アクセスマップ

会　場：六本木アカデミーヒルズ49

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

宿泊地：グランドハイアット東京

タクシー（「タクシーベイB」とお申し付けください。）
羽田空港から約40分
品川駅・東京駅からは約20分
道路状況により混雑する場合がございます。余裕を持ってお越しください。
到着後、防災センター隣のエスカレーターで2階に上がりますと後方に
「アカデミーヒルズ」の入り口があります。

地下鉄
日比谷線　六本木駅・徒歩3分（コンコースにて直結）
大江戸線　六本木駅・徒歩6分、麻布十番駅・徒歩9分
南北線　麻布十番駅・徒歩12分
千代田線　乃木坂駅・徒歩10分

当日のご連絡は、当社団の加藤（090-8844-8565）または長谷川（080-2001-4999）にお願いします。

http://www.academyhills.com/

CHAAO Chugai Academy for Advanced Oncology

一般社団法人　中外Oncology学術振興会議
〒101-0032 東京都千代田区岩本町3-9-2 PMO 岩本町ビル8F
TEL：03-5825-2012　FAX：03-5821-2886
E-mail：chaao@chaao.or.jp　URL：http://www.chaao.or.jp/

Program

INTERNATIONAL ACADEMY FOR ADVANCED ONCOLOGY

IAAO

国際フォーラム2017

Paradigm Shift in Therapeutic Strategies and Novel Treatments for Cancer

2017年7月21日（金）12:55~17:30
22日（土）9:00~15:00
六本木アカデミーヒルズ49

CHAAO Chugai Academy for Advanced Oncology

Paradigm Shift in Therapeutic Strategies and Novel Treatments for Cancer

Friday, Jul 21, 2017　12:55 ～ 17:30

Opening Remarks P.3

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

1. Innovations in Cancer Research P.6

13:00 **Lessons Learned from the First Two Decades of Targeted Therapy**
Speaker: Bruce A. Chabner (Harvard Medical School, USA)
Chair/Moderator: Makoto Ogawa (Aichi Cancer Center, Japan)

2. New Paradigm in Epigenetics P.12

13:25 **Role of Mutations in Epigenetic Modifiers in Myeloid Malignancies and Therapeutics Response**
Speaker: Ross L. Levine (Memorial Sloan Kettering Cancer Center, USA)
Chair/Moderator: Chikashi Ishioka (Tohoku University, Japan)

14:10 **Transcriptional Regulation of Cell Identity and its Misregulation in Cancer**
Speaker: Brian J. Abraham (Whitehead Institute, USA)
Chair/Moderator: Hiroyuki Mano (The University of Tokyo, Japan)

14:55 Break

3. Next Stage in Cancer Immunotherapy P.26

15:15 **How Melanoma Responds and Resists PD-1 Blockade**
Speaker: Antoni Ribas (University of California Los Angeles, USA)
Chair/Moderator: Nagahiro Saijo (Japanese Society of Medical Oncology, Japan)

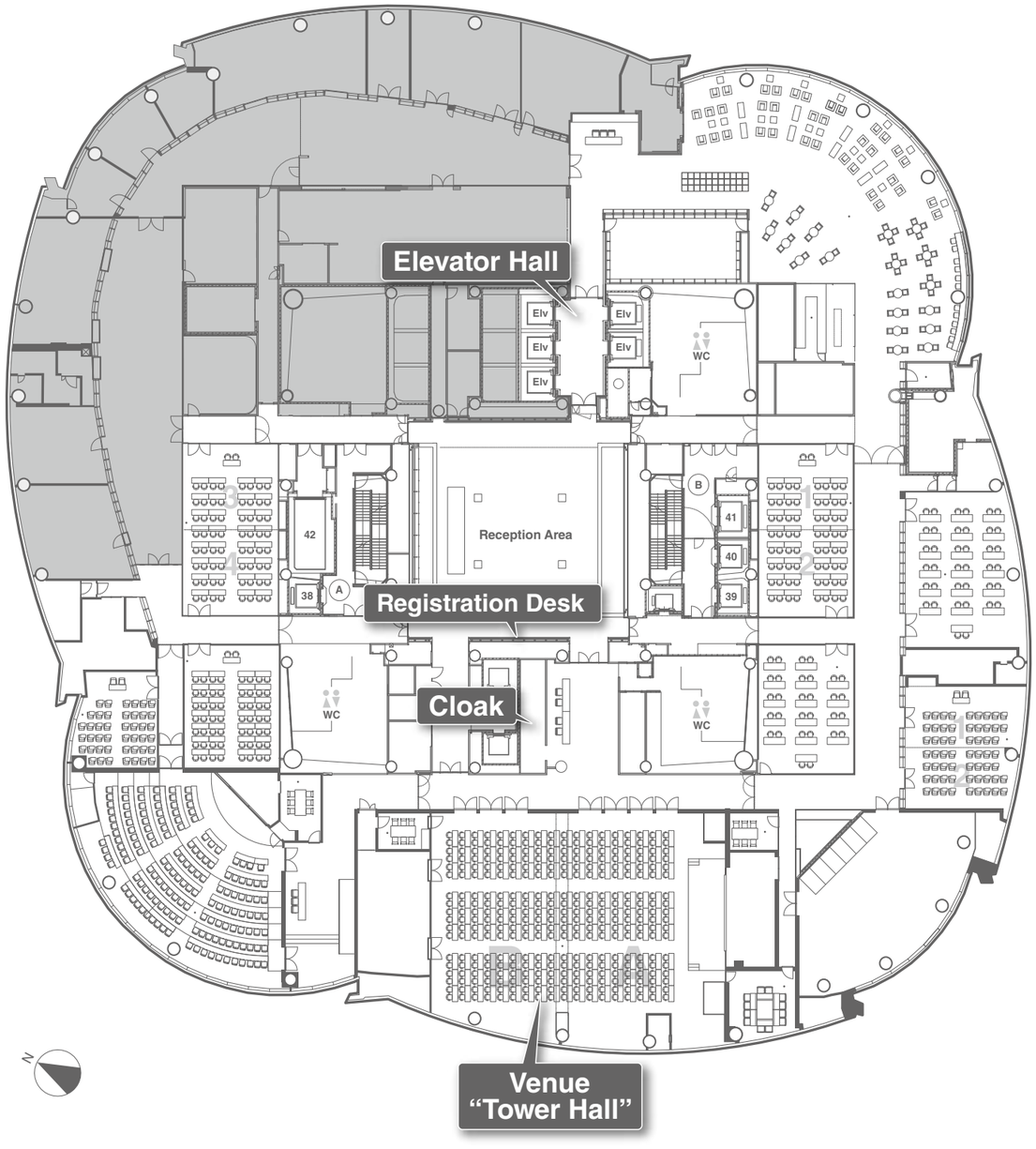
16:00 **Checkpoint Blockade for Melanoma: What's New**
Speaker: Jedd D. Wolchok (Memorial Sloan Kettering Cancer Center, USA)
Chair/Moderator: Hiroyoshi Nishikawa (National Cancer Center, Japan)

16:45 **Nutrition, Immunity and Cancer**
Speaker: Guido Kroemer (Institut National de la Santé et de la Recherche Médicale, France)
Chair/Moderator: Ryuzo Ueda (Aichi Medical University, Japan)

17:40 **RECEPTION *at Roppongi Hills Club, 51F***

オフィシャル言語 ›› 英　語
ドレスコード ›› ビジネスカジュアル

国際フォーラム2017 講演会場：六本木アカデミーヒルズ49（49階）



ウエルカム レセプション（7月21日17:40 ～）：六本木ヒルズクラブ（51階）
51階へはエレベーターをご利用ください。

Saturday, Jul 22, 2017 9:00 ～ 15:00

4. New Molecular Targeted Drugs P.46

9:00 **Allele Specific Precision Medicine for ERK-Driven Tumors**
Speaker: Neal Rosen (Memorial Sloan Kettering Cancer Center, USA)
Chair/Moderator: Mitsuaki Yoshida (Japanese Foundation For Cancer Research, Japan)

9:45 **Targeting DNA Repair in Cancer Therapy**
Speaker: Alan D. D'Andrea (Dana-Farber Cancer Institute, USA)
Chair/Moderator: Kohei Miyazono (The University of Tokyo, Japan)

10:30 **Break**

10:50 **Cyclin D-Dependent Effects of CDK4/6 Inhibitors in Cancer**
Speaker: Charles J. Sherr (St. Jude Children's Research Hospital, USA)
Chair/Moderator: Masakazu Toi (Kyoto University, Japan)

5. Cancer Genomics Impacts on Clinical Practice and Economics P.64

11:35 **Genomic Analysis of Tumors in the Clinic: Promises and Challenges**
Speaker: Anthony J. Iafrate (Harvard Medical School, USA)
Chair/Moderator: Kiyohiko Hatake (Cancer Institute Hospital, Japan)

12:20 **Lunch**

13:15 **The Clinical Outcomes and Costs of Precision Oncology**
Speaker: Lincoln D. Nadauld (Intermountain Healthcare, USA)
Chair/Moderator: Bruce A. Chabner (Harvard Medical School, USA)

14:00 **A Nation-Wide Genome Screening Consortium for New Agent Development (SCRUM-Japan)**
Speaker: Atsushi Ohtsu (National Cancer Center, Japan)
Chair/Moderator: Tomomitsu Hotta (National Cancer Center, Japan)

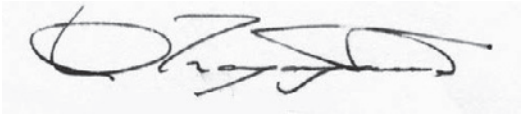
Closing Remarks

14:45 Ryuzo Ueda (Aichi Medical University, Japan)

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) 2017.

