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

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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
〒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2013

Frontier in Oncology Therapy

2013年7月26日（金）13:00~17:55
27日（土）8:30~15:50
六本木アカデミーヒルズ49

CHAAO Chugai Academy for Advanced Oncology

Frontier in Oncology Therapy

Friday, July 26th, 2013 13:00~17:55

Opening Remarks P.3

13:00 Osamu Nagayama, Chairman (Chugai Academy for Advanced Oncology)

1. Non-genetic dysregulation in tumor P.4

13:10 **TGF-β Signaling in Cancer**
Speaker: Kohei Miyazono, MD, PhD (The University of Tokyo, Japan)
Chair: Bruce A. Chabner, MD (Harvard Medical School, USA)

13:55 **Targeting Cancer Metabolism**
Speaker: Chi Van Dang, MD, PhD (The University of Pennsylvania, USA)
Chair: Kohei Miyazono, MD, PhD (The University of Tokyo, Japan)

14:40 Break

2. Genetic dysregulation in tumor P.16

15:10 **Targeting Activated HER2 in Solid Tumors**
Speaker: Mark Sliwkowski, PhD (Genentech Inc., USA)
Chair: Masakazu Toi, MD, PhD (Kyoto University, Japan)

15:55 **The Power of One: Use of Whole Genome Outlier Analysis to Identify Occult Biomarkers of Drug Response**
Speaker: David B. Solit, MD (Memorial Sloan-Kettering Cancer Center, USA)
Chair: Hiroyuki Mano, MD, PhD (The University of Tokyo, Japan)

16:40 Break

17:10 **Role of Mutations in Epigenetic Regulators in Pathogenesis of Myeloid Malignancies**
Speaker: Ross L. Levine, MD (Memorial Sloan-Kettering Cancer Center, USA)
Chair: Yuko Kitagawa, MD, PhD (Keio University, Japan)

18:00 **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

Saturday, July 27th, 2013 8:30~15:50

3. Tumor immunotolerance : basic and applications P.40

8:30 **Immune Checkpoint Blockade in Cancer Therapy: New Insights & Opportunities**
Speaker: James P. Allison, PhD (The University of Texas, USA)
Chair: Makoto Ogawa, MD (Emeritus President, Aichi Cancer Center, Japan)

9:15 **Immune Monitoring on Pre-surgical Clinical Trials with Anti-CTLA-4: Implicating the ICOS/ICOSL Pathway in Anti-tumor Immune Responses**
Speaker: Padmanee Sharma, MD, PhD (The University of Texas, USA)
Chair: Kiyohiko Hatake, MD, PhD (Cancer Institute Hospital, JFCR, Japan)

10:00 Break

4. Right drugs on right patients P.58

10:30 **Approaches to Hypothesis Based Combination Therapy for Cancer**
Speaker: Neal Rosen, MD, PhD (Memorial Sloan-Kettering Cancer Center, USA)
Chair: Mitsuaki Yoshida, PhD (Cancer Chemotherapy Center, JFCR, Japan)

11:15 **Targeting Oncogenic Drivers in Lung Cancer**
Speaker: Pasi A. Jänne, MD, PhD (Harvard Medical School, USA)
Chair: Nagahiro Saijo, MD, PhD (Japanese Society of Medical Oncology, Japan)

12:00 Lunch

12:40 **Targeting Clinically Relevant Molecular Subtypes in Colorectal Cancer**
Speaker: Patrick G. Johnston, MD, PhD (The Queen´s University of Belfast, UK)
Chair: Chikashi Ishioka, MD (Tohoku University, Japan)

13:25 **Understanding and Targeting Mechanisms of Resistance to Next Generation AR and AR Signaling Inhibitors**
Speaker: Howard I. Scher, MD (Memorial Sloan-Kettering Cancer Center, USA)
Chair: Patrick G. Johnston, MD, PhD (The Queen´s University of Belfast, UK)

14:10 Break

5. Accessibility to new drugs P.90

14:40 **Changing the Regulatory Pathway for Targeted Drugs**
Speaker: Bruce A. Chabner, MD (Harvard Medical School, USA)
Chair: Isao Kamae, MD, ScD (The University of Tokyo, Japan)

15:00 **Health Technology Assessment: Changing Landscape in Asia and Japan**
Speaker: Isao Kamae, MD, ScD (The University of Tokyo, Japan)
Chair: Yasuhiro Fujiwara, MD, PhD (National Cancer Center, Japan)
※このセッションは日本語で行います。

15:20 **Discussion**
Chair: Bruce A. Chabner, MD (Harvard Medical School, USA)

Opening Remarks

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

As chairman of Chugai Academy for Advanced Oncology (CHAAO), it is a great honor and pleasure to welcome all our distinguished guests, experts and investigators, both from overseas and from Japan, to the International Academy for Advanced Oncology 2013.

Considering the success of the forums over the last three years, I am very pleased that it was possible to organize a fourth one. The number of participants has continued to expand each time, and this year we are welcoming more than 180 attendees. Past forums have generated very positive feedback from the participants, and I sincerely hope this year will become another success as well.

As the term of Advisory Board members is three years, the forum this year marks the start of a new organizing team, including Dr. Bruce Chabner, Dr. Patrick Johnston, Dr. Fujiwara, Dr. Hatake, Dr. Ishioka, Dr. Kitagawa, Dr. Mano, Dr. Miyazono, Dr. Toi and Dr. Ueda. Under the active leadership of these 10 board members, the forum this year has brought together an extremely fascinating program with world-class speakers.

This year's theme is "Frontier in Oncology Therapy." In addition to the topics covered last year, such as personalized healthcare by biomarkers, immunotherapy and genome-based therapy, we will also be discussing areas such as Myeloid Malignancy and prostate cancer. Furthermore, as well as the scientific topics, we will also focus on regulatory issues such as Health Technology Assessment (HTA) and have a robust discussion considering the difference between the US and Asia, including Japan.

