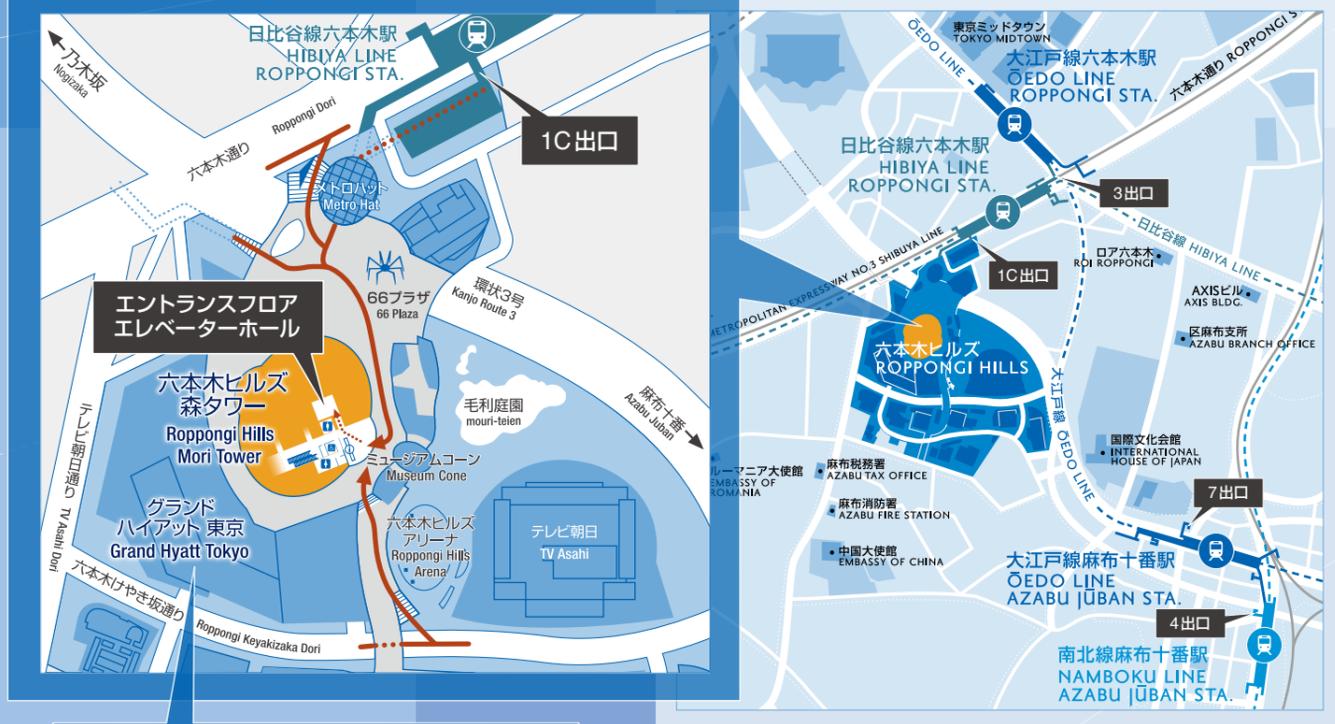


アクセスマップ

会場：六本木アカデミーヒルズ49

49階へのエレベーターは、エントランスフロア(2階)
右奥のエレベーターホールにございます。

六本木アカデミーヒルズ49 Roppongi Academyhills 49



宿泊地：グランドハイアット東京

タクシー (「タクシーベイB」とお申し付けください。)
羽田空港から約40分
品川駅・東京駅からは約20分
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。
到着後、防災センター隣のエスカレーターで2階に上がりますと後方に「アカデミーヒルズ」の入り口があります。

地下鉄

日比谷線 六本木駅・徒歩3分(コンコースにて直結)
大江戸線 六本木駅・徒歩6分、麻布十番駅・徒歩9分
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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INTERNATIONAL ACADEMY FOR ADVANCED ONCOLOGY

IAAO

国際フォーラム2014

Convergence for Breakthroughs in Oncology Therapy

2014年8月1日(金) 12:55~18:30

2日(土) 8:40~15:30

六本木アカデミーヒルズ49

Convergence for Breakthroughs in Oncology Therapy

Friday, Aug 1st, 2014 12:55~18:30

Opening Remarks

P.3

12:55 Osamu Nagayama, Chairman (Chugai Academy for Advanced Oncology)

1. Individualized Cancer Therapy

P.4

13:00 Functionalizing Data from the Cancer Genome - the Case of RAF Mutations

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

Chair: Kiyohiko Hatake (Cancer Institute Hospital, Japan)