Each year at IAAO, I am delighted to see that the size of our gathering continues to grow larger each time. This year--our eighth meeting--is no exception, with more than 230 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 "Paradigm Shift in Therapeutic Strategies and Novel Treatments for Cancer". The program will focus on cancer immunotherapies, and cancer genomics and epi-genomics, which are the essential research fields in the practice of precision medicine. We will also address cancer targeted therapies including DNA repair and kinases essential for cancer growth.

The exceptional program was organized through the active discussions and hard work of the IAAO Advisory Board members, namely Dr. Chabner, Dr. Johnston, Dr. Fujiwara,

Dr. Hatake, Dr. Ishioka, Dr. Kitagawa, Dr. Mano, Dr. Toi and Dr. Ueda. I sincerely appreciate and respect the leadership and dedication of these nine board members.

Regretfully, however, I must make one very sad announcement regarding the advisory board. Last month, long-time member, Dr. Patrick Johnston, vice-chancellor of Queen's University in Belfast, passed away suddenly at the age of 58. Dr. Johnston was regarded as one of the world's leading cancer researchers, with a focus for over 25 years on understanding the mechanisms of drug resistance to therapeutic agents. His commitment and leadership made a tremendous contribution to global health as well as to IAAO. On behalf of the Chugai Academy for Advanced Oncology (CHAAO), I would like to extend our deepest sympathies and condolences to Dr. Johnston's family, friends and colleagues.

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.

Session 1

Innovations in Cancer Research

1-1. Lessons Learned from the First Two Decades of Targeted Therapy

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

Title: Lessons Learned from the First Two Decades of Targeted Therapy

Speaker

Bruce A. Chabner, MD

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

Chairman

Makoto Ogawa, MD

Emeritus President, Aichi 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.

Recent Publications

Regarding "Oncology Drug Approvals: Evaluating Endpoints and Evidence in an Era of Breakthrough Therapies". **Chabner BA**. *Oncologist*. 2017 Jun 2. pii: theoncologist. 2017-0202.

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.

Let This Be Our New Year's Pledge. **Chabner BA**, Murphy MJ. *Oncologist*. 2017 Jan;22(1):1-2.

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.

Session 2

New Paradigm in Epigenetics

2-1. Role of Mutations in Epigenetic Modifiers in Myeloid Malignancies and Therapeutics Response

Speaker: Ross L. Levine (Memorial Sloan Kettering Cancer Center, USA)

2-2. Transcriptional Regulation of Cell Identity and its Misregulation in Cancer

Speaker: Brian J. Abraham (Whitehead Institute, USA)

Title: Role of Mutations in Epigenetic Modifiers in Myeloid Malignancies and Therapeutics Response

Speaker

Ross L. Levine, MD

Associate Member of Human Oncology and Pathgenesis Program, Attending Physician of Leukemia Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, USA
Associate Professor of Medicine, Weill Cornell Medical College, USA

Chairman

Chikashi Ishioka, MD

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

Ross L. Levine, MD

Profile

Dr. Levine is a physician-scientist focused on researching and treating blood and bone marrow cancers, including acute myeloid leukemia and the chronic myeloproliferative neoplasms polycythemia vera, essential thrombocytosis, and primary myelofibrosis.

He began medical school at The Johns Hopkins School of Medicine planning to become an academic clinical physician. One summer, to broaden his experience, he worked in the laboratory of pathologist Lora Hedrick-Ellenson, who was studying endometrial cancer. The research was fascinating, more interesting to me than any clinical experience. That brief stint in the lab caused me to consider someday becoming a physician-scientist.

Over the next four years he finished medical school and trained in internal medicine at Massachusetts General Hospital. In 2002, during his clinical fellowship in hematology/oncology at Dana-Farber Cancer Institute, he developed a specific interest

in caring for patients with leukemia; however, he soon learned that most patients are not cured with existing treatments.

This led him the following year to enter the laboratory of Gary Gilliland, a leader in leukemia genetics and a fantastic mentor. His research focused on myeloproliferative neoplasms — blood cancers — the cause of which had eluded researchers. He hoped that by identifying the cause of these cancers he could develop better therapies.

Awards and Honors: Pershing Square Sohn Prize for Cancer Research (2014), Laurence Joseph Dineen Chair in Leukemia Research (2013), Leukemia and Lymphoma Society Scholar (2012), Boyer Award for Clinical Research, Memorial Sloan Kettering Cancer Center (2011), Howard Hughes Medical Institute Early Career Award (2007), American Society of Hematology Basic Research Fellow Award (2006), American Society of Clinical Oncology Young Investigator Award (2006), American Society of Hematology 2016 Scientific Program co-chair Medical and Scientific Advisory Board, Leukemia and Lymphoma Society

Education: MD, Johns Hopkins University School of Medicine

Recent Publications

Enasidenib induces acute myeloid leukemia cell differentiation to promote clinical response. Amatangelo MD, Quek L, Shih A, Stein EM, Roshal M, David MD, Marteyn B, Rahnamay Farnoud N, de Botton S, Bernard OA, Wu B, Yen KE, Tallman MS, Papaemmanuil E, Penard-Lacronique V, Thakurta A, Vyas P, **Levine RL.** *Blood*. 2017 Jun 6. pii: blood-2017-04-779447.

Functional screen of MSI2 interactors identifies an essential role for SYNCRIP in myeloid leukemia stem cells. Vu LP, Prieto C, Amin EM, Chhangawala S, Krivtsov A, Calvo-Vidal MN, Chou T, Chow A, Minuesa G, Park SM, Barlowe TS, Taggart J, Tivnan P, Deering RP, Chu LP, Kwon JA, Meydan C, Perales-Paton J, Arshi A, Gönen M, Famulare C, Patel M, Paietta E, Tallman MS, Lu Y, Glass J, Garret-Bakelman FE, Melnick A, **Levine R**, Al-Shahrour F, Järås M, Hacohen N, Hwang A, Garippa R, Lengner CJ, Armstrong SA, Cerchietti L, Cowley GS, Root D, Doench J, Leslie C, Ebert BL, Kharas MG. *Nat Genet*. 2017 Jun;49(6):866-875.

Epigenetic Identity in AML Depends on Disruption of Non-promoter Regulatory Elements and is Affected by Antagonistic Effects of Mutations in Epigenetic Modifiers. Glass J, Hassane DC, Wouters B, Kunimoto H, Avellino R, Garrett-Bakelman FE, Guryanova OA, Bowman R, Redlich S, Intlekofer A, Meydan C, Qin T, Fall MP, Alonso A, Guzman ML, Valk PJ, Thompson CB, **Levine RL**, Elemento O, Delwel R, Melnick A, Figueroa ME. *Cancer Discov*. 2017 Apr 13. pii: CD-16-1032.

Cardiovascular disease: Commonality with cancer. Tall AR, **Levine RL.** *Nature*. 2017 Mar 2;543(7643):45-47.

Multicolor Flow Cytometry and Multigene Next-Generation Sequencing Are Complementary and Highly Predictive for Relapse in Acute Myeloid Leukemia after Allogeneic Transplantation. Getta BM, Devlin SM, **Levine RL**, Arcila ME, Mohanty AS, Zehir A, Tallman MS, Giralt SA, Roshal M. *Biol Blood Marrow Transplant*. 2017 Mar 15. pii: S1083-8791(17)30336-1.

TET2 in Normal and Malignant Hematopoiesis. Bowman RL, **Levine RL.** *Cold Spring Harb Perspect Med*. 2017 Feb 27. pii: a026518

Combination Targeted Therapy to Disrupt Aberrant Oncogenic Signaling and Reverse Epigenetic Dysfunction in *IDH2*- and *TET2*-Mutant Acute Myeloid Leukemia. Shih AH, Meydan C, Shank K, Garrett-Bakelman FE, Ward PS, Intlekofer AM, Nazir A, Stein EM, Knapp K, Glass J, Travins J, Straley K, Gliser C, Mason CE, Yen K, Thompson CB, Melnick A, **Levine RL.** *Cancer Discov.* 2017 Feb 13. doi: 10.1158/2159-8290.

CD99 is a therapeutic target on disease stem cells in myeloid malignancies. Chung SS, Eng WS, Hu W, Khalaj M, Garrett-Bakelman FE, Tavakkoli M, **Levine RL**, Carroll M, Klimek VM, Melnick AM, Park CY. *Sci Transl Med*. 2017 Jan 25;9(374). pii: eaaj2025.

Aid is a key regulator of myeloid/erythroid differentiation and DNA methylation in hematopoietic stem/progenitor cells. Kunimoto H, McKenney AS, Meydan C, Shank K, Nazir A, Rapaport F, Durham B, Garrett-Bakelman FE, Pronier E, Shih AH, Melnick A, Chaudhuri J, **Levine RL**. *Blood*. 2017 Mar 30;129(13):1779-1790.

DNMT3A mutations promote anthracycline resistance in acute myeloid leukemia via impaired nucleosome remodeling. Guryanova OA, Shank K, Spitzer B, Luciani L, Koche RP, Garrett-Bakelman FE, Ganzel C, Durham BH, Mohanty A, Hoermann G, Rivera SA, Chramiec AG, Pronier E, Bastian L, Keller MD, Tovbin D, Loizou E, Weinstein AR, Gonzalez AR, Lieu YK, Rowe JM, Pastore F, McKenney AS, Krivtsov AV, Sperr WR, Cross JR, Mason CE, Tallman MS, Arcila ME, Abdel-Wahab O, Armstrong SA, Kubicek S, Staber PB, Gönen M, Paietta EM, Melnick AM, Nimer SD, Mukherjee S, **Levine RL**. *Nat Med.* 2016 Dec;22(12):1488-1495.

