Program

International Academy for Advanced Oncology

IAAO

国際フォーラム2019

The Front Line of Innovation in Cancer Research and Therapy

2019年7月26日（金）12:55–17:50
27日（土）9:00–14:50
六本木アカデミーヒルズ49

CHAAO
Comprehensive
Academy for
Advanced Oncology

The Front Line of Innovation in Cancer Research and Therapy

Friday, July 26, 2019 12:55—17:50

Opening Remarks P.3

12:55 Osamu Nagayama (Tokyo Biochemical Research Foundation, Japan)

Opening Comment P.6

13:00 **Combination Therapy with Immuno-Oncology Drugs**
Speaker : Bruce A. Chabner (Harvard Medical School, USA)
Chair/Moderator : Yasuo Ikeda (Waseda University)

Breakthroughs in Cancer Immunology and Immunotherapy P.12

13:10 **What's Next in Cancer Immunotherapy**
Speaker : Antoni Ribas (University of California, Los Angeles, USA)
Chair/Moderator : Yusuke Nakamura (Japanese Foundation for Cancer Research, Japan)

13:50 **Targeting Regulatory T cells for Tumor Immunity**
Speaker : Shimon Sakaguchi (Immunology Frontier Research Center, Osaka Univ., Japan)
Chair/Moderator : Ryuzo Ueda (Aichi Medical University, Japan)

14:30 Coffee Break

14:50 **Enterophages: Newcomers in Immuno-Oncology 2.0**
Speaker : Laurence Zitvogel (Gustave Roussy, France)
Chair/Moderator : Noboru Yamamoto (National Cancer Center Hospital, Japan)

15:30 **Regeneration of Antigen-Specific Cytotoxic T cells with an iPSC Technology**
Speaker : Shin Kaneko (Center for iPS Cell Research and Application, Kyoto University, Japan)
Chair/Moderator : Mitsuaki Yoshida (Japanese Foundation for Cancer Research, Japan)

16:10 Coffee Break

Novel Targets for Cancer Drug Development P.38

16:30 **Predictive Markers for Immunotherapy Including EGFR and ALK Mutants**
Speaker : Bruce E. Johnson (Dana-Farber Cancer Institute, USA)
Chair/Moderator : Makoto Ogawa (Aichi Cancer Center, Japan)

17:10 **Stromal Fibroblasts Detect Genomic Stress in Cancer Cells and Modulate Therapy Responses**
Speaker : Erik Sahai (Francis Crick Institute, UK)
Chair/Moderator : Kohei Miyazono (The University of Tokyo, Japan)

18:00 Reception Dinner

Saturday, July 27, 2019 9:00—14:50

Cancer Genomics and Precision Oncology P.50

9:00 **Precision Pediatric Cancer Medicine**
Speaker : Elaine R. Mardis (Nationwide Children's Hospital, USA)
Chair/Moderator : Hiroyuki Mano (National Cancer Center Research Institute, Japan)

9:40 **Next-Generation Approaches to Assessing Hereditary Cancer Risk in the Genome Era**
Speaker : James M. Ford (Stanford University School of Medicine, USA)
Chair/Moderator : Hiroyuki Aburatani (The University of Tokyo, Japan)

10:20 Coffee Break

Translational Research in Precision Oncology P.62

10:40 **Fostering Precision Medicine in Selected Subpopulations of Patients with CRC**
Speaker : Josep Tabernero (Vall d'Hebron University Hospital, Spain)
Chair/Moderator : Tomomitsu Hotta (National Cancer Center, Japan)

11:20 **Evolving Paradigms of Precision Medicine in the Clinic**
Speaker : David Hyman (Memorial Sloan Kettering Cancer Center, USA)
Chair/Moderator : Hironobu Minami (Kobe University, Japan)

12:00 Lunch

Targeting Mutant RAS P.76

12:45 **A Novel Model for Oncogenic Activity of ERK Signal Activation in Human Cancer**
Speaker : Neal Rosen (Memorial Sloan Kettering Cancer Center, USA)
Chair/Moderator : Chikashi Ishioka (Tohoku University, Japan)

13:25 **Discovery of Direct Inhibitors of the Human Oncogene, KRAS (G12C)**
Speaker : Kevan M. Shokat (University of California, San Francisco, USA)
Chair/Moderator : Kiyohiko Hatake (International University of Health and Welfare, Japan)

14:05 **Targeting the RAS Pathway with SHP2 Inhibitors**
Speaker : Benjamin G. Neel (NYU Langone Health, USA)
Chair/Moderator : Masakazu Toi (Kyoto University, Japan)

Closing Remarks

14:45 Neal Rosen (Memorial Sloan Kettering Cancer Center, USA)

Official language » English
Dress code » Business casual

Opening Remarks

Osamu Nagayama

Chairman, The Tokyo Biochemical Research Foundation

From April 1, 2019, Chugai Academy for Advanced Oncology was integrated into the Tokyo Biochemical Research Foundation (TRBF), newly named Comprehensive Academy for Advanced Oncology (CHAAO), and continues to organize the International Academy for Advanced Oncology (IAAO).

As chairman of the TBRF, I would like to express my sincere thanks to all of the distinguished guests, experts and investigators -- both from overseas and Japan – for attending the IAAO2019.

Each year at IAAO, I am delighted to see that the size of our gathering continues to grow larger each time. This year-our tenth meeting-is no exception, with more than 250 people in attendance. We are always encouraged by the very positive feedback we receive from participants, and feel extremely happy and honored to know that more and more experts are interested in and value this event.

We are very fortunate to have so many world-class experts here to share their experience, knowledge, and insights. I am confident this will spark extensive and wide-ranging discussions. I encourage everyone to seize an opportunity in each session to actively engage in the discussions. Your comment or insight will be found truly valuable to someone else here at the forum.

The theme of this year's meeting is "*The Frontline of Innovation in Cancer Research and Therapy*". The program will focus on cancer genomics and precision oncology, which are progressing rapidly to the next stage. In cancer immunotherapy, we will address the latest breakthroughs in clinical applications. In addition, we will also focus on the novel approaches for targeting RAS mutations, and new findings around novel targets.

The exceptional program was organized through the active discussions and hard work of the IAAO Advisory Board members, namely Dr. Chabner, Dr. Rosen, Dr. Tabernero, Dr. Hatake, Dr. Ishioka, Dr. Kitagawa, Dr. Miyazono, Dr. Mano, Dr. Toi and Dr. Ueda. I sincerely appreciate and respect the leadership and dedication of these eleven board members.

In closing, allow me to once again thank you for participating this year. CHAAO's sincere wish is that this two-day event will be an extremely informative and fruitful time for everyone. Our ultimate goal is for the IAAO Forum to become an important venue for the exchange of information that advances the fight against cancer and empowers patients to deal with their treatment proactively and with hope.

Thank you very much for your attention.

Opening Comment

Combination Therapy with Immuno-Oncology Drugs

Speaker: Bruce A. Chabner (Harvard Medical School, USA)

Title: Combination Therapy with Immuno-Oncology Drugs

Bruce A. Chabner, MD

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

Speaker

Yasuo Ikeda, MD, PhD

University Professor, Waseda, Japan

Chairman

Bruce A. Chabner, MD

Profile

Dr. Chabner is a professor of medicine at Harvard Medical School and director of clinical research at the Massachusetts General Hospital Cancer Center. He graduated *summa cum laude* from Yale College in 1961. He received his M.D. from Harvard University *cum laude* in 1965.

He has had extensive experience in the field of cancer drug discovery and development. After joining the National Cancer Institute (NCI) in 1971, he participated in the training of clinical and research fellows there for the following 24 years, including three years (1976-1979) as Chief of the Clinical Pharmacology Branch; two years (1979-1981) as Director of the Clinical Oncology Program; and in 1981, one year as Acting Director, and for 13 years as permanent Director of the Division of Cancer Treatment, NCI.

In 1995, he joined the Massachusetts General Hospital as Clinical Director of its cancer

center and Chief of Hematology/Oncology. With the formation of the Dana-Farber/Harvard Cancer Center, he assumed responsibilities as Associate Director for Clinical Sciences of that consortium, which includes the Massachusetts General Hospital, Brigham & Women's Hospital, Dana-Farber Cancer Institute and Beath Israel Deaconess Medical Center. He has authored and edited the numerous textbooks of internal medicine, hematology, oncology and pharmacology.

He has received numerous awards, including Phi Beta Kappa, Alpha Omega Alpha, the Public Health Service's Distinguished Service Medal, the Karnofsky Award of the American Society for Clinical Oncology and the Bruce F. Cain Award for Drug Development of the American Association for Cancer Research. In 2006, he was the first recipient of the Bob Pinedo Award for Contributions to Improvement in the Care of Cancer Patients.

He is a senior editor for the Oncologist and serves on the executive advisory boards for some of the industry's leading innovators in drug development. In 2006, he received a presidential appointment to the National Cancer Advisory Board at the National Cancer Institute.

Recent Publications

Addressing the Financial Burden of Cancer Clinical Trial Participation: Longitudinal Effects of an Equity Intervention. Nipp RD, Lee H, Gorton E, Lichtenstein M, Kuchukhidze S, Park E, **Chabner BA**, Moy B. *Oncologist*. 2019 Apr 15. pii: theoncologist.2019-0146

Immuno-Oncology in China. Lu S, **Chabner BA**. *Oncologist*. 2019 Feb;24(Suppl 1):S1-S2.

The Other Opioid Crisis: Just Another Drug Shortage? Soumerai TE, Kamdar MM, **Chabner BA**. *Oncologist.* 2019 May;24(5):574-575.

Cell-free DNA Analysis in Cancer. Corcoran RB, **Chabner BA**. *N Engl J Med*. 2019 Jan 31;380(5):501-502.

Design and clinical validation of a point-of-care device for the diagnosis of lymphoma via contrast-enhanced microholography and machine learning. Im H, Pathania D, McFarland PJ, Sohani AR, Degani I, Allen M, Coble B, Kilcoyne A, Hong S, Rohrer L, Abramson JS, Dryden-Peterson S, Fexon L, Pivovarov M, **Chabner B**, Lee H, Castro CM, Weissleder R. *Nat Biomed Eng*. 2018 Sep;2(9):666-674.

Application of Cell-free DNA Analysis to Cancer Treatment. Corcoran RB, **Chabner BA**. *N Engl J Med*. 2018 Nov 1;379(18):1754-1765

Conflict of Interest: An Ethical Firestorm with Consequences for Cancer Research. **Chabner BA**, Bates SE. *Oncologist*. 2018 Dec;23(12):1391-1393.

Session 1

Breakthroughs in Cancer Immunology and Immunotherapy

1-1. What's Next in Cancer Immunotherapy

Speaker: Antoni Ribas (University of California, Los Angeles, USA)

1-2. Targeting Regulatory T cells for Tumor Immunity

Speaker: Shimon Sakaguchi
(Immunology Frontier Research Center, Osaka Univ., Japan)

1-3. Enterophages: Newcomers in Immuno-Oncology 2.0

Speaker: Laurence Zitvogel (Gustave Roussy, France)

1-4. Regeneration of Antigen-Specific Cytotoxic T cells with iPSC Technology

Speaker: Shin Kaneko
(Center for iPS Cell Research and Application, Kyoto University, Japan)

Title: What's Next in Cancer Immunotherapy

Speaker

Antoni Ribas, MD, PhD

Professor of Medicine, Professor of Surgery, Professor of Molecular and Medical Pharmacology at UCLA, USA
Director of the Tumor Immunology Program at the Jonsson Comprehensive Cancer Center, USA.
Vice-President of the Society for Melanoma Research and the Chair of the Melanoma Committee at SWOG, USA

Chairman

Yusuke Nakamura, MD, PhD

Director, The Cancer Precision Medicine Center, The Japanese Foundation for Cancer Research, Japan

Antoni Ribas, MD, PhD

Profile

Dr. Ribas is Professor of Medicine, Professor of Surgery, and Professor of Molecular and Medical Pharmacology at the University of California Los Angeles (UCLA), Director of the Tumor Immunology Program at the Jonsson Comprehensive Cancer Center (JCCC), Director of the Parker Institute for Cancer Immunotherapy (PICI) Center at UCLA, and Chair of the Melanoma Committee at Southwest Oncology Group (SWOG).

Dr Ribas is a physician-scientist who conducts laboratory and clinical research in malignant melanoma, focusing on gene engineered T cells, PD-1 blockade and BRAF targeted therapies. His National Cancer Institute (NCI), State of California and private foundation-supported research laboratory develops models of disease to test new therapeutic options, studies mechanism of action of treatments in patients and the molecular mechanisms of therapy resistance. He is an elected member of the American Society of Clinical Investigation (ASCI), the recipient of a AACR Richard and Hinda Rosenthal Award and a NCI Outstanding Investigator Award.

