, 2014) and identified an alcohol- and tobacco-associated GC subtype specifically found in East Asia, particularly with inactive ALDH2 genetic background (Science Advances, 2020; Nature Genetics, 2023). These discoveries have significantly advanced the understanding of gastric cancer genetics and opened new avenues for prevention and therapy.

Recently, he has been actively exploring the complex homeostasis of cancer tissues using deep learning and spatial genomics approaches. He developed methods for universal encoding of pan-cancer histology (Cell Reports, 2022) and interpretable histopathological AI for inferring biological features from H&E images (Patterns, 2023).

He has also contributed to spatial genomics, publishing a spatial cell atlas of the gastric mucosa in both healthy and diseased states (Cell Reports, 2023).

Professional Experience/Awards

Dr. Ishikawa graduated from the Faculty of Medicine at the University of Tokyo and received his PhD in Human and Diagnostic Pathology in 2004. He began his academic career as an Assistant Professor at the Genome Science Division, Research Institute of Advanced Science and Technology, the University of Tokyo. In 2013, he moved to Tokyo Medical and Dental University (currently Institute of Science Tokyo), where he served as a Professor in the Department of Genomic Pathology. In 2018, he returned to the University of Tokyo, where he currently holds the position of Professor in the Department of Preventive Medicine at the Graduate School of Medicine. He is also the Division Chief of Pathology at the Exploratory Oncology Research & Clinical Trial Center, National Cancer Center Japan from 2022.

Dr. Ishikawa has received numerous prestigious awards, including: Yamato Scientific Award (2015), Japanese Society of Pathology Academic Research Award (2015), the Young Investigator Awards of the Japanese Cancer Association (2015), the JCA-Mauvernay Award of the Japanese Cancer Association (2021), the Eiichi Tahara Award from the Japanese Society for Gastroenterological Carcinogenesis (2023)

Education

MD	2000	The University of Tokyo, Japan
PhD	2004	The University of Tokyo, Japan

Abstract of the lecture

Recent advances in deep learning have revolutionized cancer pathology by enabling the extraction and quantification of complex histological features that were previously difficult to assess objectively. This progress has allowed the application of large-scale data science approaches, akin to those used in genomics, across thousands of histopathological images. In particular, gastric cancer, a highly heterogeneous disease both clinically and pathologically, presents an ideal model for such integrative analysis.

In this study, we applied deep learning to analyze histopathological images from over 800 gastric cancer cases. From these, we extracted high-dimensional morphological features and reconstructed a continuous, quantitative spectrum of tissue architecture. This spectrum not only recapitulated conventional histological classifications but also provided a data-driven view of morphological diversity across the cohort.

To explore the biological underpinnings of this morphological continuum, we integrated the image-derived features with genomic profiles of the same tumors. This multimodal fusion uncovered systematic associations between tissue morphology, cellular composition, and specific somatic alterations. For example, certain morphological subspaces were enriched for distinct mutation profiles, highlighting the biological relevance of the visual features.

Beyond classification, this approach enables a collective intelligence paradigm in pathology—where insights emerge not from individual expert interpretation, but from comprehensive, quantitative comparisons across populations. Importantly, our findings also underscore current challenges in the field, including the need for biological interpretability and model robustness across different institutions and imaging conditions.

Overall, this integrative framework offers a novel, scalable approach to characterize tumor heterogeneity in a biologically meaningful way. By bridging the gap between tissue morphology and genomics, it holds promise for more precise diagnosis,

stratification, and treatment planning in gastric cancer and potentially other malignancies.