Genomics of primary chemoresistance and remission induction failure in paediatric and adult acute myeloid leukaemia. Brown FC, Cifani P, Drill E, He J, Still E, Zhong S, Balasubramanian S, Pavlick D, Yilmazel B, Knapp KM, Alonzo TA, Meshinchi S, Stone RM, Kornblau SM, Marcucci G, Gamis AS, Byrd JC, Gonen M, **Levine RL**, Kentsis A. *Br J Haematol*. 2017 Jan;176(1):86-91.

Title: Transcriptional Regulation of Cell Identity and its Misregulation in Cancer

Brian J. Abraham, PhD

Postdoctoral Fellow, Laboratory of Richard Young, Whitehead Institute for Biomedical Research, USA

Speaker

Hiroyuki Mano, MD, PhD

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

Chairman

Abstract

Super-enhancer drives cell identity.

- ✓ Cell identity is controlled by the genes that are transcribed.
- ✓ Transcription is controlled by the binding of transcription factor proteins to enhancers.
- ✓ Super-enhancers are clusters of enhancers that drive expression of genes that control and define cell identity, including well-characterized oncogenes in tumor cells.

Tumor cells acquire somatic mutations that generate oncogenic enhancers

- ✓ Tumor cells have super-enhancers that are inherited from healthy cells and super-enhancers that are acquired during tumorigenesis.
- ✓ Examples of mutations we discovered that nucleate enhancers at oncogenes.

Transcriptional inhibition blocks production from tumor dependency genes

- ✓ Transcriptional inhibitors THZ1 and THZ531 kill cancer cells i*n vivo* and *in vivo.*

- ✓ Transcriptional inhibitors affect gene expression programs.
- ✓ The genes most sensitive to THZ1 are involved in transcription and are super-enhancer-associated.
- ✓ The genes most sensitive to THZ531 are involved in DNA damage-response.
- ✓ Addition of transcriptional inhibitors to other targeted therapies hinders acquisition of resistance.

Brian J. Abraham, PhD

Profile

Dr. Abraham is a postdoctoral fellow in the lab of Professor Richard A. Young at the Whitehead Institute for Biomedical Research, where he is the Hope Funds for Cancer Research Grillo-Marxuach Family Fellow.

His studies focus on the molecular mechanisms that control gene transcription in mammalian cells, the use of these mechanisms in disease, and understanding how inhibitors of transcriptional components affect diseased cells. Upon joining the Young lab, he made fundamental contributions to the concept of super-enhancers and their functions. His recent work has involved characterizing transcriptional enhancers and super-enhancers that drive key tumor cell dependency genes, as well as the study of a first-in-class inhibitor of the transcriptional kinase CDK7, which has entered clinical trials.

He earned his undergraduate degrees in Information Technology and Medical Informatics from the Rochester Institute of Technology and his Ph.D. in Bioinformatics from Boston University performing his thesis research at the U.S. National Institutes of Health.

2008 BS in Medical Informatics / Rochester Institutes of Technology

2013 PhD in Bioinformatics / Boston University.

Recent Publications

A CD47-associated super-enhancer links pro-inflammatory signalling to CD47 upregulation in breast cancer. Betancur PA, **Abraham BJ**, Yiu YY, Willingham SB, Khameneh F, Zarnegar M, Kuo AH, McKenna K, Kojima Y, Leeper NJ, Ho P, Gip P, Swigut T, Sherwood RI, Clarke MF, Somlo G, Young RA, Weissman IL. *Nat Commun*. 2017 Apr 5;8:14802.

Activation of the *LMO2* oncogene through a somatically acquired neomorphic promoter in T-cell acute lymphoblastic leukemia. Rahman S, Magnussen M, León TE, Farah N, Li Z, **Abraham BJ**, Alapi KZ, Mitchell RJ, Naughton T, Fielding AK, Pizzey A, Bustraan S, Allen C, Popa T, Pike-Overzet K, Garcia-Perez L, Gale RE, Linch DC, Staal FJ, Young RA, Look AT, Mansour MR. *Blood*. 2017 Mar 7. pii: blood-2016-09-742148.

Integrated genomic analyses of de novo pathways underlying atypical meningiomas.Harmancı AS, Youngblood MW, Clark VE, Coşkun S, Henegariu O,

Duran D, Erson-Omay EZ, Kaulen LD, Lee TI, **Abraham BJ**, Simon M, Krischek B, Timmer M, Goldbrunner R, Omay SB, Baranoski J, Baran B, Carrión-Grant G, Bai H, Mishra-Gorur K, Schramm J, Moliterno J, Vortmeyer AO, Bilgüvar K, Yasuno K, Young RA, Günel M. *Nat Commun*. 2017 Feb 14;8:14433.

Small genomic insertions form enhancers that misregulate oncogenes. **Abraham BJ**, Hnisz D, Weintraub AS, Kwiatkowski N, Li CH, Li Z, Weichert-Leahey N, Rahman S, Liu Y, Etchin J, Li B, Shen S, Lee TI, Zhang J, Look AT, Mansour MR, Young RA. *Nat Commun*. 2017 Feb 9;8:14385

Covalent targeting of remote cysteine residues to develop CDK12 and CDK13 inhibitors. Zhang T, Kwiatkowski N, Olson CM, Dixon-Clarke SE, **Abraham BJ**, Greifenberg AK, Ficarro SB, Elkins JM, Liang Y, Hannett NM, Manz T, Hao M, Bartkowiak B, Greenleaf AL, Marto JA, Geyer M, Bullock AN, Young RA, Gray NS. *Nat Chem Biol.* 2016 Oct;12(10):876-84.

Session 3

Next Stage in Cancer Immunotherapy

3-1. How Melanoma Responds and Resists PD-1 Blockade

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

3-2. Checkpoint Blockade for Melanoma: What's New

Speaker: Jedd D. Wolchok (Memorial Sloan Kettering Cancer Center, USA)

3-3. Nutrition, Immunity and Cancer

Speaker: Guido Kroemer
(Institut National de la Santé et de la Recherche Médicale, France)

Title: How Melanoma Responds and Resists PD-1 Blockade

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

Speaker

Nagahiro Saijo, MD, PhD

Executive Officer of Japanese Society of Medical Oncology, Japan

Chairman

Antoni Ribas, MD, PhD

Profile

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

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

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

Recent Publications

SnapShot: Immune Checkpoint Inhibitors. Abril-Rodriguez G, **Ribas A.** *Cancer Cell.* 2017 Jun 12;31(6):848-848.

Gene Expression Profiling in *BRAF*-Mutated Melanoma Reveals Patient Subgroups With Poor Outcomes to Vemurafenib That May Be Overcome by Cobimetinib Plus Vemurafenib. Wongchenko MJ, McArthur GA, Dréno B, Larkin J, Ascierto PA, Sosman J, Andries L, Kockx M, Hurst SD, Caro I, Rooney I, Hegde PS, Molinero L, Yue H, Chang I, Amler LC, Yan Y, **Ribas A**. *Clin Cancer Res*. 2017 May 23

Interferon Receptor Signaling Pathways Regulating PD-L1 and PD-L2 Expression. Garcia-Diaz A, Shin DS, Moreno BH, Saco J, Escuin-Ordinas H, Rodriguez GA, Zaretsky JM, Sun L, Hugo W, Wang X, Parisi G, Saus CP, Torrejon DY, Graeber TG, Comin-Anduix B, Hu-Lieskovan S, Damoiseaux R, Lo RS, **Ribas A.** *Cell Rep*. 2017 May 9;19(6):1189-1201.

Targeted agents and immunotherapies: optimizing outcomes in melanoma. Luke JJ, Flaherty KT, **Ribas A**, Long GV. *Nat Rev Clin Oncol*. 2017 Apr 4.

Preparation of peptide-MHC and T-cell receptor dextramers by biotinylated dextran doping. Bethune MT, Comin-Anduix B, Hwang Fu YH, **Ribas A,** Baltimore D. *Biotechniques.* 2017 Mar 1;62(3):123-130.

Primary, Adaptive, and Acquired Resistance to Cancer Immunotherapy. Sharma P, Hu-Lieskovan S, Wargo JA, **Ribas A**. *Cell*. 2017 Feb 9;168(4):707-723.

MAPK pathway inhibition induces MET and GAB1 levels, priming BRAF mutant melanoma for rescue by hepatocyte growth factor. Caenepeel S, Cooke K, Wadsworth S, Huang G, Robert L, Moreno BH, Parisi G, Cajulis E, Kendall R, Beltran P, **Ribas A**, Coxon A, Hughes PE. *Oncotarget*. 2017 Mar 4; 8(11): 17795-17809.

Genomic and Transcriptomic Features of Response to Anti-PD-1 Therapy in Metastatic Melanoma. Hugo W, Zaretsky JM, Sun L, Song C, Moreno BH, Hu-Lieskovan S, Berent-Maoz B, Pang J, Chmielowski B, Cherry G, Seja E, Lomeli S, Kong X, Kelley MC, Sosman JA, Johnson DB, **Ribas A**, Lo RS. *Cell.* 2017 Jan 26; 168(3):542.

New Combination Strategies Using Programmed Cell Death 1/Programmed Cell Death Ligand 1 Checkpoint Inhibitors as a Backbone. Hu-Lieskovan S, **Ribas A**. *Cancer J*. 2017 Jan/Feb; 23(1):10-22.

Infiltration of CD8 T Cells and Expression of PD-1 and PD-L1 in Synovial Sarcoma. Nowicki TS, Akiyama R, Huang RR, Shintaku IP, Wang X, Tumeh PC, Singh A, Chmielowski B, Denny C, Federman N, **Ribas A**. *Cancer Immunol Re*s. 2017 Feb;5(2):118-126.