In line with the program, many experts from a broad range of specialties are participating, and I am confident the forum this year will enable everyone to share their knowledge and exchange deep insights into a wide range of fields.

In closing, let me emphasize that our sincere wish is for the two-day forum to be informative and inspiring for everyone. CHAAO's goal is to create opportunities for researchers and academics from around the world to exchange valuable information, and ultimately we hope that our activities will lead to the realization of cancer treatments that allow patients to confront cancer proactively and with hope.

Session 1

Non-genetic dysregulation in tumor

1-1. TGF-β Signaling in Cancer

Speaker: Kohei Miyazono, MD, PhD (The University of Tokyo, Japan)

1-2. Targeting Cancer Metabolism

Speaker: Chi Van Dang, MD, PhD (The University of Pennsylvania, USA)

Title: TGF-β signaling in cancer

Kohei Miyazono, MD, PhD
Professor and Chair, Department of Molecular Pathology, Graduate School of Medicine, The University of Tokyo, Japan

Speaker

Bruce A. Chabner, MD
Director of Clinical Research Cancer Center, Massachusetts General Hospital, Boston Massachusetts, USA

Chairman

Kohei Miyazono, MD, PhD

CAREER HISTORY

1981: M.D. degree, Faculty of Medicine, Univ. of Tokyo

1988: Assistant of Professor, Third Dept. Int. Med., Univ. of Tokyo

1989: Doctor of Medical Science, Faculty of Medicine, Univ. of Tokyo

1990: Assistant Member, Ludwig Institute for Cancer Research, Uppsala, Sweden

1995: Member and Chief, Department of Biochemistry, The Cancer Institute, Japanese Foundation for Cancer Research

2000: Professor, Department of Molecular Pathology, Graduate School of Medicine, Univ. of Tokyo

2011: Dean, Graduate School of Medicine, Univ. of Tokyo

AWARDS

1999: Honorary Doctor of Medicine of Uppsala University, Sweden

2000: Princess Takamatsu Cancer Research Award

2009: Medal of honor with purple ribbon from the Japanese government

2011: Japan Academy Prize

IAAO2013 Title of the Talk:

TGF-β signaling in cancer

ABSTRACT:

TGF-β elicits both pro-tumorigenic and tumor suppressive functions during progression of cancer. We present our recent findings on TGF-β signaling in progression of cancer, focusing on induction of epithelial-mesenchymal transition (EMT) by TGF-β. TGF-β induces EMT through activation of Smad and non-Smad signaling pathways. Inhibition of TGF-β signaling by Smad7 or small molecular weight TGF-β inhibitor(s) results in prevention of cancer metastasis in mouse models. Multiple transcription factors, including δEF1/ZEB1, SIP1/ZEB2, and Snail, play critical roles in TGF-β-induced EMT.
TGF-β induces EMT in normal and transformed cells. We have found that FGF-2 enhanced TGF-β-induced morphological changes and activation of ECM degradation. Normal mouse epithelial NMuMG cells treated with TGF-β and FGF-2 enhanced the invasion of co-cultured breast cancer cells into collagen gels in vitro. Thus, TGF-β and FGF-2 may cooperate with each other to produce activated fibroblasts in tumor microenvironment, and the activated fibroblasts in turn secrete some substances, e.g. MMPs, to induce invasion and metastasis of cancer.
TGF-β-induced EMT involves isoform switching of FGF receptors by alternative splicing. We have found that TGF-β induces broad alteration of splicing profiles by downregulating epithelial splicing regulatory proteins (ESRPs).
Thyroid transcription factor-1 (TTF-1/Nkx2-1) is expressed in lung cancer, but its functional roles remain to be elucidated. TTF-1 that inhibited TGF-β-mediated EMT and restored epithelial phenotype in lung adenocarcinoma cells. This effect was accompanied by down-regulation of TGF-β target genes, including Snail and Slug. Genome-wide analyses by ChIP-seq revealed that TTF-1 co-localized with Smad3 on the chromatin and altered the binding patterns of Smad3 throughout the genome. We also propose a new model of regulation of TGF-β-Smad signaling by TTF-1.

Session 1-2

Title: Targeting Cancer Metabolism

Chi Van Dang, MD, PhD
Professor of Medicine, Director, Abramson Family Cancer Research Institute, Abramson Cancer Center, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA.

Speaker

Kohei Miyazono, MD, PhD
Professor and Chair, Department of Molecular Pathology, Graduate School of Medicine, The University of Tokyo, Japan

Chairman

Chi Van Dang, MD, PhD

Chi Van Dang is Director of the Abramson Cancer Center of the University of Pennsylvania and the John H. Glick Professor. His career at Penn started in September 2011 after having been at Johns Hopkins when he was the Johns Hopkins Family Professor in Oncology Research and Vice Dean for Research of Johns Hopkins University School of Medicine. He directed the Hopkins Institute for Cell Engineering and was a Professor of Medicine, Pathology, Oncology, and Cell Biology with joint appointment in Molecular Biology and Genetics. Dr. Dang is Editor-in-Chief of Cancer & Metabolism, a scientific editor of Cancer Discovery and serves on editorial boards of Cancer Research, Clinical Translational Science, Current Cancer Therapy Reviews, eLIFE, Journal of Clinical Investigation, Journal of Molecular Medicine, Genes & Cancer, Molecular and Cellular Biology, Neoplasia, and Oncotargets. He has authored over 200 scientific and medical articles, book chapters and a book. He is a member of the Institute of Medicine of the National Academy of Sciences, American Academy of Arts & Sciences, National Cancer Institute Board of Scientific Advisors, American Society for Clinical Investigation (ASCI) and The Association of American Physicians. He was president of the ASCI (2003). He held an NIH/National Cancer Institute MERIT award, received a number of honors, and sponsored and mentored many NIH K08 physician-scientist awardees, Ph.D. doctorates and post-doctoral fellows. The Dang laboratory has contributed to the understanding of the function of the MYC cancer gene (www.myccancergene.org), which has emerged as a central transcription factor or gene switch in many different human cancers. His laboratory established the first mechanistic link between the MYC cancer gene and cellular energy metabolism, contributing to the concept that genetic alterations in cancers re-program fuel utilization by tumors and render cancers addicted to certain fuel sources. His laboratory is now exploiting these concepts for therapeutic targeting of cancer cell metabolism as a new way to treat cancer.

