アクセスマップ

会　場：六本木アカデミーヒルズ49

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

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CHAAO Chugai Academy for Advanced Oncology

一般社団法人　中外Oncology学術振興会議
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TEL：03-5825-2012　FAX：03-5821-2886
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Program

INTERNATIONAL ACADEMY FOR ADVANCED ONCOLOGY

IAAO

国際フォーラム2018

Quantum Leap to Next Horizon in Cancer Research and Therapy

2018年7月27日（金）12:55–17:55
28日（土）　9:00–14:50
六本木アカデミーヒルズ49

CHAAO Chugai Academy for Advanced Oncology

Quantum Leap to Next Horizon in Cancer Research and Therapy

Friday, July 27, 2018 12:55—17:55

Opening Remarks P.3

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

1. Next Horizon in Cancer Research and Therapy P.6

13:00 **Expanding Horizons for Cancer Genomics**
Speaker: Bruce A. Chabner (Harvard Medical School, USA)
Chair/Moderator: Makoto Ogawa (Aichi Cancer Center, Japan)

2. Breakthroughs in Cancer Immunotherapy P.12

13:15 **Neoantigens and the Molecular Basis of Personalized Cancer Immunotherapy**
Speaker: Robert D. Schreiber (Washington University School of Medicine, USA)
Chair/Moderator: Ryuzo Ueda (Aichi Medical University, Japan)

13:55 **Mechanistic Basis of Cancer Immunotherapy**
Speaker: Ira Mellman (Genentech Inc., USA)
Chair/Moderator: Yuko Kitagawa (Keio University, Japan)

14:35 Coffee Break

14:55 **Deconvolution of Cellular Determinants of Anti-Tumor Immune Responses**
Speaker: Ash A. Alizadeh (Stanford School of Medicine, USA)
Chair/Moderator: Nagahiro Saijo (Akihabara Medical Clinic, Japan)

3. New Insights in Target Discovery and Resistance P.30

15:35 **Complex Functional Analysis is Required for Optimizing Targeted Therapy**
Speaker: Neal Rosen (Memorial Sloan Kettering Cancer Center, USA)
Chair/Moderator: Kiyohiko Hatake (International University of Health and Welfare, Japan)

16:15 Coffee Break

16:35 **Discovery of a New Class of Oncogenic Drivers in Breast Cancer**
Speaker: Leif W. Ellisen (Harvard Medical School, USA)
Chair/Moderator: Mitsuaki Yoshida (Japanese Foundation For Cancer Research, Japan)

17:15 **Inflammatory Breast Cancer Biology; the Tumor Microenvironment is the Key**
Speaker: Naoto T. Ueno (The University of Texas MD Anderson Cancer Center, USA)
Chair/Moderator: Masakazu Toi (Kyoto University, Japan)

18:00 **Reception *at Roppongi Hills Club, 51F***

Saturday, July 28, 2018 9:00—14:50

4. Progress in Precision Oncology P.48

9:00 **The Genomic Landscape of Advanced Hormone Resistant Breast Cancer**
Speaker: José Baselga (Memorial Sloan Kettering Cancer Center, USA)
Chair/Moderator: Chikashi Ishioka (Tohoku University, Japan)

9:40 **The Era of Genome Driven Oncology: Making the Clinic the New Laboratory**
Speaker: David M. Hyman (Memorial Sloan Kettering Cancer Center, USA)
Chair/Moderator: Yasuhiro Fujiwara (National Cancer Center, Japan)

10:20 Coffee Break

10:40 **Tumor Evolution and Heterogeneity in Oncogene-Driven Lung Cancers**
Speaker: Alice T. Shaw (Harvard Medical School, USA)
Chair/Moderator: Kohei Miyazono (The University of Tokyo, Japan)

5. Advances in Cancer Genomics / Genetics P.66

11:20 **Chromosomal Order from Chaos in Cancer Evolution, Immune Escape and Metastases: TRACERx**
Speaker: Charles Swanton (The Francis Crick Institute, UK)
Chair/Moderator: Hiroyuki Aburatani (The University of Tokyo, Japan)

12:00 Lunch

12:45 **Holistic View of Cancer Genomics in GI Area**
Speaker: Josep Tabernero (The Vall d'Herbron University Hospital, Spain)
Chair/Moderator: Atsushi Ohtsu (National Cancer Center, Japan)

13:25 **A One-Two Punch Model for Cancer Therapy**
-Exploiting Powerful Sequential Combinations by Functional Genetics
Speaker: René Bernards (Netherlands Cancer Institute, Netherlands)
Chair/Moderator: Hiroyuki Mano (National Cancer Center Research Institute, Japan)

14:05 **Liver Cancer Progression and Wnt Signaling**
Speaker: Hiroyuki Aburatani (The University of Tokyo, Japan)
Chair/Moderator: Charles Swanton (The Francis Crick Institute, UK)

Closing Remarks

14:45 Josep Tabernero (The Vall d'Herbron University Hospital, Spain)

Official language » English
Dress code » Business casual

Opening Remarks

Osamu Nagayama

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

As chairman of Chugai Academy for Advanced Oncology (CHAAO), 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 International Academy for Advanced Oncology (IAAO) 2018.

Each year at IAAO, I am delighted to see that the size of our gathering continues to grow larger each time. This year-our ninth 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 "Quantum Leap to Next Horizon 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 research on improving clinical outcomes, novel concepts for immunomodulation, and individualization. In addition, we will also address the new findings around oncogenes and potential drug targets, and discuss the basic and clinical understandings on drug-resistance.

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. Fujiwara, 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.

Title: Expanding Horizons for Cancer Genomics

Bruce A. Chabner, MD

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

Speaker

Makoto Ogawa, MD

Emeritus President, Aichi Cancer Center, 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

Canakinumab and Lung Cancer: Intriguing, but Is It Real? **Chabner BA**, Nabel CS. *Oncologist.* 2018 Apr 17. pii: theoncologist.2018-0116.

Does Chemotherapy Induce Metastases? **Chabner BA.** *Oncologist*. 2018 Mar 2 3(3):273-274

Considerations About the Use of Biomarkers in Cancer Clinical Trials. **Chabner BA**. *Clin Pharmacol Ther*. 2018 Jan; 103 (1):25-27.

Antibody-Drug Conjugates for the Treatment of Solid Tumors: Clinical Experience and Latest Developments. Nagayama A, Ellisen LW, **Chabner B**, Bardia A. *Target Oncol.* 2017 Dec; 12(6):719-739.

Regarding "Oncology Drug Approvals: Evaluating Endpoints and Evidence in an Era of Breakthrough Therapies". **Chabner BA.** *Oncologist*. 2017 Jul; 22(7):757-758.

Advantages of a Truly Open-Access Data-Sharing Model. Bertagnolli MM, Sartor O, **Chabner BA**, Rothenberg ML, Khozin S, Hugh-Jones C, Reese DM, Murphy MJ. *N Engl J Med*. 2017 Mar 23; 376(12):1178-1181.

Limits to Precision Cancer Medicine. Clark JW, **Chabner BA**. *N Engl J Med*. 2017 Jan 5; 376(1):96.

Understanding the Precision in "Precision Medicine". **Chabner BA**. *Oncologist.* 2016 Sep; 21(9):1029-30.

Title: Neoantigens and the Molecular Basis of Personalized Cancer Immunotherapy

Speaker

Robert D. Schreiber, PhD

AM Bursky & JM Bursky Distinguished Professor, Pathology & Immunology
Director, Center for Human Immunology and Immunotherapy Programs, Washington University School of Medicine, USA

Chairman

Ryuzo Ueda, MD, PhD

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

Robert D. Schreiber, PhD

Profile

Dr. Schreiber is an immunologist and currently is the Alumni Endowed Professor of Pathology and Immunology at Washington University School of Medicine in St. Louis. He is also co-leader of the Tumor Immunology Program of Washington University's Siteman Comprehensive Cancer Center, Director of the newly formed Washington University Center for Human Immunology and Immunotherapy Programs and an Associate Director of the Scientific Advisory Board to the Cancer Research Institute. He is a co-founder of Igenica, Inc., a biotech company focused on monoclonal antibody cancer therapeutics and a senior advisor to Jounce Therapeutics, a biotech company focused on development of novel immunomodulatory cancer therapies.

He obtained his B.A. and PhD in biochemistry from the State University of New York at Buffalo. His post-doctoral training was with Han Mueller-Eberhart at the Scripps Clinic studying the complement system. He joined the Scripps faculty in 1976 and rose to

Associate Member with tenure at Scripps before joining Washington University in St. Louis as Professor of Pathology. He was given the Alumni Endowed Professorship in 1990 and became an Affiliate of the Ludwig Institute for Cancer Research in 2001.