Primary Resistance to PD-1 Blockade Mediated by JAK1/2 Mutations. Shin DS, Zaretsky JM, Escuin-Ordinas H, Garcia-Diaz A, Hu-Lieskovan S, Kalbasi A, Grasso CS,

Hugo W, Sandoval S, Torrejon DY, Palaskas N, Rodriguez GA, Parisi G, Azhdam A, Chmielowski B, Cherry G, Seja E, Berent-Maoz B, Shintaku IP, Le DT, Pardoll DM, Diaz LA Jr, Tumeh PC, Graeber TG, Lo RS, Comin-Anduix B, **Ribas A**.*Cancer Discov*. 2017 Feb;7(2):188-201.

What does PD-L1 positive or negative mean? **Ribas A**, Hu-Lieskovan S. *J Exp Med*. 2016 Dec 12; 213(13):2835-2840.

Title: Checkpoint Blockade for Melanoma: What's New

Speaker

Jedd D. Wolchok, MD, PhD

Lloyd J. Old/Virginia and Daniel K. Ludwig Chair in Clinical Investigation, Chief of Melanoma & Immunotherapeutics Service, Director of Parker Institute for Cancer Immunotherapy at Memorial Sloan Kettering Cancer Center, USA
Associate Director of Ludwig Center for Cancer Immunotherapy, Member of Ludwig Cancer Research, USA
Professor of Medicine, Weill Medical College of Cornell University, USA

Chairman

Hiroyoshi Nishikawa, MD, PhD

Director, Division of Cancer Immunology, Research Institute, Exploratory Oncology Research & Clinical Trial Center, National Cancer Center, Japan

Jedd Wolchok, MD, PhD

Profile

Dr. Wolchok received his undergraduate degree from Princeton University and both M.D and Ph.D. from New York University, where he also fulfilled his residency program. He completed his fellowship at MSK and remained on faculty with an appointment in the Melanoma Immunotherapeutics Service.

Dr. Wolchok is Chief of the Melanoma and Immunotherapeutics Service and holds The Lloyd J. Old Chair in Clinical Investigation at Memorial Sloan Kettering Cancer Center (MSK) with an expertise in the treatment of metastatic melanoma. His additional appointments include: Head of the Swim Across America - Ludwig Collaborative Laboratory; Associate Director of the Ludwig Center for Cancer Immunotherapy (LCCI); Director of the Parker Institute for Cancer Immunotherapy at MSK. He has helped establish MSK as a leader in the discovery and treatment of cancers with novel immunotherapies.

Dr. Wolchok was instrumental in the clinical development leading to the approval of ipilimumab for advanced melanoma. He has been at the forefront of cancer immunotherapy, as an active clinician scientist exploring immunotherapy and as a principal investigator in several pivotal clinical trials, including the phase III trial that led to the FDA approval of ipilimumab + nivolumab as a treatment for patients with advanced melanoma. He supervises an R01-funded basic science laboratory which is focused on investigating novel immunotherapeutic agents in pre-clinical mouse models. In 2011, he established the Immunotherapeutics Clinical Core, a specialized phase 1-2 outpatient unit at MSK that is focused on the conduct of novel immunotherapy trials, with a specific emphasis on pharmacodynamic biomarker identification. This group treats patients with a broad spectrum of malignancies.

In 2011, Dr. Wolchok was named Director of the Cancer Vaccine Collaborative (CVC), a joint initiative between the Cancer Research Institute (CRI) and the Ludwig Institute for Cancer Research (LICR). The CVC is an international academic clinical trials network dedicated to developing safe and effective therapeutic vaccines and other immunotherapies for cancer. The CVC has conducted nearly 50 early-phase clinical trials of different therapeutic cancer vaccines involving more than 950 patients with melanoma, lung, ovarian, prostate, breast, and other cancers. In 2015, Dr. Wolchok was elected to the ASCO Board of Directors.

Dr. Wolchok has been recognized for his momentous career throughout the years and has received several of awards including the Melanoma Research Foundation – Humanitarian Award in 2010, the Melanoma International Foundation's Doctor of the Year award in 2012, and the Live, Love, Laugh Foundation and was named the Virginia and Daniel K. Ludwig Chair for Clinical Investigation in 2013. He has been recognized with the American Association for Cancer Research Richard and Hinda Rosenthal Memorial Award, the Giants of Cancer Care in Melanoma Award and received the AICF Prize for Scientific excellence in Medicine. Most recently, he has received the Melvin and Sylvia Griem Lectureship in Molecular and Cellular Oncology; the Alumni Achievement Award in Clinical and Translational Science from NYU and the Alfred Taubman Prize for Excellence in Translational Medical Research.

Recent Publications

Curbing Tregs' (Lack of) Enthusiasm. Merghoub T, **Wolchok JD**. *Cell*. 2017 Jun 1;169(6):981-982.

Chromatin states define tumour-specific T cell dysfunction and reprogramming.Philip M, Fairchild L, Sun L, Horste EL, Camara S, Shakiba M, Scott AC, Viale A, Lauer P, Merghoub T, Hellmann MD, **Wolchok JD**, Leslie CS, Schietinger A. *Nature*. 2017 May 25;545(7655):452-456.

T-cell invigoration to tumour burden ratio associated with anti-PD-1 response. Huang AC, Postow MA, Orlowski RJ, Mick R, Bengsch B, Manne S, Xu W, Harmon S, Giles JR, Wenz B, Adamow M, Kuk D, Panageas KS, Carrera C, Wong P, Quagliarello F, Wubbenhorst B, D'Andrea K, Pauken KE, Herati RS, Staupe RP, Schenkel JM, McGettigan S, Kothari S, George SM, Vonderheide RH, Amaravadi RK, Karakousis GC, Schuchter LM, Xu X, Nathanson KL, **Wolchok JD**, Gangadhar TC, Wherry EJ. *Nature*. 2017 Apr 10.
Neutrophil to Lymphocyte Ratio is Associated With Outcome During Ipilimumab Treatment. Cassidy MR, Wolchok RE, Zheng J, Panageas KS, **Wolchok JD**, Coit D, Postow MA, Ariyan C. *EBioMedicine*. 2017 Mar 24. pii: S2352-3964(17)30125-1.

Patient perspectives on ipilimumab across the melanoma treatment trajectory.Shuk E, Shoushtari AN, Luke J, Postow MA, Callahan M, Harding JJ, Roth KG, Flavin M, Granobles A, Christian J, Gold G, Schoenhammer M, Gordon M, Cimaglia N, Dyson R, Goodman-Davis N, Colgan MN, Jefferson IS, Munhoz R, D'Angelo S, **Wolchok JD**, Chapman P, Chi P, Carvajal RD, Hay JL. *Support Care Cancer*. 2017 Mar 1.

Combination immunotherapy: a road map.Ott PA, Hodi FS, Kaufman HL, Wigginton JM, **Wolchok JD**. *J Immunother Cancer*. 2017 Feb 21;5:16.

Intratumoral modulation of the inducible co-stimulator ICOS by recombinant oncolytic virus promotes systemic anti-tumour immunity. Zamarin D, Holmgaard RB, Ricca J, Plitt T, Palese P, Sharma P, Merghoub T, **Wolchok JD**, Allison JP. *Nat Commun*. 2017 Feb 13;8:14340.

Peripheral CD8 effector-memory type 1 T-cells correlate with outcome in ipilimumab-treated stage IV melanoma patients. Wistuba-Hamprecht K, Martens A, Heubach F, Romano E, Geukes Foppen M, Yuan J, Postow M, Wong P, Mallardo D, Schilling B, Di Giacomo AM, Khammari A, Dreno B, Maio M, Schadendorf D, Ascierto PA, **Wolchok JD**, Blank CU, Garbe C, Pawelec G, Zeide B. *Eur J Cancer*. 2017 Mar;73:61-70.

Safety Profile of Nivolumab Monotherapy: A Pooled Analysis of Patients With Advanced Melanoma. Weber JS, Hodi FS, **Wolchok JD**, Topalian SL, Schadendorf D, Larkin J, Sznol M, Long GV, Li H, Waxman IM, Jiang J, Robert C. *J Clin Oncol.* 2017 Mar;35(7):785-792.

Efficacy and Safety of Nivolumab Alone or in Combination With Ipilimumab in Patients With Mucosal Melanoma: A Pooled Analysis. D'Angelo SP, Larkin J, Sosman JA, Lebbé C, Brady B, Neyns B, Schmidt H, Hassel JC, Hodi FS, Lorigan P, Savage KJ, Miller WH Jr, Mohr P, Marquez-Rodas I, Charles J, Kaatz M, Sznol M, Weber JS, Shoushtari AN, Ruisi M, Jiang J, **Wolchok JD**. *J Clin Oncol.* 2017 Jan 10;35(2):226-235.

Health-related quality of life with adjuvant ipilimumab versus placebo after complete resection of high-risk stage III melanoma (EORTC 18071): secondary outcomes of a multinational, randomised, double-blind, phase 3 trial. Coens C, Suciu S, Chiarion-Sileni V, Grob JJ, Dummer R, **Wolchok JD**, Schmidt H, Hamid O, Robert C, Ascierto PA, Richards JM, Lebbé C, Ferraresi V, Smylie M, Weber JS, Maio M, Bottomley A, Kotapati S, de Pril V, Testori A, Eggermont AM. *Lancet Onco*l. 2017 Mar;18(3):393-403.