IAAO2013 Title of the Talk:

Targeting Cancer Metabolism

ABSTRACT:

Canonical oncogenes and tumor suppressors involved in cell growth and proliferation are intimately linked to metabolic pathways, which in turn affect tumorigenesis. The MYC oncogene regulates gene expression and stimulates metabolism in favor of cell growth and proliferation. Deregulation of MYC in cancers is surmised to stimulate cell growth without extracellular cues, rendering tumorigenic cells addicted to glucose, glutamine, and fatty acids. In this regard, experiments to inhibit key enzymes, such as lactate dehydrogenase A (LDHA) and glutaminase (GLS), have provided proof-of-concept for targeting cancer metabolism. Because glycolysis and glutaminolysis are also used by some normal cells for growth, we also investigated an additional potential therapeutic window through the natural circadian metabolic rhythm of normal cells that is presumed to be disrupted in certain cancer cells. We found that MYC is able to directly perturb circadian transcription factors, disrupts circadian rhythm, and causes sustained metabolic deregulation, which could be exploited for chrono-metabolic therapy.

Session 2-1

Title: Targeting Activated HER2 in Solid Tumors

Mark Sliwkowski, PhD
Distinguished Staff Scientist, Research Oncology,
Genentech, Inc., USA

Speaker

Masakazu Toi, MD, PhD
Professor, Department of Surgery, Graduate School of
Medicine Kyoto University, Japan

Chairman

Mark Sliwkowski, PhD

Mark is currently a Distinguished Staff Scientist in Research Oncology at Genentech, Inc. He received his B.S. from the University of Delaware and his Ph.D. in biochemistry with a minor in physical chemistry from North Carolina State University. Mark was a postdoctoral fellow in the laboratory of Dr. Theresa C. Stadtman in the Laboratory of Biochemistry, in the National Heart, Lung, and Blood Institute at NIH. Upon leaving NIH, he joined Triton Biosciences, Inc., where he studied growth factor receptors and their ligands. Mark joined Genentech in 1991 and worked on a number of programs involving drugs directed against the human epidermal growth factor receptor family (also known as the HER or ErbB family). Dr. Sliwkowski was involved in the research and development efforts for Herceptin® (trastuzumab) and Tarceva® (erlotinib). In the last year, two drugs which arose from his laboratory's research, Perjeta® (pertuzumab) and Kadcyla® (ado-trastuzumab emtansine) have received regulatory approval. In addition, a novel "two-in-one" antibody (MEHD7945A) that targets HER3 and EGFR is about to commence phase II clinical testing in head and neck and colorectal cancer. Dr. Sliwkowski is an inventor on over 30 issued patents and has authored more than 95 scientific publications.

Education

National Institutes of Health (1982-1985)
National Heart, Lung and Blood Institute, Laboratory of Biochemistry
Staff Fellow with Dr. Thressa C. Stadtman

North Carolina State University (1978-1981)
Ph.D. in Biochemistry with minor in Physical Chemistry
Advisor: Dr. Harold E. Swaisgood

University of Delaware (1972-1976)
B.S. in Animal Science and Agricultural Biochemistry (Pre-Vet)

Experience

GENENTECH, INC.

Distinguished Staff Scientist 2012-present

Sr. Staff Scientist 2010-2012

Clinical Development Projects: Provide scientific and strategic input for Kadcyla® (T-DM1), Perjeta® (pertuzumab) and Herceptin® (trastuzumab) life cycle teams. Assist in the design and the scientific rationale for clinical trials for MEHD7945A (novel EGFR-HER3, two-in-one antibody) and direct laboratory efforts.

Early Discovery Projects: Initiated project to study and to address resistance to standard inhibitors. Participate in project to optimize linkers and non-microtuble directed drugs for conjugation to monoclonal antibodies.

Staff Scientist 2002-2010

HER3-EGFR Dual Antibody Project (DAF/MEHD7945A) (2006-present): Late Stage Research Team Leader responsible for moving project into Early Clinical Development (ECD). Current member of ECD core team.

Armed Antibody Program (2003-present): Lead multi-disciplinary research and development team efforts to assess arming monoclonal with cytotoxic agents. Served as the major liaison in coordinating collaboration with outside companies.

Trastuzumab-DM1 Program (2004-present): Research team leader and early development team leader. Considered prototype for armed antibody platform. Current member of T-DM1 life cycle team. Participate in development program.

Director 2003-2008

Formed Translational Oncology Department. Managed expansive growth from 2004-2007, including small molecule expertise. Managed Director of Assay & Automation Technology from 2005-2007.

Senior Scientist 1991-2001

Heregulin (1991-1996): Participated in the initial characterization of heregulin. Helped define a role for HER2/ErbB2 as a co-receptor with HER3, HER4 and EGFR.

HERCEPTIN® (1993-present): Member of the core project team throughout Phase II and Phase III clinical development. Responsibilities included studies on the development of an *in vitro* diagnostic assay, mechanism of action, mechanism of cardiotoxicity, coordinating biological and biochemical assays, obtaining data to support new clinical indications and designing studies to test novel chemotherapeutic combinations. Also responsible for managing all extramural research activities.

