Final Program

International Academy for Advanced Oncology

IAAO 2021

Frontline in Cancer Genomics, Novel Treatments and Precision Oncology

June 19, 2021 13:00—16:45
June 20, 2021 9:00—12:10

Zoom Webinar

CHAAO
Comprehensive Academy for Advanced Oncology

Frontline in Cancer Genomics, Novel Treatments and Precision Oncology

Saturday, June 19, 2021 13:00 - 16:45 JST Zoom Webinar

Opening Remarks P.3

13:00 Osamu Nagayama, President (The Tokyo Biochemical Research Foundation)

1. Current Status of Cancer Drug R&D P.5

13:05 **Chemotherapy in the Age of Targeted and Immune Therapies: Learning New Tricks**
Speaker : Bruce A. Chabner (Harvard Medical School, USA)
Chair/Moderator : Hitoshi Nakagama (National Cancer Center, Japan)

2. Cancer Genomics P.8

13:35 **Serial Evolution of Mutant Cancer Genes: Implications for Biology and Therapy**
Speaker : Barry S. Taylor (Loxo Oncology Inc., USA)
Chair/Moderator : Hiroyuki Mano (National Cancer Center, Japan)

14:05 **Cancer Evolution, Immune Evasion and Metastasis**
Speaker : Charles Swanton (The Francis Crick Institute, UK)
Chair/Moderator : Tetsuo Noda (Japanese Foundation for Cancer Research, Japan)

14:45 **Break**

3. Precision Oncology as a Platform for Discovery & Development P.13

15:00 **Precision Oncology: Genomic Driven Medicine into Clinical Practice A Prime-Time Reality?**
Speaker : Josep Tabernero (Vall d'Hebron University Hospital, Spain)
Chair/Moderator : Tomomitsu Hotta (National Cancer Center, Japan)

15:40 **Activity on Nationwide Cancer Genome Screening Project for Advanced Solid Tumors; SCRUM-Japan MONSTAR-SCREEN**
Speaker : Takayuki Yoshino (National Cancer Center Hospital East, Japan)
Chair/Moderator : Tomomitsu Hotta (National Cancer Center, Japan)

4. New Molecular Targets P.18

16:10 **Targeting Androgen Receptor Splicing in Prostate Cancer**
Speaker : Johann S. de Bono (The Institute of Cancer Research, UK)
Chair/Moderator : Chikashi Ishioka (Tohoku University, Japan)

16:40 **Announcement (CHAAO)**

Sunday, June 20, 2021 9:00 - 12:10 JST Zoom Webinar

4. New Molecular Targets P.18

9:00 **TBD**
Speaker : Neal Rosen (Memorial Sloan Kettering Cancer Center, USA)
Chair/Moderator : Kiyohiko Hatake (International University of Health and Welfare, Japan)

9:30 **Overcoming the 7 Deadly Hallmarks of Pancreatic Cancer**
Speaker : David A. Tuveson (Cold Spring Harbor Laboratory Cancer Center, USA)
Chair/Moderator : Kohei Miyazono (The University of Tokyo, Japan)

10:10 **Treatment of Targeted Therapy Induced Drug Persistent Disease**
Speaker : Pasi A. Jänne (Dana-Farber Cancer Institute, USA)
Chair/Moderator : Masakazu Toi (Kyoto University, Japan)

10:45 **Break**

5. Cancer Immunotherapy P.27

10:55 **Precision Targeting of Melanoma with the Immune System**
Speaker : Antoni Ribas (University of California, Los Angeles, USA)
Chair/Moderator : Hiroyoshi Nishikawa (National Cancer Center, Japan)

11:35 **Immune Suppression by Regulatory T Cells in the Tumor Microenvironment**
Speaker : Hiroyoshi Nishikawa (National Cancer Center, Japan)
Chair/Moderator : Ryuzo Ueda (Aichi Medical University, Japan)

Closing Remarks P.32

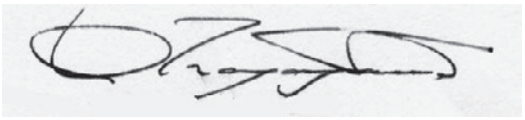
12:05 Kohei Miyazono (The University of Tokyo, Japan)

Official language » English

Opening Remarks

Osamu Nagayama

President, The Tokyo Biochemical Research Foundation



Last year, due to the worldwide spread of COVID-19 infection, we unfortunately could not hold the International Academy for Advanced Oncology (IAAO) 2020. In consideration of the ongoing pandemic situation, we first planned to hold this year's forum in a hybrid format that combines online and on-site. However, because the local incidence of the infection is still high and a State of Emergency is ongoing through June, we decided to change to a full-remote format for IAAO2021. We are truly sorry that we cannot hold the forum on-site, but we are relieved to be able to hold it at all.

As president of the Tokyo Biochemical Research Foundation (TBRF), I would like to express my sincere gratitude to all of the distinguished guests, experts and investigators attending this conference from overseas and Japan.

Each year at IAAO, I am delighted to see that the size of our gathering continues to grow every year. This year, our eleventh meeting, is no exception, and even though it is an online event, more than 250 people will be in attendance. We are always encouraged by the positive feedback that we receive from participants, and are extremely happy and honored to know that more and more experts are interested in and value this event.