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Session 5

Novel Approaches in Cancer Immunotherapy

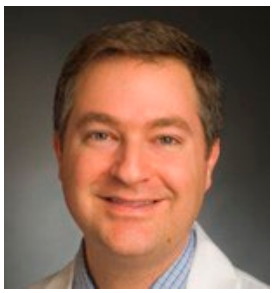
5-1. Developing CAR-T Cell Therapy to Eradicate Oncogene-Driven Drug Tolerant Persister Cells

Speaker: David Barbie, MD
(Jane Rodgers Chair, Dana-Farber Cancer Institute, USA)

5-2. Engineered and Adjuvant Enhancements of CAR-T Cell Effector Functions

Speaker: Avery Posey, PhD (Assistant Professor, University of Pennsylvania, USA)

Title: Developing CAR-T Cell Therapy to Eradicate Oncogene-Driven Drug Tolerant Persister Cells



David Barbie, MD

Director, Lowe Center for Thoracic Oncology
Associate Director, Belfer Center for Applied Cancer Research
Jane Rodgers Chair at Dana-Farber Cancer Institute
Associate Professor of Medicine, Harvard Medical School
USA

Speaker

Hiroyoshi Nishikawa, MD, PhD

Professor and Chairperson, Division of Cancer Immune Multicellular System Regulation, Center for Cancer Immunotherapy and Immunobiology (CCII), Kyoto University Graduate School of Medicine
Chief, Division of Cancer Immunology, Research Institute / Exploratory Oncology Research and Clinical Trial Center (EPOC), National Cancer Center Japan

Chair

David Barbie, MD

Research summary

Dr. David Barbie serves as the Director of the Lowe Center for Thoracic Oncology at Dana-Farber Cancer Institute and is an Associate Professor of Medicine at Harvard Medical School. His research centers on developing innovative therapies for KRAS-mutant non-small cell lung cancer (NSCLC), a subtype historically resistant to targeted treatments. Dr. Barbie's laboratory investigates the role of the innate immune system in tumor survival, particularly focusing on drug-tolerant persister (DTP) cells that evade standard therapies. Notably, his team identified that the kinase inhibitor momelotinib can inhibit TBK1 and JAK signaling pathways, demonstrating activity in KRAS-driven lung cancer models. This discovery led to a clinical trial combining momelotinib with the MEK inhibitor trametinib for patients with refractory KRAS-mutant lung cancer. In 2024, Dr. Barbie's team received the inaugural IASLC–LCRF Team Science Research Grant to explore immune-based strategies targeting DTP cells, aiming to overcome therapy resistance and improve patient outcomes.

Professional experience

Dr. David Barbie earned his AB from Harvard College in 1997 and his MD from Harvard Medical School in 2002. During medical school, he was a Howard Hughes Medical Institute Research Fellow in Dr. Edward Harlow's laboratory at Massachusetts General Hospital. He completed his residency in Internal Medicine at Massachusetts General Hospital from 2002 to 2005, serving as Chief Resident in 2006. Dr. Barbie then pursued a fellowship in Medical Oncology through the Dana-Farber/Partners CancerCare program, concluding in 2008. Subsequently, he conducted postdoctoral research in Dr. William Hahn's laboratory at Dana-Farber and the Broad Institute, focusing on cancer biology.

In 2010, Dr. Barbie was appointed as a tenure-track investigator at Dana-Farber Cancer Institute and began his clinical practice within the Lowe Center for Thoracic Oncology. He currently holds multiple leadership roles, including Associate Director of the Robert and Renée Belfer Center for Applied Cancer Science and Co-Leader of the Lung Cancer Program at the Dana-Farber/Harvard Cancer Center. Additionally, he serves as Co-Director of the DF/HCC Lung Cancer SPORE, a collaborative research initiative aimed at advancing lung cancer therapies.

Dr. Barbie's contributions to oncology have been recognized through several prestigious awards. He received the ASCO Young Investigator Award in 2009, the NIH K08 Award in 2010, the V Foundation Scholar Award in 2012, and the NIH R01 Award in 2015. In 2024, he was honored with the inaugural IASLC–LCRF Team Science Research Grant, a $2.5 million award supporting his team's work on immune elimination of drug-tolerant persister cells in oncogene-driven lung cancer.

Beyond his research and clinical duties, Dr. Barbie is committed to mentoring emerging scientists and fostering interdisciplinary collaborations to translate laboratory discoveries into clinical applications, aiming to improve outcomes for patients with thoracic malignancies.