Dr. Schreiber's career has focused on elucidating the biochemistry and molecular cell biology of cytokines and defining the role they play in promoting immune responses to cancer. He was the first to demonstrate that interferon-gamma (IFNγ) was the cytokine that activated mouse macrophage anti-tumor and anti-microbial activities and pioneered the *in vivo* use of monoclonal antibodies to define the physiologic roles of cytokines in promoting host responses to tumors and infectious agents. He subsequently was one of the first to elucidate the structure and function of the IFNγ receptor and then established the physiologic relevance of IFNγ receptor-dependent signaling by generating genetically engineered mice lacking specific components of this pathway. Using IFNγ-unresponsive- and immunodeficient gene-targeted mice, Schreiber and colleagues demonstrated that the unmanipulated immune system could eliminate spontaneous and carcinogen-induced primary tumors and thereby resolved the long-standing controversy over whether cancer immunosurveillance occurs.

He also demonstrated that immunity can promote tumor dormancy and ultimately facilitate cancer progression by shaping tumor immunogenicity. These observations led Schreiber and his collaborators to propose the cancer immunoediting hypothesis that has gained nearly universal acceptance in the last few years. Schreiber's work has thus led to a generalized appreciation of the profound effect of immunity on developing tumors and has contributed critical conceptual and practical support to the fields of tumor immunology and cancer immunotherapy. Recently, he pioneered the use of genomics approaches to define the antigenic targets of cancer immunoediting and elucidate the mechanisms that underlie the process. This latter work supports ongoing efforts to develop individualized cancer immunotherapies.

Dr. Schreiber has authored more than 300 peer reviewed and invited publications and has received many honors including the Milstein Award from the International Society for interferon and cytokine Research, The Marie T Bonazinga Award for Excellence in Leukocyte Biology Research, the William B. Coley Award for Distinguished Research in Basic and Tumor Immunology from the Cancer Research Institute, and the Charles Rodolphe Brupbacher Prize for Cancer Research. Schreiber was inducted into the American Academy of Arts and Sciences in 2010 and the National Academy of Sciences (USA) in 2013.

Recent Publications

Interferon γ and Its Important Roles in Promoting and Inhibiting Spontaneous and Therapeutic Cancer Immunity. Alspach E, Lussier DM, **Schreiber RD**. *Cold Spring Harb Perspect Biol*. 2018 Apr 16. pii: a028480.

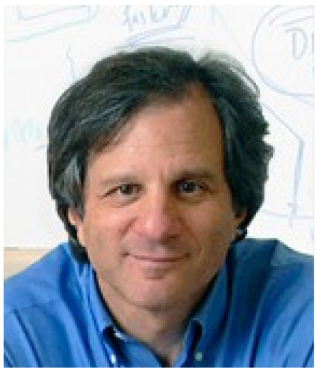
Cancer immunogenomic approach to neoantigen discovery in a checkpoint blockade responsive murine model of oral cavity squamous cell carcinoma. Zolkind P, Przybylski D, Marjanovic N, Nguyen L, Lin T, Johanns T, Alexandrov A, Zhou L, Allen CT, Miceli AP, **Schreiber RD**, Artyomov M, Dunn GP, Uppaluri R. *Oncotarget.* 2017 Dec 28;9(3):4109-4119.

Inflammatory monocytes require type I interferon receptor signaling to activate NK cells via IL-18 during a mucosal viral infection. Lee AJ, Chen B, Chew MV, Barra NG, Shenouda MM, Nham T, van Rooijen N, Jordana M, Mossman KL, **Schreiber RD**, Mack M, Ashkar AA. *J Exp Med*. 2017 Apr 3;214(4):1153-1167.

Temporally Distinct PD-L1 Expression by Tumor and Host Cells Contributes to Immune Escape. Noguchi T, Ward JP, Gubin MM, Arthur CD, Lee SH, Hundal J, Selby MJ, Graziano RF, Mardis ER, Korman AJ, **Schreiber RD.** *Cancer Immunol Res*. 2017 Feb;5(2):106-117.

Endogenous Neoantigen-Specific CD8 T Cells Identified in Two Glioblastoma Models Using a Cancer Immunogenomics Approach.Johanns TM, Ward JP, Miller CA, Wilson C, Kobayashi DK, Bender D, Fu Y, Alexandrov A, Mardis ER, Artyomov MN, **Schreiber RD**, Dunn GP. Ca*ncer Immunol Res*. 2016 Dec;4(12):1007-1015.

Title: Mechanistic Basis of Cancer Immunotherapy



Speaker

Ira Mellman, PhD

Vice President, Cancer Immunology, Genentech Inc.,USA

Chairman

Yuko Kitagawa, MD, PhD

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

Ira Mellman, PhD

Profile

Dr. Mellman was on the faculty of Yale University School of Medicine for over 20 years, holding the Sterling Professorship of Cell Biology and Immunobiology. He also served as chair of the Department of Cell Biology, Scientific Director of the Yale Cancer Center, and was an investigator with the Ludwig Institute for Cancer Research. In 2007, He moved to Genentech to apply the basic science insights learned during my academic career to cancer drug discovery. He now devote 100% of his effort to cancer immunology and immunotherapy, and have built perhaps the largest discovery unit devoted to this problem in industry or academia. With his first marketed product (atezolizumab), the larger Genentech/Roche organization has become a major player in this space, with much more still to come.

1978 Ph.D (Genetics) Yale University School of Medicine

Recent Publications

TGFβ attenuates tumour response to PD-L1 blockade by contributing to exclusion of T cells. Mariathasan S, Turley SJ, Nickles D, Castiglioni A, Yuen K, Wang Y, Kadel EE III, Koeppen H, Astarita JL, Cubas R, Jhunjhunwala S, Banchereau R, Yang Y, Guan Y, Chalouni C, Ziai J, Şenbabaoğlu Y, Santoro S, Sheinson D, Hung J, Giltnane JM, Pierce AA, Mesh K, Lianoglou S, Riegler J, Carano RAD, Eriksson P, Höglund M, Somarriba L, Halligan DL, van der Heijden MS, Loriot Y, Rosenberg JE, Fong L, **Mellman I**, Chen DS, Green M, Derleth C, Fine GD, Hegde PS, Bourgon R, Powles T. *Nature.* 2018 Feb 22;554(7693):544-548.

SUV420H2 is an epigenetic regulator of epithelial/mesenchymal states in pancreatic cancer. Viotti M, Wilson C, McCleland M, Koeppen H, Haley B, Jhunjhunwala S, Klijn C, Modrusan Z, Arnott D, Classon M, Stephan JP, **Mellman I**. *J Cell Biol.* 2018 Feb 5;217(2):763-777.

T cell costimulatory receptor CD28 is a primary target for PD-1-mediated inhibition. Hui E, Cheung J, Zhu J, Su X, Taylor MJ, Wallweber HA, Sasmal DK, Huang J, Kim JM, **Mellman I**, Vale RD. *Science.* 2017 Mar 31;355(6332):1428-1433.

Tumour and host cell PD-L1 is required to mediate suppression of anti-tumour immunity in mice. Lau J, Cheung J, Navarro A, Lianoglou S, Haley B, Totpal K, Sanders L, Koeppen H, Caplazi P, McBride J, Chiu H, Hong R, Grogan J, Javinal V, Yauch R, Irving B, Belvin M, **Mellman I**, Kim JM, Schmidt M. *Nat Commun.* 2017 Feb 21;8:14572.

Transcriptional determinants of tolerogenic and immunogenic states during dendritic cell maturation. Vander Lugt B, Riddell J, Khan AA, Hackney JA, Lesch J, DeVoss J, Weirauch MT, Singh H, **Mellman I**. *J Cell Biol*. 2017 Mar 6;216(3):779-792.
Elements of cancer immunity and the cancer-immune set point. Chen DS, **Mellman I.** *Nature*. 2017 Jan 18;541(7637):321-330.

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Title: Deconvolution of Cellular Determinants of Anti-Tumor Immune Response

Speaker

Ash A. Alizadeh, MD, PhD

Professor, Stanford School of Medicine, USA
Attending Physician, Lymphoma Oncology Clinic, Stanford Cancer Center. USA

Chairman

Nagahiro Saijo, MD, PhD

Deputy Director, Akihabara Medical Clinic, Japan

Ash A. Alizadeh, MD, PhD

Profile

Dr. Alizadeh completed his PhD in Biophysics and MD at Stanford in 2003, under mentorship of Pat Brown (Stanford Biochemistry) and Lou Staudt (NCI/NIH). Supported by the Howard Hughes Medical Institute (HHMI) and NIH Medical Scientist Training Program (MSTP), he built the Lymphochip DNA microarray platform. He and his colleagues used this platform to profile gene expression in diffuse large B cell lymphoma (DLBCL), and many other tumors. This work led to the discovery of DLBCL subtypes, and a framework for their cell of origin.