We are very fortunate to have here so many world-class experts who share their experience, knowledge, and insights. I am confident this year's forum will spark extensive and wide-ranging discussions. I encourage everyone to seize the opportunity provided by each session to actively engage in the discussions. Your comments and insights will be found truly valuable to others attending this forum.

The theme of this year's meeting is "*Frontline Cancer Genomics, Novel Treatments and Precision Oncology*". The program focuses on cancer genomics and precision oncology, which have been rapidly progressing to the next stage of cancer biology and clinical

practices. In the new molecular target session, we will hear expert lectures on novel biomarker strategies, RAS & other signaling pathways, hallmarks of pancreatic cancer, and challenges in targeted therapy. In cancer immunotherapy, the speakers will address the latest breakthroughs in clinical applications and new molecular mechanism insights of immune suppression in the tumor microenvironment.

This exceptional program was organized through active discussions and the 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. TBRF's sincere wish is that this two-day event will be a highly 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, concurrently, empowers patients to deal with their treatment proactively and with hope.

Thank you very much for your attention.

Session 1

Current Status of Cancer Drug R&D

1-1. Chemotherapy in the Age of Targeted and Immune Therapies: Learning New Tricks

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

Title: Chemotherapy in the Age of Targeted and Immune Therapies: Learning New Tricks

Speaker

Bruce A. Chabner, MD

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

Chairman

Hitoshi Nakagama, MD, PhD

President, National Cancer Center, Japan

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.

Most Recent Publications

An Homage to Two Explorers of Uncharted Cancer Waters. **Chabner BA**, DeVita V, Murphy MJ. Oncologist. 2021 Apr;26(4):350-351.

A Medical Pearl Harbor: Pandemic Uncovers Societal Fissures and Leadership Breaches. **Chabner BA**, Bates SE, Fojo AT, Murphy A, Sartor AO, Murphy MJ. Oncologist. 2021 Feb;26(2):89.

The Corruption of Science. **Chabner BA**. Oncologist. 2020 Nov;25(11):907-908.

Racism and Cancer Care: A Call for Recognition and Reform. **Chabner BA**. Oncologist. 2020 Sep;25(9):729.

Pemetrexed in Recurrent or Progressive Central Nervous System Lymphoma: A Phase I Multicenter Clinical Trial. Dietrich J, Versmee L, Drappatz J, Eichler AF, Nayak L, Norden A, Wong E, Pisapia MR, Jones SS, Gordon AB, **Chabner BA**, Hochberg F, Batchelor TT. Oncologist. 2020 Sep;25(9):747-e1273.

Session 2

Cancer Genomics

2-1. Serial Evolution of Mutant Cancer Genes: Implications for Biology and Therapy

Speaker: Barry S. Taylor (Loxo Oncology Inc., USA)

2-2. Cancer Evolution, Immune Evasion and Metastasis

Speaker: Charles Swanton (The Francis Crick Institute, UK)

Title: Serial Evolution of Mutant Cancer Genes: Implications for Biology and Therapy

Barry S. Taylor, PhD

Vice President, Loxo Oncology at Lilly, Eli Lilly, USA.

Speaker

Hiroyuki Mano, MD, PhD

Director, National Cancer Center Research Institute, Japan

Chairman

Barry S, Taylor, PhD

Profile

Dr. Taylor is vice president of Loxo Oncology at Lilly since July 2020.
He received his Ph.D. from Weill Medical College of Cornell University in 2009. He had been an Associate Member in the Human Oncology and Pathogenesis Program, Associate Attending Computational Oncologist in the Department of Epidemiology and Biostatistics, and Associate Director of the Marie-Josée and Henry R. Kravis Center for Molecular Oncology in MSKCC until last year.

He has been enthusiastic about research to define the germline and somatic abnormalities that mediate the genesis, progression, and response to therapy of human cancers. His research program lies at the interface of computational and cancer biology, employing translational genomic and functional genetic approaches to identify tumor cell-specific vulnerabilities that can be therapeutically exploited in diverse malignancies.

Dr. Taylor has been involved in many collaborative studies exploring the genomic basic of diverse human cancer types and the development of computational methodologies for cancer genome discovery. His current research centers on exploring the molecular and evolutionary origins of response and resistance to cancer therapy, and defining the mechanisms, serial genetic evolution, and both biological and therapeutic significance of common and rare driver mutations in tumorigenesis.

He has received numerous awards, including such as Research Scholar Award of American Cancer Society in 2015.

Most Recent Publications

Homing in on genomic instability as a therapeutic target in cancer. Bielski CM, **Taylor BS**. Nat Commun. 2021 Jun 16;12(1):3663.

Recurrent Mutations in Cyclin D3 Confer Clinical Resistance to FLT3 Inhibitors in Acute Myeloid Leukemia. Smith CC, Viny AD, Massi E, Kandoth C, Socci ND, Rapaport F, Najm M, Medina-Martinez JS, Papaemmanuil E, Tarver TC, Hsu HH, Le MH, West B, Bollag G, **Taylor BS**, Levine RL, Shah NP. Clin Cancer Res. 2021 Jun 8.