13:45 Maximizing Responses to Radioiodine in Thyroid Cancer by Sustained MAPK Pathway Inhibition

Speaker: James A. Fagin (Memorial Sloan-Kettering Cancer Center, USA)

Chair: Yuko Kitagawa (Keio University, Japan)

14:30 Break

14:45 Challenges and Opportunities Facing Tumor and Therapeutics Heterogeneity of Kidney Cancer

Speaker: James J. Hsieh (Memorial Sloan-Kettering Cancer Center, USA)

Chair: Chikashi Ishioka (Tohoku University, Japan)

15:30 Molecular Pathology: Detection of Gene Fusions in Cancer

Speaker: Anthony J. Iafrate (Harvard Medical School, USA)

Chair: Makoto Ogawa (Aichi Cancer Center, Japan)

16:15 Break

16:35 Q&A session

2. Towards a More Productive Relationship Between Academia and Industry

P.28

16:50 The European Cancer Patient Bill of Rights: A Catalyst for Change

Speaker: Patrick G. Johnston (The Queen's University Belfast, UK)

Chair: Yasuhiro Fujiwara (National Cancer Center, Japan)

17:15 Academic-Industry Collaboration Drives Cancer Drug Development

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

Chair: Nagahiro Saijo (Japanese Society of Medical Oncology, Japan)

17:40 Industry-Academia Relationship after Diovon Scandal in Japan

Speaker: Yasuhiro Fujiwara (National Cancer Center, Japan)