Following his clinical subspecialty Hematology and Medical Oncology training at Stanford, he completed his postdoctoral studies with Ron Levy and Irv Weissman. During this time he worked on molecular outcome prediction in DLBCL, developing a statistical framework for identification of small numbers of genes for robust risk

stratification and prognosis. Working with Irv Weissman, he identified CD47 expression as an adverse prognostic factor in non-Hodgkin lymphomas, and a therapeutic target of novel monoclonal antibodies that synergize to eradicate tumors.

The Alizadeh lab studies genomic biomarkers of tumors, whether detected through biopsy of primary tissues, or non-invasively through monitoring blood using circulating tumor DNA (ctDNA). His group developed Cancer Personalized Profiling by deep Sequencing (CAPP-Seq) as a novel method for ctDNA detection, and developed a novel cell deconvolution framework (CIBERSORT). His group applies such genomic tools for early detection, diagnosis, and monitoring of diverse tumors. In this effort, his group builds and employ tools from functional genomics, computational biology, molecular genetics, and mouse models.

2003: M.D. Stanford Medical School
2003: Ph.D. Stanford Medical School, Biophysics/Dept. of Biochemistry

Recent Publications

Combination Approach for Detecting Different Types of Alterations in Circulating Tumor DNA in Leiomyosarcoma. Przybyl J, Chabon JJ, Spans L, Ganjoo KN, Vennam S, Newman AM, Forgó E, Varma S, Zhu S, Debiec-Rychter M, **Alizadeh AA**, Diehn M, van de Rijn M.*Clin Cancer Res*. 2018 Feb 20. doi: 10.1158/1078-0432.

Profiling Tumor Infiltrating Immune Cells with CIBERSORT. Chen B, Khodadoust MS, Liu CL, Newman AM, **Alizadeh AA**. *Methods Mol Biol.* 2018;1711:243-259.

KLHL6 Is Preferentially Expressed in Germinal Center-Derived B-Cell Lymphomas. Kunder CA, Roncador G, Advani RH, Gualco G, Bacchi CE, Sabile JM, Lossos IS, Nie K, Tibshirani RJ, Green MR, **Alizadeh AA**, Natkunam Y. *Am J Clin Pathol.* 2017 Nov 20;148(6):465-476.

Early Detection of Molecular Residual Disease in Localized Lung Cancer by Circulating Tumor DNA Profiling. Chaudhuri AA, Chabon JJ, Lovejoy AF, Newman AM, Stehr H, Azad TD, Khodadoust MS, Esfahani MS, Liu CL, Zhou L, Scherer F, Kurtz DM, Say C, Carter JN, Merriott DJ, Dudley JC, Binkley MS, Modlin L, Padda SK, Gensheimer MF, West RB, Shrager JB, Neal JW, Wakelee HA, Loo BW Jr, **Alizadeh AA**, Diehn M. *Cancer Discov*. 2017 Dec;7(12):1394-1403.

Data normalization considerations for digital tumor dissection. Newman AM, Gentles AJ, Liu CL, Diehn M, **Alizadeh AA.** *Genome Biol.* 2017 Jul 5;18(1):128.

High-throughput sequencing for noninvasive disease detection in hematologic malignancies. Scherer F, Kurtz DM, Diehn M, **Alizadeh AA**.*Blood*. 2017 Jul 27;130(4):440-452.

Antigen presentation profiling reveals recognition of lymphoma immunoglobulin neoantigens. Khodadoust MS, Olsson N, Wagar LE, Haabeth OA, Chen B, Swaminathan K, Rawson K, Liu CL, Steiner D, Lund P, Rao S, Zhang L, Marceau C, Stehr H, Newman AM, Czerwinski DK, Carlton VE, Moorhead M, Faham M, Kohrt HE, Carette J, Green MR, Davis MM, Levy R, Elias JE, **Alizadeh AA**. *Nature*. 2017 Mar 30;543(7647):723-727.

Title: Complex Functional Analysis is Required for Optimizing Targeted Therapy.

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. 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.

Recent Publications

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 Jun 7. pii: CD-17-1263.

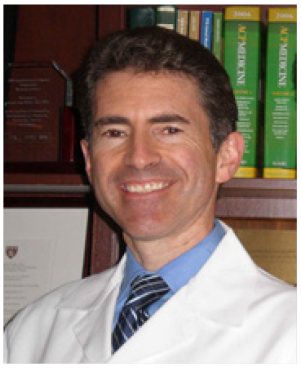
Allele-Specific Mechanisms of Activation of MEK1 Mutants Determine Their Properties. Gao Y, Chang MT, McKay D, Na N, Zhou B, Yaeger R, Torres NM, Muniz K, Drosten M, Barbacid M, Caponigro G, Stuart D, Moebitz H, Solit DB, Abdel-Wahab O, Taylor BS, Yao Z, **Rosen N.** *Cancer Discov*. 2018 May;8(5):648-661.

Clinical Sequencing Defines the Genomic Landscape of Metastatic Colorectal Cancer. Yaeger R, Chatila WK, Lipsyc MD, Hechtman JF, Cercek A, Sanchez-Vega F, Jayakumaran G, Middha S, Zehir A, Donoghue MTA, You D, Viale A, Kemeny N, Segal NH, Stadler ZK, Varghese AM, Kundra R, Gao J, Syed A, Hyman DM, Vakiani E, **Rosen N**, Taylor BS, Ladanyi M, Berger MF, Solit DB, Shia J, Saltz L, Schultz N. *Cancer Cell*. 2018 Jan 8;33(1):125-136.e3.

Accelerating Discovery of Functional Mutant Alleles in Cancer. Chang MT, Bhattarai TS, Schram AM, Bielski CM, Donoghue MTA, Jonsson P, Chakravarty D, Phillips S, Kandoth C, Penson A, Gorelick A, Shamu T, Patel S, Harris C, Gao J, Sumer SO, Kundra R, Razavi P, Li BT, Reales DN, Socci ND, Jayakumaran G, Zehir A, Benayed R, Arcila ME, Chandarlapaty S, Ladanyi M, Schultz N, Baselga J, Berger MF, **Rosen N**, Solit DB, Hyman DM, Taylor BS. *Cancer Discov*. 2018 Feb;8(2):174-183.

Genetic Predictors of Response to Systemic Therapy in Esophagogastric Cancer. Janjigian YY, Sanchez-Vega F, Jonsson P, Chatila WK, Hechtman JF, Ku GY, Riches JC, Tuvy Y, Kundra R, Bouvier N, Vakiani E, Gao J, Heins ZJ, Gross BE, Kelsen DP, Zhang L, Strong VE, Schattner M, Gerdes H, Coit DG, Bains M, Stadler ZK, Rusch VW, Jones DR, Molena D, Shia J, Robson ME, Capanu M, Middha S, Zehir A, Hyman DM, Scaltriti M, Ladanyi M, **Rosen N**, Ilson DH, Berger MF, Tang L, Taylor BS, Solit DB, Schultz N. *Cancer Discov.* 2018 Jan;8(1):49-58.

Title: Discovery of a New Class of Oncogenic Drivers in Breast Cancer



Speaker

Leif W. Ellisen, MD, PhD

Professor of Medicine, Harvard Medical School Program Director, Breast Medical Oncology, MGH Cancer Center
Clinical Director, Breast and Ovarian Cancer Genetics, MGH Cancer Center, USA

Chairman

Mitsuaki Yoshida, PhD

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

Leif W. Ellisen, MD, PhD

Profile

Dr. Ellisen is the Program Director of Breast Medical Oncology and a researcher at the Massachusetts General Hospital (MGH) Cancer Center, and Professor of Medicine at Harvard Medical School. Basic breast cancer research in the laboratory focuses on altered transcription factor function and cellular signaling in cancer initiation and progression, while their translational research emphasizes the application of germline and somatic tumor genetic testing for cancer risk and therapeutic prediction. He is dedicated to training and mentoring the next generation of successful cancer clinicians and scientists, through work focused in the fields of cancer biology, translational therapeutics, and cancer genetics. He directs a clinical research program involving 13 breast cancer physicians and >30 active clinical trials. He serves on numerous grant review committees and editorial boards, and his work on personalized cancer medicine has been featured in the news media including the *Wall Street Journal* and the ABC Evening News

1992 MD, PhD Medicine and Cancer Biology, Stanford University
2007 Associate Professor of Medicine, Harvard Medical School
2014 Professor of Medicine, Harvard Medical School

Recent Publications

Developmental History Provides a Roadmap for the Emergence of Tumor Plasticity. Tata PR, Chow RD, Saladi SV, Tata A, Konkimalla A, Bara A, Montoro D, Hariri LP, Shih AR, Mino-Kenudson M, Mou H, Kimura S, **Ellisen LW**, Rajagopal J. *Dev Cell*. 2018 Mar 26;44(6):679-693.