Respiratory complex and tissue lineage drive recurrent mutations in tumour mtDNA. Gorelick AN, Kim M, Chatila WK, La K, Hakimi AA, Berger MF, **Taylor BS**, Gammage PA, Reznik E. Nat Metab. 2021 Apr;3(4):558-570

The Genetic Evolution of Treatment-Resistant Cutaneous, Acral, and Uveal Melanomas. Makohon-Moore AP, Lipson EJ, Hooper JE, Zucker A, Hong J, Bielski CM, Hayashi A, Tokheim C, Baez P, Kappagantula R, Kohutek Z, Makarov V, Riaz N, Postow MA, Chapman PB, Karchin R, Socci ND, Solit DB, Chan TA, **Taylor BS**, Topalian SL, Iacobuzio-Donahue CA. Clin Cancer Res. 2021 Mar 1;27(5):1516-1525.

AKT1 E17K Inhibits Cancer Cell Migration by Abrogating β-Catenin Signaling. Gao SP, Kiliti AJ, Zhang K, Vasani N, Mao N, Jordan E, Wise HC, Shrestha Bhattarai T, Hu W, Dorso M, Rodrigues JA, Kim K, Hanrahan AJ, Razavi P, Carver B, Chandarlapaty S, Reis-Filho JS, **Taylor BS**, Solit DB. Mol Cancer Res. 2021 Apr;19(4):573-584.

Title: Cancer Evolution, Immune Evasion and Metastasis

Speaker

Charles Swanton, FRCP, PhD

Chair, Personalized Cancer Medicine, Cancer Research-UK
Group Leader, Translational Cancer Therapeutics Laboratory
Professor, Francis Crick Institute and University College London Hospital, UK

Chairman

Tetsuo Noda, MD, PhD

Director, Cancer Institute, Japanese Foundation for Cancer Research, Japan

Charles Swanton, FRCP, PhD

Profile

Dr. Swanton completed his MD, PhD in 1999 at the Imperial Cancer Research Fund Laboratories and Cancer Research UK clinician/scientist medical oncology training in 2008. He combines his laboratory research at the Francis Crick Institute with clinical duties focused on biological mechanisms of cancer drug resistance. He was made Fellow of the Royal College of Physicians in April 2011 and Chair in Personalized Cancer Medicine and Consultant Thoracic Medical Oncologist at UCL Hospitals in November 2011.

He is the Chief Investigator of the CRUK TRACERx lung cancer evolution study and was awarded the Royal College of Physicians Goulstonian lecture and Graham Bull Prize for Clinical Sciences in 2013, Fellow of the European Academy of Cancer Sciences in 2013, and Fellow of the Academy of Medical Sciences in 2015. He was awarded the Jeremy Jass Prize (2014), Stand up to Cancer Translational Cancer Research Prize (2015), GlaxoSmithKline Biochemical Society Prize in recognition of distinguished research leading to new advances in medical science and the Ellison-

Cliffe Medal and Lecture, Royal Society of Medicine (2016). He was appointed Napier Professor in Cancer by the Royal Society in 2016.

Most Recent Publications

AMBRA1 regulates cyclin D to guard S-phase entry and genomic integrity. Maiani E, Milletti G, Nazio F, Holdgaard SG, Bartkova J, Rizza S, Cianfanelli V, Lorente M, Simoneschi D, Di Marco M, D'Acunzo P, Di Leo L, Rasmussen R, Montagna C, Raciti M, De Stefanis C, Gabicagogeascoa E, Rona G, Salvador N, Pupo E, Merchut-Maya JM, Daniel CJ, Carinci M, Cesarini V, O'sullivan A, Jeong YT, Bordi M, Russo F, Campello S, Gallo A, Filomeni G, Lanzetti L, Sears RC, Hamerlik P, Bartolazzi A, Hynds RE, Pearce DR, **Swanton C**, Pagano M, Velasco G, Papaleo E, De Zio D, Maya-Mendoza A, Locatelli F, Bartek J, Cecconi F. Nature. 2021 Apr 14.

Characterizing genetic intra-tumor heterogeneity across 2,658 human cancer genomes. Dentro SC, Leshchiner I, Haase K, Tarabichi M, Wintersinger J, Deshwar AG, Yu K, Rubanova Y, Macintyre G, Demeulemeester J, Vázquez-García I, Kleinheinz K, Livitz DG, Malikic S, Donmez N, Sengupta S, Anur P, Jolly C, Cmero M, Rosebrock D, Schumacher SE, Fan Y, Fittall M, Drews RM, Yao X, Watkins TBK, Lee J, Schlesner M, Zhu H, Adams DJ, McGranahan N, **Swanton C**, Getz G, Boutros PC, Imielinski M, Beroukhim R, Sahinalp SC, Ji Y, Peifer M, Martincorena I, Markowetz F, Mustonen V, Yuan K, Gerstung M, Spellman PT, Wang W, Morris QD, Wedge DC, Van Loo P; PCAWG Evolution and Heterogeneity Working Group and the PCAWG Consortium. Cell. 2021 Apr 15;184(8):2239-2254

Tracking Cancer Evolution through the Disease Course. Bailey C, Black JRM, Reading JL, Litchfield K, Turajlic S, McGranahan N, Jamal-Hanjani M, **Swanton C**. Cancer Discov. 2021 Apr;11(4):916-932.