1990 M.D., University of Barcelona, Spain
1997 Ph.D., Autonomous University of Barcelona, Spain

Ribas' laboratory has made major advancements in the treatment of melanoma. Most significantly, he led the clinical program that demonstrated the effectiveness of the drug pembrolizumab (marketed as Keytruda), which ushered in a paradigm shift in the way melanoma is treated. The drug blocks a protein called PD-1 that sits on the surface of immune cells and keeps them from recognizing and attacking cancer cells. This was the first of the class of PD-1 blocking antibodies to be approved by the Food and Drug Administration for the treatment of any cancer. Keytruda is now used in the treatment of inoperable, metastatic melanoma, non-small cell lung cancers and other malignancies including Hodgkin's lymphoma. Ribas is conducting several clinical trials of cutting-edge treatments including both immunotherapies and targeted stem cell-based therapies. In 2017, he launched a first-of-its-kind trial that involves genetically engineering blood-forming stem cells to produce cancer-fighting T cells to treat melanomas and sarcomas and later multiple myeloma. The clinical trial involves a dual approach intended to provide patients with both short and long-term immune responses to their cancer. This is accomplished by giving patients modified blood-forming stem cells and modified mature T cells in a single transplant. Upon transplant, the modified mature T cells begin fighting the cancer immediately, while the modified blood-forming stem cells work to generate an on-going supply of new modified T cells, resulting in a lasting immune response to the cancer. Ribas also studies how the immune system responds to and develops resistance to immunotherapies, and how combination therapies may be used to overcome treatment resistance. One such treatment the Ribas lab is evaluating combines pembrolizumab with a targeted therapy that blocks a protein that leads to mutations in the BRAF gene. The BRAF gene makes a protein called B-RAF, which is involved in cell communication and growth. When BRAF genes are mutated, they can increase the growth and spread of cancer cells; approximately one - half of all patients with melanoma have mutations in the BRAF gene. An additional area of focus in the Ribas lab is molecular imaging and advanced monitoring of the immune system. Ribas and his team utilize molecular imaging technology such as PET scans to investigate and understand precisely how novel immunotherapies work on a molecular level. They aim to use these technologies to guide and evaluate new therapeutic strategies for melanoma. Ribas earned both his medical and doctoral degrees from the University of Barcelona in Spain**.** He completed an internship and residency at Hospital Vall d'Hebron and fellowships in surgical oncology and hematology/oncology at the UCLA David Geffen School of Medicine. He is an elected member of the American Society of Clinical Investigation.

Recent Publications

Effect of concomitant dosing with acid-reducing agents and vemurafenib dose on survival in patients with $BRAF_{V600}$ mutation-positive metastatic melanoma treated with vemurafenib ± cobimetinib. Lewis K, Hauschild A, Larkin J, **Ribas A**, Flaherty KT, McArthur GA, Dréno B, McKenna E, Zhu Q, Mun Y, Ascierto PA. *Eur J Cancer*. 2019 Jun 4;116:45-55.

Combined BRAF and MEK inhibition with PD-1 blockade immunotherapy in BRAF-mutant melanoma. **Ribas A**, Lawrence D, Atkinson V, Agarwal S, Miller WH Jr, Carlino

MS, Fisher R, Long GV, Hodi FS, Tsoi J, Grasso CS, Mookerjee B, Zhao Q, Ghori R, Moreno BH, Ibrahim N, Hamid O. *Nat Med*. 2019 Jun;25(6):936-940.

Dabrafenib, trametinib and pembrolizumab or placebo in BRAF-mutant melanoma. Ascierto PA, Ferrucci PF, Fisher R, Del Vecchio M, Atkinson V, Schmidt H, Schachter J, Queirolo P, Long GV, Di Giacomo AM, Svane IM, Lotem M, Bar-Sela G, Couture F, Mookerjee B, Ghori R, Ibrahim N, Moreno BH, **Ribas A**. *Nat Med*. 2019 Jun;25(6):941-946.

Phenotypic heterogeneity and evolution of melanoma cells associated with targeted therapy resistance. Su Y, Bintz M, Yang Y, Robert L, Ng AHC, Liu V, **Ribas A**, Heath JR, Wei W. *PLoS Comput Bio*l. 2019 Jun 5;15(6):e1007034.

Five-Year Outcomes with Dabrafenib plus Trametinib in Metastatic Melanoma. Robert C, Grob JJ, Stroyakovskiy D, Karaszewska B, Hauschild A, Levchenko E, Chiarion Sileni V, Schachter J, Garbe C, Bondarenko I, Gogas H, Mandalá M, Haanen JBAG, Lebbé C, Mackiewicz A, Rutkowski P, Nathan PD, **Ribas A**, Davies MA, Flaherty KT, Burgess P, Tan M, Gasal E, Voi M, Schadendorf D, Long GV. *N Engl J Med.* 2019 Jun 4.

Anti-CTLA-4 Immunotherapy Does Not Deplete FOXP3+ Regulatory T Cells (Tregs) in Human Cancers-Response. Sharma A, Subudhi SK, Blando J, Vence L, Wargo J, Allison JP, **Ribas A**, Sharma P. *Clin Cancer Res*. 2019 Jun 1;25(11):3469-3470.

Tumor characteristics associated with benefit from pembrolizumab in advanced non-small cell lung cancer. Hu-Lieskovan S, Lisberg A, Zaretsky JM, Grogan TR, Rizvi H, Wells DK, Carroll J, Cummings A, Madrigal J, Jones B, Gukasyan J, Shintaku IP, Slamon DJ, Dubinett SM, Goldman JW, Elashoff DA, Hellmann MD, **Ribas A**, Garon EB. *Clin Cancer Res.* 2019 May 21. pii: clincanres.4275.2018.

Interleukin 32 expression in human melanoma. Paz H, Tsoi J, Kalbasi A, Grasso CS, McBride WH, Schaue D, Butterfield LH, Maurer DM, **Ribas A**, Graeber TG, Economou JS. *J Transl Med*. 2019 Apr 5;17(1):113.

Autoimmune genetic risk variants as germline biomarkers of response to melanoma immune-checkpoint inhibition. Chat V, Ferguson R, Simpson D, Kazlow E, Lax R, Moran U, Pavlick A, Frederick D, Boland G, Sullivan R, **Ribas A**, Flaherty K, Osman I, Weber J, Kirchhoff T. *Cancer Immunol Immunother*. 2019 Jun;68(6):897-905.

Title: Targeting Regulatory T cells for Tumor Immunity

Speaker

Shimon Sakaguchi, MD, PhD

Professor, Experimental Immunology, The Immunology Frontier Research Center (iFReC), Japan

Chairman

Ryuzo Ueda, MD, PhD

Professor Emeritus, Senior Advisor, Nagoya City University, Japan
Professor, Dept. of Tumor Immunology, Aichi Medical University, Japan

Shimon Sakaguchi, MD, PhD

Profile

Dr. Sakaguchi is an immunologist and a Distinguished Professor of Osaka University. He is best known for the discovery of regulatory T cells and to describe their role in the immune system. This discovery is used in the treatment of cancer and autoimmune diseases.

Dr. Sakaguchi studied at the University of Kyoto; he obtained a Master's degree in 1976 and then a Ph.D in 1982. In Kyoto, he continued his study of pathology and immunology. As postdoc, he worked at the Johns Hopkins University and to Stanford University in the United States. In 1989, he began his teaching career and became an assistant professor at the Scripps Research Institute, and then returned to Japan in 1991, where he became a researcher at the RIKEN and director of the Department of Pathology immune Metropolitan Institute Tokyo. In 1999 he became professor of experimental pathology at Kyoto University. Since 2007 he is a teacher in his own laboratory at the Osaka University.

Awards

2004: William B. Coley Award

2008: Keio Medical Science Prize

2009: Medals of Honor (Japan), purple ribbon

2011: Asahi Prize

2012: Foreign associate of the National Academy of Sciences

2015: Gairdner Foundation International Award

2017: Crafoord Prize

2017: Person of Cultural Merit

Dr. Sakaguchi's main contribution to immunology is his discovery of regulatory T (Treg) cells and elucidation of the molecular and cellular basis of their development and function in disease and healthy states. Dr. Sakaguchi discovered in 1995 a subpopulation of T cells that was naturally present in the normal immune system, constituting approximately 5% of T cells, and specialized for immunosuppression. He named the population as Treg cells and showed that removal of the population from normal animals elicited spontaneous development of a spectrum of autoimmune diseases immunopathologically similar to the human counterparts (such as type 1 diabetes, autoimmune thyroiditis, and autoimmune arthritis). This was a clear demonstration that Treg cells are engaged in the maintenance of natural self-tolerance and their dysfunction can be a direct cause of autoimmune diseases. He subsequently demonstrated that reduction of Treg cells was able to elicit effective cancer immunity while enhancement of Treg-mediated suppression can induce tolerance to organ transplants. His group then showed in 2003 that Treg cells were specifically expressing the transcription factor Foxp3. This is a direct demonstration that natural Treg cells play a crucial role in immunological self-tolerance and homeostasis in humans because mutations of the Foxp3 gene impair Treg development / function, and cause human genetic diseases called IPEX (immune dysregulation, polyendocrinopathy, enteropathy, X-linked) syndrome, which is characterized by autoimmune diseases such as type 1 diabetes and thyroiditis, inflammatory bowel disease, and severe allergy. Dr. Sakaguchi has analyzed how Foxp3 controls Treg cell function and development, and also extended his research to the analysis of human Foxp3+ Treg cells. He has shown that human Foxp3+ T cells can be dissected into subpopulations, whose numerical and functional changes bear a good correlation with pathophysiology of immunological disorders. His recent contribution to human immunology is the characterization of cancer antigens in adult T cell leukemia/lymphoma, which is induced by HTLV-1 (human T-lymphotropic virus-1) endemic in Japan, as malignant transformation of human Treg cells. Based on Dr. Sakaguchi's research accomplishments, Treg cells are now under active investigation in laboratories and clinics all over the world to apply them for the treatment and prevention of immunological diseases and also control of a variety of physiological and pathological immune responses as in the setting of

autoimmunity, tumor immunity, organ transplantation, microbial immunity, allergy, and feto-maternal tolerance.

References

Regulatory roles of IL-10-producing human follicular T cells. Cañete PF, Sweet RA, Gonzalez-Figueroa P, Papa I, Ohkura N, Bolton H, Roco JA, Cuenca M, Bassett KJ, Sayin I, Barry E, Lopez A, Canaday DH, Meyer-Hermann M, Doglioni C, Fazekas de St Groth B, **Sakaguchi** S, Cook MC, Vinuesa CG. *J Exp Med*. 2019 Jun 17. pii: jem.20190493.

Theoretical modeling reveals that regulatory T cells increase T cell-interaction with antigen-presenting cells for stable immune-tolerance. Yamaguchi T, Teraguchi S, Furusawa C, Machiyama H, Watanabe TM, Fujita H, **Sakaguchi S**, Yanagida T. *Int Immunol*. 2019 May 25. pii: dxz043.

Functional Roles of the IgM Fc Receptor in the Immune System. Kubagawa H, Honjo K, Ohkura N, **Sakaguchi S**, Radbruch A, Melchers F, Jani PK. *Front Immunol.* 2019 May 3;10:945

PD-1$_+$ regulatory T cells amplified by PD-1 blockade promote hyperprogression of cancer. Kamada T, Togashi Y, Tay C, Ha D, Sasaki A, Nakamura Y, Sato E, Fukuoka S, Tada Y, Tanaka A, Morikawa H, Kawazoe A, Kinoshita T, Shitara K, **Sakaguchi S**, Nishikawa H. *Proc Natl Acad Sci U S A.* 2019 May 14;116(20):9999-10008.

Human FOXP3$_+$ Regulatory T Cell Heterogeneity and Function in Autoimmunity and Cancer. Wing JB, Tanaka A, **Sakaguchi S**. *Immunity*. 2019 Feb 19;50(2):302-316.

Satb1 regulates the effector program of encephalitogenic tissue Th17 cells in chronic inflammation. Yasuda K, Kitagawa Y, Kawakami R, Isaka Y, Watanabe H, Kondoh G, Kohwi-Shigematsu T, **Sakaguchi S**, Hirota K. *Nat Commun.* 2019 Feb 1;10(1):549.

Differential control of human Treg and effector T cells in tumor immunity by Fc-engineered anti-CTLA-4 antibody. Ha D, Tanaka A, Kibayashi T, Tanemura A, Sugiyama D, Wing JB, Lim EL, Teng KWW, Adeegbe D, Newell EW, Katayama I, Nishikawa H, **Sakaguchi S**. *Proc Natl Acad Sci U S A*. 2019 Jan 8;116(2):609-618.

Regulatory T cells expressing abundant CTLA-4 on the cell surface with a proliferative gene profile are key features of human head and neck cancer. Matoba T, Imai M, Ohkura N, Kawakita D, Ijichi K, Toyama T, Morita A, Murakami S, **Sakaguchi S**, Yamazaki S. *Int J Cancer*. 2019 Jun 1;144(11):2811-2822.