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Expressed Gene Fusions as Frequent Drivers of Poor Outcomes in Hormone Receptor-Positive Breast Cancer. Matissek KJ, Onozato ML, Sun S, Zheng Z, Schultz A, Lee J, Patel K, Jerevall PL, Saladi SV, Macleay A, Tavallai M, Badovinac-Crnjevic T, Barrios C, Beşe N, Chan A, Chavarri-Guerra Y, Debiasi M, Demirdögen E, Egeli Ü, Gökgöz S, Gomez H, Liedke P, Tasdelen I, Tolunay S, Werutsky G, St Louis J, Horick N, Finkelstein DM, Le LP, Bardia A, Goss PE, Sgroi DC, Iafrate AJ, **Ellisen LW**. *Cancer Discov*. 2018 Mar;8(3):336-353.

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A wound-healing program is hijacked to promote cancer metastasis. **Ellisen LW**. *J Exp Med.* 2017 Oct 2;214(10):2813-2815.

A mutational signature reveals alterations underlying deficient homologous recombination repair in breast cancer. Polak P, Kim J, Braunstein LZ, Karlic R, Haradhavala NJ, Tiao G, Rosebrock D, Livitz D, Kübler K, Mouw KW, Kamburov A, Maruvka YE, Leshchiner I, Lander ES, Golub TR, Zick A, Orthwein A, Lawrence MS, Batra RN, Caldas C, Haber DA, Laird PW, Shen H, **Ellisen LW**, D'Andrea AD, Chanock SJ, Foulkes WD, Getz G. *Nat Genet*. 2017 Oct;49(10):1476-1486.

Recurrent and functional regulatory mutations in breast cancer. Rheinbay E, Parasuraman P, Grimsby J, Tiao G, Engreitz JM, Kim J, Lawrence MS, Taylor-Weiner A, Rodriguez-Cuevas S, Rosenberg M, Hess J, Stewart C, Maruvka YE, Stojanov P, Cortes ML, Seepo S, Cibulskis C, Tracy A, Pugh TJ, Lee J, Zheng Z, **Ellisen LW**, Iafrate AJ, Boehm JS, Gabriel SB, Meyerson M, Golub TR, Baselga J, Hidalgo-Miranda A, Shioda T, Bernards A, Lander ES, Getz G. *Nature*. 2017 Jul 6;547(7661):55-60.

Title: Inflammatory Breast Cancer Biology; the Tumor Microenvironment is the Key

Naoto T. Ueno, MD, PhD

Professor of Medicine, Department of Breast Medical Oncology
Nylene Eckles Distinguished Professor in Breast Cancer Research
Executive Director of Morgan Welch Inflammatory Breast Cancer Research Program and Clinic
Chief, Section of Translational Breast Cancer Research
Enhanced Drug-Development Guidance and Evaluation (EDGE) Preclinical Solutions
The University of Texas MD Anderson Cancer Center, USA

Speaker

Masakazu Toi, MD, PhD

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

Chairman

Naoto T. Ueno, MD, PhD

Profile

Dr. Ueno has a strong background in translational breast cancer research in the areas of cancer biology and molecular therapeutics, with specific training and expertise in the key research areas of EGFR/ERK signaling and *in vivo* modeling. As a Ph.D student at The University of Texas Graduate School of Biomedical Sciences, he carried out preclinical research on the role of the HER2 pathway in chemosensitization of paclitaxel in breast cancer. In addition to his basic research background, he trained as a medical oncologist at MD Anderson and simultaneously learned how to conduct clinical research and perform data analysis related to breast cancer. He is now a practicing physician who has experience in conducting both targeted and gene therapy clinical trials.

Since becoming a faculty member at MD Anderson, he has expanded my research to include the EGFR/ERK pathway in both breast and ovarian cancer (HER2, JNK, TIG1, FOXO3, epigenetic, etc.). Over the past 10 years, he have successfully managed

projects in breast cancer biology related to triple-negative breast cancer, inflammatory breast cancer, metastasis, cancer stem cells, and drug resistance of cancer cells. Currently he serves as an executive director of Morgan Welch Inflammatory Breast Cancer (MWIBC) Research Program and Clinic and Section of Translational Breast Cancer Research (TBCR). MD Anderson MWIBC is the world's largest IBC specific research program that conducts IBC-specific clinical trials, understanding the aggressiveness of caners by studying cancer stem cells, and the impact of microenviroment (inflamation and immunolgoical efect). For the section of TBCR, the program focuses on reducing the suffering of breast cancer patients through our unique, rapid drug development platforms via enhanced value of novel therapeutic approach and guiding to investigator-initiated clinical trials or standard of care.

Recent Publications

Clinically relevant inflammatory breast cancer patient-derived xenograft-derived ex vivo model for evaluation of tumor-specific therapies. Eckhardt BL, Gagliardi M, Iles L, Evans K, Ivan C, Liu X, Liu CG, Souza G, Rao A, Meric-Bernstam F, **Ueno NT**, Bartholomeusz GA. *PLoS One*. 2018 May 16;13(5):e0195932.

International Consensus on the Clinical Management of Inflammatory Breast Cancer from the Morgan Welch Inflammatory Breast Cancer Research Program 10th Anniversary Conference.**Ueno NT**, Espinosa Fernandez JR, Cristofanilli M, Overmoyer B, Rea D, Berdichevski F, El-Shinawi M, Bellon J, Le-Petross HT, Lucci A, Babiera G, DeSnyder SM, Teshome M, Chang E, Lim B, Krishnamurthy S, Stauder MC, Parmar S, Mohamed MM, Alexander A, Valero V, Woodward WA.*J Cancer*. 2018 Apr ;9(8):1437-1447.

Survivorship and Advocacy in Inflammatory Breast Cancer. Alexander A, Arnold TL, Bishnoi S, Ballinger C, Shaitelman SF, Schaverien MV, Cohen L, Dev M, **Ueno NT**.*J Cancer*. 2018 Apr 6;9(8):1430-1436.

Inflammatory breast cancer biology: the tumour microenvironment is key. Lim B, Woodward WA, Wang X, Reuben JM, **Ueno NT**.*Nat Rev Cancer*. 2018 Apr 27. doi: 10.

Expression of Programmed Death Ligand 1 (PD-L1) in Posttreatment Primary Inflammatory Breast Cancers and Clinical Implications. He J, Huo L, Ma J, Zhao J, Bassett RL, Sun X, **Ueno NT**, Lim B, Gong Y.*Am J Clin Pathol.* 2018 Feb 17;149(3):253-261.

Dynamic changes in CD44v-positive cells after preoperative anti-HER2 therapy and its correlation with pathologic complete response in HER2-positive breast cancer. Yamauchi T, Espinosa Fernandez JR, Imamura CK, Yamauchi H, Jinno H, Takahashi M, Kitagawa Y, Nakamura S, Lim B, Krishnamurthy S, Reuben JM, Liu D, Tripathy D, Chen H, Takebe N, Saya H, **Ueno NT**. *Oncotarget*. 2018 Jan 4;9(6):6872-6882.

Development of CNS metastases and survival in patients with inflammatory breast cancer. Uemura MI, French JT, Hess KR, Liu D, Raghav K, Hortobagyi GN, Arun BK, Valero V, **Ueno NT**, Alvarez RH, Woodward WA, Debeb BG, Moulder SL, Lim B, Tripathy D, Ibrahim NK. *Cancer*. 2018 Mar 26. doi: 10.1002/cncr.31336.

Title: The Genomic Landscape of Advanced Hormone Resistant Breast Cancer

José Baselga, MD, PhD

Physician-in-Chief and Chief Medical Officer, Memorial Sloan Kettering Cancer Center, USA.