Clonal architecture in mesothelioma is prognostic and shapes the tumour microenvironment. Zhang M, Luo JL, Sun Q, Harber J, Dawson AG, Nakas A, Busacca S, Sharkey AJ, Waller D, Sheaff MT, Richards C, Wells-Jordan P, Gaba A, Poile C, Baitei EY, Bzura A, Dzialo J, Jama M, Le Quesne J, Bajaj A, Martison L, Shaw JA, Pritchard C, Kamata T, Kuse N, Brannan L, De Philip Zhang P, Yang H, Griffiths G, Wilson G, **Swanton C**, Dudbridge F, Hollox EJ, Fennell DA. Nat Commun. 2021 Mar 19;12(1):1751.

Understanding the impact of immune-mediated selection on lung cancer evolution. Rosenthal R, **Swanton C**, McGranahan N. Br J Cancer. 2021 Feb 24.

Session 3

Precision Oncology as a Platform for Discovery & Development

3-1. Precision Oncology: Genomic Driven Medicine into Clinical Practice A Prime-Time Reality?

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

3-2. Activity on Nationwide Cancer Genome Screening Project for Advanced Solid Tumors; SCRUM-Japan MONSTAR-SCREEN

Speaker: Takayuki Yoshino (National Cancer Center Hospital East, Japan)

Title: Precision Oncology: Genomic Driven Medicine into Clinical Practice A Prime-Time Reality?

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 dysregulation. 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.

Most Recent Publications

Precision oncology in metastatic colorectal cancer - from biology to medicine. Di Nicolantonio F, Vitiello PP, Marsoni S, Siena S, **Tabernero J**, Trusolino L, Bernards R, Bardelli A. Nat Rev Clin Oncol. 2021 Apr 16.

Building Bridges Between Drug Development and Cancer Science: A Tribute to José Baselga's Legacy. Hyman DM, Soria JC, **Tabernero J**. Ann Oncol. 2021 Apr 7:S0923-7534(21)01119-4.

Management of BRAF-mutant metastatic colorectal cancer: a review of treatment options and evidence-based guidelines. Grothey A, Fakih M, **Tabernero J**. Ann Oncol. 2021 Apr 6:S0923-7534(21)01112-1.

Assessment of Pembrolizumab Therapy for the Treatment of Microsatellite Instability-High Gastric or Gastroesophageal Junction Cancer Among Patients in the KEYNOTE-059, KEYNOTE-061, and KEYNOTE-062 Clinical Trials. Chao J, Fuchs CS, Shitara K, **Tabernero J**, Muro K, Van Cutsem E, Bang YJ, De Vita F, Landers G, Yen CJ, Chau I, Elme A, Lee J, Özgüroglu M, Catenacci D, Yoon HH, Chen E, Adelberg D, Shih CS, Shah S, Bhagia P, Wainberg ZA. JAMA Oncol. 2021 Apr 1.

Quantifying the Long-term Survival Benefit of Pembrolizumab for Patients With Advanced Gastric Cancer-Reply. Shitara K, **Tabernero J**. JAMA Oncol. 2021 Apr 1;7(4):633.

Title: Activity on Nationwide Cancer Genome Screening Project for Advanced Solid Tumors: SCRUM-Japan MONSTAR-SCREEN

Takayuki Yoshino, MD, PhD

Director, Gastroenterology and Gastrointestinal Oncology,
National Cancer Center Hospital East, Japan

Speaker

Tomomitsu Hotta, MD, PhD

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

Chairman

Takayuki Yoshino, MD, PhD

Profile

Dr. Takayuki Yoshino, MD, PhD currently works at the National Cancer Center Hospital East (NCCE) in Chiba, Japan, where he is the Director for the Department of Gastroenterology and Gastrointestinal Oncology and the Head of the Clinical Research Coordinating Division. He has a particular interest in chemotherapy for gastrointestinal cancers, especially for colorectal cancer (CRC), where he focuses on various investigational new agent and translational research.
Dr. Yoshino received his medical degree from the National Defense Medical College in 1995 and after completing his first residency there, he moved to the NCCE where he specialized in gastrointestinal oncology. He later spent five years at the Shizuoka Cancer Center and during this time, he studied in the USA at several world-renowned institutions, including the Mayo Clinic, Dana-Farber Cancer Institute and the Vanderbilt-Ingram Cancer Center.

In 2007 Dr. Yoshino returned to the NCCE and has had over 150 peer-review scholar journal publications on metastatic CRC (mCRC), with several articles published in the Lancet Journal, Journal of Clinical Oncology, and the New England Journal of Medicine. In addition, he holds several professional appointments, serving on an international guideline member of the European Society for Medical Oncology (ESMO), a chair of Pan-Asian adapted ESMO Guideline for mCRC, a guideline member of the Japanese Society for Cancer of the Colon and Rectum and an international affairs committee member of the Japanese Society of Medical Oncology as well the administrative board for The Japanese Association for Molecular Target Therapy of Cancer.