Pertuzumab (PERJETA®) (1997-present): As part of our heregulin studies, recognized the potential of blocking ligand-activated HER2 as an anti-cancer therapy. Led research and developmental research teams. Participated on developmental assessment team that resulted in rhuMAb 2C4/pertuzumab being moved into development in August 2000. Helped facilitate Roche decision to co-develop rhuMAb 2C4. Currently lead research effort and serve on pertuzumab life cycle team.

Tarceva® (2000-2007): One of several Genentech employees that encouraged Business Development to pursue in-licensing OSI-774. Participated in due diligence team. Led research effort on Tarceva and served on Tarceva core team.

Triton Biosciences, Inc. (Berlex Biosciences, Inc.)

Staff Scientist 1990 – 1991
Initiated a program for the identification and isolation of ligands for receptor tyrosine kinases. Participated in project to establish structure-activity relationship for TGFα. Supervised protein and peptide chemistry laboratories consisting of 2 scientists and 5 research associates.

Senior Research Scientist 1987 – 1990
Project Leader for development stage of HTLV-1 program. (Interdisciplinary team consisting of 3 scientists and 8 research associates.) Developed folding procedure for TGFα. Collaborated extensively with Immunology group on projects involving differentiation and cytotoxicity.

Research Scientist 1985 – 1987
One of the first bench scientists hired. Established protein chemistry laboratory purified recombinant retroviral proteins for development of diagnostic viral immunoassay.

NIH Postdoctoral Position 1982 – 1985
Studied mechanisms by which selenium is incorporated into bacterial proteins. Purified several selenium-containing proteins and gained extensive experience in peptide mapping.

Awards

Genentech, Inc. Ralph Schwall Memorial Award, 2012
Genentech, Inc. Keynote Speaker New Scientists' Offsite, 2011
Genentech, Inc. Most Commercially Significant Patent Award, 2010 (Patent No. 7,537,931 B2)
Genentech, Inc. Most Commercially Significant Patent Award, 2009 (Patent No. 7,344,840)
Genentech, Inc. Outstanding Commercial Collaborator Award, 2008
North Carolina State University, Outstanding Alumni Award, 2008
Genentech, Inc. Most Commercially Significant Patent Award, 2007 (Patent No. 7,097,840)
Genentech, Inc. Most Commercially Significant Patent Award, 2006 (Patent No. 6,949,245)
Industry Scientist of the Year, Pharmaceutical Achievement Award, 2005
Triton R&D Award, 1989
Industrial Initiative for Science and Math Education Award, 1989
American Society of Biological Chemistry Travel Grant, 1985
Phi Lambda Upsilon Chemistry Honor Society, 1981
Gamma Delta Sigma Agricultural Honor Society, 1981
Outstanding Graduate Student Teaching Award, 1979

Professional Affiliations

Advisory Committee for African Americans in Biotechnology
American Society of Clinical Oncology
American Association for Cancer Research
American Society for Biochemistry and Molecular Biology

Invited Lectures (Since 2010)

Keynote Speaker Experimental Therapeutics MD Anderson, Houston, TX March 2013
Israeli Society for Clinical Oncology and Radiation Therapy, Eilat, Israel, January 2013
Weizmann Institute of Science, Rehovat, Israel, January 2013
Antibody Engineering and Antibody Therapeutics, IBC Conference, San Diego, CA, December 2012
University of California San Francisco Cancer Center, CA, September 2012
CIMT Annual Meeting, Mainz, Germany, May 2012
University of North Carolina Cancer Center, Chapel Hill, NC, March 2012
Keynote Speaker, 10 years of HER2 Targeting in Belgium, Brussels, Belgium, January 2012
Japanese Foundation Cancer Research, Tokyo, Japan, January 2012
Cancer Research Institute: Cancer Immunotherapy 2011, New York City, NY, October 2011
Keynote Speaker Antibodies as Drugs, Keystone Symposium, Keystone, CO, February 2011
Antibody Therapeutics, IBC Conference, San Diego, CA, December 2010
EORTC/NCI/AACR, Berlin, Germany, November 2010
iSBTc, Workshop on Monoclonal Antibodies, Washington, DC, October 2010
Keynote Speaker International Bio Forum, Tokyo, Japan, June 2010

PUBLICATIONS (selected from 99 publications)

1. Bijay S. Jaiswal, Noelyn M. Kljavin, Eric W. Stawiski, Emily Chan, Chaitali Parikh, Steffen Durinck, Subhra Chaudhuri, Kanan Pujara, Joseph Guillory, Kyle A. Edgar, Vasantharajan Janakiraman, Rolf-Peter Scholz, Krista K. Bowman, Maria Lorenzo, Hong Li, Jiansheng Wu, Wenlin Yuan, Brock A. Peters, Zhengyan Kan, Jeremy Stinson, Michelle Mak, Zora Modrusan, Charles Eigenbrot, Ron Firestein, Howard M. Stern, Krishnaraj Rajalingam, Gabriele Schaefer, Mark A. Merchant, Mark X. Sliwkowski, Frederic J. de Sauvage, Somasekar Seshagiri. Oncogenic ERBB3 Mutations in Human Cancers. Cancer Cell 2013;23:1-15

2. Huang SM, Li C, Armstrong EA, Peet CR, Saker J, Amler LC, Sliwkowski MX, Harari P. Dual targeting of EGFR and HER3 with MEHD7945A overcomes acquired resistance to EGFR inhibitors and radiation. Cancer Res 2012 Nov 20 (Epub ahead of print)

3. Sliwkowski MX. Pari passu dimers of dimers. Proc Natl Acad Sci U S A 2012.

4. Shen BQ, Xu K, Liu L, Raab H, Bhakta S, Kenrick M, Parsons-Reponte KL, Tien J, Yu SF, Mai E, Li D, Tibbitts J, Baudys J, Saad OM, Scales SJ, McDonald PJ, Hass PE, Eigenbrot C, Nguyen T, Solis WA, Fuji RN, Flagella KM, Patel D, Spencer SD, Khawli LA, Ebens A, Wong WL, Vandlen R, Kaur S, Sliwkowski MX, Scheller RH, Polakis P, Junutula JR. Conjugation site modulates the in vivo stability and therapeutic activity of antibody-drug conjugates. Nat Biotechnol 2012;30:184-9.