Speaker

Chikashi Ishioka, MD

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

Chairman

José Baselga, MD, PhD

Profile

Dr. Baselga received his MD and PhD degrees from the Autonomous University of Barcelona in 1982. He completed a fellowship in Medical Oncology at Memorial Sloan-Kettering Cancer Center in New York, and subsequently stayed on as a faculty member of the Breast Medicine Service at Memorial Sloan-Kettering.

From 1996 to 2010, he was the Chairman of the Medical Oncology Service and Founding Director of the recently established Vall d'Hebron Institute of Oncology (VHIO) at the Vall d'Hebron University Hospital in Barcelona. From 2010 to 2012, he was the chief of the Division of Hematology/Oncology and associate director of the MGH Cancer Center in Massachusetts

He joined Memorial Sloan Kettering as Physician-in-Chief and Chief Medical Officer in 2013 from Massachusetts General Hospital (MGH), where he was Chief of the Division of Hematology/Oncology and Associate Director of the MGH Cancer Center.

He pioneered the development of treatments for women with HER2-positive breast cancer; conducted the first clinical trial to demonstrate that patients with advanced HER2-positive breast cancer benefited from treatment with the anti-HER2 monoclonal antibody trastuzumab; and continue to lead state-of-the-art international clinical trials with trastuzumab for women before and after breast cancer surgery. In addition, he led the clinical development of the second anti-HER2 monoclonal antibody to receive US Food and Drug Administration approval, pertuzumab, and the pivotal study that led to the approval of everolimus for the treatment of patients with hormone receptor–positive breast cancer. His most recent focus in the laboratory and clinic has been on mechanisms of resistance to anti-HER2 and anti-PI3K agents. (The PI3K pathway is one of the most important pathways in cancer metabolism and growth.) He is also studying compensatory pathway activation and the development of therapeutic combination approaches, including PI3K inhibitors and anti-estrogen therapies.

He have been actively involved in the American Association for Cancer Research (AACR) for more than 20 years. He is a founding co-editor-in-chief of the AACR's high-impact scientific journal, *Cancer Discovery, and* have served the AACR in many other key capacities, including as president from 2015 to 2016. In addition, He have served as chair of numerous AACR committees, including the Clinical Trials Committee from 2012 to 2013 and the Research Grant Review Committee); he was a member of the Landon Foundation-AACR Innovator Award for International Collaboration in Cancer Research Committee from 2006 to 2008, the Pezcoller Foundation-AACR International Award for Cancer Research Committee from 2004 to 2005, and the AACR Award for Outstanding Achievement in Cancer Research Award Committee from 2002 to 2003. He was also inaugurated into the 2014 class of fellows of the AACR Academy. Additionally, he is a principal of the Stand Up To Cancer Dream Team "Targeting the PI3K Pathway in Women's Cancers."

As Physician-in-Chief, he oversee the clinical component of MSK. This includes the management of patient care in Memorial Hospital as well as at our outpatient clinics and regional locations. He takes an active role in efforts aimed at enhancing and expanding MSK's programs in clinical and translational research. He truly believe that MSK is one of our nation's premier cancer institutions, executing the new ideas that are transforming patients' lives on an almost daily basis. Their vision is to bring treatments to patients that were not available before — indeed, that didn't even exist before. His primary, overarching focus is on maintaining our clinical excellence. They are who we are because they have the best people anywhere — the best physicians, nurses, and support staff — and we are all committed to the patients who are at the heart of our mission. They are the reason we come to work every day. He has been in oncology for many years and he has never seen the acceleration of progress that he is seeing today. While it's difficult to make predictions — and cancer is anything but simple — major advances in their understanding of cancer biology are changing the way they think about treating these diseases. His MSK colleagues are energizing and inspiring, and he feel privileged to play a part in their communal efforts to conquer cancer.

Recent Publications

HER kinase inhibition in patients with HER2- and HER3-mutant cancers. Hyman DM, Piha-Paul SA, Won H, Rodon J, Saura C, Shapiro GI, Juric D, Quinn DI, Moreno V, Doger B, Mayer IA, Boni V, Calvo E, Loi S, Lockhart AC, Erinjeri JP, Scaltriti M, Ulaner GA, Patel J, Tang J, Beer H, Selcuklu SD, Hanrahan AJ, Bouvier N, Melcer M, Murali R, Schram AM, Smyth LM, Jhaveri K, Li BT, Drilon A, Harding JJ, Iyer G, Taylor BS, Berger MF, Cutler RE Jr, Xu F, Butturini A, Eli LD, Mann G, Farrell C, Lalani AS, Bryce RP, Arteaga CL, Meric-Bernstam F, **Baselga J**, Solit DB. *Nature.* 2018 Feb 8;554(7691):189-194.

Phosphatidylinositol 3-Kinase α-Selective Inhibition With Alpelisib (BYL719) in PIK3CA-Altered Solid Tumors: Results From the First-in-Human Study. Juric D, Rodon J, Tabernero J, Janku F, Burris HA, Schellens JHM, Middleton MR, Berlin J, Schuler M, Gil-Martin M, Rugo HS, Seggewiss-Bernhardt R, Huang A, Bootle D, Demanse D, Blumenstein L, Coughlin C, Quadt C, **Baselga J**. *J Clin Oncol.* 2018 May 1;36(13):1291-1299.

Accelerating Discovery of Functional Mutant Alleles in Cancer. Chang MT, Bhattarai TS, Schram AM, Bielski CM, Donoghue MTA, Jonsson P, Chakravarty D, Phillips S, Kandoth C, Penson A, Gorelick A, Shamu T, Patel S, Harris C, Gao J, Sumer SO, Kundra R, Razavi P, Li BT, Reales DN, Socci ND, Jayakumaran G, Zehir A, Benayed R, Arcila ME, Chandarlapaty S, Ladanyi M, Schultz N, **Baselga J**, Berger MF, Rosen N, Solit DB, Hyman DM, Taylor BS. *Cancer Discov.* 2018 Feb;8(2):174-183.

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Advances in the management of HER2-positive early breast cancer. **Baselga J**, Coleman RE, Cortés J, Janni W. *Crit Rev Oncol Hematol.* 2017 Nov;119:113-122.

Title: The Era of Genome Driven Oncology: Making the Clinic the New Laboratory

Speaker

David M. Hyman, MD

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

Chairman

Yasuhiro Fujiwara, MD, PhD

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

David M. Hyman, MD

Profile

Dr. Hyman is a medical oncologist. 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. His clinical research is focused on developing new treatments for ovarian cancer and uterine sarcomas. He serves as principal investigator on a national research study for women with recurrent uterine sarcoma. He also specializes in early-phase clinical trials (sometimes called Phase I trials). These studies give patients new cancer medicines or new combinations of cancer medicines for the first time. He is working to improve the design of these trials.

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

Recent Publications

A Randomized Trial of Prophylactic Extended Carboplatin Infusion to Reduce Hypersensitivity Reactions in Recurrent Ovarian Cancer. LaVigne K, **Hyman DM**, Zhou QC, Iasonos A, Tew WP, Aghajanian C, Makker V, Hensley ML, Konner J, Grisham RN, Cangemi N, Soldan K, Spriggs DR, Sabbatini PJ, O'Cearbhaill RE. *Int J Gynecol Cancer*. 2018 May 4.

Rates of TP53 Mutation are Significantly Elevated in African American Patients with Gastric Cancer. van Beek EJAH, Hernandez JM, Goldman DA, Davis JL, McLaughlin K, Ripley RT, Kim TS, Tang LH, Hechtman JF, Zheng J, Capanu M, Schultz N, **Hyman DM**, Ladanyi M, Berger MF, Solit DB, Janjigian YY, Strong VE. *Ann Surg Oncol*. 2018 May 3

HER kinase inhibition in patients with HER2- and HER3-mutant cancers. **Hyman DM**, Piha-Paul SA, Won H, Rodon J, Saura C, Shapiro GI, Juric D, Quinn DI, Moreno V, Doger B, Mayer IA, Boni V, Calvo E, Loi S, Lockhart AC, Erinjeri JP, Scaltriti M, Ulaner GA, Patel J, Tang J, Beer H, Selcuklu SD, Hanrahan AJ, Bouvier N, Melcer M, Murali R, Schram AM, Smyth LM, Jhaveri K, Li BT, Drilon A, Harding JJ, Iyer G, Taylor BS, Berger MF, Cutler RE Jr, Xu F, Butturini A, Eli LD, Mann G, Farrell C, Lalani AS, Bryce RP, Arteaga CL, Meric-Bernstam F, Baselga J, Solit DB. *Nature.* 2018 Feb 8; 554(7691):189-194.