Morphological characterization of colorectal cancers in The Cancer Genome Atlas reveals distinct morphology-molecular associations: clinical and biological implications. Shia J, Schultz N, Kuk D, Vakiani E, Middha S, Segal NH, Hechtman JF, Berger MF, Stadler ZK,

Title: Nutrition, Immunity and Cancer

Speaker

Guido Kroemer, MD, PhD

Director of Apoptosis, Cancer and Immunology at Institut National de la Santé et de la Recherche Médcale (INSERM), France
Professor of Faculty of Medicine, University of Paris Descarte, France
Director of the Metabolomics facility of the Institut Gustave Roussy, France

Chairman

Ryuzo Ueda, MD, PhD

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

Abstract

Quantitative and qualitative aspects of nutrition have a profound effect on leukocytes, thereby affecting pro-inflammatory carcinogenic effects or anticancer immune responses. As a result, nutrition affects the incidence, natural progression and therapeutic response of malignant disease, both in humans and in preclinical models. Here, we discuss the molecular mechanisms through which alimentary cues modulates metabolic, microbial and neuroendocrine circuitries that affect the probability to develop premalignant lesions, to progress to clinically manifest disease and to respond to therapeutic intervention. For this, we will examine each of the connections that compose the triangle composed by nutrition, immune/inflammatory reactions and cancer, while focusing on the mechanistic aspects of this relationship.

Guido Kroemer, MD, PhD

Profile

Dr. Kroemer is currently Professor at the Faculty of Medicine of the University of Paris Descartes, Director of the research team "Apoptosis, Cancer and Immunity" of the French Medical Research Council (INSERM), Director of the Metabolomics and Cell Biology platforms of the Gustave Roussy Comprehensive Cancer Center, and Hospital Practitioner at the Hôpital Européen George Pompidou, Paris, France. He is also a Foreign Adjunct Professor at the Karolinska Institute, Stockholm, Sweden.

Prior to joining INSERM (1994), Dr. Kroemer was Senior Scientist of the European Community at the Spanish National Research Council (CSIC), at the National Center of Molecular Biology (1990-1992) and at the National Center of Biotechnology (1993). Dr. Kroemer did his post-doctoral training at the Collège de France, Nogent-sur-Marne (1988-1989) and at the University of Innsbruck, Austria, after receiving his PhD/MD degree at the same University in 1985. He also holds a PhD degree in Molecular Biology (Autonomous University of Madrid, 1992).

Dr. Kroemer has made important contributions to medical research through his groundbreaking work in the fields of cell biology and cancer research. He is best known for the discovery that the permeabilization of mitochondrial membranes constitutes a decisive step in programmed cell death. Kroemer has explored the fine mechanisms of mitochondrial cell death control, the molecular pathways that explain the inhibition of cell death in cancer cells, upstream of or at the level of mitochondria, and the mechanisms that make cancer cell death immunogenic. His work has had far reaching implications for the comprehension, detection and therapeutic manipulation of cellular demise. He has published some 1050 papers including in Science (12x), Cell (10x), Nature (5x), Nature Medicine (14x), Journal of Experimental Medicine (25x), EMBO Journal (18x), Journal of Clinical Investigation (15x), Molecular Cell (12x), Nature Cell Biology (11x), Cell Research (9x), Immunity (7x), Cell Metabolism (5x), Journal of Cell Biology (5x), Cancer Cell (4x), Science Translational Medicine (3x), Nature Communications (2x), Nature Structural Biology (2x), Proceedings of the National Academy of Sciences of the USA (2x), and New England Journal of Medicine.

Dr. Kroemer’s contributions have been recognized with numerous awards, including the Monika Kutzner Prize of the Berlin-Brandenburg Academy of Sciences (1998), the Gallet & Breton Prize of the French Academy of Medicine (1999), the Descartes Prize of the European Union (2006), the Carus Medal of the German Academy of Sciences (2007), the Grand Prix Mergier-Bourdeix of the French Academy of Sciences (2007), the Lucien Dautrebande Prize of the Belgian Royal Academy of Medicine (2009), the Duquesne Prize of the French National League against Cancer (2010), the "Coup d'Elan" Prize of the Bettencourt-Schueller Foundation (2011), the Léopold Griffuel Prize of the French Association for Cancer Research (2012), an Advanced Investigator Award from the European Research Council (2013), the Mitjavile Prize of the French Academy of Medicine (2014), the Galien Prize for Pharmacological Resarch (2015), the Grand Prix Claude Bernard of the City of Paris (2016), and the Brupbacher Prize for Cancer Research (2017), among others.

Dr. Kroemer currently serves on the Editorial Boards of Cell Death & Differentiation, Cell Research, EMBO Journal, EMBO Molecular Medicine, Oncogene, Oncotarget, Molecular & Cellular Biology, and Science Signaling. Kroemer is also the founding

Editor-in-Chief of five journals: Cell Death & Disease, Cell Stress, OncoImmunology, Microbial Cell, and Molecular & Cellular Oncology. He is member of the European Molecular Biology Organization (EMBO), German Academy of Sciences (Leopoldina), Austrian Academy of Sciences, Academia Europaea, European Academy of Sciences (EAS), European Academy of Sciences and Arts (EASA), European Academy of Cancer Sciences (EACS), and Institut Universitaire de France (IUF). He is the Director of the Paris Alliance of Cancer Research Institutes (PACRI), the Founding Director of the European Research Institute for Integrated Cellular Pathology (ERI-ICP), the Director of the LabEx Immuno-Oncology, and the Founding President of the European Academy of Tumor Immunology (EATI).

Five major publications

Autophagy-dependent anticancer immune responses induced by chemotherapeutic agents in mice. Michaud M, Martin I, Sukkuwala A, Adjemian S, Ma Y, Pellegati P, Shen S, Kepp O, Scoazec M, Mignot G, Rello-Varona S, Tailler M, Menger L, Vacchelli E, Galluzzi L, Ghiringhelli F, Galluzzi L, di Virgilio F, Zitvogel L, **Kroemer G**. *Science*. 2011 Dec16;334:1573-1577.

An immunosurveillance mechanism controls cancer cell ploidy. Senovilla L, Vitale I, Martins I, Tailler M, Pailleret C, Michaud M, Galluzzi L, Adjemian S, Kepp O, Niso-Santano M, Shen S, Mariño G, Criollo A, Boilève A, Job B, Ladoire S, Ghiringhelli F, Sistigu A, Yamazaki T, Rello-Varona S, Locher C, Poirier-Colame V, Talbot M, Valent A, Berardinelli F, Antoccia A, Ciccosanti F, Fimia GM, Piacentini M, Fueyo A, Messina NL, Li M, Chan CJ, Sigl V, Pourcher G, Ruckenstuhl C, Carmona-Gutierrez D, Lazar V, Penninger JM, Madeo F, López-Otín C, Smyth MJ, Zitvogel L, Castedo M, **Kroemer G**. *Science*. 2012 Sep 28;337(6102):1678-84.

Anticancer chemotherapy-induced intratumoral recruitment and differentiation of antigen-presenting cells.Ma Y, Adjemian S, Mattarollo SR, Yamazaki T, Aymeric L, Yang H, Portela Catani JP, Hannani D, Duret H, … Van Endert P, Solary E, Smyth MJ, Zitvogel L, **Kroemer G**. *Immunity*. 2013 Apr 18;38(4):729-41.

Essential role of formyl peptide receptor 1 in anticancer chemotherapy*.* Vacchelli E, Ma Y, Baracco EE, Sistigu A, Enot DP, Pietrocola F, Yang H, Adjemian S, Chaba K, Semeraro M, Signore M, de Ninno A, Lucarini V, Peschiaroli F, Businaro L, Gerardino A, Manic G, Ulas T, Günther P, Schultze JL, Kepp O, Stoll G, Lefebvre C, Mulot C, Castoldi F, Rusakiewicz S, Ladoire S, Apetoh L, Bravo-San Pedro JM, Lucattelli M, Delarasse C, Boige V, Ducreux M, Delaloge S, Borg C, André F, Schiavoni G, Vitale I, Laurent-Puig P, Mattei F, Zitvogel L, **Kroemer G**. *Science*. 2015 Nov 20;350(6263):972-8.

Caloric restriction mimetics reinforce anticancer immunosurveillance. Pietrocola F, Pol J, Vacchelli E, Rao S, Enot DP, Baracco EE, Levesque S, Castoldi F, Jacquelot N, Yamazaki T, Senovilla L, Marino G, Aranda F, Durnand, S, Sica V, Chery A, Lachkar S, Sigl V, Bloy N, Buque A, Falzoni S, Ryffel B, Apetoh L, DiVirgilio F, Madeo F, Maiuri MC, Zitvogel L, Levine B, Penninger J, **Kroemer G**.. *Cancer Cell.* 2016 Jul 11;30(1):147-60.

Recent Publications

Pro-necrotic molecules impact local immunosurveillance in human breast cancer. Stoll G, Ma Y, Yang H, Kepp O, Zitvogel L, **Kroemer G**. Oncoimmunology. 2017 Apr 17;6(4):e1299302

DNA Damage in Stem Cells. Vitale I, Manic G, De Maria R, **Kroemer G**, Galluzzi L. Mol Cell. 2017 May 4;66(3):306-319.

Activating autophagy to potentiate immunogenic chemotherapy and radiation therapy. Galluzzi L, Bravo-San Pedro JM, Demaria S, Formenti SC, **Kroemer G**. *Nat Rev Clin Oncol.* 2017 Apr;14(4):247-258.

Immunogenic cell death in cancer and infectious disease. Galluzzi L, Buqué A, Kepp O, Zitvogel L, **Kroemer G**. *Nat Rev Immunol*. 2017 Feb;17(2):97-111.

Calreticulin and type I interferon: An unsuspected connection. Galluzzi L, **Kroemer G**. *Oncoimmunology*. 2017 Feb 6;6(3):e1288334.

Mouse models in oncoimmunology. Zitvogel L, Pitt JM, Daillère R, Smyth MJ, **Kroemer G**. *Nat Rev Cance*r. 2016 Dec;16(12):759-773.

Spontaneous DNA damage propels tumorigenicity. Vitale I, **Kroemer G**. *Cell Res*. 2017 Mar 31

Immunological Mechanisms Underneath the Efficacy of Cancer Therapy. Galluzzi L, Zitvogel L, **Kroemer G**. *Cancer Immunol Res*. 2016 Nov;4(11):895-902.