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

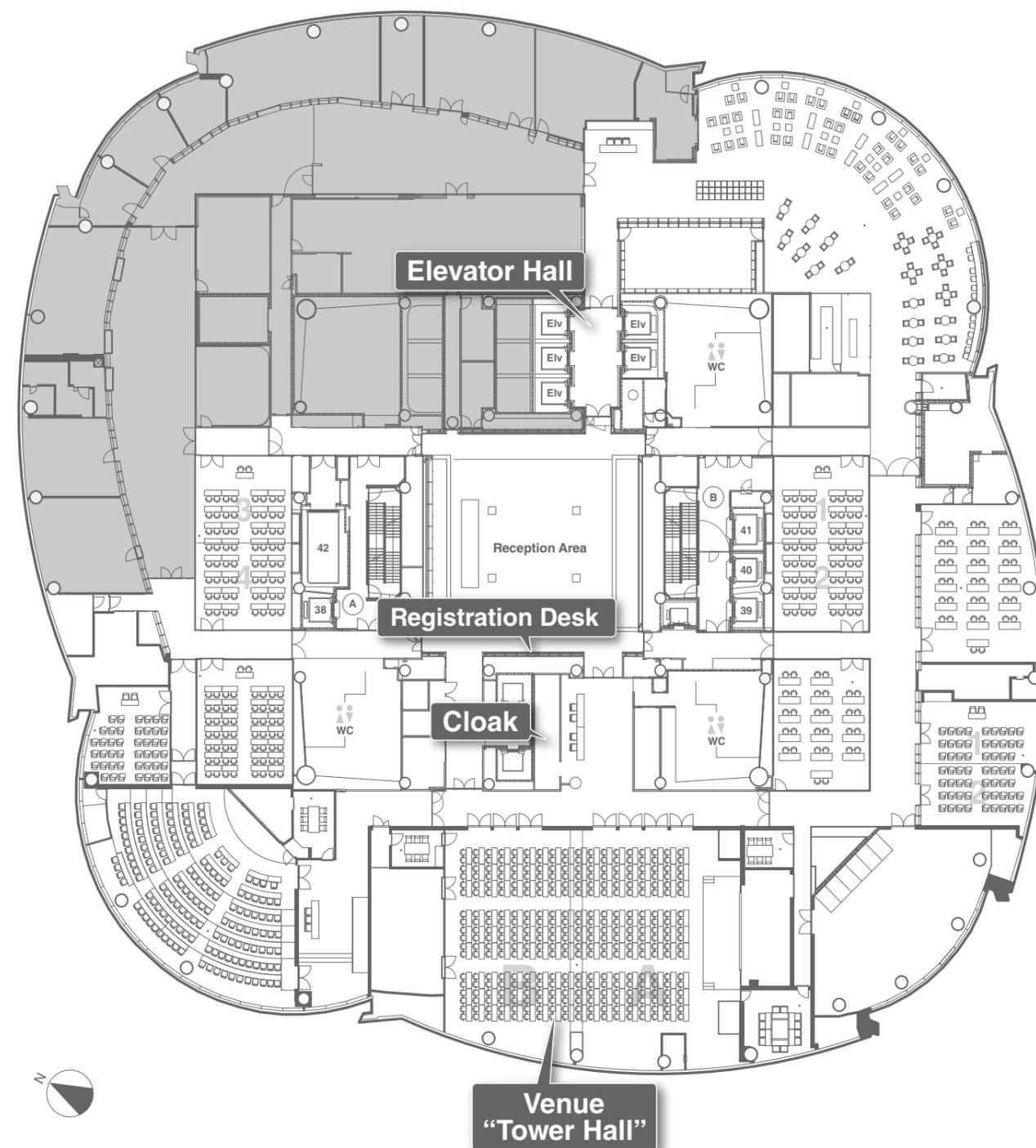
18:00 Panel Discussion

Discussants: P. G. Johnston, B. A. Chabner, Y. Fujiwara, N. Saijo

Moderator: Patrick G. Johnston (The Queen's University Belfast, UK)

18:30 Reception at Roppongi Hills Club, 51F

国際フォーラム2014 講演会場：六本木アカデミーヒルズ49 (49階)



ウェルカム レセプション (8月1日 18:30 ~) : 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。

Saturday, Aug 2nd, 2014 8:40~15:30

3. Physiological Versatility of Cancer

P.46

8:40 Defining the Underlying Principles of Resistance to Targeted Cancer Therapeutics

Speaker: Levi A. Garraway (Harvard Medical School, USA)

Chair: Hiroyuki Mano (The University of Tokyo, Japan)

9:25 Pharmacology, Feedback, and Novel Agents in the MAP Kinase Pathway

Speaker: Keith T. Flaherty (Harvard Medical School, USA)

Chair: Chikashi Ishioka (Tohoku University, Japan)

10:10

Break

10:25 Beyond Oncogenes: What Will Be the Next Generations of AntiCancer Targets?

Speaker: Tak W. Mak (Research at University Health Network, Canada)

Chair: Kohei Miyazono (The University of Tokyo, Japan)

11:25

Q&A session

4. Immunology in Cancer Treatment

P.64

11:35 Translating Cancer Immunoediting Principles to Cancer Immunotherapy

Speaker: Robert D. Schreiber (Washington University, USA)

Chair: Mitsuaki Yoshida (Japanese Foundation For Cancer Research, Japan)

12:35

Lunch

13:10 Control of Tumor Immunity by Regulatory T Cells

Speaker: Shimon Sakaguchi (Osaka University, Japan)

Chair: Ryuzo Ueda (Aichi Medical University, Japan)

14:10 Tumor Site Immune Modulation Therapy

Speaker: Lieping Chen (Yale University, USA)

Chair: Hirotohi Akita (Hokkaido University, Japan)

15:10

Q&A session

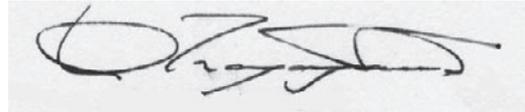
オフィシャル言語 >> 英語
ドレスコード >> ビジネスカジュアル

Opening Remarks



Osamu Nagayama

Chairman, Chugai Academy for Advanced Oncology
(CHAAO), Incorporated Association



As chairman of Chugai Academy for Advanced Oncology (CHAAO), it is my greatest pleasure and honor to welcome all of our distinguished guests, experts and investigators, both from overseas and Japan, to the International Academy for Advanced Oncology 2014.

Following the success of previous Forums, I am delighted that today we have realized the fifth opportunity to meet together with more than 220 oncologists participating. We have received highly positive feedback from the participants in past years, which is very encouraging to us, and I am confident that this year will be equally successful.

The forum was organized through the active discussions among the new Advisory Board team launched last year, namely Dr. Chabner, Dr. Johnston, Dr. Fujiwara, Dr. Hatake, Dr. Ishioka, Dr. Kitagawa, Dr. Mano, Dr. Miyazono, Dr. Toi and Dr. Ueda. I sincerely appreciate the leadership and positive efforts of these 10 board members to put together an exceptional program with so many outstanding speakers.

The main theme chosen for this year is “Convergence for Breakthroughs in Oncology Therapy.” This reflects our strong belief that a convergence of technology, science, and resources is required to pursue and ultimately realize innovations in cancer treatment.