Title: Enterophages: Newcomers in Immuno-Oncology 2.0

Speaker

Laurence Zitvogel, MD, PhD

The Scientific Director at the Gustave Roussy Cancer Centre, Professor of Immunobiology at the University of Paris XI Medical School, France

Chairman

Noboru Yamamoto, MD, PhD

Director, Department of Experimental Therapeutics
National Cancer Center Hospital, Japan

Laurence Zitvogel, MD, PhD

Profile

1987 MD, School of Medicine, Pitié Salpétrière, University of Paris VI, France
1992 Board Certificate, Medical Oncology, University Paris VII, France
1995 PhD, Immunology, University Paris VII-Pittsburgh Cancer Institute, France-USA
1998 Habilitation Research Director, University Paris XI, France

CURRENT POSITIONS

1990 Master in Tumor Immunology of tumors, Prof. Fridman's lab., Institut Curie
1992-1994 Instructor, University of Pittsburgh, Pittsburgh Cancer Institute, USA
1994-1995 Assistant Professor, University of Pittsburgh, Pittsburgh Cancer Institute, USA
1995-2000 Associate Professor, Clinical attending, Medical University of Paris XI, IGR
1995-1998 Post-doctoral fellowship, Adenovirus Gene therapy, Pr Pericaudet's lab, IGR
1998-2016 Hospital Practioner, Breast Cancer Department, Clinical attending, IGR

2002- Co-Director, Center of Clinical Investigations in Biotherapies of Cancer, GRCC-Curie, Paris
2003- Full Professor, Immunology Biology, School of Medicine, University Paris XI
2000- Director, Laboratory "Tumor immunology and immunotherapy" INSERM U1015
2014- Scientific Director, OncoImmunology Program, Gustave Roussy Cancer Center

Prof. L. Zitvogel's current research is divided into three main areas. First, she is studying different modes of action of immune checkpoint inhibitors and looking for predictors of response to immune-modulation. Second, she is trying to characterize how the gut microbiome plays a part in cancer immune-surveillance. Finally, she is working to identify the molecular mechanisms behind immunogenic cell death, a form of cancer cell death that triggers the activation of T-cells toward the remaining cancer cells.

Prof. L. Zitvogel has published more than 452 papers, quite a few of them in high ranking journals, such as „Nature Reviews Immunology", „Science" and „Nature Medicine". Since 2012, she has been member of France's National Academy of Medicine as well as a permanent member in the European Academy of Cancer Sciences. In 2017, Prof. Dr. L. Zitvogel was (among others) awarded the Charles Rodolphe Brupbacher Prize for Cancer Research and in 2014, she received the SWISS BRIDGE Award for Cancer Research.

Jakob-Herz Prize 2018
On 2 February 2018, the Jakob-Herz Prize has been awarded for the fifth time. The award honors outstanding scientific success in the whole field of theoretical and clinical medicine. This year's awardee was Professor Laurence Zitvogel, MD, PhD, from Paris who is widely recognized for being a pioneer in the field of oncology and for her innovative achievements in the field of cancer immunotherapy.

Recent Publications

Interferon-γ induces cancer cell ferroptosis. **Zitvogel L**, Kroemer G. *Cell Res*. 2019 Jun 3. doi: 10.1038/s41422-019-0186-z

Tumor lysis with LTX-401 creates anticancer immunity. Xie W, Mondragón L, Mauseth B, Wang Y, Pol J, Lévesque S, Zhou H, Yamazaki T, Eksteen JJ, **Zitvogel L**, Sveinbjørnsson B, Rekdal Ø, Kepp O, Kroemer G. *Oncoimmunology*. 2019 Apr 13;8(7):1594555.

Trial watch: dietary interventions for cancer therapy. Lévesque S, Pol JG, Ferrere G, Galluzzi L, **Zitvogel L**, Kroemer G. *Oncoimmunology*. 2019 Apr 3;8(7):1591878.

Crizotinib-induced immunogenic cell death in non-small cell lung cancer.
Liu P, Zhao L, Pol J, Levesque S, Petrazzuolo A, Pfirschke C, Engblom C, Rickelt S, Yamazaki T, Iribarren K, Senovilla L, Bezu L, Vacchelli E, Sica V, Melis A, Martin T, Xia L, Yang H, Li Q, Chen J, Durand S, Aprahamian F, Lefevre D, Broutin S, Paci A, Bongers A, Minard-Colin V, Tartour E, **Zitvogel L**, Apetoh L, Ma Y, Pittet MJ, Kepp O, Kroemer G. *Nat Commun*. 2019 Apr 2;10(1):1486.

Failure of immunosurveillance accelerates aging. Perez-Lanzon M, **Zitvogel L**, Kroemer G. *Oncoimmunology*. 2019 Feb 9;8(4):e1575117.

Anticancer effects of anti-CD47 immunotherapy *in vivo*. Iribarren K, Buque A, Mondragon L, Xie W, Lévesque S, Pol J, Z**itvogel L**, Kepp O, Kroemer G. *Oncoimmunology*. 2018 Dec 11;8(3):1550619.

Systemic autophagy in the therapeutic response to anthracycline-based chemotherapy. Castoldi F, Vacchelli E, **Zitvogel L**, Maiuri MC, Pietrocola F, Kroemer G. *Oncoimmunology*. 2018 Oct 1;8(1):e1498285.

Title: Regeneration of Antigen-Specific Cytotoxic T cells with an iPSC Technology

Speaker

Shin Kaneko, MD, PhD

Associate Professor, The Center for iPS Cell Research and Application, Kyoto University, Japan

(Photo: Courtesy of KO SASAKI)

Chairman

Mitsuaki Yoshida, PhD

Research Unit, Japanese Foundation of Cancer Research, Japan
Professor Emeritus, The University of Tokyo, Japan

Shin Kaneko, MD, PhD

Profile

1995	School of Medicine and Medical Sciences, University of Tsukuba, Japan
1995-1997	Resident, University of Tsukuba Hospital, Japan
1997-1998	Graduate School of Medicine, Ehime University, Japan
1998-2002	Division of Biomedical Science (Immunology), University of Tsukuba, Japan
2002-2005	Research Fellow of the Japan Society for the Promotion of Science
2003-2007	Lecturer, University of Tsukuba, Japan
2005-2007	Postdoctoral Fellow, San Raffaele Scientific Institute, Italy
2008-2012	Assistant Professor, Graduate School of Medicine, The University of Tokyo, Japan
2012-	Associate Professor, Center for iPS Cell Research and Application (CiRA), Kyoto University, Japan

Research Interest:

To realize iPS cell-based regenerative therapy, facilities and technologies are needed to produce iPS cells, and the differentiated cells derived from them, of sufficient quality for use in patient treatment. The Center for iPS Cell Research and Application (CiRA) operates the Facility for iPS cell Therapy (FiT), a cell-processing center which is equipped to carry out all operational stages from the generation of iPS cells to induction of differentiation in accordance with the standards of Good Manufacturing Practice (GMP). Our operation of this facility and development of GMP culture technology supports a wide variety of projects, within CiRA and beyond, through cell processing operations ranging from generation of iPS cells for clinical use to induction of cell differentiation.

We are also engaged in research aimed at ensuring the safety of iPS cells and realizing immunotherapy by exploiting the special characteristics of iPS cells. T lymphocytes are a type of white blood cell whose functions are activated by antigen-specific recognition of target cells; the T cell receptors (TCR) which enable recognition of the target antigens are formed by gene rearrangement involving deletion of a genome sequence. However, iPS cells created by reprogramming T lymphocytes (T-iPS cells) retain the TCR gene sequence of the original T lymphocytes. We have established a method of inducing redifferentiation of rejuvenated cytotoxic T cells in large quantities from antigen-specific human T-iPS cells. As well as continuing with research to bring this technology to the clinical stage, we are progressing with research to achieve redifferentiation of the numerous other T lymphocyte subsets from antigen-specific T lymphocytes and to exploit the special characteristics of each subset for the development of immune regenerative therapy. To improve the safety of iPS cell therapy, we are continuing the development of a system to eliminate cancerous cells using selective cell death-inducing genes.

Through these research projects, our aim is to contribute to making regenerative therapy a reality and to improving therapeutic outcomes.

Recent Publications

Junctional Adhesion Molecule 2 Represents a Subset of Hematopoietic Stem Cells with Enhanced Potential for T Lymphopoiesis. Radulovic V, van der Garde M, Koide S, Sigurdsson V, Lang S, **Kaneko S**, Miharada K. *Cell Rep*. 2019 Jun 4;27(10):2826-2836.

Targeted Disruption of HLA Genes via CRISPR-Cas9 Generates iPSCs with Enhanced Immune Compatibility. Xu H, Wang B, Ono M, Kagita A, Fujii K, Sasakawa N, Ueda T, Gee P, Nishikawa M, Nomura M, Kitaoka F, Takahashi T, Okita K, Yoshida Y, **Kaneko S**, Hotta A. *Cell Stem Cel*l. 2019 Apr 4;24(4):566-578

Toward the development of true "off-the-shelf" synthetic T-cell immunotherapy. Iriguchi S, **Kaneko S**. *Cancer Sci*. 2019 Jan;110(1):16-22.

Enhancing T Cell Receptor Stability in Rejuvenated iPSC-Derived T Cells Improves Their Use in Cancer Immunotherapy. Minagawa A, Yoshikawa T, Yasukawa M, Hotta A, Kunitomo M, Iriguchi S, Takiguchi M, Kassai Y, Imai E, Yasui Y, Kawai Y, Zhang R, Uemura Y, Miyoshi H, Nakanishi M, Watanabe A, Hayashi A, Kawana K, Fujii T, Nakatsura T, **Kaneko S**. *Cell Stem Ce*ll. 2018 Dec 6;23(6):850-858.

Generation of HIV-Resistant Macrophages from IPSCs by Using Transcriptional Gene Silencing and Promoter-Targeted RNA. Higaki K, Hirao M, Kawana-Tachikawa A, Iriguchi S, Kumagai A, Ueda N, Bo W, Kamibayashi S, Watanabe A, Nakauchi H, Suzuki K, **Kaneko S**. *Mol Ther Nucleic Acids*. 2018 Sep 7;12:793-804.

Repurposing the Cord Blood Bank for Haplobanking of HLA-Homozygous iPSCs and Their Usefulness to Multiple Populations. Lee S, Huh JY, Turner DM, Lee S, Robinson J, Stein JE, Shim SH, Hong CP, Kang MS, Nakagawa M, **Kaneko S**, Nakanishi M, Rao MS, Kurtz A, Stacey GN, Marsh SGE, Turner ML, Song J. *Stem Cells*. 2018 Oct;36(10):1552-1566.

Generation of TCR-Expressing Innate Lymphoid-like Helper Cells that Induce Cytotoxic T Cell-Mediated Anti-leukemic Cell Response. Ueda N, Uemura Y, Zhang R, Kitayama S, Iriguchi S, Kawai Y, Yasui Y, Tatsumi M, Ueda T, Liu TY, Mizoro Y, Okada C, Watanabe A, Nakanishi M, Senju S, Nishimura Y, Kuzushima K, Kiyoi H, Naoe T, **Kaneko S**. *Stem Cell Repor*ts. 2018 Jun 5;10(6):1935-1946.

Session 2

Novel Targets for Cancer Drug Development

2-1. Predictive Markers for Immunotherapy Including EGFR and ALK Mutants

Speaker: Bruce E. Johnson (Dana-Farber Cancer Institute, USA)

2-2. Stromal Fibroblasts Detect Genomic Stress in Cancer Cells and Modulate Therapy Responses

Speaker: Erik Sahai (Francis Crick Institute, UK)

Title: Predictive Markers for Immunotherapy Including EGFR and ALK Mutants

Speaker

Bruce E. Johnson, MD

Professor, Medicine, Harvard Medical School, USA.
Professor of Medicine, Adult Oncology, Dana-Farber Cancer Institute, USA

Chairman

Makoto Ogawa, MD

Emeritus President, Aichi Cancer Center, Japan

Bruce E. Johnson, MD

Profile

Dr. Johnson received his MD from the University of Minnesota in 1979 and his postgraduate training at the University of Chicago and the National Cancer Institute. After serving at NCI, where he most recently headed the Lung Cancer Biology Section, he joined DFCI in 1999. He currently leads the Dana-Farber/Harvard Cancer Center Lung Cancer Program and is the Chief Clinical Research Officer at the Dana-Farber Cancer Institute.

Research Abstract

The translational research on patients with adenocarcinoma of the lung here at the Dana- Farber/Harvard Cancer Center has helped identify patient subsets that respond differently to targeted agents. Women, patients with adenocarcinoma, and those who do not smoke cigarettes are more likely to have a favorable response to gefitinib and erlotinib therapy (Iressa and Tarceva) than patients with other types of lung cancer and men respectively. This prompted my laboratory to assemble tumor cell lines from

women with adenocarcinoma who either did or did not smoke cigarettes to characterize their response to gefitinib. A team composed of our laboratory and the laboratory led by Dr. Sellers and Meyerson at the Dana-Farber Cancer Institute discovered that most patients who have a clinical response to gefitinib treatment have either point mutations or deletion of amino acids from the tyrosine kinase domain of the epidermal growth factor receptor. Our laboratory showed lung cancer cell lines with epidermal growth factor cell lines with these point mutations or deletions are 100 fold more sensitive to treatment gefitinib than cell lines with wild type sequence of the epidermal growth factor receptor. The lung cancer cell lines with mutations in the epidermal growth factor receptor treated with 100 nM of gefitinib have downregulation of phosphorylated epidermal growth factor receptor. This also leads to downregulation of the downstream targets including phospho-Akt and phospho-Erk1/2 kinase. Treatment of lung cancer cells with mutated epidermal growth factor receptor with 1 micromolar gefitinib leads to apoptosis while the cells with wild type epidermal growth factor receptor undergo a G1/S arrest. Future studies will study the relationship between different mutations in the epidermal growth factor receptor, their susceptibility to different epidermal growth factor receptor inhibitors, and the signaling pathways. Prospective trials will test the impact of these epidermal growth factor receptor mutations on the treatment of patients with non-small cell lung cancer. The studies will include erlotinib treatment in previously untreated elderly patients with advanced non-small cell lung cancer (older than 70) and women with adenocarcinoma who are either never smokers or former smokers. These patients will have their tumor DNA studied for the epidermal growth factor receptor sequence, and their response, response duration, subsequent response to other chemotherapy, and survival will be recorded. This will be done to determine if there is a relationship between the epidermal growth factor receptor sequence and the outcome of patients with non-small cell lung cancer after treatment with erlotinib.