Autophagy-dependent danger signaling and adaptive immunity to poorly immunogenic tumors. **Kroemer G**, Galluzzi L. *Oncotarget.* 2017 Jan 24;8(4):5686-5691

Session 4

New Molecular Targeted Drugs

4-1. Allele Specific Precision Medicine for ERK-Driven Tumors

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

4-2. Targeting DNA Repair in Cancer Therapy

Speaker: Alan D. D'Andrea (Dana-Farber Cancer Institute, USA)

4-3. Cyclin D-Dependent Effects of CDK4/6 Inhibitors in Cancer

Speaker: Charles J. Sherr (St. Jude Children's Research Hospital, USA)

Title: Allele Specific Precision Medicine for ERK-Driven Tumors

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

Mitsuaki Yoshida, PhD

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

Phenformin Enhances the Efficacy of ERK Inhibition in NF1-Mutant Melanoma. Trousil S, Chen S, Mu C, Shaw FM, Yao Z, Ran Y, Shakuntala T, Merghoub T, Manstein D, **Rosen N**, Cantley LC, Zippin JH, Zheng B. *J Invest Dermatol*. 2017 May;137(5):1135-1143.

A brain-penetrant RAF dimer antagonist for the noncanonical BRAF oncoprotein of pediatric low-grade astrocytomas. Sun Y, Alberta JA, Pilarz C, Calligaris D, Chadwick EJ, Ramkissoon SH, Ramkissoon LA, Garcia VM, Mazzola E, Goumnerova L, Kane M, Yao Z, Kieran MW, Ligon KL, Hahn WC, Garraway LA, **Rosen N**, Gray NS, Agar NY, Buhrlage SJ, Segal RA, Stiles CD. *Neuro Oncol. 2017 Jan 12.*

Kinase Regulation of Human MHC Class I Molecule Expression on Cancer Cells. Brea EJ, Oh CY, Manchado E, Budhu S, Gejman RS, Mo G, Mondello P, Han JE, Jarvis CA, Ulmert D, Xiang Q, Chang AY, Garippa RJ, Merghoub T, Wolchok JD, **Rosen N**, Lowe SW, Scheinberg DA. *Cancer Immunol Res*. 2016 Nov;4(11):936-947.

Sustained ERK inhibition maximizes responses of BrafV600E thyroid cancers to radioiodine. Nagarajah J, Le M, Knauf JA, Ferrandino G, Montero-Conde C, Pillarsetty N, Bolaender A, Irwin C, Krishnamoorthy GP, Saqcena M, Larson SM, Ho AL, Seshan V, Ishii N, Carrasco N, **Rosen N**, Weber WA, Fagin JA. *J Clin Invest.* 2016 Nov 1;126(11):4119-4124.

Integrated molecular pathway analysis informs a synergistic combination therapy targeting PTEN/PI3K and EGFR pathways for basal-like breast cancer. She QB, Gruvberger-Saal SK, Maurer M, Chen Y, Jumppanen M, Su T, Dendy M, Lau YK, Memeo L, Horlings HM, van de Vijver MJ, Isola J, Hibshoosh H, **Rosen N**, Parsons R, Saal LH. *BMC Cancer*. 2016 Aug 2;16:587.

Mechanistically distinct cancer-associated mTOR activation clusters predict sensitivity to rapamycin. Xu J, Pham CG, Albanese SK, Dong Y, Oyama T, Lee CH, Rodrik-Outmezguine V, Yao Z, Han S, Chen D, Parton DL, Chodera JD, **Rosen N**, Cheng EH, Hsieh JJ. *J Clin Invest*. 2016 Sep 1;126(9):3526-40.

A combinatorial strategy for treating KRAS-mutant lung cancer. Manchado E, Weissmueller S, Morris JP 4th, Chen CC, Wullenkord R, Lujambio A, de Stanchina E, Poirier JT, Gainor JF, Corcoran RB, Engelman JA, Rudin CM, **Rosen N**, Lowe SW. *Nature*. 2016 Jun 30;534(7609):647-51.

Overcoming mTOR resistance mutations with a new-generation mTOR inhibitor. Rodrik-Outmezguine VS, Okaniwa M, Yao Z, Novotny CJ, McWhirter C, Banaji A, Won H, Wong W, Berger M, de Stanchina E, Barratt DG, Cosulich S, Klinowska T, **Rosen N**, Shokat KM. *Nature*. 2016 Jun 9;534(7606):272-6.

Title: Targeting DNA Repair in Cancer Therapy

Speaker

Alan D. D'Andrea, MD

Professor of Pediatrics, Harvard Medical School, USA
The Fuller-American Cancer Society Professor, Department of Radiation Oncology and Pediatric, Harvard Medical School, USA
Director, Center for DNA Damage and Repair,
Director, Susan F. Smith Center for Women's Cancers,
Dana-Farber Cancer Institute, USA

Chairman

Kohei Miyazono, MD, PhD

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

Alan D. D'Andrea, MD

Profile

Dr. D'Andrea received his MD from Harvard Medical School in 1983. He completed his residency in Pediatrics at Children's Hospital of Philadelphia, and a fellowship in hematology-oncology at DFCI and Children's Hospital, Boston. Dr. D'Andrea also completed a research fellowship at the Whitehead Institute of Biomedical Research at MIT where he cloned the receptor for erythropoietin while working in the laboratory of Harvey Lodish. Dr. D'Andrea joined the staff at DFCI in 1990. His research focused on the molecular cause of leukemia for many years. He also investigates the pathogenesis of Fanconi anemia, a human genetic disease characterized by bone marrow failure and AML in children.

Dr. D'Andrea is internationally known for his research in the area of DNA damage and DNA repair. He is currently the Fuller-American Cancer Society Professor of Radiation Oncology at Harvard Medical School and the Director of the Center for DNA Damage and Repair at the Dana-Farber Cancer Institute. A recipient of numerous academic

awards, Dr. D'Andrea is a former Stohlman Scholar of the Leukemia and Lymphoma Society, and serves on their Medical and Scientific Advisory Board. He recently served as Chairman of the Career Development Selection Committee of the LLS, and Chairman of the NIH Molecular and Cellular Hematology Study Section. Dr. D'Andrea is a Distinguished Clinical Investigator of the Doris Duke Charitable Trust, and a Fellow of the American Association for the Advancement of Science. He is also the recipient of the 2001 E. Mead Johnson Award, the highest award in Pediatric Research, and the 2012 G.H.A. Clowes Memorial Award from the American Association for Cancer Research. He is also currently the Team Leader of the Stand Up To Cancer-Ovarian Cancer Research Fund-Ovarian Cancer National Alliance-National Ovarian Cancer Coalition Dream Team Translational Research Grant. Through his work on DNA Repair Biomarkers, Dr. D'Andrea participates in a wide range of clinical trials, largely focused on ovarian, breast, prostate, and bladder cancers. In 2017, he became the Director of the Susan Smith Center for Women's Cancer at the Dana-Farber Cancer Institute.

Recent Publications

Aldehydes Pose a Threat to BRCA2 Mutation Carriers. Parmar K, **D'Andrea AD**. *Cell.* 2017 Jun 1;169(6):979-981.

Clear cell ovarian cancers with microsatellite instability: A unique subset of ovarian cancers with increased tumor-infiltrating lymphocytes and PD-1/PD-L1 expression. Howitt BE, Strickland KC, Sholl LM, Rodig S, Ritterhouse LL, Chowdhury D, **D'Andrea AD**, Matulonis UA, Konstantinopoulos PA. *Oncoimmunology*. 2017 Jan 6;6(2):e1277308.

Small Molecule Inhibition of the Ubiquitin-specific Protease USP2 Accelerates cyclin D1 Degradation and Leads to Cell Cycle Arrest in Colorectal Cancer and Mantle Cell Lymphoma Models. Davis MI, Pragani R, Fox JT, Shen M, Parmar K, Gaudiano EF, Liu L, Tanega C, McGee L, Hall MD, McKnight C, Shinn P, Nelson H, Chattopadhyay D, **D'Andrea AD**, Auld DS, DeLucas LJ, Li Z, Boxer MB, Simeonov A. *J Biol Chem*. 2016 Nov 18;291(47):24628-24640.

CDK12 Inhibition Reverses De Novo and Acquired PARP Inhibitor Resistance in BRCA Wild-Type and Mutated Models of Triple-Negative Breast Cancer. Johnson SF, Cruz C, Greifenberg AK, Dust S, Stover DG, Chi D, Primack B, Cao S, Bernhardy AJ, Coulson R, Lazaro JB, Kochupurakkal B, Sun H, Unitt C, Moreau LA, Sarosiek KA, Scaltriti M, Juric D, Baselga J, Richardson AL, Rodig SJ, **D'Andrea AD**, Balmaña J, Johnson N, Geyer M, Serra V, Lim E, Shapiro GI. *Cell Rep*. 2016 Nov 22;17(9):2367-2381.

Genomic Evolution after Chemoradiotherapy in Anal Squamous Cell Carcinoma. Mouw KW, Cleary JM, Reardon B, Pike J, Braunstein LZ, Kim J, Amin-Mansour , Miao D, Damish A, Chin J, Ott PA, Fuchs CS, Martin NE, Getz G, Carter S, Mamon HJ, Hornick JL, Van Allen EM, **D'Andrea AD.** *Clin Cancer Re*s. 2016 Nov 16. doi: 10.1158/1078-0432

FANCD2 Maintains Fork Stability in BRCA1/2-Deficient Tumors and Promotes Alternative End-Joining DNA Repair. Kais Z, Rondinelli B, Holmes A, O'Leary C, Kozono D, **D'Andrea AD**, Ceccaldi R. *Cell Rep*. 2016 Jun 14;15(11):2488-99

Title: Cyclin D- Dependent Effects of CDK4/6 Inhibitors in Cancer

Speaker

Charles J. Sherr, MD, PhD

Chair, Tumor Cell Biology Department, Herrick Foundation
Chair, St. Jude Children's Research Hospital, USA
Investigator, Howard Hughes Medical Institute, USA

Chairman

Masakazu Toi, MD, PhD

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

Charles J. Sherr, MD, PhD

Profile

Dr. Sherr pioneered studies of the mechanics of cell division cycle control and the manner by which the functions of key cell cycle regulators are perturbed in cancer. He is an Investigator of the Howard Hughes Medical Institute and Herrick Foundation Chairman of the Department of Tumor Cell Biology at St. Jude Children's Research Hospital.