Most Recent Publications

Health-related quality of life in patients with microsatellite instability-high or mismatch repair deficient metastatic colorectal cancer treated with first-line pembrolizumab versus chemotherapy (KEYNOTE-177): an open-label, randomised, phase 3 trial. Andre T, Amonkar M, Norquist JM, Shiu KK, Kim TW, Jensen BV, Jensen LH, Punt CJA, Smith D, Garcia-Carbonero R, Sevilla I, De La Fouchardiere C, Rivera F, Elez E, Diaz LA Jr, **Yoshino T**, Van Cutsem E, Yang P, Farooqui M, Le DT. Lancet Oncol. 2021 Apr 1:S1470-2045(21)00064-4.

Combined Analysis of Concordance between Liquid and Tumor Tissue Biopsies for RAS Mutations in Colorectal Cancer with a Single Metastasis Site: The METABEAM Study. Kagawa Y, Elez E, García-Foncillas J, Bando H, Taniguchi H, Vivancos A, Akagi K, García A, Denda T, Ros J, Nishina T, Baraibar I, Komatsu Y, Ciardiello D, Oki E, Kudo T, Kato T, Yamanaka T, Tabernero J, **Yoshino T**. Clin Cancer Res. 2021 Feb 18.

Real-world data on microsatellite instability status in various unresectable or metastatic solid tumors. Akagi K, Oki E, Taniguchi H, Nakatani K, Aoki D, Kuwata T, **Yoshino T**. Cancer Sci. 2021 Mar;112(3):1105-1113.

Post-marketing surveillance study of trifluridine/tipiracil in patients with metastatic colorectal cancer. **Yoshino T**, Uetake H, Funato Y, Yamaguchi Y, Koyama T, Ozawa D, Tajiri M, Muro K. Jpn J Clin Oncol. 2021 Jan 13:hyaa243.

ASO Author Reflections: Circulating Tumor DNA (ctDNA) as a Potentially Practice-Changing Innovation to Evolve "Precision Onco-Surgery" in Resectable Colorectal Liver Metastases. Kobayashi S, Nakamura Y, Takahashi S, Taniguchi H, **Yoshino T**. Ann Surg Oncol. 2021 Jan 4.

Session 4

New Molecular Targets

4-1. Targeting Androgen Receptor Splicing in Prostate Cancer

Speaker: Johann S. de Bono (The Institute of Cancer Research, UK)

4-2. TBD

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

4-3. Overcoming the 7 Deadly Hallmarks of Pancreatic Cancer

Speaker: David A. Tuveson (Cold Spring Harbor Laboratory Cancer Center, USA)

4-4. Treatment of Targeted Therapy Induced Drug Persistent Disease

Speaker: Pasi A. Jänne (Dana-Farber Cancer Institute, USA)

Title: Targeting Androgen Receptor Splicing in Prostate Cancer

Speaker

Johann S. de Bono, MRCP, PhD

Professor, Head of division and Team Leader
The Institute of Cancer Research, UK

Chairman

Chikashi Ishioka, MD, PhD

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

Johann S. de Bono, MRCP, PhD

Profile

Professor Johann de Bono is Regius Professor of Cancer Research and a Professor in Experimental Cancer Medicine at The Institute of Cancer Research and The Royal Marsden NHS Foundation Trust. He is also the Director of the Drug Development Unit, overseeing the conduct of phase I trials, with a particular interest in innovative trial designs, circulating biomarkers and prostate cancer. Additionally, he leads the Prostate Cancer Targeted Therapy Group and the Cancer Biomarkers laboratory team. He graduated from the University of Glasgow medical school in 1989 and became a Member of the Royal College of Physicians (MRCP) in 1992.

Professor de Bono is also a key opinion leader in the development of novel cancer therapies, and co-founded and now runs The Royal Marsden Drug Development Unit, one of the world's largest such trials units for cancer patients. He has been involved in the development of many novel agents, many of which are now approved drugs.

He is a world leader in prostate cancer research, having changed the treatment of prostate cancer multiple times through trials of the ICR-discovered drug abiraterone, cabazitaxel, enzalutamide and olaparib. He also led on the identification of germline and somatic DNA repair defects in lethal prostate cancer, and co-led studies mapping the genomics of these diseases. His work has changed international guidelines on germline testing in men with advanced prostate cancer and the first molecular stratification for this commonest of male cancers. He has also recently led studies of pembrolizumab, talazoparib, ipatasertib and lutetium-PSMA for men suffering from advanced prostate cancer.

His laboratory has led on the study of liquid biopsies in advanced prostate cancer including circulating tumour cells, whole blood expression profiling, and plasma circulating tumour DNA in metastatic prostate cancer patients. He helped to pioneer the concept of patient molecular stratification in early clinical trials through the Pharmacological Audit Trial.

Dr de Bono has received numerous awards, including the 2018 AACR–Joseph H. Burchenal Memorial Award for Outstanding Achievement in Clinical Cancer Research.

Most Recent Publications

Phase I trial of MEDI3726, a prostate-specific membrane antigen-targeted antibody-drug conjugate, in patients with mCRPC after failure of abiraterone or enzalutamide. **de Bono JS**, Fleming MT, Wang JS, Cathomas R, Selvi Miralles M, Bothos J, Hinrichs MJ, Zhang Q, He P, Williams M, Rosenbaum AI, Liang M, Vashisht K, Cho S, Martinez P, Petrylak DP. Clin Cancer Res. 2021 Apr 1.