Recent Publications

Tumor Volume Analysis as a Predictive Marker for Prolonged Survival in Anaplastic Lymphoma Kinase-rearranged Advanced Non-Small Cell Lung Cancer Patients Treated With Crizotinib. Hida T, Dahlberg SE, Lydon CA, Hatabu H, Johnson BE, Awad MM, Nishino M. J Thorac Imaging. 2019 Apr 12. doi: 10.

Interstitial lung abnormality in stage IV non-small cell lung cancer: A validation study for the association with poor clinical outcome. Araki T, Dahlberg SE, Hida T, Lydon CA, Rabin MS, Hatabu H, Johnson BE, Nishino M. Eur J Radiol Open. 2019 Mar 29;6:128-131.

Use of targeted next generation sequencing to characterize tumor mutational burden and efficacy of immune checkpoint inhibition in small cell lung cancer. Ricciuti B, Kravets S, Dahlberg SE, Umeton R, Albayrak A, Subegdjo SJ, Johnson BE, Nishino M, Sholl LM, Awad MM. J Immunother Cancer. 2019 Mar 28;7(1):87.

Review: Thyroid hormone therapy does not improve QoL or symptoms in subclinical hypothyroidism.Johnson BE. Ann Intern Med. 2019 Feb 19;170(4):JC17.

Characteristics and Outcomes of Patients With Metastatic KRAS-Mutant Lung Adenocarcinomas: The Lung Cancer Mutation Consortium Experience.

El Osta B, Behera M, Kim S, Berry LD, Sica G, Pillai RN, Owonikoko TK, Kris MG, Johnson BE, Kwiatkowski DJ, Sholl LM, Aisner DL, Bunn PA, Khuri FR, Ramalingam SS. J Thorac Oncol. 2019 May;14(5):876-889.

Clinical Cancer Advances 2019: Annual Report on Progress Against Cancer From the American Society of Clinical Oncology. Pal SK, Miller MJ, Agarwal N, Chang SM, Chavez-MacGregor M, Cohen E, Cole S, Dale W, Magid Diefenbach CS, Disis ML, Dreicer R, Graham DL, Henry NL, Jones J, Keedy V, Klepin HD, Markham MJ, Mittendorf EA, Rodriguez-Galindo C, Sabel MS, Schilsky RL, Sznol M, Tap WD, Westin SN, Johnson BE. J Clin Oncol. 2019 Apr 1;37(10):834-849.

M1b Disease in the 8th Edition of TNM Staging of Lung Cancer: Pattern of Single Extrathoracic Metastasis and Clinical Outcome. Park H, Dahlberg SE, Lydon CA, Araki T, Hatabu H, Rabin MS, Johnson BE, Nishino M. Oncologist. 2019 Jan 29. pii: theoncologist.2018-0596.

Real-world treatment patterns and survival of patients with BRAF V600-mutated metastatic non-small cell lung cancer. Horn L, Bauml J, Forde PM, Davis KL, Myall NJ, Sasane M, Dalal A, Culver K, Wozniak AJ, Baik CS, Mutebi A, Zhang P, Wakelee HA, Johnson BE. Lung Cancer. 2019 Feb;128:74-90.

Race, Poverty, and Initial Implementation of Precision Medicine for Lung Cancer. Kehl KL, Lathan CS, Johnson BE, Schrag D. J Natl Cancer Inst. 2019 Apr 1;111(4):431-434.

Automated image analysis tool for tumor volume growth rate to guide precision cancer therapy: EGFR-mutant non-small-cell lung cancer as a paradigm. Nishino M, Wakai S, Hida T, Dahlberg SE, Ozaki M, Hatabu H, Tachizaki H, Johnson BE.
Eur J Radiol. 2018 Dec;109:68-76.

A Cancer Cell Program Promotes T Cell Exclusion and Resistance to Checkpoint Blockade. Jerby-Arnon L, Shah P, Cuoco MS, Rodman C, Su MJ, Melms JC, Leeson R, Kanodia A, Mei S, Lin JR, Wang S, Rabasha B, Liu D, Zhang G, Margolais C, Ashenberg O, Ott PA, Buchbinder EI, Haq R, Hodi FS, Boland GM, Sullivan RJ, Frederick DT, Miao B, Moll T, Flaherty KT, Herlyn M, Jenkins RW, Thummalapalli R, Kowalczyk MS, Cañadas I, Schilling B, Cartwright ANR, Luoma AM, Malu S, Hwu P, Bernatchez C, Forget MA, Barbie DA, Shalek AK, Tirosh I, Sorger PK, Wucherpfennig K, Van Allen EM, Schadendorf D, Johnson BE, Rotem A, Rozenblatt-Rosen O, Garraway LA, Yoon CH, Izar B, Regev A. Cell. 2018 Nov 1;175(4):984-997

Impact of BRAF Mutation Class on Disease Characteristics and Clinical Outcomes in BRAF-mutant Lung Cancer. Dagogo-Jack I, Martinez P, Yeap BY, Ambrogio C, Ferris LA, Lydon C, Nguyen T, Jessop NA, Iafrate AJ, Johnson BE, Lennerz JK, Shaw AT, Awad MM. Clin Cancer Res. 2019 Jan 1;25(1):158-165.

Title: Stromal Fibroblasts Detect Genomic Stress in Cancer Cells and Modulate Therapy Responses

Speaker

Erik Sahai, PhD

Group Leader, the Francis Crick Institute, London, UK

Chairman

Kohei Miyazono, MD, PhD

Professor and Chair, Department of Molecular Pathology, Graduate School of Medicine, The University of Tokyo, Japan

Erik Sahai, PhD

Profile

Erik obtained his PhD with Richard Treisman in London studying RhoGTPases and their effectors. He then carried out post-doctoral work in both London (Chris Marshall) and New York (John Condeelis) before setting up his own group at the Cancer Research UK London Research Institute in 2004 (now part of the Francis Crick Institute).

1998 PhD in Biochemistry, University College, London, UK

1998 Postdoctoral Fellow, Institute of Cancer Research, UK

2003 Postdoctoral Fellow, Albert Einstein College of Medicine, USA

2004 Established lab at the London Research Institute, Cancer Research UK

2015 Group Leader, Francis Crick Institute, London, UK

Research Interest

Dr. Sahai is studying the most lethal aspects of cancer: how it spreads through the body and why it becomes resistant to cancer therapies. Most cancer deaths are caused by a combination of the disease spreading from the initial tumor to other parts of the body, known as metastasis, and it becoming resistant to treatment. Both processes can be hard to predict and are strongly influenced by the interplay of tumor cells with other non-cancerous cells in the body. By carefully studying patient data together with experimental models we can start to uncover recurring patterns in the behavior of cancers. In particular, we are carrying out in-depth studies of the cellular environment around a tumor, investigating the genetic and molecular changes that enable cancer cells to break away and start moving towards new sites. For example, we are listening in on the signals that are sent between cancer cells and their neighbors to find out how they might accelerate metastasis or prevent chemotherapy from working. We are also using cutting-edge microscopy techniques to watch tumors growing and spreading in real time inside a living organism. And we are growing cancer cells together with normal cells from patients, using computer modelling to understand the complex molecular dialoague between different cells within a tumor. Tackling metastasis and treatment failure are two of the biggest challenges in cancer research. Our work is leading to new ways to predict how the disease will spread, and pointing towards potential targets for treatments that might be able to stop it in its tracks.

Recent Publications

The importance of developing therapies targeting the biological spectrum of metastatic disease. Zijlstra A, Von Lersner A, Yu D, Borrello L, Oudin M, Kang Y, **Sahai E,** Fingleton B, Stein U, Cox TR, Price JT, Kato Y, Welm AL, Aguirre-Ghiso JA; Board Members of the Metastasis Research Society. *Clin Exp Metastasis*. 2019 May 17. doi: 10.1007/s10585-019-09972-3.

Tissue clonality of dendritic cell subsets and emergency DCpoiesis revealed by multicolor fate mapping of DC progenitors. Cabeza-Cabrerizo M, van Blijswijk J, Wienert S, Heim D, Jenkins RP, Chakravarty P, Rogers N, Frederico B, Acton S, Beerling E, van Rheenen J, Clevers H, Schraml BU, Bajénoff M, Gerner M, Germain RN, **Sahai E**, Klauschen F, Reis E Sousa C. *Sci Immunol*. 2019 Mar 1;4(33). pii: eaaw1941.

TRPS1 shapes YAP/TEAD-dependent transcription in breast cancer cells. Elster D, Tollot M, Schlegelmilch K, Ori A, Rosenwald A, **Sahai E**, von Eyss B. *Nat Commun*. 2018 Aug 6;9(1):3115. doi: 10.1038/s41467-018-05370-7.

Heterogeneity in tumor chromatin-doxorubicin binding revealed by in vivo fluorescence lifetime imaging confocal endomicroscopy. Sparks H, Kondo H, Hooper S, Munro I, Kennedy G, Dunsby C, French P, **Sahai E**. *Nat Commun*. 2018 Jul 9;9(1):2662.

Mechanisms and impact of altered tumour mechanics. Mohammadi H, **Sahai E**. *Nat Cell Biol.* 2018 Jul;20(7):766-774.

Quantitative Analysis Reveals that Actin and Src-Family Kinases Regulate Nuclear YAP1 and Its Export. Ege N, Dowbaj AM, Jiang M, Howell M, Hooper S, Foster C, Jenkins RP, **Sahai E**. *Cell Syst*. 2018 Jun 27;6(6):692-708.e13.

Session 3

Cancer Genomics and Precision Oncology

3-1. Precision Pediatric Cancer Medicine

Speaker: Elaine R. Mardis (Nationwide Children's Hospital, USA)

3-2. Next-Generation Approaches to Assessing Hereditary Cancer Risk in the Genome Era

Speaker: James M. Ford (Stanford University School of Medicine, USA)

Title: Precision Pediatric Cancer Medicine

Speaker

Elaine R. Mardis, PhD

The Nationwide Foundation Endowed Chair in Genomic Medicine, Co-Executive Director of the Institute for Genomic Medicine, Nationwide Children's Hospital, Professor of Pediatrics, The Ohio State University College of Medicine, USA.

Chairman

Hiroyuki Mano, MD, PhD

Director, National Cancer Center Research Institute, Japan

Elaine R. Mardis, PhD

Profile

Dr. Mardis holds the Nationwide Foundation Endowed Chair in Genomic Medicine and is co-executive director of the Institute for Genomic Medicine at Nationwide Children's Hospital in Columbus, Ohio. She also is professor of pediatrics at The Ohio State University College of Medicine.

Dr. Mardis is a world-renowned researcher whose work centers on the genomic characterization of cancer and its implications for precision cancer medicine. She has presented keynote addresses and other invited remarks at international conferences on topics including cancer genomics, next-generation sequencing technology, personalized medicine, and cancer immunogenomics.
An active member of the AACR since 2009, Dr. Mardis' contributions to the AACR have been vast and far-reaching. She is currently serving as an AACR Project GENIE Advisory Board member, an AACR Special Conferences committee member, and is a senior editor of the AACR journal Molecular Cancer Research. She previously served on the Board of Directors (2015–2018), as chair of the AACR Annual Meeting 2018

Program Committee, as a committee member for the Pezcoller Foundation-AACR Award (2017), and as a member of the Steering Committee for the AACR Cancer Progress Report 2014. In addition, she was co-chair of the AACR Precision Medicine Series: Integrating Clinical Genomics and Cancer Therapy conference in Salt Lake City, and has served on the organizing committees of several other conferences.

Dr. Mardis has received many awards and honors in recognition of her exceptional research accomplishments. She was elected to the 2019 class of Fellows of the AACR Academy, and was the recipient of the Precision Medicine World Congress 2017 Luminary Award, the American Association for Clinical Chemistry Morton K. Schwartz Award for Significant Contributions in Cancer Research Diagnostics (2016), the George Engelmann Interdisciplinary Award (2012), St. Louis Academy of Science (2012), and the Scripps Research Institute Translational Medicine Award (2010).

Dr. Mardis received a bachelor's degree, summa cum laude, and her PhD from the University of Oklahoma. She spent much of her early career at the Washington University School of Medicine in St. Louis, Missouri, as a professor, researcher, and ultimately, co-director of The McDonnell Genome Institute.

Research Interests

Large-scale cancer genomics (discovery-based research into the genetic drivers of cancer onset and progression); computational analysis of cancer genomics data; immunogenomic applications and analysis of cancer samples; building and populating knowledge-bases of curated cancer genes, their mutations and aspects of prognosis, diagnosis and therapy response; characterization of cancer intratumoral heterogeneity and its implications in therapy resistance prediction; genomic and immunogenomic characterization of mouse models of cancer; applications of genomics to clinical characterization of individual patients for therapeutic and diagnostic purposes, including germline susceptibility.