He earned his A.B. degree with honors at Oberlin College in 1966, and received both the M.D. and Ph.D. degrees in 1972 from New York University School of Medicine and Graduate School of Arts and Sciences, respectively. Dr. Sherr joined the National Cancer Institute in 1973, where he initiated early studies of retroviral oncogenes. In 1983, he relocated to St. Jude Children's Research Hospital in Memphis, Tennessee, as the founder of the Department of Tumor Cell Biology and was appointed to the Howard Hughes Medical Institute in 1988. Dr. Sherr continues as an HHMI Investigator

and has remained at St. Jude Children's Research Hospital throughout the development and expansion of its scientific programs over the last 32 years.

Dr. Sherr's laboratory discovered the FMS oncogene, demonstrated that it encoded the cell surface receptor for colony-stimulating factor-1 (CSF-1), and mapped receptor mutations that induced aberrantly constitutive signaling and oncogenic activity. His subsequent identification of growth factor-responsive mammalian D-type cyclins and cyclin-dependent kinase-4 (CDK-4), and the demonstration that cyclin D-CDK4 complexes triggered the phosphorylation of the retinoblastoma protein (RB), helped to reveal how mammalian cells respond to extracellular cues in regulating their cell division cycle. Investigations of CDK4 inhibitory ("INK4") proteins led to the discovery of the ARF tumor suppressor, an oncogene-activated arbiter of the p53 transcriptional response. Mutations affecting the expression of genes encoding many of these proteins – namely, the D-type cyclins, CDK4, INK4A, RB, ARF, and p53 – are among the most frequently observed events in human cancer.

Dr. Sherr was elected to the National Academy of Sciences in 1995, to the Institute of Medicine in 2004, and to the American Academy of Arts and Sciences in 2013. He was elected to the American Society of Clinical Investigation in 1986 and to the Association of American Physicians in 1991; he became a Fellow of the American Society for Microbiology in 1994, of the American Association for the Advancement of Science in 2010, and was chosen as an Inaugural Fellow of the Academy of the American Association for Cancer Research in 2013. Among several prestigious awards, Dr. Sherr received the AACR Pezcoller International Award for Cancer Research and the Bristol-Myers Squibb Award for Distinguished Achievement in Cancer Research in 2000, the AACR-Landon Prize for Basic Cancer Research in 2003, and the General Motors Cancer Foundation Charles S. Mott Prize in 2004.

Recent Publications

Inactivation of Ezh2 Upregulates Gfi1 and Drives Aggressive Myc-Driven Group 3 Medulloblastoma. Vo BT, Li C, Morgan MA, Theurillat I, Finkelstein D, Wright S, Hyle J, Smith SM, Fan Y, Wang YD, Wu G, Orr BA, Northcott PA, Shilatifard A, **Sherr CJ**, Roussel MF. *Cell Rep*. 2017 Mar 21;18(12):2907-2917.

A New Cell-Cycle Target in Cancer - Inhibiting Cyclin D-Dependent Kinases 4 and 6. **Sherr CJ**. *N Engl J Med*. 2016 Nov 17;375(20):1920-1923.

Targeting CDK4 and CDK6: From Discovery to Therapy. **Sherr CJ**, Beach D, Shapiro GI. *Cancer Discov.* 2016 Apr;6(4):353-67.

Forging a signature of in vivo senescence. Sharpless NE, **Sherr CJ**. *Nat Rev Cancer.* 2015 Jul;15(7):397-408.

Session 5

Cancer Genomics Impacts on Clinical Practice and Economics

5-1. Genomic Analysis of Tumors in the Clinic: Promises and Challenges

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

5-2. The Clinical Outcomes and Costs of Precision Oncology

Speaker: Lincoln D. Nadauld (Intermountain Healthcare, USA)

5-3. A Nation-Wide Genome Screening Consortium for New Agent Development (SCRUM-Japan)

Speaker: Atsushi Ohtsu (National Cancer Center, Japan)

Title: Genomic Analysis of Tumors in the Clinic: Promises and Challenges

Speaker

Anthony J. Iafrate, MD, PhD

Professor of Pathology, Harvard Medical School, USA
Director, Center for Integrated Diagnostics, MGH, USA

Chairman

Kiyohiko Hatake, MD, PhD

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

Anthony J. Iafrate, MD, PhD

Profile

Dr. Iafrate is a Professor of Pathology at Harvard Medical School, and is director of the Director of the Center for Integrated Diagnostics (CID), a clinical laboratory for molecular diagnostics at the Massachusetts General Hospital (MGH).

Dr. Iafrate received his MD/PhD dual degree from the State University of New York at Stony Brook in 2000 and was trained in anatomic and molecular genetic pathology at Brigham and Women's Hospital. Dr. Iafrate is a board-certified Pathologist, and has been on staff at MGH since 2005. The CID provides rapid personalized genomic testing to help inform cancer treatment decisions for patients. His research is focused on lung and brain tumors, where he has been closely involved in the clinical development of crizotinib and companion diagnostics in ALK- and ROS1 positive lung cancers. His lab has developed several technologies for sequencing tumors, including

SNaPshot and the next-generation sequencing-based Anchored Multiplex PCR, both techniques have been widely used in the molecular diagnostics community.

Recent Publications

KIF13B-NRG1 Gene Fusion and KRAS Amplification in a Case of Natural Progression of Lung Cancer. Xia D, Le LP, **Iafrate AJ**, Lennerz J. *Int J Surg Pathol*. 2017 May;25(3):238-240.

Decoupling genetics, lineages, and microenvironment in IDH-mutant gliomas by single-cell RNA-seq. Venteicher AS, Tirosh I, Hebert C, Yizhak K, Neftel C, Filbin MG, Hovestadt V, Escalante LE, Shaw ML, Rodman C, Gillespie SM, Dionne D, Luo CC, Ravichandran H, Mylvaganam R, Mount C, Onozato ML, Nahed BV, Wakimoto H, Curry WT, **Iafrate AJ**, Rivera MN, Frosch MP, Golub TR, Brastianos PK, Getz G, Patel AP, Monje M, Cahill DP, Rozenblatt-Rosen O, Louis DN, Bernstein BE, Regev A, Suvà ML. *Science.* 2017 Mar 31;355(6332).

Primitive Neuroectodermal Tumors of the Female Genital Tract: A Morphologic, Immunohistochemical, and Molecular Study of 19 Cases. Chiang S, Snuderl M, Kojiro-Sanada S, Quer Pi-Sunyer A, Daya D, Hayashi T, Bosincu L, Ogawa F, Rosenberg AE, Horn LC, Wang L, **Iafrate AJ**, Oliva E. *Am J Surg Patho*l. 2017 Mar 14

Analytical Validation of the Next-Generation Sequencing Assay for a Nationwide Signal-Finding Clinical Trial: Molecular Analysis for Therapy Choice Clinical Trial. Lih CJ, Harrington RD, Sims DJ, Harper KN, Bouk CH, Datta V, Yau J, Singh RR, Routbort MJ, Luthra R, Patel KP, Mantha GS, Krishnamurthy S, Ronski K, Walther Z, Finberg KE, Canosa S, Robinson H, Raymond A, Le LP, McShane LM, Polley EC, Conley BA, Doroshow JH, **Iafrate AJ**, Sklar JL, Hamilton SR, Williams PM. *J Mol Diagn*. 2017 Mar;19(2):313-327.

Polyclonal Secondary *FGFR2* Mutations Drive Acquired Resistance to FGFR Inhibition in Patients with FGFR2 Fusion-Positive Cholangiocarcinoma. Goyal L, Saha SK, Liu LY, Siravegna G, Leshchiner I, Ahronian LG, Lennerz JK, Vu P, Deshpande V, Kambadakone A, Mussolin B, Reyes S, Henderson L, Sun JE, Van Seventer EE, Gurski JM Jr, Baltschukat S, Schacher-Engstler B, Barys L, Stamm C, Furet P, Ryan DP, Stone JR, **Iafrate AJ**, Getz G, Porta DG, Tiedt R, Bardelli A, Juric D, Corcoran RB, Bardeesy N, Zhu AX. *Cancer Discov*. 2017 Mar;7(3):252-263.

ROS1 Fusions Rarely Overlap with Other Oncogenic Drivers in Non-Small Cell Lung Cancer. Lin JJ, Ritterhouse LL, Ali SM, Bailey M, Schrock AB, Gainor JF, Ferris LA, Mino-Kenudson M, Miller VA, **Iafrate AJ**, Lennerz JK, Shaw AT. *J Thorac Oncol*. 2017 Jan 11.

IDH2 Mutations Define a Unique Subtype of Breast Cancer with Altered Nuclear Polarity. Chiang S, Weigelt B, Wen HC, Pareja F, Raghavendra A, Martelotto LG, Burke KA, Basili T, Li A, Geyer FC, Piscuoglio S, Ng CK, Jungbluth AA, Balss J, Pusch S, Baker GM, Cole KS, von Deimling A, Batten JM, Marotti JD, Soh HC, McCalip BL, Serrano J, Lim RS, Siziopikou KP, Lu S, Liu X, Hammour T, Brogi E, Snuderl M, **Iafrate AJ**, Reis-Filho JS, Schnitt SJ. *Cancer Res.* 2016 Dec 15;76(24):7118-7129.