During the program, we will cover a broad range of topics, such as immunotherapy, personalized health care (PHC), and genome therapy. In addition to the scientific topics, we will also discuss the relationship between academia and industry and how the collaboration between them can be made more efficient and effective.

To have extensive discussion on such a broad range of topics, I am extremely pleased that we could invite so many world-class experts to share their experience, knowledge and insights.

In closing, on behalf of the organizer, CHAAO, our sincere wish is that this two-day forum will become an extremely informative and engaging time for everyone. Our goal is for CHAAO to facilitate a valuable exchange of information, paving the way toward cancer treatments that enable patients to confront cancer proactively and with hope. New challenges and issues are constantly appearing in cancer treatment, but I believe CHAAO can make a contribution to the search for solutions.

Session 1

IAAO

Individualized Cancer Therapy

1-1. Functionalizing Data from the Cancer Genome - the Case of RAF Mutations

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

1-2. Maximizing Responses to Radioiodine in Thyroid Cancer by Sustained MAPK Pathway Inhibition

Speaker: James A. Fagin (Memorial Sloan-Kettering Cancer Center, USA)

1-3. Challenges and Opportunities Facing Tumor and Therapeutics Heterogeneity of Kidney Cancer

Speaker: James J. Hsieh (Memorial Sloan-Kettering Cancer Center, USA)

1-4. Molecular Pathology: Detection of Gene Fusions in Cancer

Speaker: Anthony J. Iafrate (Harvard Medical School, USA)

Title: Functionalizing Data from the Cancer Genome - the Case of RAF Mutations



Speaker

Neal Rosen, MD, PhD

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



Chairman

Kiyohiko Hatake, MD, PhD

Chief, Department of Hematology, Cancer Institute Hospital,
Japanese Foundation for Cancer Research (JFCR), Japan

Neal Rosen, MD, PhD

Profile

Dr Neal Rosen is the Director 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 Chemistry and the incumbent of the Enid A Haupt Chair in Medical Oncology.

Dr Rosen's 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. Dr. Rosen has played a leading role in the development of inhibitors of tyrosine kinase-mediated 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.

Dr Rosen 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.

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Title: Maximizing Responses to Radioiodine in Thyroid Cancer by Sustained MAPK Pathway Inhibition



James A. Fagin, MD

Chief, Endocrinology Service, Member, Human Oncology Pathogenesis Program, Memorial Sloan Kettering Cancer Center

Speaker



Yuko Kitagawa, MD, PhD

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

Chairman

James A. Fagin, MD

Profile

Dr Fagin's group has been instrumental in characterizing somatic genetic changes associated with thyroid tumor initiation and progression, and in defining the functional consequences using in vitro and in vivo experimental models. We have focused in particular on the role of MAP kinase effectors, because these tumors are associated with non-overlapping mutations of the tyrosine kinase receptors RET and NTRK, the three RAS genes and BRAF. Our group is also exploring the activity of selective kinase inhibitors on thyroid cancer cell growth and responsiveness to radioactive iodine, and studying potential mechanisms of resistance in vitro, in mouse genetic models and in patients.

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Julio C. Ricarte-Filho et al. Identification of kinase fusion oncogenes in post-Chernobyl radiation-induced thyroid cancers
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Debyani Chakravarty et al. Small-molecule MAPK inhibitors restore radioiodine incorporation in mouse thyroid cancers with conditional BRAF activation.
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Oncogene (2013), 1–8 doi:10.1038/onc.2013.489

Title: Challenges and Opportunities Facing Tumor and Therapeutics Heterogeneity of Kidney Cancer



Speaker

James J. Hsieh, MD, PhD

Founding Director/Translational Kidney Cancer Research Program

Associate Member/Human Oncology & Pathogenesis Program, Associate Attending/GU Oncology/Medicine, Memorial Sloan-Kettering Cancer Center



Chairman

Chikashi Ishioka, MD

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

James J. Hsieh, MD, PhD

Profile

As a medical intern taking care of cancer patients in 1990, Dr. James Hsieh witnessed the hopelessness that metastatic cancer patient faces and decided to devote his life to the fight against cancer. He stated in his graduate school application “I want to study the molecular mechanisms of gene regulation in human cells, particularly those concerning cellular differentiation and transformation”. His Ph.D. thesis at Johns Hopkins Medical School focused on dissecting the mechanisms by which EBV EBNA2 hijacks Notch signaling for tumorigenesis, which resulted in a two-authored Science paper^{1,2}. After graduation, Dr. Hsieh entered Washington University and Dana Farber Cancer Institute for Medicine and Oncology training, respectively. After completing medical oncology training, he joined the late Dr. Korsmeyer’s laboratory as an HHMI Physician-Scientist Fellowship Awardee, where he discovered the proteolytic processing of MLL, purified the culprit protease, and named it “Taspase1” in a three-authored Cell paper^{3,4}.