Recent Publications

Expanding the clinical history associated with syndromic Klippel-Feil: A unique case of comorbidity with medulloblastoma. Schieffer KM, Varga E, Miller KE, Agarwal V, Koboldt DC, Brennan P, Kelly B, Dave-Wala A, Pierson CR, Finlay JL, AbdelBaki MS, White P, Magrini V, Wilson RK, **Mardis ER**, Cottrell CE. *Eur J Med Genet*. 2019 Jun 10:103701.

MiRNAs and long-term breast cancer survival: Evidence from the WHEL Study. Natarajan L, Pu M, Davies SR, Vickery TL, Nelson SH, Pittman E, Parker BA, Ellis MJ, Flatt SW, **Mardis ER**, Marinac CR, Pierce JP, Messer K. *Cancer Epidemiol Biomarkers Prev*. 2019 Jun 11. pii: cebp.1322.2018

Precision oncogenomics. Ferreira-Gonzalez A, **Mardis ER**. *Cold Spring Harb Mol Case Stud*. 2019 Apr 1;5(2). pii: a004150.

Detection of neoantigen-specific T cells following a personalized vaccine in a patient with glioblastoma. Johanns TM, Miller CA, Liu CJ, Perrin RJ, Bender D, Kobayashi DK,

Campian JL, Chicoine MR, Dacey RG, Huang J, Fritsch EF, Gillanders WE, Artyomov MN, **Mardis ER**, Schreiber RD, Dunn GP. *Oncoimmunolo*gy. 2019 Jan 5;8(4):e1561106

No evidence that G6PD deficiency affects the efficacy or safety of daunorubicin in acute lymphoblastic leukemia induction therapy. Robinson KM, Yang W, Karol SE, Kornegay N, Jay D, Cheng C, Choi JK, Campana D, Pui CH, Wood B, Borowitz MJ, Gastier-Foster J, Larsen EC, Winick N, Carroll WL, Loh ML, Raetz EA, Hunger SP, Devidas M, **Mardis ER**, Fulton RS, Relling MV, Jeha S. *Pediatr Blood Cancer.* 2019 Jun;66(6):e27681.

The Clonal Evolution of Metastatic Osteosarcoma as Shaped by Cisplatin Treatment. Brady SW, Ma X, Bahrami A, Satas G, Wu G, Newman S, Rusch M, Putnam DK, Mulder HL, Yergeau DA, Edmonson MN, Easton J, Alexandrov LB, Chen X, **Mardis E**R, Wilson RK, Downing JR, Pappo AS, Raphael BJ, Dyer MA, Zhang J. *Mol Cancer Res*. 2019 Apr;17(4):895-906.

Association of Tumor Microenvironment T-cell Repertoire and Mutational Load with Clinical Outcome after Sequential Checkpoint Blockade in Melanoma. Yusko E, Vignali M, Wilson RK, **Mardis E**R, Hodi FS, Horak C, Chang H, Woods DM, Robins H, Weber J. *Cancer Immunol Res*. 2019 Mar;7(3):458-465.

Accounting for proximal variants improves neoantigen prediction. Hundal J, Kiwala S, Feng YY, Liu CJ, Govindan R, Chapman WC, Uppaluri R, Swamidass SJ, Griffith OL, **Mardis ER**, Griffith M. *Nat Gene*t. 2019 Jan;51(1):175-179.

Next-Generation Sequencing Technologies. McCombie WR, McPherson JD, **Mardis ER**. *Cold Spring Harb Perspect Med*. 2018 Nov 26. pii: a036798.

A deep learning approach to automate refinement of somatic variant calling from cancer sequencing data. Ainscough BJ, Barnell EK, Ronning P, Campbell KM, Wagner AH, Fehniger TA, Dunn GP, Uppaluri R, Govindan R, Rohan TE, Griffith M, **Mardis ER**, Swamidass SJ, Griffith OL. *Nat Genet*. 2018 Dec;50(12):1735-1743.

The Impact of Next-Generation Sequencing on Cancer Genomics: From Discovery to Clinic. M**ardis ER**. *Cold Spring Harb Perspect Med*. 2018 Nov 5. pii: a036269.

Recurrent WNT pathway alterations are frequent in relapsed small cell lung cancer. Wagner AH, Devarakonda S, Skidmore ZL, Krysiak K, Ramu A, Trani L, Kunisaki J, Masood A, Waqar SN, Spies NC, Morgensztern D, Waligorski J, Ponce J, Fulton RS, Maggi LB Jr, Weber JD, Watson MA, O'Conor CJ, Ritter JH, Olsen RR, Cheng H, Mukhopadhyay A, Can I, Cessna MH, Oliver TG, **Mardis ER**, Wilson RK, Griffith M, Griffith OL, Govindan R. *Nat Commun*. 2018 Sep 17;9(1):3787.

The prognostic effects of somatic mutations in ER-positive breast cancer. Griffith OL, Spies NC, Anurag M, Griffith M, Luo J, Tu D, Yeo B, Kunisaki J, Miller CA, Krysiak K, Hundal J, Ainscough BJ, Skidmore ZL, Campbell K, Kumar R, Fronick C, Cook L, Snider JE, Davies S, Kavuri SM, Chang EC, Magrini V, Larson DE, Fulton RS, Liu S, Leung S, Voduc D, Bose R, Dowsett M, Wilson RK, Nielsen TO, **Mardis ER**, Ellis MJ. *Nat Commun.* 2018 Sep 4;9(1):3476.

Title: Next-Generation Approaches to Assessing Hereditary Cancer Risk in the Genome Era

Speaker

James M. Ford, MD

Professor of Medicine, Pediatrics and Genetics
Director, Stanford Program for Clinical Cancer Genetics
Stanford University School of Medicine, California, USA

Chairman

Hiroyuki Aburatani, MD, PhD

Professor, LSBM, Research Center for Advanced Science and Technology, The University of Tokyo, Japan

James M. Ford, MD

Profile

Dr. Ford is a medical oncologist and geneticist at Stanford, devoted to studying the genetic basis of breast and GI cancer development, treatment and prevention. Dr. Ford graduated in 1984 Magna Cum Laude (Biology) from Yale University where he later received his M.D. degree from the School of Medicine in 1989. He was a internal medicine resident (1989-91), Clinical Fellow in Medical Oncology (1991-94), Research Fellow of Biological Sciences (1993-97) at Stanford, and joined the faculty in 1998. He is currently Professor of Medicine (Oncology) and Genetics, and Director of the Stanford Cancer Genetics Clinic and the Cancer Genomics Program at the Stanford University Medical Center.

Dr. Ford's research goals are to understand the role of genetic changes in cancer genes in the risk and development of common cancers. He studies the role of the p53 and BRCA1 tumor suppressor genes in DNA repair, and uses techniques for high-

throughput genomic analyses of cancer to identify molecular signatures for targeted therapies. Dr. Ford's clinical interests include the diagnosis and treatment of patients with a hereditary pre-disposition to cancer. He runs the Stanford Cancer Genetics Clinic,that sees patients for genetic counseling and testing of hereditary cancer syndromes for prevention and early diagnosis of cancer in high-risk individuals and populations. He has recently been named the Director of Stanford's new Cancer Genomics Program, performing next-generation tumor profiling to identify novel genetic targets for personalized targeted therapies, and directs the Molecular Tumor Board.

Recent Publications

Comprehensive genomic characterization of breast tumors with BRCA1 and BRCA2 mutations. Lal A, Ramazzotti D, Weng Z, Liu K, **Ford JM**, Sidow A. *BMC Med Genomics*. 2019 Jun 10;12(1):84.

High-Resolution Bisulfite-Sequencing of Peripheral Blood DNA Methylation in Early-Onset and Familial Risk Breast Cancer Patients. Chen J, Haanpää MK, Gruber JJ, Jäger N, **Ford JM,** Snyder MP. *Clin Cancer Res*. 2019 Jun 7. pii: clincanres.2423.2018.

From the Past to the Present: Insurer Coverage Frameworks for Next-Generation Tumor Sequencing. Trosman JR, Weldon CB, Gradishar WJ, Benson AB 3rd, Cristofanilli M, Kurian AW, **Ford JM**, Balch A, Watkins J, Phillips KA. *Value Health*. 2018 Sep;21(9):1062-1068.

Surgical and molecular characterization of primary and metastatic disease in a neuroendocrine tumor arising in a tailgut cyst.
Erdrich J, Schaberg KB, Khodadoust MS, Zhou L, Shelton AA, Visser BC, Ford JM, Alizadeh AA, Quake SR, Kunz PL, Beausang JF.
Cold Spring Harb Mol Case Stud. 2018 Oct 1;4(5). pii: a003004.

Precision oncology in advanced cancer patients improves overall survival with lower weekly healthcare costs. Haslem DS, Chakravarty I, Fulde G, Gilbert H, Tudor BP, Lin K, **Ford JM**, Nadauld LD. *Oncotarge*t. 2018 Feb 2;9(15):12316-12322.

Higher Absolute Lymphocyte Counts Predict Lower Mortality from Early-Stage Triple-Negative Breast Cancer. Afghahi A, Purington N, Han SS, Desai M, Pierson E, Mathur MB, Seto T, Thompson CA, Rigdon J, Telli ML, Badve SS, Curtis CN, West RB, Horst K, Gomez SL, **Ford JM**, Sledge GW, Kurian AW. **Clin Cancer Res**. 2018 Jun 15;24(12):2851-2858.

Session 4

Translational Research in Precision Oncology

4-1. Fostering Precision Medicine in Selected Subpopulations of Patients with CRC

Speaker: Josep Tabernero (Vall d'Hebron University Hospital, Spain)

4-2. Evolving Paradigms of Precision Medicine in the Clinic

Speaker: David Hyman (Memorial Sloan Kettering Cancer Center, USA)

Title: Fosterling Precision Medicine in Selected Subpopulations of Patients with CRC

Speaker

Josep Tabernero, MD, PhD

Director, Vall d'Hebron Institute of Oncology (VHIO), Spain
Head of the Medical Oncology Department., Zall d'Hebron University Hospital, Spain
Director, Clinical Research, VHIO, Spain

Chairman

Tomomitsu Hotta, MD, PhD

Honorary President, National Cancer Center, Japan
Honorary Director, NHO Nagoya Medical Center, Japan

Josep Tabernero, MD, PhD

Profile

Dr.Tabernero holds MD and PhD degrees from the Universitat Autònoma de Barcelona, Spain. He is currently Head of the Medical Oncology Department at the Vall d'Hebron Barcelona Hospital Campus, Director of the Vall d'Hebron Institute of Oncology (VHIO), and leads the Research Innovation of Catalonian Cancer Centers Network.

He also directs VHIO´s Gastrointestinal and Endocrine Tumors Group, the Research Unit for Molecular Therapy of Cancer (UITM) – "la Caixa", and is Principal Investigator of several Phase I pharmacodynamic studies and translational projects with molecular targeted therapies, with particular emphasis on EGFR-family inhibitors and IGFR-PI3K-Akt-mTOR pathway inhibitors, as well as phase II and III studies with novel chemotherapeutics.

Based on the idea that each tumor has an independent genetic identity, his group aims at potentiating molecular therapies targeting specific oncoproteins and accelerating more effective personalized cancer medicines for patients displaying genetic lesions or pathway disregulation. One of his team´s main objectives is to establish novel predictive markers of response to anti-cancer therapies and identify markers of primary resistance (de novo) and secondary treatment.

At preclinical level, in collaboration with VHIO´s cancer researchers and physician-scientists, he develops new xenograft models with explant tumors from patients ("xenopatients") in mice in order to mimic the patient's disease and study tumor development in optimal research models. He also leads research into the study of circulating biomarkers (detection and genotyping of circulating free DNA), and is dedicated to advancing the immuno-oncology field through a large portfolio of trials with some of the most promising targets in immune checkpoints and cytokines. By paring immune therapeutics with oncogenomics, his team seeks to render anti-cancer therapies more precise.

Dr.Tabernero serves on the Editorial Boards of various top tier journals including *Annals of Oncology, ESMO Open, Cancer Discovery* and *Clinical Cancer Research*. He has (co) authored approximately 350 peer-reviewed papers.

He is currently ESMO President (2018 – 2019) of the European Society for Medical Oncology (ESMO) and an Executive Board Member. He is also member of the American Association for Cancer Research (AACR), the American Society of Clinical Oncology (ASCO), and has been appointed as member of several Educational and Scientific Committees of ESMO, ECCO, ASCO, AACR, AACR/NCI/EORTC, ASCO Gastrointestinal, and WCGIC meetings.

Recent Publications

Binimetinib, Encorafenib, and Cetuximab Triplet Therapy for Patients With *BRAF* V600E-Mutant Metastatic Colorectal Cancer: Safety Lead-In Results From the Phase III BEACON Colorectal Cancer Study.Van Cutsem E, Huijberts S, Grothey A, Yaeger R, Cuyle PJ, Elez E, Fakih M, Montagut C, Peeters M, Yoshino T, Wasan H, Desai **J**, Ciardiello F, Gollerkeri A, Christy-Bittel **J**, Maharry K, Sandor V, Schellens JHM, Kopetz S, **Tabernero J**. *J Clin Oncol*. 2019 Jun 10;37(17):1460-1469.