Single-cell RNA-seq supports a developmental hierarchy in human oligodendroglioma. Tirosh I, Venteicher AS, Hebert C, Escalante LE, Patel AP, Yizhak K, Fisher JM, Rodman C, Mount C, Filbin MG, Neftel C, Desai N, Nyman J, Izar B, Luo CC, Francis JM, Patel AA, Onozato ML, Riggi N, Livak KJ, Gennert D, Satija R, Nahed BV, Curry WT, Martuza RL, Mylvaganam R, **Iafrate AJ**, Frosch MP, Golub TR, Rivera MN, Getz G, Rozenblatt-Rosen O, Cahill DP, Monje M, Bernstein BE, Louis DN, Regev A, Suvà ML. *Nature*. 2016 Nov 10;539(7628):309-313.

Next-generation sequencing adds value to the preoperative diagnosis of pancreatic cysts. Rosenbaum MW, Jones M, Dudley JC, Le LP, **Iafrate AJ**, Pitman MB. *Cancer*. 2017 Jan;125(1):41-47.

Metastatic Breast Cancer With ESR1 Mutation: Clinical Management Considerations From the Molecular and Precision Medicine (MAP) Tumor Board at Massachusetts General Hospital. Bardia A, **Iafrate AJ**, Sundaresan T, Younger J, Nardi V. *Oncologist*. 2016 Sep;21(9):1035-40.

Health Care Infrastructure for Financially Sustainable Clinical Genomics. Lennerz JK, McLaughlin HM, Baron JM, Rasmussen D, Sumbada Shin M, Berners-Lee N, Miller Batten J, Swoboda KJ, Gala MK, Winter HS, Schmahmann JD, Sweetser DA, Boswell M, Pacula M, Stenzinger A, Le LP, Hynes W, Rehm HL, Klibanski A, Black-Schaffer SW, Golden JA, Louis DN, Weiss ST, **Iafrate AJ**. *J Mol Diagn*. 2016 Sep;18(5):697-706.

Acquired Resistance to Crizotinib in NSCLC with MET Exon 14 Skipping. Heist RS, Sequist LV, Borger D, Gainor JF, Arellano RS, Le LP, Dias-Santagata D, Clark JW, Engelman JA, Shaw AT, **Iafrate AJ**. *J Thorac Oncol*. 2016 Aug;11(8):1242-5.

Title: The Clinical Outcomes and Costs of Precision Oncology

Speaker

Lincoln D. Nadauld, MD, PhD

Executive Director, Precision Genomics, Intermountain Healthcare, USA
Consulting Assistant Professor, Stanford School of Medicine, USA.

Chairman

Bruce A. Chabner, MD

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

Lincoln D. Nadauld, MD, PhD

Profile

Dr. Nadauld is the Executive Director of Precision Medicine and Precision Genomics at Intermountain Healthcare, an integrated healthcare system where he oversees the clinical implementation of genomic cancer medicine across 22 hospitals and 180 physician clinics.

He is on the research faculty at Stanford University School of Medicine in the Division of Oncology focusing on cancer genomics and personalized cancer medicine. His work has been published extensively in journals such as Nature Medicine, Journal of Clinical Oncology, and Genome Medicine. He also serves on the Board of Directors of the Gastric Cancer Foundation, and reviews grant applications on behalf of the Department of Defense. He participated in the Precision Medicine Initiative Summit and roundtables at the White House with President Barack Obama. He is Associate Editor of Journal of Clinical Oncology-Precision Oncology.

Dr. Nadauld received a B.S. from Brigham Young University and a combined M.D./Ph.D. from the University of Utah. He completed clinical training in Medical Oncology at Stanford University School of Medicine, where he also completed a postdoctoral fellowship in solid tumor genomics, receiving the prestigious Young Investigator Award from the American Society of Clinical Oncology. In his spare time, Dr. Nadauld enjoys spending time with his wife and five children, attending his children's sporting events, fishing, hiking, boating, and skiing.

Recent Publications

A Retrospective Analysis of Precision Medicine Outcomes in Patients With Advanced Cancer Reveals Improved Progression-Free Survival Without Increased Health Care Costs. Haslem DS, Van Norman SB, Fulde G, Knighton AJ, Belnap T, Butler AM, Rhagunath S, Newman D, Gilbert H, Tudor BP, Lin K, Stone GR, Loughmiller DL, Mishra PJ, Srivastava R, Ford JM, **Nadauld LD**. *J Oncol Pract*. 2016 Sep 6

Metastatic tumor evolution and organoid modeling implicate TGFBR2 as a cancer driver in diffuse gastric cancer. **Nadauld LD**, Garcia S, Natsoulis G, Bell JM, Miotke L, Hopmans ES, Xu H, Pai RK, Palm C, Regan JF, Chen H, Flaherty P, Ootani A, Zhang NR, Ford JM, Kuo CJ, Ji HP. G*enome Biol*. 2014 Aug 27;15(8):428.

Oncogenic transformation of diverse gastrointestinal tissues in primary organoid culture. Li X, **Nadauld LD**, Ootani A, Corney DC, Pai RK, Gevaert O, Cantrell MA, Rack PG, Neal JT, Chan CW, Yeung T, Gong X, Yuan J, Wilhelmy J, Robine S, Attardi LD, Plevritis SK, Hung KE, Chen CZ, Ji HP, Kuo CJ. *Nat Med*. 2014 Jul; 20(7):769-77

Molecular profiling of gastric cancer: toward personalized cancer medicine. **Nadauld LD**, Ford JM. *J Clin Oncol*. 2013 Mar 1;31(7):838-9

Title: A Nation-Wide Genome Screening Consortium for New Agent Development (SCRUM-Japan)

Speaker

Atsushi Ohtsu, MD, PhD

Director, National Cancer Center Hospital East, Japan

Chairman

Tomomitsu Hotta, MD, PhD

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

Astushi Ohtsu, MD, PhD

Profile

Dr. Ohtsu received his MD in 1983 and PhD in 2002 from Tohoku University in Sendai, Japan. From 2002, he has been working in the gastrointestinal oncology department at the National Cancer Center Hospital East, excluding the period of his visit to MD Anderson Cancer Center, USA in 1997.

In 2012, he became Director of the Exploratory Oncology Research & Clinical Trial Center (NCC-EPOC), which involves preclinical, TR, and early and exploratory clinical research in NCC. Since 2015, he has also been acting as a scientific board member of the Japan Agency for Medical Research and Development (AMED). He has published more than 270 articles that have appeared in peer-reviewed journals such as *NEJM*, *The Lancet, Journal of Clinical Oncology*, *The Lancet Oncology*, and the *Journal of the National Cancer Institute*.

Dr Ohtsu is also acting as an international affair committee member of the American Society of Clinical Oncology (ASCO) and Director of the Japanese Society of Medical Oncology (he served as the chair of the international affair committee) and the Japanese Cancer Association. He is also serving as a member or advisory expert of various committees of the PMDA, MHLW, and MEXT.

Recent Publications

Trastuzumab emtansine versus taxane use for previously treated HER2-positive locally advanced or metastatic gastric or gastro-oesophageal junction adenocarcinoma (GATSBY): an international randomised, open-label, adaptive, phase 2/3 study. Thuss-Patience PC, Shah MA, **Ohtsu A**, Van Cutsem E, Ajani JA, Castro H, Mansoor W, Chung HC, Bodoky G, Shitara K, Phillips GD, van der Horst T, Harle-Yge ML, Althaus BL, Kang YK. *Lancet Onco*l. 2017 Mar 23. pii: S1470-2045(17)30111-0.

Comparison between neoadjuvant chemotherapy followed by surgery and definitive chemoradiotherapy for overall survival in patients with clinical Stage II/III esophageal squamous cell carcinoma (JCOG1406-A). Nomura M, Kato K, Ando N, **Ohtsu A**, Muro K, Igaki H, Abe T, Takeuchi H, Daiko H, Gotoh M, Kataoka K, Wakabayashi M, Kitagawa Y. *Jpn J Clin Oncol.* 2017 Mar 17:1-7.

Nivolumab treatment for oesophageal squamous-cell carcinoma: an open-label, multicentre, phase 2 trial. Kudo T, Hamamoto Y, Kato K, Ura T, Kojima T, Tsushima T, Hironaka S, Hara H, Satoh T, Iwasa S, Muro K, Yasui H, Minashi K, Yamaguchi K, **Ohtsu A**, Doki Y, Kitagawa Y. *Lancet Oncol.* 2017 Mar 14.

NC-6004 Phase I study in combination with gemcitabine for advanced solid tumors and population PK/PD analysis. Doi T, Hamaguchi T, Shitara K, Iwasa S, Shimada Y, Harada M, Naito K, Hayashi N, Masada A, **Ohtsu A.** *Cancer Chemother Pharmacol.* 2017 Mar;79(3):569-578

Relationship between Pulmonary Adverse Events and Everolimus Exposure in Japanese and Non-Japanese Patients: A Meta-Analysis of Oncology Trials. Noguchi S, Shinohara N, Ito T, **Ohtsu A**, Ravaud A, Jerusalem G, Ohno N, Gallo J, Bouillaud E, Fan J, Nonomura N. *Oncology*. 2017 Feb 21

Gastrointestinal Perforation and Fistula Formation in 5 Patients With Colorectal Cancer During Treatment With Regorafenib. Doi A, Kuboki Y, Shitara K, Fukuoka S, Bando H, Okamoto W, Kojima T, Doi T, **Ohtsu A**, Yoshino T. *Clin Colorectal Cancer.* 2016 Dec 28.