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JMJD6 Is a Druggable Oxygenase That Regulates AR-V7 Expression in Prostate Cancer. Paschalis A, Welti J, Neeb AJ, Yuan W, Figueiredo I, Pereira R, Ferreira A, Riisnaes R, Rodrigues DN, Jiménez-Vacas JM, Kim S, Uo T, Micco PD, Tumber A, Islam MS, Moesser MA, Abboud M, Kawamura A, Gurel B, Christova R, Gil VS, Buroni L, Crespo M, Miranda S, Lambros MB, Carreira S, Tunariu N, Alimonti A, Al-Lazikani B, Schofield CJ, Plymate SR, Sharp A, **de Bono JS**; SU2C/PCF International Prostate Cancer Dream Team. Cancer Res. 2021 Feb 15;81(4):1087-1100.

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Title: TBD

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

Kiyohiko Hatake, MD, PhD

Professor, Department of Hematology,
International University of Health and Welfare, School of Medicine, 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 and a Member in the Program in Molecular Pharmacology and Chemistry. 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.

His major interests include the study of the key molecular events and growth signaling pathways responsible for human cancers, and the use of this information for developing effective therapies. Dr. Rosen has played a leading role in the development of inhibitors of tyrosine kinase and RAS-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 includes the elucidation of the biochemical and biologic mechanisms of action of RAF inhibitors, the mechanisms underlying resistance to these compounds, and studies on the role of

ERK-dependent feedback in tumors with RAF or RAS mutation. This research has led to many international clinical trials with promising early results.

Dr. Rosen will continue to improve combination therapies and target other pathways to treat breast and uterine cancers. While there are therapies available to treat endometrial and metastatic breast cancer (MBC)—breast cancer that has spread to other tissues—these cancers will progress, even if they initially respond to treatment. Dr. Rosen is focused on the protein PI3K, which activates a pathway that drives the growth of many MBC and endometrial cancers. He and his team have recently developed two new drugs that, when combined in laboratory studies, target these pathways and kill tumor cells.

Most Recent Publications

Regulation of PTEN translation by PI3K signaling maintains pathway homeostasis. Mukherjee R, Vanaja KG, Boyer JA, Gadal S, Solomon H, Chandarlapaty S, Levchenko A, **Rosen N**. Mol Cell. 2021 Feb 18;81(4):708-723.

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Therapeutic Implications of Detecting MAPK-Activating Alterations in Cutaneous and Unknown Primary Melanomas. Shoushtari AN, Chatila WK, Arora A, Sanchez-Vega F, Kantheti HS, Rojas Zamalloa JA, Krieger P, Callahan MK, Betof Warner A, Postow MA, Momtaz P, Nair S, Ariyan CE, Barker CA, Brady MS, Coit DG, **Rosen N**, Chapman PB, Busam KJ, Solit DB, Panageas KS, Wolchok JD, Schultz N. Clin Cancer Res. 2021 Apr 15;27(8):2226-2235.

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Title: Overcoming the 7 Deadly Hallmarks of Pancreatic Cancer

Speaker

David A. Tuveson, MD, PhD

Director and Professor, Cold Spring Harbor Laboratory Cancer Center, USA

Chairman

Kohei Miyazono, MD, PhD

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

David A. Tuveson, MD, PhD

Profile

Dr. David Tuveson received an M.D.-Ph.D. from the Johns Hopkins School of Medicine in 1994. His laboratory uses murine and human models of pancreatic cancer to explore the fundamental biology of malignancy and thereby identify new diagnostic and treatment strategies. The lab's approaches run the gamut from designing new model systems of disease to developing new therapeutic and diagnostic approaches for rapid evaluation in preclinical and clinical settings. The lab's studies make use of organoid cultures—three-dimensional cultures of normal or cancerous epithelia—as ex vivo models to probe cancer biology. Current projects in the lab explore changes in redox metabolism associated with pancreatic cancer tumorigenesis, dissect signaling by the Ras oncogene, discover new biomarkers of early pancreas cancer, and identify mechanisms of cross-talk between pancreatic cancer cells and the tumor stroma. Novel treatment approaches suggested by these studies are then tested by performing therapeutic experiments in mouse models. To dissect molecular changes associated with pancreatic tumorigenesis, the Tuveson lab has generated a large collection of

human patient-derived organoid models. By measuring the therapeutic sensitivities of patient-derived organoids, the lab is working to identify novel strategies to treat patients as well as markers of therapeutic response. The Tuveson Laboratory maintains strong links to clinical research, and the ultimate goal is confirmation of preclinical findings in early-phase trials. Collectively, the lab's bench-to-bedside approach is codified as the "Cancer Therapeutics Initiative," and this initiative will provide these same approaches to the entire CSHL cancer community.

Dr. Tuveson serves as Director of the Cold Spring Harbor Laboratory Cancer Center and the Chief Scientist for the Lustgarten Foundation. He has received the Rita Allen Foundation Scholar award. the Waldenström Award for outstanding researchers, and Hamdan Award for Medical Research Excellence, Pancreatic Diseases.

Most Recent Publications

Fighting the Sixth Decade of the Cancer War with Better Cancer Models. **Tuveson DA**. Cancer Discov. 2021 Apr;11(4):801-804.