A First-in-Human Phase 1 Study of LY3023414, an Oral PI3K/mTOR Dual Inhibitor, in Patients with Advanced Cancer. Bendell JC, Varghese AM, **Hyman DM**, Bauer TM, Pant S, Callies S, Lin J, Martinez R, Wickremsinhe ER, Fink A, Wacheck V, Moore KN. *Clin Cancer Res*. 2018 Apr 10.

Phase I Study of MEDI3617, a Selective Angiopoietin-2 Inhibitor Alone and Combined with Carboplatin/Paclitaxel, Paclitaxel, or Bevacizumab for Advanced Solid Tumors. **Hyman DM**, Rizvi N, Natale R, Armstrong DK, Birrer M, Recht L, Dotan E, Makker V, Kaley T, Kuruvilla D, Gribbin M, McDevitt J, Lai DW, Dar M. *Clin Cancer Res*. 2018 Mar 20.

NTRK Fusions Define a Novel Uterine Sarcoma Subtype With Features of Fibrosarcoma. Chiang S, Cotzia P, **Hyman DM**, Drilon A, Tap WD, Zhang L, Hechtman JF, Frosina D, Jungbluth AA, Murali R, Park KJ, Soslow RA, Oliva E, Iafrate AJ, Benayed R, Ladanyi M, Antonescu CR. *Am J Surg Pathol*. 2018 Jun; 42(6):791-798.

Efficacy of Larotrectinib in TRK Fusion-Positive Cancers in Adults and Children. Drilon A, Laetsch TW, Kummar S, DuBois SG, Lassen UN, Demetri GD, Nathenson M, Doebele RC, Farago AF, Pappo AS, Turpin B, Dowlati A, Brose MS, Mascarenhas L, Federman N, Berlin J, El-Deiry WS, Baik C, Deeken J, Boni V, Nagasubramanian R, Taylor M, Rudzinski ER, Meric-Bernstam F, Sohal DPS, Ma PC, Raez LE, Hechtman JF, Benayed R, Ladanyi M, Tuch BB, Ebata K, Cruickshank S, Ku NC, Cox MC, Hawkins DS, Hong DS, **Hyman DM**. *N Engl J Med.* 2018 Feb 22;378(8):731-739.

HER kinase inhibition in patients with HER2- and HER3-mutant cancers. **Hyman DM**, Piha-Paul SA, Won H, Rodon J, Saura C, Shapiro GI, Juric D, Quinn DI, Moreno V,

Doger B, Mayer IA, Boni V, Calvo E, Loi S, Lockhart AC, Erinjeri JP, Scaltriti M, Ulaner GA, Patel J, Tang J, Beer H, Selcuklu SD, Hanrahan AJ, Bouvier N, Melcer M, Murali R, Schram AM, Smyth LM, Jhaveri K, Li BT, Drilon A, Harding JJ, Iyer G, Taylor BS, Berger MF, Cutler RE Jr, Xu F, Butturini A, Eli LD, Mann G, Farrell C, Lalani AS, Bryce RP, Arteaga CL, Meric-Bernstam F, Baselga J, Solit DB. *Nature*. 2018 Feb 8;554 (7691):189-194.

First-in-Class ERK1/2 Inhibitor Ulixertinib (BVD-523) in Patients with MAPK Mutant Advanced Solid Tumors: Results of a Phase I Dose-Escalation and Expansion Study. Sullivan RJ, Infante JR, Janku F, Wong DJL, Sosman JA, Keedy V, Patel MR, Shapiro GI, Mier JW, Tolcher AW, Wang-Gillam A, Sznol M, Flaherty K, Buchbinder E, Carvajal RD, Varghese AM, Lacouture ME, Ribas A, Patel SP, DeCrescenzo GA, Emery CM, Groover AL, Saha S, Varterasian M, Welsch DJ, **Hyman DM**, Li BT. *Cancer Discov*. 2018 Feb;8 (2):184-195.

Accelerating Discovery of Functional Mutant Alleles in Cancer. Chang MT, Bhattarai TS, Schram AM, Bielski CM, Donoghue MTA, Jonsson P, Chakravarty D, Phillips S, Kandoth C, Penson A, Gorelick A, Shamu T, Patel S, Harris C, Gao J, Sumer SO, Kundra R, Razavi P, Li BT, Reales DN, Socci ND, Jayakumaran G, Zehir A, Benayed R, Arcila ME, Chandarlapaty S, Ladanyi M, Schultz N, Baselga J, Berger MF, Rosen N, Solit DB, **Hyman DM**, Taylor BS. *Cancer Discov.* 2018 Feb; 8(2):174-183.

Patient HLA class I genotype influences cancer response to checkpoint blockade immunotherapy. Chowell D, Morris LGT, Grigg CM, Weber JK, Samstein RM, Makarov V, Kuo F, Kendall SM, Requena D, Riaz N, Greenbaum B, Carroll J, Garon E, **Hyman DM**, Zehir A, Solit D, Berger M, Zhou R, Rizvi NA, Chan TA. *Science*. 2018 Feb 2; 359 (6375):582-587.

Title: Tumor Evolution and Heterogeneity in Oncogene-Driven Lung Cancers

Speaker

Alice T. Shaw, MD, PhD

Professor of Medicine, Harvard Medical School
Attending Physician, Thoracic Cancer Program,
Massachusetts General Hospital, USA

Chairman

Kohei Miyazono, MD, PhD

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

Alice T. Shaw, MD, PhD

Profile

Dr. Shaw is an associate professor of medicine at Harvard Medical School and an attending physician in the Thoracic Oncology Division at Massachusetts General Hospital. She received her AB in biochemistry from Harvard and her MD and PhD degrees from Harvard Medical School. She did her residency in internal medicine at Massachusetts General Hospital and completed a fellowship in hematology/oncology at Dana-Farber/Massachusetts General Hospital. She completed her postdoctoral work in the laboratory of Dr. Tyler Jacks at MIT.

In addition to caring for patients with lung cancer, Dr. Shaw also performs clinical and translational research. Her research focuses on anaplastic lymphoma kinase (ALK), ROS1 and RET rearrangements in non-small cell lung carcinoma (NSCLC). She was the lead investigator for the global registration studies of crizotinib and ceritinib, which led to regulatory approval of both drugs in advanced ALK-rearranged NSCLC. She was also the lead investigator for crizotinib in ROS1-rearranged NSCLC. Her research focuses on elucidating mechanisms of resistance to targeted therapies, and she is

currently leading several clinical trials and translational efforts aimed at overcoming drug resistance

Recent Publications

STK11/LKB1 Mutations and PD-1 Inhibitor Resistance in KRAS-Mutant Lung Adenocarcinoma. Skoulidis F, Goldberg ME, Greenawalt DM, Hellmann MD, Awad MM, Gainor JF, Schrock AB, Hartmaier RJ, Trabucco SE, Gay L, Ali SM, Elvin JA, Singal G, Ross JS, Fabrizio D, Szabo PM, Chang H, Sasson A, Srinivasan S, Kirov S, Szustakowski J, Vitazka P, Edwards R, Bufill JA, Sharma N, Ou SI, Peled N, Spigel DR, Rizvi H, Jimenez Aguilar E, Carter BW, Erasmus J, Halpenny DF, Plodkowski AJ, Long NM, Nishino M, Denning WL, Galan-Cobo A, Hamdi H, Hirz T, Tong P, Wang J, Rodriguez-Canales J, Villalobos PA, Parra ER, Kalhor N, Sholl LM, Sauter JL, Jungbluth AA, Mino-Kenudson M, Azimi R, Elamin YY, Zhang J, Leonardi GC, Jiang F, Wong KK, Lee JJ, Papadimitrakopoulou VA, Wistuba II, Miller VA, Frampton GM, Wolchok JD, **Shaw AT**, Jänne PA, Stephens PJ, Rudin CM, Geese WJ, Albacker LA, Heymach JV. *Cancer Discov*. 2018 May 17. pii: CD-18-0099.

Exploratory Analysis of Brigatinib Activity in Patients With Anaplastic Lymphoma Kinase-Positive Non-Small-Cell Lung Cancer and Brain Metastases in Two Clinical Trials. Camidge DR, Kim DW, Tiseo M, Langer CJ, Ahn MJ, **Shaw AT**, Huber RM, Hochmair MJ, Lee DH, Bazhenova LA, Gold KA, Ou SI, West HL, Reichmann W, Haney J, Clackson T, Kerstein D, Gettinger SN. *J Clin Oncol.* 2018 May 16:JCO2017775841.