5. Pastuskovas CV, Mundo EE, Williams SP, Nayak TK, Ho J, Ulufatu S, Clark S, Ross S, Cheng E, Parsons-Reponte K, Cain G, Van Hoy M, Majidy N, Bheddah S, dela Cruz Chuh J, Kozak KR, Lewin-Koh N, Nauka P, Bumbaca D, Sliwkowski M, Tibbitts J, Theil FP, Fielder PJ, Khawli LA,

Boswell CA. Effects of anti-VEGF on pharmacokinetics, biodistribution, and tumor penetration of trastuzumab in a preclinical breast cancer model. Mol Cancer Ther 2012;11:752-62.

6. Kamath AV, Lu D, Gupta P, Jin D, Xiang H, Wong A, Leddy C, Crocker L, Schaefer G, Sliwkowski MX, Damico-Beyer LA. Preclinical pharmacokinetics of MEHD7945A, a novel EGFR/HER3 dual-action antibody, and prediction of its human pharmacokinetics and efficacious clinical dose. Cancer Chemother Pharmacol 2012;69:1063-9.
7. Hurvitz SA, Betting DJ, Stern HM, Quinaux E, Stinson J, Seshagiri S, Zhao Y, Buyse M, Mackey J, Driga A, Damaraju S, Sliwkowski MX, Robert NJ, Valero V, Crown J, Falkson C, Brufsky A, Pienkowski T, Eiermann W, Martin M, Bee V, Marathe O, Slamon DJ, Timmerman JM. Analysis of Fcgamma receptor IIIa and IIa polymorphisms: lack of correlation with outcome in trastuzumab-treated breast cancer patients. Clin Cancer Res 2012;18:3478-86.
8. Arteaga CL, Sliwkowski MX, Osborne CK, Perez EA, Puglisi F, Gianni L. Treatment of HER2-positive breast cancer: current status and future perspectives. Nat Rev Clin Oncol 2012;9:16-32.
9. Lee-Hoeflich ST, Pham, TQ, Dowbenko D, Munroe X, Lee J, Li L, Zhou W, Haverty PM, Pujara K, Stinson J, Chan SM, Eastham-Anderson J, Pandita A, Seshagiri S, Hoeflich KP, Turashvili G, Gelmon KA, Aparicio SA, Davis DP, Sliwkowski MX, Stern HM. PPM1H is a p27 phosphatase implicated in trastuzumab resistance. Cancer Discovery 2011;1:326-337
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11. Lorusso PM, Weiss D, Guardino E, Girish S, Sliwkowski MX. Trastuzumab emtansine: a unique antibody-drug conjugate in development for human epidermal growth factor receptor 2-positive cancer. Clin Cancer Res 2011 Oct 15;17(20)6437-47
12. Burris HA 3rd, Tibbits J, Holden SN, Sliwkowski MX, Lewis Phillips GD. Trastuzumab emtansine (T-DM1): a novel agent for targeting HER2+ breast cancer. Clin Breast Cancer 2011 Oct;11(5):275-82
13. Makhija S, Amler LC, Glenn D, Ueland FR, Gold MA, Dizon DS, Paton V, Lin CY, Januario T, Ng K, Strauss A, Kelsey S, Sliwkowski MX, Matulonis U. Clinical activity of gemcitabine plus pertuzumab in platinum-resistant ovarian cancer, fallopian tube cancer, or primary peritoneal cancer. J Clin Oncol 2010;28:1215-23.
14. Krop IE, Beeram M, Modi S, Jones SF, Holden SN, Yu W, Girish S, Tibbitts J, Yi JH, Sliwkowski MX, Jacobson F, Lutzker SG, Burris HA. Phase I study of trastuzumab-DM1, an HER2 antibody-drug conjugate, given every 3 weeks to patients with HER2-positive metastatic breast cancer. J Clin Oncol 2010;28:2698-704.
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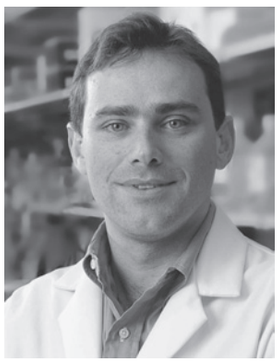
Session 2-1

IAAO2013 Title of the Talk:

Targeting Activated HER2 in Solid Tumors

ABSTRACT:

Title: The Power of One: Use of Whole Genome Outlier Analysis to Identify Occult Biomarkers of Drug Response



David B. Solit, MD
Director, Developmental Therapeutics
Laboratory Head, Human Oncology and Pathogenesis Program Attending Physician, Department of Medicine
Memorial Sloan-Kettering Cancer Center, USA.

Speaker

Hiroyuki Mano, MD, PhD
Professor, Division of Molecular Cell Biology, Center for Disease Biology and Integrative Medicine, Graduate School of Medicine, The University of Tokyo

Chairman

David B. Solit, MD

EDUCATIONAL BACKGROUND

BA, University of Pennsylvania, Philadelphia, PA, 1991

MD, University of Pennsylvania School of Medicine, Philadelphia, PA, 1995

CAREER

PROFESSIONAL POSITIONS AND EMPLOYMENT

Title	*Institution name and location*	*Dates held*
Intern in Internal Medicine	Barnes Hospital, St. Louis, MO. St. Louis, MO	1995-1996
Resident in Internal Medicine	Barnes-Jewish Hospital St. Louis, MO	1996-1998

Fellow in Medical Oncology and Hematology	Memorial Sloan-Kettering Cancer Center of Medicine New York, NY	1998-2001
Fellow in Medicine	Joan and Sanford I. Weill Medical College of Cornell University New York, NY	1998-2001