Phase I dose-escalation of trifluridine/tipiracil in combination with oxaliplatin in patients with metastatic colorectal cancer. Argilés G, André T, Hollebecque A, Calvo A, Dahan L, Cervantes A, Leger C, Amellal N, Fougeray R, **Tabernero J**. *Eur J Cancer*. 2019 May;112:12-19.

Comparative Assessment of Clinical Benefit Using the ESMO-Magnitude of Clinical Benefit Scale Version 1.1 and the ASCO Value Framework Net Health Benefit Score. Cherny NI, de Vries EGE, Dafni U, Garrett-Mayer E, McKernin SE, Piccart M, Latino NJ, Douillard JY, Schnipper LE, Somerfield MR, Bogaerts **J**, Karlis D, Zygoura P, Vervita K, Pentheroudakis G, **Tabernero J**, Zielinski C, Wollins DS, Schilsky RL. ***J** Clin Oncol.* 2019 Feb 1;37(4):336-349.

Prospective multicenter real-world RAS mutation comparison between OncoBEAM-based liquid biopsy and tissue analysis in metastatic colorectal cancer. García-Foncillas **J**, **Tabernero J**, Élez E, Aranda E, Benavides M, Camps C, Jantus-Lewintre

E, López R, Muinelo-Romay L, Montagut C, Antón A, López G, Díaz-Rubio E, Rojo F, Vivancos A. *Br **J** Cancer*. 2018 Dec;119(12):1464-1470.

Galunisertib plus gemcitabine vs. gemcitabine for first-line treatment of patients with unresectable pancreatic cancer. Melisi D, Garcia-Carbonero R, Macarulla T, Pezet D, Deplanque G, Fuchs M, Trojan **J**, Oettle H, Kozloff M, Cleverly A, Smith C, Estrem ST, Gueorguieva I, Lahn MMF, Blunt A, Benhadji KA, **Tabernero J**. *Br **J** Cancer*. 2018 Nov;119(10):1208-1214.

Cancer Core Europe: A European cancer research alliance realizing a research infrastructure with critical mass and programmatic approach to cure cancer in the 21st century. Calvo F, Apolone G, Baumann M, Caldas C, Celis JE, de Lorenzo F, Ernberg I, Ringborg U, Rowell **J**, **Tabernero J**, Voest E, Eggermont A. *Eur **J** Cancer.* 2018 Nov;103:155-159

Title: Evolving Paradigms of Precision Medicine in the Clinic

Speaker

David M. Hyman, MD, PhD

Chief, Early Drug Development Service,
Memorial Sloan Kettering Cancer Center, USA

Chairman

Hironobu Minami, MD, PhD

Professor ,Kobe University Graduate School of Medicine,
Japan

David M. Hyman, MD, PhD

Profile

He graduated from Joan & Sanford I. Weill Medical College of Cornell University in 2006. His clinical practice is focused on the care of women with gynecologic cancers including ovarian, endometrial, and cervical cancers. In addition, he has a special interest in treating women with uterine sarcomas. He works as part of a multidisciplinary team of surgeons, radiation oncologists, and pathologists who all specialize in the diagnosis and treatment of gynecologic cancers.

He is a clinical researcher and Chief of the Early Drug Development Service at MSKCC. In this capacity he leads a multispecialty team of oncologists to conduct a variety of early phase clinical studies including first-in-human studies, novel combinations of investigational therapy, and histology-independent, molecularly selected “basket” studies. They enroll approximately 300 patients each year to our clinical trial portfolio of 30+ open studies. He collaborates closely with translational scientists on all my studies

in order to better understand how the consequences of pathway inhibition vary as a function of tumor cell lineage and the complement of co-mutations within tumor cells. He has also published numerous articles on methods to improve the design and efficiency of early phase studies.

His clinical expertise is in gynecologic oncology and he holds a dual appointment to the Gynecologic Medical Oncology service. He has worked extensively within the NCI National Clinical Trials Network mechanism for my gynecologic oncology research and served as leader for several national cooperative group studies. His gynecologic cancer research has primarily involved on biomarker driven studies translating insights gained from his Developmental Therapeutics research.

Specialties: Gynecologic Oncology, Developmental Therapeutics, Phase I Studies, Basket Studies

Clinical Expertise**:** Gynecologic Cancers (Ovarian, Endometrial, Cervical); Uterine Sarcomas; Clinical Trials (First-in-Human Phase I; Phase II)

Recent Publications

Efficacy of MEK inhibition in patients with histiocytic neoplasms. Diamond EL, Durham BH, Ulaner GA, Drill E, Buthorn J, Ki M, Bitner L, Cho H, Young RJ, Francis JH, Rampal R, Lacouture M, Brody LA, Ozkaya N, Dogan A, Rosen N, Iasonos A, Abdel-Wahab O, **Hyman DM**. *Nature*. 2019 Mar;567(7749):521-524

Use, Safety, and Efficacy of Single-Patient Use of the US Food and Drug Administration Expanded Access Program. Feit NZ, Goldman DA, Smith E, Deighan J, Iasonos A, Zivanovic O, **Hyman DM**. *JAMA Oncol.* 2019 Feb 28. doi: 10.1001/jamaoncol.2018.7002.

Colorectal Carcinomas Containing Hypermethylated MLH1 Promoter and Wild-Type BRAF/KRAS Are Enriched for Targetable Kinase Fusions. Cocco E, Benhamida J, Middha S, Zehir A, Mullaney K, Shia J, Yaeger R, Zhang L, Wong D, Villafania L, Nafa K, Scaltriti M, Drilon A, Saltz L, Schram AM, Stadler ZK, **Hyman DM**, Benayed R, Ladanyi M, Hechtman JF. *Cancer Res*. 2019 Mar 15;79(6):1047-1053.

Next-Generation Sequencing-Based Assessment of JAK2, PD-L1, and PD-L2 Copy Number Alterations at 9p24.1 in Breast Cancer: Potential Implications for Clinical Management. Gupta S, Vanderbilt CM, Cotzia P, Arias-Stella JA 3rd, Chang JC, Zehir A, Benayed R, Nafa K, Razavi P, **Hyman DM**, Baselga J, Berger MF, Ladanyi M, Arcila ME, Ross DS. *J Mol Diagn*. 2019 Mar;21(2):307-317.

RAF inhibitor PLX8394 selectively disrupts BRAF dimers and RAS-independent BRAF-mutant-driven signaling. Yao Z, Gao Y, Su W, Yaeger R, Tao J, Na N, Zhang Y, Zhang C, Rymar A, Tao A, Timaul NM, Mcgriskin R, Outmezguine NA, Zhao H, Chang Q, Qeriqi B, Barbacid M, de Stanchina E, **Hyman DM**, Bollag G, Rosen N. *Nat Med*. 2019 Feb;25(2):284-291.

Early disease progression and treatment discontinuation in patients with advanced ovarian cancer receiving immune checkpoint blockade. Boland JL, Zhou Q, Martin M,

Callahan MK, Konner J, O'Cearbhaill RE, Friedman CF, Tew W, Makker V, Grisham RN, Hensley ML, Zecca N, Iasonos AE, Snyder A, **Hyman DM**, Sabbatini P, Aghajanian C, Cadoo KA, Zamarin D. *Gynecol Oncol*. 2019 Feb;152(2):251-258

A phase Ib dose-escalation and expansion study of the oral MEK inhibitor pimasertib and PI3K/MTOR inhibitor voxtalisib in patients with advanced solid tumours. Schram AM, Gandhi L, Mita MM, Damstrup L, Campana F, Hidalgo M, Grande E, **Hyman DM**, Heist RS. *Br J Cancer*. 2018 Dec;119(12):1471-1476.

Microsatellite Instability Is Associated With the Presence of Lynch Syndrome Pan-Cancer. Latham A, Srinivasan P, Kemel Y, Shia J, Bandlamudi C, Mandelker D, Middha S, Hechtman J, Zehir A, Dubard-Gault M, Tran C, Stewart C, Sheehan M, Penson A, DeLair D, Yaeger R, Vijai J, Mukherjee S, Galle J, Dickson MA, Janjigian Y, O'Reilly EM, Segal N, Saltz LB, Reidy-Lagunes D, Varghese AM, Bajorin D, Carlo MI, Cadoo K, Walsh MF, Weiser M, Aguilar JG, Klimstra DS, Diaz LA Jr, Baselga J, Zhang L, Ladanyi M, **Hyman DM**, Solit DB, Robson ME, Taylor BS, Offit K, Berger MF, Stadler ZK. *J Clin Oncol.* 2019 Feb 1;37(4):286-295.

Prospective Genotyping of Hepatocellular Carcinoma: Clinical Implications of Next-Generation Sequencing for Matching Patients to Targeted and Immune Therapies. Harding JJ, Nandakumar S, Armenia J, Khalil DN, Albano M, Ly M, Shia J, Hechtman JF, Kundra R, El Dika I, Do RK, Sun Y, Kingham TP, D'Angelica MI, Berger MF, **Hyman DM**, Jarnagin W, Klimstra DS, Janjigian YY, Solit DB, Schultz N, Abou-Alfa GK. *Clin Cancer Res*. 2019 Apr 1;25(7):2116-2126.

Widespread Selection for Oncogenic Mutant Allele Imbalance in Cancer. Bielski CM, Donoghue MTA, Gadiya M, Hanrahan AJ, Won HH, Chang MT, Jonsson P, Penson AV, Gorelick A, Harris C, Schram AM, Syed A, Zehir A, Chapman PB, **Hyman DM**, Solit DB, Shannon K, Chandarlapaty S, Berger MF, Taylor BS. *Cancer Cell.* 2018 Nov 12;34(5):852-862.

BRAF Inhibition in $BRAF_{V600}$-Mutant Gliomas: Results From the VE-BASKET Study. Kaley T, Touat M, Subbiah V, Hollebecque A, Rodon J, Lockhart AC, Keedy V, Bielle F, Hofheinz RD, Joly F, Blay JY, Chau I, Puzanov I, Raje NS, Wolf J, DeAngelis LM, Makrutzki M, Riehl T, Pitcher B, Baselga J, **Hyman DM**. *J Clin Oncol*. 2018 Oct 23:JCO2018789990.

Clinical Utility of Prospective Molecular Characterization in Advanced Endometrial Cancer. Soumerai TE, Donoghue MTA, Bandlamudi C, Srinivasan P, Chang MT, Zamarin D, Cadoo KA, Grisham RN, O'Cearbhaill RE, Tew WP, Konner JA, Hensley ML, Makker V, Sabbatini P, Spriggs DR, Troso-Sandoval TA, Charen AS, Friedman C, Gorsky M, Schweber SJ, Middha S, Murali R, Chiang S, Park KJ, Soslow RA, Ladanyi M, Li BT, Mueller J, Weigelt B, Zehir A, Berger MF, Abu-Rustum NR, Aghajanian C, DeLair DF, Solit DB, Taylor BS, **Hyman DM**. *Clin Cancer Res*. 2018 Dec 1;24(23):5939-5947

Rates of *ERBB2* Alterations across Melanoma Subtypes and a Complete Response to Trastuzumab Emtansine in an *ERBB2*-Amplified Acral Melanoma. Gottesdiener LS, O'Connor S, Busam KJ, Won H, Solit DB, **Hyman DM**, Shoushtari AN. *Clin Cancer Res*. 2018 Dec 1;24(23):5815-5819

Clinical tumour sequencing for precision oncology: time for a universal strategy. Cheng ML, Berger MF, **Hyman DM**, Solit DB. *Nat Rev Cancer*. 2018 Sep;18(9):527-528.

Genome doubling shapes the evolution and prognosis of advanced cancers.
Bielski CM, Zehir A, Penson AV, Donoghue MTA, Chatila W, Armenia J, Chang MT, Schram AM, Jonsson P, Bandlamudi C, Razavi P, Iyer G, Robson ME, Stadler ZK, Schultz N, Baselga J, Solit DB, **Hyman DM**, Berger MF, Taylor BS. *Nat Genet*. 2018 Aug;50(8):1189-1195.

Session 5

Targeting Mutant RAS

5-1. A Novel Model for Oncogenic Activity of ERK Signal Activation in Human Cancer

Speaker: Neal Rosen (Memorial Sloan Kettering Cancer Center, USA)

5-2. Discovery of Direct Inhibitors of the Human Oncogene, KRAS (G12C)

Speaker: Kevan M. Shokat (University of California, San Francisco, USA)

5-3. Targeting the RAS Pathway with SHP2 Inhibitors

Speaker: Benjamin G. Neel (New York University Langone Medical Center, USA)

Title: A Novel Model for Oncogenic Activity of ERK Signal Activation in Human Cancer

Speaker

Neal Rosen, MD, PhD

Chair, Center for Mechanism-Based Therapeutics,
Enid A. Haupt Chair in Medical Oncology,
Member, Program in Molecular Pharmacology,
Memorial Sloan Kettering Cancer Center, USA

Chairman

Chikashi Ishioka, MD, PhD

Professor, Institute of Development, Aging and Cancer,
Tohoku University, Japan

Neal Rosen, MD, PhD

Profile

Dr. Rosen is the Chair of the Center for Mechanism-Based Therapeutics at Memorial Sloan Kettering Cancer Center, where he is also a Member in the Program in Molecular Pharmacology and the incumbent of the Enid A Haupt Chair in Medical Oncology.