Improved Overall Survival and Locoregional Disease Control With Concurrent PD-1 Pathway Inhibitors and Stereotactic Radiosurgery for Lung Cancer Patients With Brain Metastases. Schapira E, ubbeling H, Yeap BY, Mehan WA Jr., **Shaw AT**, Oh K, Gainor JF, Shih HA. *Int J Radiat Oncol Biol Phys*. 2018 Mar 22. pii: S0360-3016(18)30542..

Sequential ALK Inhibitors Can Select for Lorlatinib-Resistant Compound *ALK* Mutations in ALK-Positive Lung Cancer. Yoda S, Lin JJ, Lawrence MS, Burke BJ, Friboulet L, Langenbucher A, Dardaei L, Prutisto-Chang K, Dagogo-Jack I, Timofeevski S, Hubbeling H, Gainor JF, Ferris LA, Riley AK, Kattermann KE, Timonina D, Heist RS, Iafrate AJ, Benes CH, Lennerz JK, Mino-Kenudson M, Engelman JA, Johnson TW, Hata AN, **Shaw AT**. *Cancer Discov*. 2018 Apr 12. doi: 10.1158/2159-8290.

Clinical Utility of Cell-Free DNA for the Detection of *ALK* Fusions and Genomic Mechanisms of ALK Inhibitor Resistance in Non-Small Cell Lung Cancer. McCoach CE, Blakely CM, Banks KC, Levy B, Chue BM, Raymond VM, Le AT, Lee CE, Diaz J, Waqar SN, Purcell WT, Aisner DL, Davies KD, Lanman RB, **Shaw AT**, Doebele RC. *Clin Cancer Res*. 2018 Mar 29. doi: 10.1158/1078-0432.CCR-17-2588.

SHP2 inhibition restores sensitivity in ALK-rearranged non-small-cell lung cancer resistant to ALK inhibitors. Dardaei L, Wang HQ, Singh M, Fordjour P, Shaw KX, Yoda S, Kerr G, Yu K, Liang J, Cao Y, Chen Y, Lawrence MS, Langenbucher A, Gainor JF, Friboulet L, Dagogo-Jack I, Myers DT, Labrot E, Ruddy D, Parks M, Lee D, DiCecca RH, Moody S, Hao H, Mohseni M, LaMarche M, Williams J, Hoffmaster K, Caponigro G, **Shaw AT**, Hata AN, Benes CH, Li F, Engelman JA. *Nat Med*. 2018 May;24(4):512-517.

Genomic and Functional Fidelity of Small Cell Lung Cancer Patient-Derived Xenografts. Drapkin BJ, George J, Christensen CL, Mino-Kenudson M, Dries R, Sundaresan T,

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Title: Chromosomal Order from Chaos in Cancer Evolution, Immune Escape and Metastases: TRACERx

Speaker

Charles Swanton, MD, 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

Hiroyuki Aburatani, MD, PhD

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

Charles Swanton, MD, 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 focussed on biological mechanisms of cancer drug resistance. He was made Fellow of the Royal College of Physicians in April 2011 and Chair in Personalised 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), Glaxo Smithkline 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.

Recent Publications

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Tracking Cancer Evolution Reveals Constrained Routes to Metastases: TRACERx Renal. Turajlic S, Xu H, Litchfield K, Rowan A, Chambers T, Lopez JI, Nicol D, O'Brien T, Larkin J, Horswell S, Stares M, Au L, Jamal-Hanjani M, Challacombe B, Chandra A, Hazell S, Eichler-Jonsson C, Soultati A, Chowdhury S, Rudman S, Lynch J, Fernando A, Stamp G, Nye E, Jabbar F, Spain L, Lall S, Guarch R, Falzon M, Proctor I, Pickering L, Gore M, Watkins TBK, Ward S, Stewart A, DiNatale R, Becerra MF, Reznik E, Hsieh JJ, Richmond TA, Mayhew GF, Hill SM, McNally CD, Jones C, Rosenbaum H, Stanislaw S, Burgess DL, Alexander NR, **Swanton C**; PEACE; TRACERx Renal Consortium.*Cell*. 2018 Apr 19;173(3):581-594.

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Evolution and clinical impact of co-occurring genetic alterations in advanced-stage EGFR-mutant lung cancers. Blakely CM, Watkins TBK, Wu W, Gini B, Chabon JJ, McCoach CE, McGranahan N, Wilson GA, Birkbak NJ, Olivas VR, Rotow J, Maynard A, Wang V, Gubens MA, Banks KC, Lanman RB, Caulin AF, St John J, Cordero AR, Giannikopoulos P, Simmons AD, Mack PC, Gandara DR, Husain H, Doebele RC, Riess JW, Diehn M, **Swanton C**, Bivona TG. *Nat Genet*. 2017 Dec;49(12):1693-1704.

Title: Holistic View of Cancer Genomics in GI Area

Speaker

Josep Tabernero, MD, PhD

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

Chairman

Atsushi Ohtsu, MD, PhD

Director, National Cancer Center Hospital East, 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

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MODUL-a multicenter randomized clinical trial of biomarker-driven maintenance therapy following first-line standard induction treatment of metastatic colorectal cancer: an adaptable signal-seeking approach. Schmoll HJ, Arnold D, de Gramont A, Ducreux M, Grothey A, O'Dwyer PJ, Van Cutsem E, Hermann F, Bosanac I, Bendahmane B, Mancao C, **Tabernero J**. *J Cancer Res Clin Oncol*. 2018 Jun;144(6):1197-1204.

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Combined BRAF, EGFR, and MEK Inhibition in Patients with *BRAF*^{V600E}-Mutant Colorectal Cancer. Corcoran RB, André T, Atreya CE, Schellens JHM, Yoshino T, Bendell JC, Hollebecque A, McRee AJ, Siena S, Middleton G, Muro K, Gordon MS, **Tabernero J**, Yaeger R, O'Dwyer PJ, Humblet Y, De Vos F, Jung AS, Brase JC, Jaeger S, Bettinger S, Mookerjee B, Rangwala F, Van Cutsem E. *Cancer Discov*. 2018 Apr;8(4):428-443.

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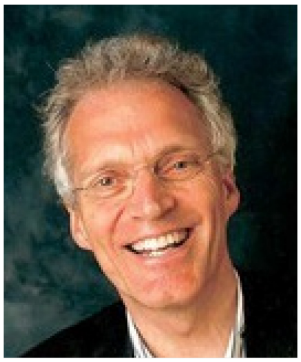
Bradley CA, Salto-Tellez M, Laurent-Puig P, Bardelli A, Rolfo C, Tabernero J, Khawaja HA, Lawler M, Johnston PG, Van Schaeybroeck S; MErCuRIC consortium. Nat Rev Clin Oncol. 2018 Jan 23;15(3):150.

Title: A One-Two Punch Model for Cancer Therapy - Exploiting Powerful Sequential Combinations by Functional Genetics



Speaker

René Bernards, PhD

Head, the Division of Molecular Carcinogenesis, the Netherlands Cancer Institute
Professor of Molecular Carcinogenesis, Utrecht University, Netherlands

Chairman

Hiroyuki Mano, MD, PhD

Director, National Cancer Center Research Institute, Japan

René Bernards, PhD

Profile

Dr. Bernards is a professor of molecular carcinogenesis at the Netherlands Cancer Institute. His laboratory uses functional genomic approaches to find vulnerabilities of cancers that can be exploited therapeutically. His laboratory identified the combination of a BRAF inhibitor and an EGFR inhibitor as effective for the treatment of *BRAF* mutant colon cancer. He also developed the first clinically used gene expression test for early breast cancer prognosis: MammaPrint. Amongst his honors are the Pezcoller Foundation award, the Ernst Bertner Award for Cancer Research from the M.D. Anderson Cancer Center and the ESMO Lifetime Achievement Award. He is also a member of the Royal Netherlands Academy of Sciences and of the AACR Academy.

Cancer remains difficult to treat, even with the new generation of targeted cancer drugs. By far the most formidable obstacle is the rapid emergence of therapy resistance.