Education

AB	1997	Harvard College, USA
MD	2002	Harvard Medical School, USA

Abstract of the lecture

EGFR tyrosine kinase inhibitors (TKIs) have dramatically improved outcomes for EGFR-mutated non-small cell lung cancer (NSCLC) patients, but relapse frequently occurs due to drug tolerant persister (DTP) cells that can evolve and develop diverse mechanisms of drug resistance. In tumor samples obtained from patients with EGFR-mutated NSCLC treated with EGFR-TKIs in the neoadjuvant setting, we observed enriched expression of the cell surface protein TROP2, a target of clinically active antibody drug conjugates (ADCs). We confirmed these findings across multiple EGFR-mutated NSCLC cell line and patient-derived xenograft models treated with osimertinib in vivo. As compared with other clinically actionable cell surface targets such as HER3, TROP2 levels were more substantially and consistently induced in the EGFR TKI induced DTP cell state and linked with the expression of TROP2 associated embryonic gene signatures. Treatment with the TROP2 ADC sacituzumab govitecan at the time of osimertinib-induced minimal residual disease only modestly delayed tumor recurrence in vivo, whereas a single infusion of sacituzumab-based TROP2 directed CAR-T cells significantly prolonged relapse-free survival, with evidence of cure. In parallel, we explored the potential of CAR-T cell engineering to optimize the performance of TROP2 CAR-T cells, benchmarking activity against the same CAR-T cells derived using the single chain variable fragment (scFv) from sacituzumab. We performed epitope mapping of a novel series of nanobodies (VHH antibodies) derived against

TROP2, uncovering distinct binders targeting multiple TROP2 extracellular domains. Construction of biparatopic TROP2 CAR-T cells with these dual domain VHH binders resulted in superior in vivo activity against EGFR mutant NSCLC xenograft models. These data highlight the potential of engineering TROP2 CAR-T cell therapy to eliminate EGFR DTPs in patients, preventing acquired resistance and resulting in durable tumor control.

Title: Engineered and Adjuvant Enhancements of CAR-T Cell Effector Functions

Avery Posey, PhD

Assistant Professor, Department of Systems Pharmacology and Translational Therapeutics, Perelman School of Medicine, University of Pennsylvania
USA

Speaker

Hiroyoshi Nishikawa, MD, PhD

Professor and Chairperson, Division of Cancer Immune Multicellular System Regulation, Center for Cancer Immunotherapy and Immunobiology (CCII), Kyoto University Graduate School of Medicine
Chief, Division of Cancer Immunology, Research Institute / Exploratory Oncology Research and Clinical Trial Center (EPOC), National Cancer Center Japan

Chair

Avery Posey, PhD

Research summary

Dr. Avery Posey, an Assistant Professor at the University of Pennsylvania's Perelman School of Medicine, leads the Posey Laboratory, which focuses on developing novel cellular immune therapies by genetically modifying patients' T cells to enhance their ability to combat cancer and other diseases. His research encompasses antigen discovery to identify tumor-specific targets, engineering strategies to overcome the tumor microenvironment, and modifying T cell signaling to achieve robust immune efficacy. Notably, Dr. Posey's work includes the development of glycosylation-specific chimeric antigen receptors (CARs) that precisely target tumor-associated glycoforms, such as those found in MUC1. His lab's innovative approaches aim to improve the effectiveness of CAR T cell therapies, particularly in solid tumors.

Professional experience

Dr. Posey earned dual Bachelor of Science degrees in Biochemistry & Molecular Biology and Bioinformatics & Computational Biology from the University of Maryland, Baltimore County (UMBC) in 2005. He then obtained his PhD in Genetics from the

University of Chicago in 2011. His doctoral research focused on dysfunctional cellular processes underlying muscular dystrophy and cardiomyopathy.

Following his PhD, Dr. Posey completed postdoctoral training in the laboratory of Dr. Carl June at the University of Pennsylvania, where he developed glycosylation-specific CARs targeting tumor-associated glycoforms. In 2016, he joined the faculty at the Perelman School of Medicine as an Assistant Professor in the Department of Systems Pharmacology and Translational Therapeutics. He also serves as the Director of Equal Opportunity Engagement at the Center for Cellular Immunotherapy.