As an NCI K01 Howard Temin Awardee, Dr. Hsieh joined the faculty at Washington University in 2004. The discovery on MLL regulation by the Hsieh laboratory laid the foundation for the compassionate use of FDA approved proteasome inhibitor Bortezomib on a small cohort of MLL

leukemia patients, showing clinical benefits⁵⁻⁷. To probe the function of Taspase1 and its respective cleavages of MLL, MLL2, TFIIA, and ALF, the Hsieh laboratory generated and reported studies on Taspase1 knockout and non-cleavable MLL1, MLL2, and TFIIA knockin mice⁸⁻¹⁰. Dr. Hsieh was inducted into the American Society for Clinical Investigation in 2010.

As a physician scientist taking care of metastatic kidney cancer patients, Dr. Hsieh joined Memorial Sloan Kettering Cancer Center to fully integrate his research and clinical interests in 2010, and founded the Translational Kidney Cancer Research Program (TKCRP) in 2011 to enable seamless collaboration among basic, preclinical, and clinical cancer research. The MSK TKCRP serves as a platform to integrate necessary disciplines inside (Medicine, Surgery, Radiology, Epidemiology & Biostatistics, Computational Biology, Human Oncology & Pathogenesis Program, etc.) and collaborate with major kidney cancer research groups in the USA (TCGA, Harvard, MDACC, UPMC, Cleveland Clinic, UCLA, UNC, Mayo Clinic and NCI)¹¹. They primarily utilize patient materials to directly decode the molecular basis underlying tumorigenesis, treatment response, tumor heterogeneity, and cancer metastasis, and thereby offer personalized treatment regimens^{12,13}. TKCRP employs state-of-art research platforms to interrogate kidney cancer genomics, transcriptomics, proteomics, and metabolomics¹⁴⁻¹⁶. Through building the molecular blueprint of kidney cancer pathogenesis, Dr. Hsieh and his colleagues wish to develop novel mechanism-based therapeutics to better treat and eventually cure kidney cancer.

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Title: Molecular Pathology: Detection of Gene Fusions in Cancer



Speaker

Anthony J. Iafrate, MD

Director, Center for Integrated Diagnostics,
Massachusetts General Hospital



Chairman

Makoto Ogawa, MD

Emeritus President, Aichi Cancer Center, Japan

Anthony J. Iafrate, MD

Profile

Dr. Iafrate has focused on translational cancer research and molecular pathology and is the director of clinical molecular diagnostics and the translational research laboratory at the Massachusetts General Hospital. He has a strong interest in the clinical implementation of genetic screening technologies that can help direct targeted therapies. His recent contributions in the treatment of tumors with rearrangement of the ALK and ROS1 tyrosine kinases or with MET amplification with small molecule kinase inhibitors has underscored the promise of personalized cancer care. His lab is currently focused on the implementation of next generation sequencing technologies in genotyping primary and recurrent tumors.

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Session 2

IAAO

Towards a More Productive Relationship Between Academia and Industry

2-1. The European Cancer Patient Bill of Rights: A Catalyst for Change

Speaker: Patrick G. Johnston (The Queen's University Belfast, UK)

2-2. Academic-Industry Collaboration Drives Cancer Drug Development

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

2-3. Industry-Academia Relationship after Diovan Scandal in Japan

Speaker: Yasuhiro Fujiwara (National Cancer Center, Japan)

Title: The European Cancer Patient Bill of Rights: A Catalyst for Change



Speaker

Patrick G. Johnston, MD, PhD

President and Vice-Chancellor, The Queen's University Belfast



Chairman

Yasuhiro Fujiwara, MD, PhD

Director-General, Strategic Planning Bureau of the National Cancer Center

Patrick G. Johnston, MD, PhD

Profile

Prof. Johnston is President and Vice-Chancellor, Queen's University Belfast. Prof. Johnston has published over 250 research articles and 5 books, and holds over 25 patents. His research is focused on cellular signalling pathways in human colorectal cancer, primarily related to molecular targeted cancer, therapeutics, personalised cancer medicine and mechanisms of drug resistance.

He received his medical degree with distinction from University College Dublin in 1982, followed by his PhD in Medicine in 1988. He obtained a fellowship at the National Cancer Institute (NCI USA) in 1987 where he pursued further clinical training in medical oncology and doctoral studies in molecular pharmacology, drug resistance and drug development.