Inhibition of Hedgehog Signaling Alters Fibroblast Composition in Pancreatic Cancer. Steele NG, Biffi G, Kemp SB, Zhang Y, Drouillard D, Syu L, Hao Y, Oni TE, Brosnan E, Elyada E, Doshi A, Hansma C, Espinoza C, Abbas A, The S, Irizarry-Negron V, Halbrook CJ, Franks NE, Hoffman MT, Brown K, Carpenter ES, Nwosu ZC, Johnson C, Lima F, Anderson MA, Park Y, Crawford HC, Lyssiotis CA, Frankel TL, Rao A, Bednar F, Dlugosz AA, Preall JB, **Tuveson DA**, Allen BL, Pasca di Magliano M. Clin Cancer Res. 2021 Apr 1;27(7):2023-2037.

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Title: Treatment of Targeted Therapy Induced Drug Persistent Disease

Pasi A. Jänne, MD, PhD

Director and Professor, Lowe Center for Thoracic Oncology, Dana-Farber Cancer Institute and Harvard Medical School, USA

Speaker

Masakazu Toi, MD, PhD

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

Chairman

Pasi A. Jänne, MD, PhD

Profile

Dr. Jänne received his MD and PhD from the University of Pennsylvania in 1996. He completed postgraduate training in internal medicine at Brigham and Women's Hospital and in medical oncology at DFCI in 2001. He is the director of the Lowe Center for Thoracic Oncology and the Scientific Director of the Belfer Center for Applied Cancer Science. His main research interests include studying the therapeutic relevance of oncogenic alterations in lung cancer. He was one of the co-discoverers of epidermal growth factor receptor (EGFR) mutations and has led the development of therapeutic strategies for patients with EGFR mutant lung cancer.

Dr. Jänne's laboratory work focuses on studying preclinical models of lung cancers that harbor oncogenic alterations. The main focus of his work is to understand how oncogenic alterations found in lung cancer lead to sensitivity of targeted therapies. Furthermore, his laboratory members extensively study both model systems and

patient derived tumors to uncover mechanisms of drug resistance. Through these studies his laboratory members have been able to identify novel therapeutic strategies for patients with different genomic subtypes of lung cancer.

Most Recent Publications

The Promising Evolution of Targeted Therapeutic Strategies in Cancer. Peters S, Mok T, Passaro A, **Jänne PA**. Cancer Discov. 2021 Apr;11(4):810-814.

Targeting MET Dysregulation in Cancer. Recondo G, Che J, **Jänne PA**, Awad MM. Cancer Discov. 2020 Jul;10(7):922-934.

Plasma IL-6 changes correlate to PD-1 inhibitor responses in NSCLC. Keegan A, Ricciuti B, Garden P, Cohen L, Nishihara R, Adeni A, Paweletz C, Supplee J, **Jänne PA**, Severgnini M, Awad MM, Walt DR. J Immunother Cancer. 2020 Oct;8(2):e000678.

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Devil in the detail: MET overexpression fails as surrogate marker for MET exon 14 splice site mutations in NSCLC. Strickland MR, **Jänne PA**. Ann Transl Med. 2020 Dec;8(23):1612.

Session 5

Cancer Immunotherapy

5-1. **Precision Targeting of Melanoma with the Immune System**

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

5-2. Immune Suppression by Regulatory T Cells in the Tumor Microenvironment

Speaker: Hiroyoshi Nishikawa (National Cancer Center, Japan)

Title: Precision Targeting of Melanoma with the Immune System

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

Hiroyoshi Nishikawa, MD, PhD

Professor, Department of Immunology, Nagoya University Graduate School of Medicine, Japan
Chief, Division of Cancer Immunology, Research Institute/Exploratory Oncology Research & Clinical Trial Center (EPOC), National Cancer Center 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) and the Chair of the Melanoma Committee at SWOG. Dr. Ribas received his M.D. from University of Barcelona, Spain in 1990, and his Ph.D. from Autonomous University of Barcelona in 1997. Trained at the University of Barcelona, with postdoctoral research and clinical fellowships at UCLA. Dr Ribas is a physician-scientist who conducts laboratory and clinical research in malignant melanoma, focusing on gene engineered adoptive cell transfer (ACT) therapies, anti-CTLA4 antibodies, anti-PD-1 antibodies, BRAF and MEK inhibitors and nanoparticle-siRNA.

His NCI, State of California and private foundation-supported research laboratory develops models of disease to test new therapeutic options and studies mechanism of action of treatments in patients. He has been instrumental in the clinical development of several agents approved by the FDA, including pembrolizumab (Keytruda),

vemurafenib (Zelboraf), cobimetinib (Cotellic), dabrafenib (Tafinlar) and trametinib (Mekinist). He is an elected member of the American Society of Clinical Investigation (ASCI), the recipient of the AACR Richard and Hinda Rosenthal Award and a National Cancer Institute (NCI) Outstanding Investigator Award.

Dr. Ribas has been a member of the AACR Board of Directors since 2016. In addition to his role as president, Ribas served as Program Chair for the AACR Annual Meeting 2020.