Dr. Posey's contributions to cancer immunotherapy have been recognized with several prestigious awards. In 2021, he received the inaugural AACR-Lustgarten Foundation Career Development Award for Pancreatic Cancer Research in honor of Congressman John Robert Lewis. He was also awarded the V Scholar Grant for Black/African American Cancer Researchers (2021–2023) and the CureSearch Young Investigator Award (2018–2020) for his work on neuroblastoma.

Beyond his research, Dr. Posey is committed to mentoring the next generation of scientists, particularly those from underrepresented backgrounds. He directs the SUIP-CCI and PICI RISE research training programs in cancer immunology and immunotherapy at the University of Pennsylvania.

Education

BS	2005	University of Maryland, Baltimore County (UMBC), USA
PhD	2011	University of Chicago, USA

Abstract of the lecture

Advances in chimeric antigen receptor (CAR) T-cell engineering have enabled the targeting of tumor-specific post-translational modifications, particularly aberrant glycosylation patterns associated with malignant transformation. One such target, the Tn antigen—a truncated O-glycan composed of a single N-acetylgalactosamine (GalNAc) residue—emerges from disruptions in COSMC, a molecular chaperone essential for core 1 O-glycan synthesis. In pancreatic ductal adenocarcinoma (PDAC) models, COSMC knockout leads to increased Tn antigen expression, resulting in enhanced tumor proliferation, accelerated in vivo growth, and a shift toward an immunosuppressive tumor microenvironment. This includes elevated infiltration of granulocytic myeloid-derived suppressor cells (gMDSCs), loss of central memory $CD8^+$ T cells, and upregulation of extracellular matrix and myeloid recruitment genes. IL-34 was identified as a key mediator of gMDSC accumulation downstream of Tn antigen expression. Complementary to these findings, a novel CAR T-cell therapy (CART-TnMUC1) was developed to target the Tn-modified form of MUC1, incorporating CD2-based costimulation to enhance cytotoxic activity. To further augment CAR T-cell efficacy, cytokine-armored CAR constructs were engineered to secrete pro-inflammatory cytokines (e.g., IL-12, IL-18, IL-23), demonstrating improved tumor clearance in preclinical models. A modular approach using linker-targeted immunocytokines—specifically anti-(G_4S)-IL12 constructs—allowed selective stimulation of CAR T cells via their peptide linker domains. These constructs significantly boosted anti-tumor activity and survival in vivo but also revealed toxicity risks in immunocompetent models, likely due to off-target immune activation. Mutant IL-12 variants with reduced binding to endogenous IL-12 receptors retained efficacy while mitigating systemic activation, suggesting a viable path toward safer, pan-CAR T-cell enhancement strategies.

Session 6

Breakthrough Technology Session: Innovative Drug Discovery Technologies

6-1. Dendritic-T Cell Crosstalk in Shaping Immunotherapy Responses

Speaker: Rony Dahan, PhD
(The Rina Gudinski Career Development Chair, Weizmann Institute of Science, Israel)

6-2. Shaping the Future of Cancer Care: Chugai's Cutting-Edge Technologies

Speaker: Tomoyuki Igawa, PhD
(Associate Vice President, Chugai Pharmaceutical Co., Ltd.)

Title: Dendritic-T Cell Crosstalk in Shaping Immunotherapy Responses

Speaker

Rony Dahan, PhD

The Rina Gudinski Career Development Chair,
Weizmann Institute of Science, Israel

Chair

Kiyohiko Hatake, MD, PhD

Professor, Akasaka Sanno Medical Center, Japan

Rony Dahan, PhD

Research Summary

Dr. Rony Dahan leads the Cancer Immunology and Immunotherapy Lab at the Weizmann Institute of Science, focusing on enhancing immune responses against cancer through advanced antibody engineering. His research delves into the Fc regions of antibodies and their interactions with Fcγ receptors (FcγRs), aiming to optimize the efficacy of antibody-based immunotherapies. By utilizing humanized mouse models, his team investigates the mechanisms governing both natural and therapeutic antibodies, striving to develop next-generation antibodies with improved anti-tumor activity. Notably, he has pioneered the creation of dendritic cell-selective bispecific antibodies and dendritic-T cell engagers, some of which are progressing through clinical development stages.