Academic positions

Title	*Institution name and location*	*Dates held*
Assistant Member (Level 1)	Memorial Sloan-Kettering Cancer Center, New York, NY	2001-2005
Instructor in Medicine	Joan and Sanford I. Weill Medical College of Cornell University New York, NY	2001-2006
Assistant Member	Memorial Sloan-Kettering Cancer Center, New York, NY	2005-2011
Assistant Professor of Medicine	Weill Cornell Medical College, New York, NY	2006-2011
Associate Member	Memorial Sloan-Kettering Cancer Center, New York, NY	2011-present

Hospital positions

Title	*Institution name, city and state*	*Dates*
Assistant Attending Physician	Genitourinary Oncology Service Memorial Hospital for Cancer and Allied Diseases, NY, NY	2001-2011
Laboratory Head	Memorial Hospital for Cancer and Allied Diseases, NY, NY	2006-present
Assistant Attending Physician	Human Oncology & Pathogenesis Program (HOPP)	2007-2011
Elizabeth and Felix Rohatyn Chair for Junior Faculty	Memorial Hospital for Cancer and Allied Diseases, NY, NY	2007-2011
Associate Attending Physician	Genitourinary Oncology Service Memorial Hospital for Cancer and Allied Diseases, NY, NY	2011-present
Associate Attending Physician	Human Oncology & Pathogenesis Program (HOPP)	2011-present
Director	Developmental Therapeutics	2013-present

PROFESSIONAL MEMBERSHIPS (medical and scientific societies)

Member, American Society of Clinical Oncology	1999-present
Member, American Association for Cancer Research	1999-present
Member, American Society for Clinical Investigation	2011-present

HONORS AND AWARDS

Inductee, American Society for Clinical Investigation	2011
Boyer Award for Excellence in Clinical Research	2007
Elizabeth and Felix Rohatyn Chair for Junior Faculty	2007
Kimmel Scholars Award	2007
Prostate Cancer Foundation Investigator Award	2004
ASCO Career Development Award	2002
ASCO Young Investigator Award	2001
ASCO Merit Award	2001
Doris Duke Translational Award	2001
NIH Clinical Scholars Research Fellow	2000
Phi Beta Kappa, University of Pennsylvania	1992
Summa Cum Laude, University of Pennsylvania	1991
Rensselaer Math and Science Medal	1987
National Merit Scholar	1987

BIBLIOGRAPHY

Articles in professional peer-reviewed journals (selected from 99 publications)

Published/In Press Articles:

1. Vakiani E, Janakiraman M, Shen R, Sinha R, Zeng Z, Shia J, Cercek A, Kemeny N, D'Angelica M, Viale A, Heguy A, Paty P, Chan T, Saltz L, Weiser M, Solit D. Comparative genomic analysis of primary versus metastatic colorectal carcinomas. J Clin Oncol, 2012 20;30(24):2956-62. Jun 4. [Epub ahead of print]. PMID: 22665543. PMCID: PMC3417049.
2. Misale S, Yaeger R, Hobor S, Scala E, Janakiraman M, Liska D, Valtorta E, Schiavo R, Buscarino M, Siravegna G, Bencardino K, Cercek A, Chen C, Veronese S, Zanon C, Sartore-Bianchi A, Gambacorta M, Gallicchio M, Vakiani E, Boscaro V, Medico E, Weiser M, Siena S, Di Nicolantonio F, Solit D, Bardelli A. Emergence of KRAS mutations and acquired resistance to anti-EGFR therapy in colorectal cancer. Nature, 2012 Jun 28; 486(7404):532-6. PMID: 22722830. (The last two authors contributed equally to this study).
3. Straussman R, Morikawa T, Shee K, Barzily-Rokni M, Qian Z, Du J, Davis A, Mongare M, Gould J, Frederick D, Cooper Z, Chapman P, Solit D, Lo R, Flaherty K, Ogino S, Wargo J, Golub T. Tumour micro-environment elicits innate resistance to RAF inhibitors through HGF secretion. Nature, 2012 Jul 26;487(7408):500-4, Jul 4. [Epub ahead of print]. PMID: 22763439.
4. Sherer E, Sale M, Pollock B, Belani C, Egorin M, Ivy P, Lieberman J, Manuck S, Marder S, Muldoon M, Scher H, Solit D, Bies R. Application of a single-objective, hybrid genetic algorithm approach to pharmacokinetic model building. J Pharmacokinet Pharmacodyn, 2012 Jul 6. [Epub ahead of print]. PMID: 22767341. PMCID: PMC3400037.
5. Dahlman K, Xia J, Hutchinson K, Ng C, Hucks D, Jia P, Atefi M, Su Z, Branch S, Lyle P, Hicks D, Bozon V, Glaspy J, Rosen N, Solit D, Netterville J, Vnencak-Jones C, Sosman J, Ribas A, Zhao Z, Pao W. BRAF L597 mutations in melanoma are associated with sensitivity to MEK inhibitors. Cancer Discovery, 2012 Jul 13. [Epub ahead of print]. PMID: 22798288.
6. Cancer Genome Atlas Network (Muzny DM, Bainbridge MN,…, Solit D,..., Thomson E), Comprehensive molecular characterization of human colon and rectal cancer. Nature, 2012, 487(7407):330-7. PMID: 22810696. PMCID: PMC3401966.
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8. Grisham R, Iyer G, Garg K, Delair D, Hyman D, Zhou Q, Iasonos A, Berger M, Dao D, Levine D, Aghajanian C, Solit D. BRAF Mutation is Associated with Early Stage Disease and Improved Outcome in Patients with Low-Grade Serous Ovarian Cancer. Cancer, 2012 Aug 28. [Epub ahead of print]. PMID: 22930283.
9. Callahan MK, Rampal R, Harding J, Klimek V, Chung Y, Merghoub T, Wolchok J, Solit D, Rosen N, Abdel-Wahab O, Levine RL, Chapman, P. Progression of RAS-mutant Leukemia during RAF Inhibitor Treatment. N Engl J Med, 2012 13;367(24):2316-21. Epub 2012 Nov 7. PMID: 23134356.
10. Wang Y, Velho S, Vakiani E, Peng S, Bass A, Chu G, Gierut J, Bugni J, Der C, Philips M, Solit D, Haigis K. Mutant N-RAS protects colorectal cancer cells from stress-induced apoptosis and contributes to cancer development and progression. Cancer Discov, 2012 Dec 28. [Epub ahead of print]. PMID: 23274911.
11. Morris L, Kaufman A, Gong Y, Walsh LA, Turcan S, Eng S, Kannan K, Peng L, Zou Y, Banuchi V, Paty P, Zeng Z, Vakiani E, Zou Y, Peng L, Solit D, Singh B, Ganly I, Liau L, Cloughesy T, Mischel P, Mellinghoff I, Chan TA. Recurrent somatic mutation of FAT1 in multiple human cancers leads to aberrant Wnt activation. Nat Genetics, 2013 Jan 27. PMID: 23354438.
12. Redelman-Sidi G, Iyer G, Solit D, Glickman M. Oncogenic activation of Pak1 dependent Macropinocytosis pathway determines BCG entry into bladder cancer cells. Cancer Res, 2013 Feb 1. PMID: 23378476.
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14. Milowsky M, Iyer G, Regazzi A, Al-Ahmadie H, Gerst SR, Ostrovnaya I, Gellert LL, Kaplan R, Garcia-Grossman I, Pendse D, Balar AV, Flaherty AM, Trout A, Solit DB, Bajorin DF. Phase II Study of Everolimus in Metastatic Urothelial Cancer. BJU Int, 2013 Apr 3. [Epub ahead of print]. PMID: 23551593.
15. Iyer G, Al-Ahmadie H, Schultz N, Hanrahan A, Balar A, Kim P, Lin O, Weinhold N, Sander C, Ostrovnaya I, Zabor E, Janakiraman M, Garcia-Grossman I, Heguy A, Viale A, Bochner B, Reuter V, Bajorin D, Milowsky M, Taylor B, Solit D, Prevalence and co-occurrence of actionable genomic alterations in high-grade bladder cancer, JCO, in press, 2012.