His major interests are the identification and study of the key molecular events and growth signaling pathways responsible for the development of human cancers, and the use of this information for the development of mechanism-based therapeutic strategies. He has played a leading role in the development of inhibitors of tyrosine kinasemediated signaling and has pioneered the concept that feedback reactivation of parallel signaling pathways is a common cause of adaptive resistance to selective pathway inhibitors.
Recent work from the Rosen laboratory included the elucidation of the mechanism whereby RAF inhibitors are selectively effective in mutant BRAF tumors. These

mechanistic studies predicted several of the cellular mechanisms whereby tumors develop resistance to vemurafenib and other selective RAF inhibitors. This work, in addition to other recent studies by the Rosen laboratory on the consequences of relief of negative feedback by oncoprotein inhibitors, has also led to multiple clinical trials of combination therapies at Memorial Sloan-Kettering and other cancer centers in the United States and internationally that have shown promising early results.

He received his undergraduate degree in chemistry from Columbia College and an MD/PhD in Molecular Biology from the Albert Einstein College of Medicine. He completed a residency in Internal Medicine at the Brigham and Women's Hospital, and postdoctoral training and a fellowship in Medical Oncology at the National Cancer Institute. He was on the senior staff of the Medicine Branch at the NCI prior to joining the faculty of Memorial Sloan Kettering Cancer Center.

Research Interests

ERK signaling and its therapeutic inhibition in cancer
One major focus of our lab is the study and development of selective inhibitors of the ERK pathway to treat the tumors driven by ERK hyperactivation. Previously we found that activation of ERK output is dependent upon the mechanisms by which oncogenic mutants evade ERK-dependent feedback regulation. The loss of feedback regulation not only drives constitutive activation of the ERK pathway, but also sensitizes the tumors to specific inhibitors of pathway components. As we have reported, the BRAF and RAS mutant tumors are more sensitive to ERK pathway inhibition than the RAF/RAS wild type tumors. We are now investigating the biochemical actions and anti-tumor activities of the different inhibitors (mutant RAS selective inhibitors, RAF monomer selective inhibitors, RAF dimer inhibitors, allosteric MEK inhibitors, ATP-competitive MEK inhibitors, and ERK inhibitors) in tumors expressing different RAS, RAF, or NF1 mutants.

PI3K signaling and its inhibition in cancer
We have shown that tumors with HER2 amplification or PI3K mutation are selectively dependent for growth on the PI3K pathway and are sensitive to specific inhibitors of PI3K or AKT. Inhibition of PI3K signaling in tumors has metabolic, pro-apoptotic, and anti-proliferative effects, but relief of potent feedback inhibition of upstream receptors increases their activation and expression, attenuating the antitumor benefit of the drugs. We have shown that inhibitors of PI3K, AKT, and mTOR all relieve feedback, but the details of their effects differ, which suggests why these drugs vary in their in efficacy and toxicity. This work has enhanced our understanding of the oncogenic signaling network, with implications for developing more effective therapeutic strategies.

Hsp90 signaling and its inhibition in cancer
The evaluation of Hsp90 as a therapeutic target in cancer patients is another major focus of our lab. Hsp90 is a chaperone required for maintaining the proper conformation of several important signaling proteins, including transmembrane tyrosine kinases and steroid receptors. The laboratory is studying the role of Hsp90 family members in maintaining the transformed phenotype of cancer cells. Our recent work has shown that Hsp90 is critical for oncogenic RAF kinase-driven ERK activation. The combination of Hsp90 inhibitors with RAF or MEK inhibitors may achieve a better pathway inhibition in RAS and/or BRAF mutant tumors. This work will contribute significantly toward better patient treatments.

Recent Publications

Efficacy of MEK inhibition in patients with histiocytic neoplasms. Diamond EL, Durham BH, Ulaner GA, Drill E, Buthorn J, Ki M, Bitner L, Cho H, Young RJ, Francis JH, Rampal R, Lacouture M, Brody LA, Ozkaya N, Dogan A, **Rosen N**, Iasonos A, Abdel-Wahab O, Hyman DM. *Nature.* 2019 Mar;567(7749):521-524

RAF inhibitor PLX8394 selectively disrupts BRAF dimers and RAS-independent BRAF-mutant-driven signaling. Yao Z, Gao Y, Su W, Yaeger R, Tao J, Na N, Zhang Y, Zhang C, Rymar A, Tao A, Timaul NM, Mcgriskin R, Outmezguine NA, Zhao H, Chang Q, Qeriqi B, Barbacid M, de Stanchina E, Hyman DM, Bollag G, **Rosen N.** *Nat Med.* 2019 Feb;25(2):284-291.

Loss of the FAT1 Tumor Suppressor Promotes Resistance to CDK4/6 Inhibitors via the Hippo Pathway. Li Z, Razavi P, Li Q, Toy W, Liu B, Ping C, Hsieh W, Sanchez-Vega F, Brown DN, Da Cruz Paula AF, Morris L, Selenica P, Eichenberger E, Shen R, Schultz N, **Rosen N**, Scaltriti M, Brogi E, Baselga J, Reis-Filho JS, Chandarlapaty S. *Cancer Cell.* 2018 Dec 10;34(6):893-905.

Synergistic anti-angiogenic treatment effects by dual FGFR1 and VEGFR1 inhibition in FGFR1-amplified breast cancer. Golfmann K, Meder L, Koker M, Volz C, Borchmann S, Tharun L, Dietlein F, Malchers F, Florin A, Büttner R, **Rosen N**, Rodrik-Outmezguine V, Hallek M, Ullrich RT. *Oncogene*. 2018 Oct;37(42):5682-5693.

A Secondary Mutation in *BRAF* Confers Resistance to RAF Inhibition in a $BRAF_{V600E}$-Mutant Brain Tumor. Wang J, Yao Z, Jonsson P, Allen AN, Qin ACR, Uddin S, Dunkel IJ, Petriccione M, Manova K, Haque S, Rosenblum MK, Pisapia DJ, **Rosen N**, Taylor BS, Pratilas CA. *Cancer Discov.* 2018 Sep;8(9):1130-1141.

Title: Discovery of Direct Inhibitors of the Human Oncogene, KRAS(G12C)

Speaker

Kevan M. Shokat, PhD

Professor and Vice-Chair, Department of Cellular and Molecular Pharmacology, at the University of California, San Francisco, Professor in the Department of Chemistry at the University of California, Berkeley, USA

Chairman

Kiyohiko Hatake, MD, PhD

Professor, Department of Hematology,
International University of Health and Welfare, School of Medicine, Japan

Kevan M. Shokat, PhD

Profile

Dr. Shokat is an American Chemical Biologist. He is a Professor and Chair in the Department of Cellular and Molecular Pharmacology at University of California, San Francisco, a Professor in the Department of Chemistry at University of California, Berkeley, and an Investigator with the Howard Hughes Medical Institute.

Dr, Shokat received his B.A, in chemistry from Reed College in 1986, completing his thesis, "Synthesis of a precursor of PRCPCP, a non-hydrolyzable analog of phosphoribosylpyrophosphate (PRPP)," with Ron McClard, and his Ph.D. from University of California, Berkeley in 1991, under Peter G. Schultz.

Dr,Shokat is one of the leading figures in the field of chemical genetics.[1] He uses methods of bioorganic chemistry to elucidate signal transduction pathways at the single cell and whole organism levels, and is particularly interested in protein kinases, and developing methods to elucidate the particular targets of each kinase.

Research Interests

Drugging the most common oncogene: K-Ras: In the area of cancer we have made a breakthrough by discovering a way to block the function of the GTPase, K-Ras. Somatic mutations in the K-Ras are the most common activating lesions found in human cancer, and are generally associated with poor response to standard therapies. Efforts to directly target this oncogene have faced difficulties due to its picomolar affinity for GTP/GDP and the absence of known allosteric regulatory sites. We were able to develop small molecules that irreversibly bind to a common oncogenic mutant, K-Ras G12C (PMID: 24256730). These compounds rely on the mutant cysteine for binding and therefore do not affect the wild type protein (WT). Using crystallography we identified a new pocket that is not apparent in previous structures of Ras, beneath the effector binding switch-II region. Our results and those from Wellspring Biosciences (PMID: 26739882) (PMID: 29373830) provide structure-based validation of a novel allosteric regulatory site on Ras that is targetable in a mutant-specific manner. This approach has been recently validated in clinical studies. We have uncovered additional druggable vulnerabilities in KRAS which we seek to exploit to develop additional KRAS targeted drugs (PMID: 29033317)(PMID: 28621541)(PMID: 31138768).

New generations of mTOR inhibitors for the treatment of cancer: The PIK3CA gene product, phosphatidylinositol 3-kinase a is the second most frequently mutated oncogene across all cancers. Several steps downstream of PIK3CA in the growth factor pathway lies the integrator of nutrient availability and growth hormones, the mechanistic Target of Rapamycin (mTOR) kinase. The natural product Rapamycin serves to inhibit mTOR via a molecular glue mechanism by recruiting the cellular chaperone FKBP12 to mTOR via its FRB domain. In 2008 we published a second generation ATP competitive inhibitor of mTOR, PP242 (PMID: 19209957) and then in collaboration with scientists at Intellikine, optimized this for human clinical studies, now named INK128/Sapanisertib (PMID: 22367541) undergoing phase II clinical studies. In 2016 we reported a third generation “bitopic” inhibitor of mTOR, termed RapaLink which has exceptionally high affinity even for mutants of mTOR which are resistant to first and second generation inhibitors (PMID: 27279227). We continue to explore chemical modifications to RapaLink and ways to exploit the molecular glue mechanism of Rapamycin (bioRxiv 619551).

Neo-substrates as a new strategy for drug discovery: In an attempt to develop a drug to treat Parkinson’s Disease we have developed a small molecule which helps to protect neurons from dying due to various types of stress. Mitochondria have long been implicated in the pathogenesis of Parkinson’s disease (PD). Mutations in the mitochondrial kinase PINK1 that reduce kinase activity are associated with mitochondrial defects and result in an autosomal-recessive form of early- onset PD. Therapeutic approaches for enhancing the activity of PINK1 have not been considered because no allosteric regulatory sites for PINK1 are known. We have shown that an alternative strategy, a neo-substrate approach involving the ATP analog kinetin triphosphate (KTP), can be used to increase the activity of both PD-related mutant PINK1G309D and PINK1WT (PMID: 23953109). Discovery of neo-substrates for kinases could provide a heretofore unappreciated modality for regulating kinase activity.

Identification of the Direct Substrates of Every Protein Kinase: The search for the complete set of all protein kinase substrates is a major goal of many laboratories. It is estimated that one third of the proteome is phosphorylated making the tracing of the substrates of >500 kinases extremely challenging. To address this problem we have devised a chemical method for tagging the direct substrates of any protein kinase

(PMID: 9108016) using a [g-S] labeled ATP analog, N6-(benzyl)ATP (PMID: 17486086)(PMID: 18234856). The ATP analog, N6-(benzyl)ATP is a poor substrate of wild-type protein kinases, but is efficiently accepted by any kinase of interest by virtue of a mutation which enlarges ATP binding site to accommodate the N6-benzyl substituent. Identification of the thiophosphate labeled proteins via chemical capture allows for hundreds of novel substrates of over 50 widely divergent kinases, such as v-Src, CDK2, JNK, Cdc28, Erk2, Srb10, and kin28 (PMID: 23836541). The ability to directly affinity purify substrates of any kinase in the will allow for the complete mapping of any kinase pathway in a cell and development of a complete picture of the complex networks of kinase signal transduction pathways. It is our long term goal to identify all the direct substrates of each kinase in the human genome using these chemical tools.
Protein Kinase Inhibitors: We have developed a powerful chemical genetic method for the generation of target-specific inhibitors of any protein kinase in the genome (PMID: 11014197). This strategy utilizes a functionally silent active site mutation to sensitize a target kinase to inhibition by a small molecule that does not inhibit wild-type kinases. Tyrosine and serine/threonine kinases are equally amenable to the drug-sensitization approach, which has been used to generate selective inhibitors of mutant Src family kinases, Abl family kinases, cyclin-dependent kinases (CDKs), mitogen-activated kinases (MAPKs), p21-activated kinases (PAKs), Ca2+/calmodulin-dependent kinases (CAMKs), and over 50 other protein kinases. The ability to generate the very first inhibitors of many diverse protein kinases has allowed for the discovery of fundamentally new roles of kinases in transcription, cell cycle, cell-fate determination, the unfolded protein response, oncogenic transformation, and many others.

Recent Publications

$KRAS_{G12C}$ inhibition produces a driver-limited state revealing collateral dependencies. Lou K, Steri V, Ge AY, Hwang YC, Yogodzinski CH, Shkedi AR, Choi ALM, Mitchell DC, Swaney DL, Hann B, Gordan JD, **Shokat KM**, Gilbert LA. *Sci Signal*. 2019 May 28;12(583). pii: eaaw9450.