Professional Experience/Awards

Dr. Rony Dahan obtained his BSc in Molecular Biology (2004) and PhD in Molecular Immunology (2010) from the Technion – Israel Institute of Technology. He conducted postdoctoral research at Rockefeller University (2013–2017) under Prof. Jeffrey Ravetch, where he contributed to elucidating the role of FcγRs in the activity of checkpoint antibodies, including anti-PD-1/L1, and to the development of the Fc-

engineered CD40 antibody, 2141-V11, now in Phase II clinical trials.

In 2017, Dr. Dahan established his laboratory at the Weizmann Institute, where he serves as a senior scientist in the Department of Systems Immunology. His work has addressed key challenges in the development of immunomodulatory antibodies, providing new insights into their mechanisms of action. Based on his discoveries, he has pioneered novel immunotherapies, including dendritic cell-selective bispecific antibodies and dendritic-T cell engagers, several of which are advancing through clinical development.

Dr. Dahan's contributions have been recognized with several awards, including the Technion's Presidential Excellency Award (2004), the Pollack Prize for Academic Excellence (2007), the Sigma Prize for Outstanding Research by the Israel Immunological Society (2010), the Sanford Kaplan Prize for Creative Management in 21st Century High Technology (2011), the Immune Therapies Training Award from the Juvenile Diabetes Research Foundation (2011), the Hershel Rich Technion Innovation Award (2011), and the Cancer Research Institute Irvington Postdoctoral Fellowship (2014), the Israel Cancer Research Fund (ICRF) – Research Career Development Award (2018), The Harry J. Lloyd Charitable Trust (HJLCT) Career Development Award (2019), and the Melanoma Research Alliance (MRA) Young Investigator Award (2019)..

In 2022, Dr. Dahan was awarded the European Research Council (ERC) Consolidator Grant, further acknowledging his significant contributions to the field of cancer immunotherapy.

Education

BS	2004	Technion – Israel Institute of Technology, Israel
PhD	2010	Technion – Israel Institute of Technology, Israel

Abstract of the lecture

Effective cancer immunotherapy requires the orchestration of multiple immune components, yet many approaches, including immune checkpoint blockade, yield limited and variable clinical success. In this presentation, I will highlight how dendritic–T cell crosstalk serves as a pivotal axis in determining the success of immunotherapeutic interventions, drawing on two distinct yet complementary studies.

First, I will describe our development of a novel bispecific DC–T cell engager (BiCE) that promotes productive interactions between PD-1$^+$ T cells and conventional type 1 dendritic cells (cDC1). While anti–PD-1 monoclonal antibodies (aPD-1 mAbs) have shown promise, their efficacy is often hindered by insufficient engagement of the broader immune network. BiCEs enhance dendritic–T cell communication within tumors and tumor-draining lymph nodes, resulting in superior immune reprogramming compared to standard aPD-1 therapy. Single-cell and physical interaction analyses reveal that BiCE treatment fosters enriched immune cell circuits, translating into more durable and potent anti-tumor responses.

Second, I will discuss how Fc-engineered agonistic antibodies targeting the co-stimulatory receptor GITR (glucocorticoid-induced TNFR-related protein) can potentiate anti-tumor immunity through enhanced CD4$^+$ T cell–dendritic cell interactions. By optimizing Fc glycan and protein domains to selectively enhance binding to activating Fcγ receptors (FcγRIIa and FcγRIIIa), we achieved more effective Treg depletion and immune activation. Using humanized FcγR mouse models, we demonstrate that these Fc-optimized GITR mAbs drive robust immunologic synapses between CD4$^+$ T cells and dendritic cells, amplifying anti-tumor responses through both innate and adaptive pathways.

Together, these studies underscore the critical role of dendritic–T cell communication in shaping therapeutic outcomes and offer novel strategies to enhance immune

coordination in the tumor microenvironment. Understanding and leveraging this cellular crosstalk may be key to expanding the efficacy of cancer immunotherapies.