In 1997 he moved to Queen's University Belfast as Professor of Oncology and became Director of the Centre for Cancer Research and Cell Biology in 2004. He became Dean of the School of Medicine, Dentistry and Biomedical Sciences at Queen's University Belfast in 2007. In 2014 he has become vice-chancellor and President of Queen's University Belfast.

He has been awarded many national and international awards, is a Fellow of the Academy of Medical Sciences, and sits on a number of influential national and international scientific and government advisory boards. He is the Founder of the Society for Translational Oncology and the biotechnology company, Almac Diagnostics.

Title: Academic-Industry Collaboration Drives Cancer Drug Development



Speaker

Bruce A. Chabner, MD

Professor of Medicine, Harvard Medical School
Director of Clinical Research, Mass General Hospital
Cancer Center.



Chairman

Nagahiro Saijo, MD, PhD

Executive Officer of Japanese Society of Medical
Oncology, Japan

Bruce A. Chabner, MD

Profile

Dr. Bruce Chabner is a Professor of Medicine at Harvard Medical School and Director of Clinical Research at the Massachusetts General Hospital Cancer Center.

Dr. Chabner graduated *summa cum laude* from Yale College in 1961. He received his M.D. from Harvard University *cum laude* in 1965.

Dr. Chabner 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 Beeth Israel Deaconess Medical Center.

He has authored and edited the numerous textbooks of internal medicine, hematology, oncology and pharmacology.

Dr. Chabner 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.

Dr. Chabner 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, Dr. Chabner received a presidential appointment to the National Cancer Advisory Board at the National Cancer Institute.

Title: Industry-Academia Relationship after Diovon Scandal in Japan



Yasuhiro Fujiwara, MD, PhD

Director-General, Strategic Planning Bureau of the National Cancer Center

Speaker



Bruce A. Chabner, MD

Professor of Medicine, Harvard Medical School
Director of Clinical Research, Mass General Hospital
Cancer Center.

Chairman

Yasuhiro Fujiwara, MD, PhD

Profile

Yasuhiro Fujiwara, MD, PhD is Director-General, Strategic Planning Bureau of the National Cancer Center, Japan. Before joining NCCH, he was a deputy director of the Evaluation Division II of the Pharmaceuticals and Medical Devices Evaluation Center (so-called “Japanese FDA”) of the Ministry of Health Labour and Welfare. He was also a staff scientist at National Cancer Center Research Institute, and was an assistant professor of internal medicine at Hiroshima University School of Medicine. Between Jan 2011 to Feb 2013, he was a Deputy Secretary General of Office of Medical Innovation, Cabinet Secretariat of Japan.

Dr Fujiwara is a medical oncologist and has authored or co-authored about 180 original articles in peer-reviewed journals. He is an active member of American Society of Clinical Oncology (between 2003 and 2006, he was International Affairs Committee’s member), an active member of AACR, etc, and board member of Japanese Society of Medical Oncology; Society for Regulatory Science of Medical Products. He is on the Editorial Board of Cancer Chemotherapy

and Pharmacology; Investigational New Drugs,; Asian-Pacific Journal of Clinical Oncology;
Japanese Journal of Clinical Oncology.

Session 3

IAAO

Physiological Versatility of Cancer

3-1. Defining the Underlying Principles of Resistance to Targeted Cancer Therapeutics

Speaker: Levi A. Garraway (Harvard Medical School, USA)

3-2. Pharmacology, Feedback, and Novel Agents in the MAP Kinase Pathway

Speaker: Keith T. Flaherty (Harvard Medical School, USA)

3-3. Beyond Oncogenes: What Will Be the Next Generations of AntiCancer Targets?

Speaker: Tak W. Mak (Research at University Health Network, Canada)

Title: Defining the Underlying Principles of Resistance to Targeted Cancer Therapeutics



Speaker

Levi A. Garraway, MD, PhD

Associate Professor, Harvard Medical School
Director, Center for Cancer Precision Medicine,
Dana-Farber Cancer Institute Senior Associate
Member, Broad Institute



Chairman

Hiroyuki Mano, MD, PhD

Professor, Department of Cellular Signaling, Graduate
School of Medicine, The University of Tokyo

Levi A. Garraway, MD, PhD

Profile

Dr. Levi Garraway is an Associate Professor of Medicine at Harvard Medical School, Senior Associate Member of the Broad Institute, and the inaugural Director of the Joint Center for Cancer Precision Medicine (CCPM) at the Dana-Farber Cancer Institute, the Brigham and Women's Hospital, and the Broad Institute.