IAAO2013 Title of the Talk:

The Power of One: Use of Whole Genome Outlier Analysis to Identify Occult Biomarkers of Drug Response

ABSTRACT:

Session 2-3

Title: Role of Mutations in Epigenetic Regulators in Pathogenesis of Myeloid Malignancies

Speaker

Ross L. Levine, MD
Associate Member, Human Oncology and Pathogenesis Program, Associate Attending Physician, Leukemia Service, Department of Medicine, Memorial Sloan Kettering Cancer Center
Associate Professor of Medicine, Weill Cornell Medical College, USA

Chairman

Yuko Kitagawa, MD, PhD
Professor, Department of Surgery, Graduate School of Medicine, Keio University, Japan

Ross L. Levine, MD

Education and Training

2002-2006	Dana Farber Cancer Institute/Partners Cancer Care, Boston, MA Fellow, Hematology/Medical Oncology
1999-2002	Massachusetts General Hospital, Boston, MA. Intern/Resident in Internal Medicine
1994-1999	Johns Hopkins University School of Medicine, Baltimore, MD. Doctor of Medicine
1990-1994	Harvard College, Cambridge, MA. A.B., Biology, *magna cum laude*

Research/Fellowships

2003-2007	Postdoctoral Research Fellow Brigham and Women's Hospital/Harvard Medical School D. Gary Gilliland, Ph.D. M.D., Professor of Medicine, Investigator, Howard Hughes Medical Institute
1997-1999	Howard Hughes Medical Institute Research Training Fellowship

Johns Hopkins University School of Medicine
Lora Hedrick Ellenson, M.D., Associate Professor of Pathology, Gynecology and Obstetrics, and Oncology

1991-1994 Undergraduate Research Assistant
Brigham and Women's Hospital/Harvard Medical School
Gary S. Richardson, M.D., Instructor in Medicine

Positions and Employment

2007-2011 Assistant Member, Human Oncology and Pathogenesis Program & Leukemia Service, Memorial Sloan Kettering Cancer Center, tenure-track

2007-2011 Assistant Professor of Medicine, Weill Cornell Medical College

2011- Associate Member, Human Oncology and Pathogenesis Program &Leukemia Service, Memorial Sloan Kettering Cancer Center, tenure-track

2011- Associate Professor of Medicine, Weill Cornell Medical College

Honors and Awards

2012 Laurence Baker Visiting Professor, University of Michigan

2012 Leukemia and Lymphoma Society Scholar

2011 Boyer Award for Clinical Research, Memorial Sloan Kettering Cancer Center 2011 American Society of Clinical Investigation

2011 Sir William Osler Young Investigator Award, Interurban Clinical Club

2007 Geoffrey Beene Junior Chair

2007 Howard Hughes Medical Institute Early Career Award

2006 Doris Duke Charitable Foundation Clinical Scientist Development Award

2006 American Society of Hematology Basic Research Fellow Award

2006 American Society of Clinical Oncology Young Investigator Award

1999 *Alpha Omega Alpha,* Johns Hopkins School of Medicine

1998-1999 Howard Hughes Medical Institute Award for Completion of Medical Studies

1994 Harvard University, *magna cum laude*

1991-1994 Harvard University, John Harvard Scholarship

Licensure and Board Certification

2002 Certification, Internal Medicine (American Board of Internal Medicine)

2005 Certification, Hematology (American Board of Internal Medicine)

2005 Certification, Medical Oncology (American Board of Internal Medicine)

2007 Medical License, State of New York, #245520

Professional Societies

2002- Member, American Society of Hematology

2008- Member, American Association for Cancer Research

Publications (selected from 107 publications)