Phosphoregulation of the oncogenic protein regulator of cytokinesis 1 (PRC1) by the atypical CDK16/CCNY complex. Hernández-Ortega S, Sánchez-Botet A, Quandt E, Masip N, Gasa L, Verde G, Jiménez J, Levin RS, Rutaganira FU, Burlingame AL, Wolfgeher D, Ribeiro MPC, Kron SJ, **Shokat KM**, Clotet J. *Exp Mol Med*. 2019 Apr 16;51(4):44.

A Legionella pneumophila Kinase Phosphorylates the Hsp70 Chaperone Family to Inhibit Eukaryotic Protein Synthesis. Moss SM, Taylor IR, Ruggero D, Gestwicki JE, **Shokat KM**, Mukherjee S. *Cell Host Microbe*. 2019 Mar 13;25(3):454-462.

Chronic TGF-β exposure drives stabilized EMT, tumor stemness, and cancer drug resistance with vulnerability to bitopic mTOR inhibition. Katsuno Y, Meyer DS, Zhang Z, **Shokat KM**, Akhurst RJ, Miyazono K, Derynck R. *Sci Signal.* 2019 Feb 26;12(570). pii: eaau8544.

Chemically reprogramming the phospho-transfer reaction to crosslink protein kinases to their substrates. Wong AW, Urisman A, Burlingame AL, **Shokat KM**. P*rotein Sci.* 2019 Mar;28(3):654-662.

A Patient-derived Xenograft Model of Pancreatic Neuroendocrine Tumors Identifies Sapanisertib as a Possible New Treatment for Everolimus-resistant Tumors.

Chamberlain CE, German MS, Yang K, Wang J, VanBrocklin H, Regan M, **Shokat KM**, Ducker GS, Kim GE, Hann B, Donner DB, Warren RS, Venook AP, Bergsland EK, Lee D, Wang Y, Nakakura EK. *Mol Cancer Ther*. 2018 Dec;17(12):2702-2709.

Type II Kinase Inhibitors Targeting Cys-Gatekeeper Kinases Display Orthogonality with Wild Type and Ala/Gly-Gatekeeper Kinases. Ocasio CA, Warkentin AA, McIntyre PJ, Barkovich KJ, Vesely C, Spencer J, **Shokat KM**, Bayliss R. *ACS Chem Biol.* 2018 Oct 19;13(10):2956-2965.

Title: Targeting the RAS Pathway with SHP2 Inhibition

Benjamin G. Neel, MD, PhD

Director, Laura and Isaac Perlmutter Cancer Center
Professor, Department of Medicine, NYU Langone Health, NY, USA

Speaker

Masakazu Toi, MD, PhD

Professor, Department of Surgery, Graduate School of Medicine,
Kyoto University, Japan

Chairman

Benjamin G. Neel, MD, PhD

Profile

As the director of Perlmutter Cancer Center, Dr. Neel leads a rigorous academic community of clinician–scientists and basic scientists, as well as a team of compassionate physicians who are dedicated to our patients. Through their clinical trials, they give patients unprecedented access to novel therapies and experimental treatments. He also oversees the advancement of our translational programs in immunotherapy, cancer genetics, targeted therapies, and epigenetics, as well as imaging, community outreach, and supportive oncology.

One of his goals as director is to foster collaboration between physicians and researchers. He creates new opportunities for them to meaningfully engage with one another and form multidisciplinary partnerships. They have the best chance at dramatically impacting patient survival when they work together to understand the

essence of cancer and its vulnerabilities, as well as the progress that has been made in cancer biology.

We are at a historic time in the field — We finally understand a range of factors that cause cancer, from one's environment to molecular defects in cancer cells. When he was a graduate student, they didn't know a single gene mutation that causes cancer, nor did they understand cancer's molecular basis. Now we know that different cancers are caused by different agents, and we have identified between 500 and 1,000 gene mutations that, in various combinations, can lead to cancer. With this knowledge, we have created a bevy of treatments that we can use against the disease, such as epigenetic therapy and immunotherapy.

His research focuses on cell signaling in cancer and developmental disease, as well as the biology of breast and ovarian cancer. In addition to authoring more than 200 original papers, 25 reviews, and 2 books, He has received multiple grants from the National Institutes of Health and National Cancer Institute, as well as private foundations.He was the inaugural recipient of the Gertrude Elion Award of the American Association for Cancer Research, have held multiple named lectureships, and serve on editorial board of several journals, including *Cancer Cell*, *Molecular Cell*, and *Cancer Discovery*, among others. I am an elected member of the Association of American Physicians, a former member of the board of directors of the American Association for Cancer Research, and co-founder of Northern Biologics, a biotechnology company developing new therapies for cancer and fibrosis.

Recent Publications

Phase I study of local radiation and tremelimumab in patients with inoperable locally recurrent or metastatic breast cancer. Jiang DM, Fyles A, Nguyen LT, **Neel BG**, Sacher A, Rottapel R, Wang BX, Ohashi PS, Sridhar SS. *Oncotarget*. 2019 Apr 26;10(31):2947-2958

The Noonan Syndrome-linked Raf1L613V mutation drives increased glial number in the mouse cortex and enhanced learning. Holter MC, Hewitt LT, Koebele SV, Judd JM, Xing L, Bimonte-Nelson HA, Conrad CD, Araki T, **Neel BG**, Snider WD, Newbern JM. *PLoS Genet*. 2019 Apr 24;15(4):e1008108.

An organoid platform for ovarian cancer captures intra- and interpatient heterogeneity. Kopper O, de Witte CJ, Lõhmussaar K, Valle-Inclan JE, Hami N, Kester L, Balgobind AV, Korving J, Proost N, Begthel H, van Wijk LM, Revilla SA, Theeuwsen R, van de Ven M, van Roosmalen MJ, Ponsioen B, Ho VWH, **Neel BG**, Bosse T, Gaarenstroom KN, Vrieling H, Vreeswijk MPG, van Diest PJ, Witteveen PO, Jonges T, Bos JL, van Oudenaarden A, Zweemer RP, Snippert HJG, Kloosterman WP, Clevers H. *Nat Med*. 2019 May;25(5):838-849.

N-Glycoproteomics of Patient-Derived Xenografts: A Strategy to Discover Tumor-Associated Proteins in High-Grade Serous Ovarian Cancer. Sinha A, Hussain A, Ignatchenko V, Ignatchenko A, Tang KH, Ho VWH, **Neel BG**, Clarke B, Bernardini MQ, Ailles L, Kislinger T. *Cell Syst*. 2019 Apr 24;8(4):345-351.e4.

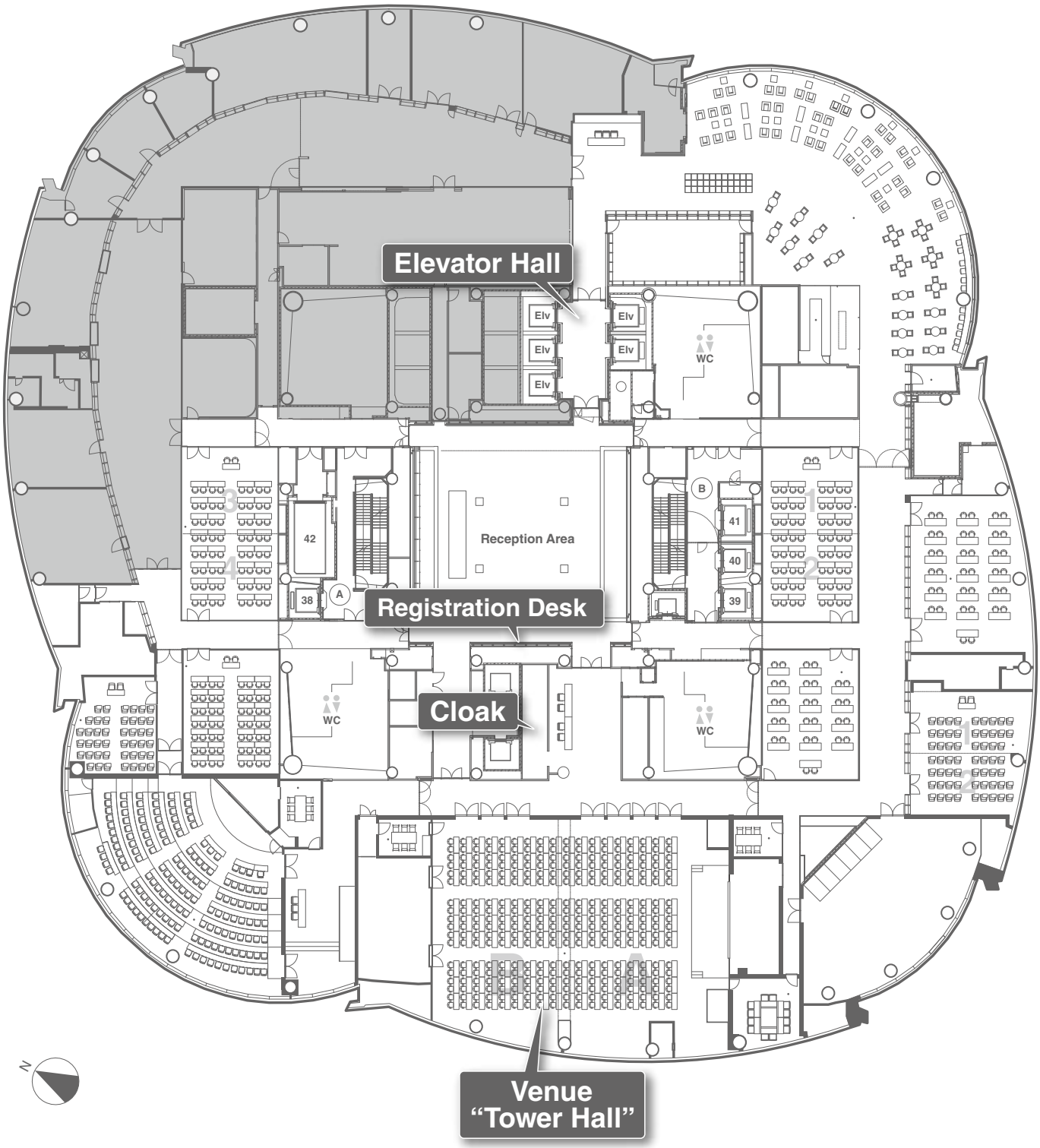
The *Gp1ba-Cre* transgenic mouse: a new model to delineate platelet and leukocyte functions. Nagy Z, Vögtle T, Geer MJ, Mori J, Heising S, Di Nunzio G, Gareus R,

Tarakhovsky A, Weiss A, **Neel BG**, Desanti GE, Mazharian A, Senis YA. *Blood*. 2019 Jan 24;133(4):331-343.

Pathologic Oxidation of PTPN12 Underlies ABL1 Phosphorylation in Hereditary Leiomyomatosis and Renal Cell Carcinoma. Xu Y, Taylor P, Andrade J, Ueberheide B, Shuch B, Glazer PM, Bindra RS, Moran MF, Linehan WM, **Neel BG**. *Cancer Res*. 2018 Dec 1;78(23):6539-6548.

Off-target inhibition by active site-targeting SHP2 inhibitors. Tsutsumi R, Ran H, **Neel BG**. *FEBS Open Bio*. 2018 Aug 1;8(9):1405-1411.

国際フォーラム2019 講演会場：六本木アカデミーヒルズ49（49階）



ウエルカム レセプション（7月26日18:00 ～）：六本木ヒルズクラブ（51階）
51階へはエレベーターをご利用ください。

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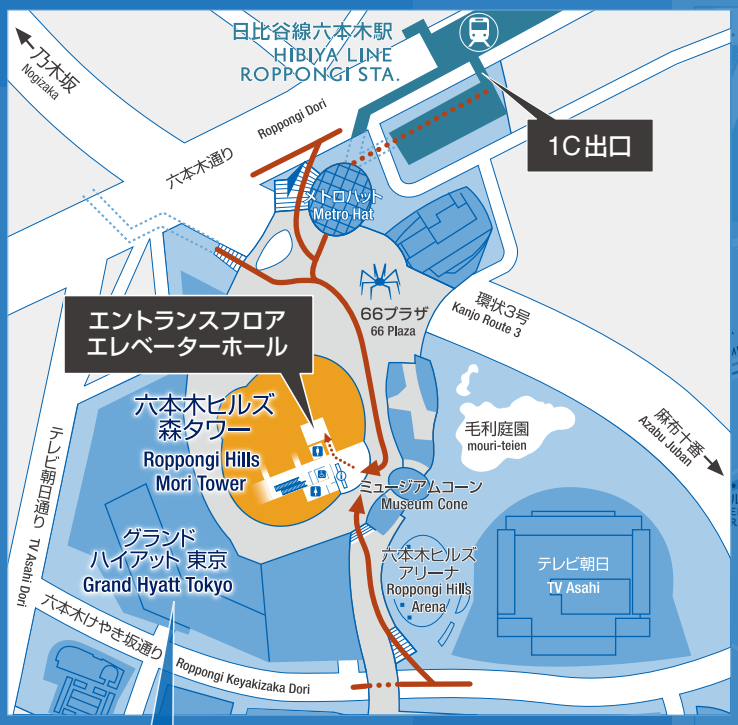

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羽田空港から約40分
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道路状況により混雑する場合がございます。余裕を持ってお越しください。
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南北線　麻布十番駅・徒歩12分
千代田線　乃木坂駅・徒歩10分

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CHAAO Comprehensive Academy for Advanced Oncology

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