References

1. **Dahan R** and Korman AJ. Fc-optimized checkpoint antibodies for cancer immunotherapy. *Trends Mol Med* 2024; S1471-4914(24): 00275-2.
2. Shapir Itai Y, Barboy O, ..., Amit I, **Dahan R**. Bispecific dendritic-T cell engager potentiates anti-tumor immunity', *Cell* 2024; 187: 375-389. (Shapir Itai and Barboy are equal contributors; Amit and Dahan are equal contributors)
3. Cohen Saban N, Yalin A, ..., Amit I, **Dahan R**. 2023, Fc glycoengineering of a PD-L1 antibody harnesses Fcγ receptors for increased antitumor efficacy. *Science immunology*; 8: 81.
4. Salomon R, Rotem H, ..., Amit I, **Dahan R**. Bispecific antibodies increase the therapeutic window of CD40 agonists through selective dendritic cell targeting. *Nat Cancer* 2022; 3: 287-302. (Salomon and Rotem are equal contributors)
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Title: Shaping the Future of Cancer Care: Chugai's Cutting-Edge Technologies

Speaker

Tomoyuki Igawa, PhD

Associate Vice President and Head of the Translational Research Division at Chugai Pharmaceutical Co., Ltd.

Chair

Kiyohiko Hatake, MD, PhD

Professor, Akasaka Sanno Medical Center, Japan

Tomoyuki Igawa, PhD

Research Summary

Dr. Tomoyuki Igawa, Associate Vice President and Head of the Translational Research Division at Chugai Pharmaceutical Co., Ltd., is a leading figure in therapeutic antibody engineering. His work focuses on developing innovative antibody technologies to address unmet medical needs. Notably, he has contributed to the creation of bispecific antibodies, such as Hemlibra® (emicizumab) for hemophilia A, and recycling antibodies like Enspring® (satralizumab) and crovalimab, which can bind to antigens repeatedly, enhancing therapeutic efficacy. He has also worked on half-life extension technologies exemplified by Mitchga® (nemolizumab). Dr. Igawa's research integrates antibody engineering with disease mechanisms, aiming to develop next-generation biologics. His contributions have significantly advanced Chugai's and Roche's pipelines, with over 40 peer-reviewed publications and more than 100 patents in antibody drug discovery.

Professional Experience/Awards

Dr. Tomoyuki Igawa earned his Ph.D. in Engineering, Chemistry, and Biotechnology from the University of Tokyo. He began his career at Chugai Pharmaceutical, a member of the Roche group, where he played a pivotal role in developing novel antibody engineering technologies. His contributions include the development of bispecific antibodies like emicizumab, recycling antibodies such as satralizumab and

crovalimab, and half-life extension technologies exemplified by nemolizumab.

Dr. Igawa served as CEO and Research Head of Chugai Pharmabody Research Pte. Ltd. in Singapore, where he led efforts in antibody drug discovery and cancer immunotherapy research. In this role, he oversaw biological discovery research in both Japan and Singapore, focusing on integrating antibody technology with disease mechanisms to address unmet medical needs.

In April 2022, Dr. Igawa was appointed Associate Vice President and Head of the Translational Research Division at Chugai Pharmaceutical Co., Ltd. In this capacity, he is responsible for early clinical development and continues to lead innovative research in therapeutic antibodies.

Dr. Igawa's contributions to drug discovery have been recognized with several awards. Notably, he received the Pharmaceutical Society of Japan Award for Drug Research and Development in 2022 for his work on the discovery and development of the recycling antibody satralizumab.

With over 40 peer-reviewed publications and more than 100 patents in antibody drug discovery, Dr. Igawa continues to be a leading figure in the field, driving innovation in therapeutic antibody engineering.