Dr. Garraway received his A.B. in biochemical sciences from Harvard College, and his M.D. and Ph.D. from Harvard Medical School. He completed his internship and residency in internal medicine at the Massachusetts General Hospital and his fellowship training in medical oncology at the Dana-Farber Cancer Institute.

Dr. Garraway has made seminal research contributions in cancer genomics, drug resistance, and genomics-driven (or "precision") cancer medicine. He was the first to describe "lineage dependence" as an oncogenic mechanism in melanoma. He has led major genomics initiatives in melanoma, including the discovery of TERT promoter mutations in over 70% of cases. TERT promoter mutations are prevalent in many cancers, thus highlighting the potential importance of regulatory mutations in tumorigenesis. He published the first genome sequencing studies of

aggressive primary prostate cancer, where he discovered an unusual rearrangement pattern (“chromoplexy”) that informs a “punctuated” model of cancer evolution.

Dr. Garraway was the first to describe a mechanism of clinical resistance to MEK and RAF inhibitors (MEK mutations). He pioneered the use of systematic gain-of-function screens to characterize cancer drug resistance, discovering several additional resistance pathways and themes that are guiding the design of new clinical trials and therapeutic combinations in melanoma.

Dr. Garraway is perhaps best known for his contributions to precision cancer medicine. He described the first high-throughput adaptation of a genomic technology to profile human tumors for hundreds of “actionable” cancer gene mutations. This established tumor mutation profiling as a means to stratify cancer patients for clinical trial enrollment and, in the future, optimal therapeutic choices. He also demonstrated the promise of massively parallel sequencing for clinical tumor genomic profiling. This research has inspired precision medicine initiatives at many cancer centers worldwide.

Garraway has been the recipient of several awards and honors, including the Paul Marks Prize for Cancer Research, the Jane Cooke Wright Award from the American Association for Cancer Research, the Block Award for outstanding cancer research from the Ohio State University, and the prestigious New Innovator Award from the National Institutes of Health. He is President-elect of the American Society for Clinical Investigation.

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Session 3-1

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Title: Pharmacology, Feedback, and Novel Agents in the MAP Kinase Pathway



Speaker

Keith T. Flaherty, MD

Director, Termeer Center for Targeted Therapy,
Massachusetts General Hospital



Chairman

Chikashi Ishioka, MD

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

Keith T. Flaherty, MD

Profile

The goal of Dr. Flaherty's group is to understand the molecular and clinical consequences of inhibiting oncogenes and oncogenic pathways in melanoma with the aim of establishing individual approaches as therapies and constructing rational combination therapies. BRAF mutant melanoma represents a large subpopulation for which single-agent oncogene targeting has been established and the focus is now to understand the consequences and limits of BRAF inhibition as a way of developing rational combination targeted therapy regimens. Given that 50% of advanced melanoma patients are BRAF wild-type establishing foundation of single-agent or combination targeted therapies in this large and heterogeneous subgroup is a current unmet need. For BRAF mutant patients, the goals are to circumvent mechanisms of de novo and acquired resistance.

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Title: Beyond Oncogenes: What Will Be the Next Generations of AntiCancer Targets?



Speaker

Tak W. Mak, OC, PhD, DSc, FRSC, FRS

Director of The Campbell Family Institute at Princess Margaret Cancer Centre, University Health Network.

Senior Staff Scientist at Ontario Cancer Institute

University Professor at the University of Toronto.



Chairman

Kohei Miyazono, MD, PhD

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

Tak W. Mak, OC, PhD, DSc, FRSC, FRS

Profile

Dr. Tak W. Mak is the Director of the Campbell Family Institute for Breast Cancer Research at the Princess Margaret Cancer Centre, and a University Professor in the Departments of Medical Biophysics and Immunology at the University of Toronto.