Indeed, many of the new cancer drugs elicit powerful initial responses, leading to dramatic effects on progression free survival, but far less long-term benefit is seen in terms of overall survival. Combination therapies can help fight therapy resistance, but with an arsenal of over 1000 cancer drugs in clinical development, the number of possible combinations seems nearly endless. In his laboratory they employ functional genetic screens to find powerful combinations of cancer drugs by exploiting the concept of "synthetic lethality". Using RNA interference-based genetic screens with collections of shRNAs that target drugable gene families, they search for genes whose inactivation is particularly synergistic with clinically-relevant cancer drugs. Such screens can identify drug combinations that are far more powerful than the sum of the two single agents. They aim to understand the molecular rationale for the observed synergy between two cancer drugs. Once they have insight into the molecular mechanism, they aim to bring such rationally-designed combinations to the cancer clinic as soon as possible through collaboration with clinicians in our comprehensive cancer center

Recent Publications

ARID1A mutation sensitizes most ovarian clear cell carcinomas to BET inhibitors. Berns K, Caumanns JJ, Hijmans EM, Gennissen AMC, Severson TM, Evers B, Wisman GBA, Jan Meersma G, Lieftink C, Beijersbergen RL, Itamochi H, van der Zee AGJ, de Jong S, **Bernards R**.*Oncogene*. 2018 May 15. doi: 10.1038/s41388-018-0300-6.

An Acquired Vulnerability of Drug-Resistant Melanoma with Therapeutic Potential. Wang L, Leite de Oliveira R, Huijberts S, Bosdriesz E, Pencheva N, Brunen D, Bosma A, Song JY, Zevenhoven J, Los-de Vries GT, Horlings H, Nuijen B, Beijnen JH, Schellens JHM, **Bernards R**.*Cell*. 2018 Apr 28. pii: S0092-8674(18)30505-1

Integrative kinome profiling identifies mTORC1/2 inhibition as treatment strategy in ovarian clear cell carcinoma. Caumanns JJ, Berns K, Wisman GBA, Fehrmann RSN, Tomar T, Klip H, Meersma GJ, Hijmans EM, Gennissen A, Duiker EW, Weening D, Itamochi H, Kluin RJ, Reyners AKL, Birrer MJ, Salvesen HB, Vergote I, Van Nieuwenhuysen E, Brenton JD, Braicu EI, Kupryjanczyk J, Spiewankiewicz B, Mittempergher L, **Bernards R**, van der Zee AGJ, de Jong S. *Clin Cancer Res*. 2018 Apr 23. pii: clincanres.3060.2017.

Anti-cancer therapy: senescence is the new black. Leite de Oliveira R, **Bernards R**. *EMBO J.* 2018 May 15;37(10). pii: e99386.

A CRISPR screen identifies CDK7 as a therapeutic target in hepatocellular carcinoma. Wang C, Jin H, Gao D, Wang L, Evers B, Xue Z, Jin G, Lieftink C, Beijersbergen RL, Qin W, **Bernards R**. *Cell Res*. 2018 Mar 5. doi: 10.1038/s41422-018-0020-z.

A Computational Workflow Translates a 58-Gene Signature to a Formalin-Fixed, Paraffin-Embedded Sample-Based Companion Diagnostic for Personalized Treatment of the BRAF-Mutation-Like Subtype of Colorectal Cancers. In 't Veld SGJG, Duong KN, Snel M, Witteveen A, Beumer IJ, Delahaye LJMJ, Wehkamp D, **Bernards R**, Glas AM, Tian S. *High Throughput.* 2017 Nov 6;6(4). pii: E16.

PIM Kinases Are a Potential Prognostic Biomarker and Therapeutic Target in Neuroblastoma. Brunen D, de Vries RC, Lieftink C, Beijersbergen RL, **Bernards R**. *Mol Cancer Ther*. 2018 Apr;17(4):849-857.

Title: Liver Cancer Progression and Wnt Signaling

Hiroyuki Aburatani, MD, PhD

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

Speaker

Charles Swanton, MD, 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

Hiroyuki Aburatani, MD, PhD

Profile

Dr Aburatani is a Professor of Genome Science at Research Center for Advanced Science and Technology, The University of Tokyo, since 2001. From 2008, his group has participated in the International Cancer Genome Consortium, where he studied the genomic alterations in liver and gastric cancers. He has also contributed to cancer genomics projects in Japan, providing his expertise in genomic analysis to examine genetic and epigenetic alterations in various cancers, e.g. clonal evolution of brain tumors after alkylating agent treatment. He has co-authored more than 480 peer-reviewed scientific publications.

1980. 03 Medical School, The University of Tokyo (UTokyo)
1980. 06 Third Department of Internal Medicine, UTokyo Hospital
1983. 09 Research Associate, Third Department of Internal Medicine, UTokyo Hospital
1988. 08 Research Fellow, MIT Center for Cancer Research
1995. 01 Research Associate, Third Department of Internal Medicine, UTokyo Hospital

1999. 03 Associate Professor, RCAST, UTokyo
2001. 09 Professor, RCAST, UTokyo

They are working with systems biology and medicine to understand complex biological systems through a functional genomics approach. High throughput technology and novel algorithms are required for collecting, integrating and visualizing the enormous amount of data on gene expression, protein expression, and protein interactions arising in the wake of the Human Genome Project. Alliance with external academics and industry will be crucial to the success of the new "systems biology", that is, understanding biological systems as more than the sum of their parts.

1. Personal cancer genome: The variety of genetic and epigenetic alterations that accumulate in cancer genomes cause activation of oncogenes and inactivation of tumor suppressor genes, leading to cellular transformation. Next generation sequencing technology has enabled us to obtain individual genomic information within feasible cost and time constraints. Since 2008 his group have participated in the International Cancer Genome Consortium and are studying the genomic alterations in liver and pancreatic cancer.

2. Epigenomics: Epigenetic processes are essential for the packaging and interpretation of the genome, fundamental to normal development and cell differentiation, and increasingly recognized as being involved in human disease. Epigenetic mechanisms, which include histone modification, positioning of histone variants, nucleosome remodelling, DNA methylation, and non-coding RNAs, are considered as "cellular memory". They have applied genomic technologies, such as ChIP-sequencing, to map these epigenetic marks throughout the genome and to elucidate how these marks are written and read.

3. Translational research: Functional genomic approaches are applied to identify novel biomarkers for disease diagnostics and therapeutics.

Recent Publications

BHD-associated kidney cancer exhibits unique molecular characteristics and a wide variety of variants in chromatin remodeling genes.HasumiH, FuruyaM, TatsunoK, Yamamoto S, Baba M, HasumiY, IsonoY, Suzuki K, JikuyaR, OtakeS, Muraoka K, Osaka K, Hayashi N, MakiyamaK, Miyoshi Y, Kondo K, NakaigawaN, Kawahara T, Izumi K, TeranishiJ, YumuraY, UemuraH, NagashimaY, MetwalliAR, Schmidt LS, **Aburatani H**, LinehanWM, Yao M. *Hum MolGenet.* 2018 May 14.

Epigenetic landscape influences the liver cancer genome architecture. Hama N, TotokiY, Miura F, TatsunoK, Saito-Adachi M, Nakamura H, Arai Y, HosodaF, UrushidateT, OhashiS, Mukai W, HiraokaN, **Aburatani H**, Ito T, Shibata T. *Nat Commun*. 2018 Apr 24; 9(1):1643.

Histone demethylase JMJD1A coordinates acute and chronic adaptation to cold stress via thermogenic phospho-switch. Abe Y, Fujiwara Y, Takahashi H, Matsumura Y, Sawada T, Jiang S, NakakiR, Uchida A, Nagao N, Naito M, KajimuraS, Kimura H, Osborne TF, **Aburatani H**, Kodama T, Inagaki T, Sakai J. *Nat Commun*. 2018 Apr 19; 9(1):1566.

Overexpression of p54nrb/NONO induces differential *EPHA6*splicing and contributes to castration-resistant prostate cancer growth. Yamamoto R, OsawaT, Sasaki Y, Yamamoto S, AnaiM, Izumi K, Matsumura Y, Sakai J, **Aburatani H**, MizokamiA, Kodama T, Tanaka T. *Oncotarget*. 2018 Jan 8; 9(12):10510-10524.

EZH2 regulates neuroblastoma cell differentiation via NTRK1 promoter epigenetic modifications. Li Z, TakenobuH, SetyawatiAN, Akita N, HarutaM, Satoh S, ShinnoY, ChikaraishiK, MukaeK, AkterJ, SuginoRP, NakazawaA, NakagawaraA, **Aburatani H**, OhiraM, KamijoT. *Oncogene*. 2018 May; 37(20):2714-2727.

Identification of a novel fusion gene HMGA2-EGFR in glioblastoma. KomuroA, Raja E, Iwata C, Soda M, IsogayaK, Yuki K, InoY, MorikawaM, TodoT, **Aburatani H**, Suzuki H, RanjitM, NatsumeA, MukasaA, Saito N, Okada H, Mano H, Miyazono K, KoinumaD. *IntJ Cancer*. 2018 Apr 15; 142(8):1627-1639.