Education

PhD 2011 The University of Tokyo, Japan

Abstract of the lecture

Despite the advent of remarkable therapies, cancer remains a disease with high unmet medical needs across many tumor types. Over the years, research into novel anti-cancer drugs has contributed to a gradual reduction in cancer-related mortality; however, numerous patient populations—particularly those diagnosed with hard-to-treat malignancies—continue to lack sufficient treatment options. Chugai Pharmaceutical has consistently pursued innovation in drug discovery, developing medicines, including anti-cancer agents, through a rigorous, technology-driven approach. By integrating deep insights into tumor biology with a sustained commitment to overcoming existing therapeutic limitations, we seek to address persistent clinical gaps and work toward improving patient outcomes across diverse cancer indications.

A key element of our research platform is an uncompromising dedication to quality at every stage of drug discovery. We leverage advanced antibody technologies, such as highly potent T cell engager antibodies[1)], which utilize the immune system to target and eliminate malignant cells, and "Switch" antibodies[2,3)], designed with the goal of providing precise and local activity in the tumor microenvironment while minimizing systemic adverse effects. Additionally, our proprietary mid-size molecule technologies[4)] enable us to pursue previously inaccessible targets, thereby broadening our therapeutic capabilities across a wide range of tumor types, including those that are resistant and refractory. Collectively, these technological platforms create a strong foundation for continuous innovation in oncology drug development.

In this presentation, we will highlight six promising development programs: SOF10, ALPS12, SAIL66, STA551, and ROSE12, which demonstrate the potential of next-generation antibody therapeutics for potent and selective antitumor activity; and LUNA18, which illustrates how our mid-size molecule approach may open novel therapeutic pathways previously considered undruggable.

By continuously refining these technologies, we strive to advance promising scientific concepts into potential new treatment options. Through steadfast dedication to scientific excellence, we remain committed to furthering the field of cancer therapy and ultimately supporting meaningful improvements in patient care and quality of life.

References

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2. Mimoto F, Tatsumi K, ..., Hattori K, **Igawa T**. Exploitation of Elevated Extracellular ATP to Specifically Direct Antibody to Tumor Microenvironment. *Cell Rep* 2020; 33: 108542.
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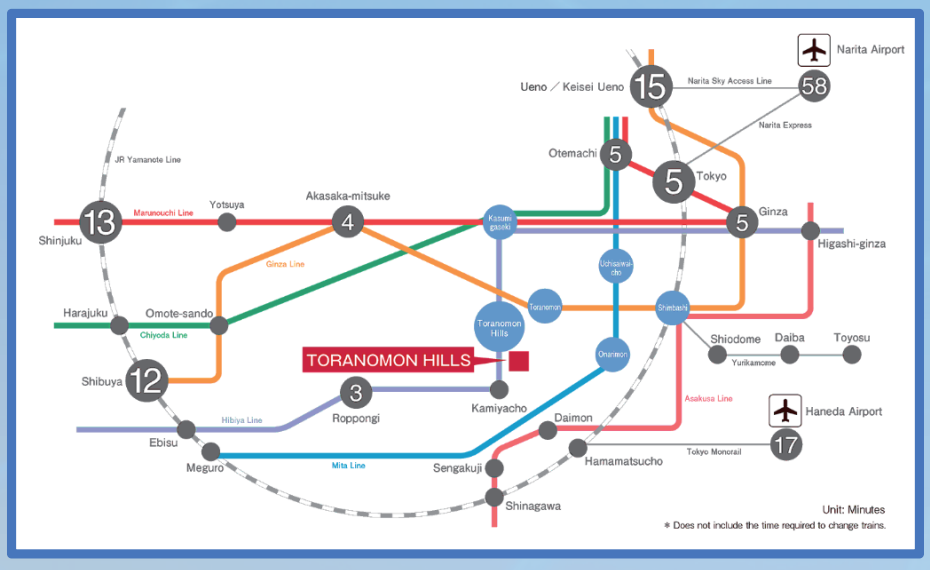
Access Map

Venue: Toranomon Hills Forum

5F, Toranomon Hills Mori Tower, 1 Chome-23-1 Toranomon,
Minato City, Tokyo 105-6390



11-minute walk from the Karasumoriguchi Exit of Shimbashi Stn.

Subway:
Hibiya Line
Toranomon Hills Stn
1. B1 Exit
2. A1b Exit

Ginza Line
Toranomon Stn
1. B1 Exit
2. B4 Exit

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