Dr. Mak received his B.Sc. and M.Sc. degrees from the University of Wisconsin (Madison) and his Ph.D. degree from the University of Alberta. His postdoctoral work was performed at the Ontario Cancer Institute under the supervision of Dr. Ernest McCulloch. Dr. Mak's research interests center on immune cell recognition/regulation, molecular mechanisms underlying the survival and death of normal or malignant cells, as well as the role of inflammation in the progression of autoimmune disease and cancer. He is best known as the lead scientist of the group that first cloned the genes of the human T cell antigen receptor, a discovery that provided essential insights into the molecular basis of cellular immunity. In addition, Dr. Mak has devoted a large portion of his research to investigating the pathogenesis of cancer. In particular, he is interested in mechanisms of metabolic transformation in order to identify potential targets for novel cancer therapeutics. Dr. Mak has published over 800 peer-reviewed research papers and holds many patents. His many accomplishments have been recognized by the scientific community through numerous prestigious awards and honours, such as the, Emil von Behring

Prize, Gairdner International Award, King Faisal International Prize for Medicine, Sloan Prize, and Novartis Immunology Prize. He is a Fellow of the Royal Society of London, a Foreign Associate of the National Academy of Sciences (USA), an Officer of the Order of Ontario, Canada and an Inductee, Fellow of American Association for Cancer Research Academy (USA)

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Session 4

IAAO

Immunology in Cancer Treatment

4-1. Translating Cancer Immunoediting Principles to Cancer Immunotherapy

Speaker: Robert D. Schreiber (Washington University, USA)

4-2. Control of Tumor Immunity by Regulatory T Cells

Speaker: Shimon Sakaguchi (Osaka University, Japan)

4-3. Tumor Site Immune Modulation Therapy

Speaker: Lieping Chen (Yale University, USA)

Title: Translating Cancer Immunoediting Principles to Cancer Immunotherapy



Speaker

Robert D. Schreiber, PhD

Alumni Endowed Professor of Pathology and Immunology; Director, Center for Human Immunology and Immunotherapy Programs; Co-Leader, Tumor Immunology, Siteman Cancer Center, Washington University School of Medicine



Chairman

Mitsuaki Yoshida, PhD

Director, The Cancer Chemotherapy Center of Japanese Foundation of Cancer Research (JFCR) Professor Emeritus, The University of Tokyo, Japan

Robert Schreiber, PhD

Profile

Dr. Schreiber is internationally recognized for his work on natural and therapeutically induced immune responses to cancer, interferon biology and IFN receptor signaling. His group developed the concept of cancer immunoediting wherein the immune system not only protects the host against cancer but also favors cancer outgrowth by shaping tumor cell immunogenicity. He developed the STAT1^{-/-} mouse model of human luminal breast cancer. In the course of his 40-year research career, Dr. Schreiber generated a number of key monoclonal antibody reagents that neutralize cytokines or block cytokine receptors and validated their *in vivo* use to assess the role of cytokines in preventing or inducing diseases. He also produced a number of gene targeted mice that display either systemic or tissue specific defects in cytokine signaling. Most recently, Dr. Schreiber and colleagues pioneered the use of genomics to identify key tumor specific antigens and employ them therapeutically.

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Title: Control of Tumor Immunity by Regulatory T Cells



Speaker

Shimon Sakaguchi, MD, PhD

Professor, Immunology Frontier Research Center,
Osaka University for “Control of Immune Responses
by Regulatory T Cells”



Chairman

Ryuzo Ueda, MD, PhD.

Professor Emeritus, Senior Adviser, Nagoya City
University

Professor, Dept. of Tumor Immunology,
Aichi Medical University, Japan

Shimon Sakaguchi, MD, PhD

Profile

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 fetomaternal tolerance.

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Title: Tumor Site Immune Modulation Therapy



Speaker

Lieping Chen, MD, PhD

United Technologies Corporation Professor in Cancer Research
Professor of Immunobiology, Dermatology and Medicine
Director, Cancer Immunology Program at Yale Cancer Center, Yale University School of Medicine



Chairman

Hirotoshi Akita, MD, PhD

Professor, Department of Medical Oncology, Hokkaido University, Graduate School of Medicine

Lieping Chen, MD, PhD

Profile

Dr. Lieping Chen is a Director of Cancer Immunology at the Yale Cancer Center, Yale University, New Haven, Connecticut. From 1997 to 2010, he served as a Professor of Dermatology and Oncology and Director of Dermatology Research at the Johns Hopkins University School of Medicine. Previously, Dr. Chen worked for Bristol-Myers Squibb Co. in Seattle as a research scientist, and as a Professor in the Department of Immunology, Mayo Clinic in Rochester, Minnesota. Dr. Chen's laboratory was the first to use costimulation to enhance tumor immunity in 1992 and has identified and characterized a series of molecules in the B7 and the TNF receptor/ligand superfamilies. Dr. Chen has published more than 200 scientific papers, review articles and book chapters, and edited two books. He has delivered more than 150 seminars, lecturer and speeches and served in many committees and advisory boards for US federal government and private organizations.

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