Most Recent Publications

Repurposing of anticancer drugs expands possibilities for antiviral and anti-inflammatory discovery in COVID-19. Aldea M, Michot JM, Danlos FX, **Ribas A**, Soria JC. Cancer Discov. 2021 Apr 12, PMID: 33846172

IFNg is Critical for CAR T Cell Mediated Myeloid Activation and Induction of Endogenous Immunity. Alizadeh D, Wong RA, Gholamin S, Maker M, Aftabizadeh M, Yang X, Pecoraro JR, Jeppson JD, Wang D, Aguilar B, Starr R, Larmonier CB, Larmonier N, Chen MH, Wu X, **Ribas A**, Badie B, Forman SJ, Brown CE. Cancer Discov. 2021 Apr 9, PMID: 33837065

T Cells as the Future of Cancer Therapy. **Ribas A**. Cancer Discov. 2021 Apr;11(4):798-800.

RNA Dysregulation: An Expanding Source of Cancer Immunotherapy Targets. Pan Y, Kadash-Edmondson KE, Wang R, Phillips J, Liu S, **Ribas A**, Aplenc R, Witte ON, Xing Y. Trends Pharmacol Sci. 2021 Apr;42(4):268-282.

Cardiotoxicities of novel cancer immunotherapies. Stein-Merlob AF, Rothberg MV, **Ribas A**, Yang EH. Heart. 2021 Mar 15, PMID: 33722826

Title: Immune Suppression by Regulatory T Cells in the Tumor Microenvironment

Hiroyoshi Nishikawa, MD, PhD

Professor, Department of Immunology, Nagoya University Graduate School of Medicine, Japan
Chief, Division of Cancer Immunology, Research Institute/Exploratory Oncology Research & Clinical Trial Center (EPOC), National Cancer Center Research, Japan

Speaker

Ryuzo Ueda, MD, PhD

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

Chairman

Hiroyoshi Nishikawa, MD, PhD

Profile

Dr Hiroyoshi Nishikawa is Professor - Department of Immunology, Nagoya University Graduate School of Medicine, and Chief - Division of Cancer Immunology, Research Institute/Exploratory Oncology Research & Clinical Trial Center (EPOC), National Cancer Center. Dr. Nishikawa received his M.D. from Mie University School of Medicine, Japan in 1995, and his Ph.D. from Mie University Graduate School of Medicine in 2002.

Dr. Nishikawa has studied the mechanisms by which the immunosuppressive network, including CD4+ regulatory T (Treg) cells, suppresses anti-tumor immune responses, and has also been developing therapeutic strategies to overcome these mechanisms. In particular, he found the typical phenotypes of effector T cells, which are important for anti-tumor immune responses, that are suppressed by Treg cells depending on the nature of the antigen (exhaust for non-self and anergy for self-antigens). These findings are extremely important for understanding not only tumor immunity, but also various

immune responses such as autoimmunity, allergy, infection and transplantation. In addition, he has recently proposed a novel concept in the carcinogenic process in which genomic aberrations of cancer cells affect the immune response and establish an immunosuppressive network in the tumor microenvironment, and commits to develop immunogenomic precision medicine.

Dr. Nishikawa was conferred the 2020 SITC Team Science Award. The honour was in recognition to his work as a member of the team lead by the late Lloyd J. Old, MD, who established the research field of cancer immunology.

Most Recent Publications

Importance of lymph node immune responses in MSI-H/dMMR colorectal cancer. Inamori K, Togashi Y, Fukuoka S, Akagi K, Ogasawara K, Irie T, Motooka D, Kobayashi Y, Sugiyama D, Kojima M, Shiiya N, Nakamura S, Maruyama S, Suzuki Y, Ito M, **Nishikawa H**. JCI Insight. 2021 Mar 23:137365.

Flow cytometry analysis of peripheral Tregs in patients with multiple myeloma under lenalidomide maintenance. Nozaki K, Fujioka Y, Sugiyama D, Ishikawa J, Iida M, Shibata M, Kosugi S, **Nishikawa H**, Shibayama H. Int J Hematol. 2021 May;113(5):772-774.

Transcriptional regulatory network for the establishment of CD8+ T cell exhaustion. Seo W, Jerin C, **Nishikawa H**. Exp Mol Med. 2021 Feb;53(2):202-209.

A simple method to distinguish residual elotuzumab from monoclonal paraprotein in immunofixation assays for multiple myeloma patients. Chen S, Kiguchi T, Nagata Y, Tamai Y, Ikeda T, Kajiya R, Ono T, Sugiyama D, **Nishikawa H**, Akatsuka Y. Int J Hematol. 2021 Apr;113(4):473-479.

HSP90 inhibition overcomes EGFR amplification-induced resistance to third-generation EGFR-TKIs. Watanabe S, Goto Y, Yasuda H, Kohno T, Motoi N, Ohe Y, **Nishikawa H**, Kobayashi SS, Kuwano K, Togashi Y. Thorac Cancer. 2021 Mar;12(5):631-642.

Closing Remarks

Kohei Miyazono, MD, PhD

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

Kohei Miyazono, MD, PhD

Profile

Dr. Miyazono graduated from the Faculty of Medicine of the University of Tokyo in 1981, working as a researcher at the Ludwig Institute for Cancer Research in Sweden and the Director of Department of Biochemistry at Japanese Foundation for Cancer Research. He has been a Professor at the Graduate School of Medicine at the University of Tokyo since 2000. He has been studying TGF-β and cancer for many years.

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The Tokyo Biochemical Research Foundation
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