1. Doege CA, Inoue K, Yamashita T, Rhee DB, Travis S, Fujita R, Guarnieri P, Bhagat G, Vanti WB, Shih A, **Levine R.L.**, Nik S, Chen EI, Abeliovich A. Early-stage epigenetic modification during somatic cell reprogramming by Parp1 and Tet2. *Nature*. 2012 Aug 30;488(7413):652-5. PMID: 22902501

2. Diab A, Zickl L, Abdel-Wahab O, Jhanwar S, Gulam MA, Panageas KS, Patel JP, Jurcic J, Maslak P, Paietta E, Mangan JK, Carroll M, Fernandez HF, Teruya-Feldstein J, Luger SM, Douer D, Litzow MR, Lazarus HM, Rowe JM, **Levine R.L.**, Tallman MS. Acute myeloid leukemia with translocation t(8;16) presents with features which mimic acute promyelocytic leukemia and is associated with poor prognosis. *Leuk Res*. 2013 Jan;37(1):32-6. PMID: 23102703.

3. Kämpjärvi K, Mäkinen N, Kilpivaara O, Arola J, Heinonen HR, Böhm J, Abdel-Wahab O, Lehtonen HJ, Pelttari LM, Mehine M, Schrewe H, Nevanlinna H, **Levine R.L.**, Hokland P, Böhling T, Mecklin JP, Bützow R, Aaltonen LA, Vahteristo P. Somatic MED12 mutations in uterine leiomyosarcoma and colorectal cancer. *Br J Cancer*. 2012 Nov 6;107(10):1761-5. PMID: 23132392.

4. Busque L, Patel JP, Figueroa, ME, Vasanthakumar A, Provost S, Hamilou Z, Mollica L, Li J, Viale, A, Heguy, A, Hassimi M, Socci N, Bhatt PK, Gönen, M, Mason CE, Melnick, A, Godley LA, Brennan C, Abdel-Wahab, O, and **Levine, R.L.,** Recurrent Somatic TET2 Mutations in Normal Elderly Individuals With Clonal Hematopoiesis. *Nature Genetics.* 2012 Nov; 44(11):1179-81. PMCID:PMC3483435

5. Callahan MK, Rampal R, Harding JJ, Klimek VM, Chung YR, Merghoub T, Wolchok, JD, Solit DB, Rosen N, Abdel-Wahab O, **Levine R.L.**, Chapman PB. Progression of RAS-Mutant Leukemia during RAF Inhibitor Treatment. *N Engl J Med*. 2012 Dec 13;367(24):2316-21. PMID: 23134356.

6. Pollyea DA, Zehnder J, Coutre S, Gotlib J, Gallegos L, Abdel-Wahab O, Greenberg P, Zhang B, Liedtke M, Berube C, **Levine R.L.**, Mitchell BS, Medeiros BC. Sequential azacitidine plus lenalidomide combination for elderly patients with untreated acute myeloid leukemia. *Haematologica*. 2012 Dec 14. [Epub ahead of print] PubMed PMID: 23242596

7. Baljevic M, Abdel-Wahab O, Rampal R, Maslak PG, Klimek VM, Rosenblat TL, Douer D, **Levine R.L.**, Tallman MS. Translocation t(11;17) in de novo Myelodysplastic Syndrome Not Associated with Acute Myeloid or Acute Promyelocytic Leukemia. *Acta Haematol*. 2013;129(1):48-54. PMID: 23147462.

8. Ward PS, Lu C, Cross JR, Abdel-Wahab O, **Levine R.L.**, Schwartz GK, Thompson CB. The Potential for Isocitrate Dehydrogenase Mutations to Produce 2-Hydroxyglutarate Depends on Allele Specificity and Subcellular CompartmentalizationI. 2013 Feb 8;288(6):3804-15. PMC3567635.

9. Shih AH, Chung SS, Dolezal EK, Zhang SJ, Abdel-Wahab OI, Park CY, Nimer SD, **Levine R.L.**, Klimek VM. Mutational analysis of therapy-related myelodysplastic syndromes and acute myelogenous leukemia. Haematologica. 2013 Jan 24. [Epub ahead of print] PubMed PMID: 23349305.

10. Gautier EL, Westerterp M, Bhagwat N, Cremers S, Shih A, Abdel-Wahab O, Lütjohann D, Randolph GJ, **Levine R.L.**, Tall AR, Yvan-Charvet L. HDL and Glut1 inhibition reverse a hypermetabolic state in mouse models of myeloproliferative disorders. J Exp Med. 2013 2013 Feb 11;210(2):339-53. PMID: 23319699

11. Lobry C, Ntziachristos P, Ndiaye-Lobry D, Oh P, Cimmino L, Zhu N, Araldi E, Hu W, Freund J, Abdel-Wahab O, Ibrahim S, Skokos D, Armstrong SA, **Levine R.L.**, Park CY, Aifantis I. Notch pathway activation targets AML-initiating cell homeostasis and differentiation. *J Exp Med.* 2013 2013 Feb 11;210(2):301-19.PMID: 23359070

12. Meyer JA, Wang J, Hogan LE, Yang JJ, Dandekar S, Patel JP, Tang Z, Zumbo P, Li S, Zavadil J, **Levine R.L.**, Cardozo T, Hunger SP, Raetz EA, Evans WE, Morrison DJ, Mason CE, Carroll WL. Relapse-specific mutations in NT5C2 in childhood acute lymphoblastic leukemia. *Nat Genet*. 2013 Mar;45(3):290-4. PMID: 23377183

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14. Sanda T, Tyner JW, Gutierrez A, Ngo VN, Glover J, Chang BH, Yost A, Ma W, Fleischman AG, Zhou W, Yang Y, Kleppe M, Ahn Y, Tatarek J, Kelliher M, Neuberg D, **Levine R.L.**, Moriggl R, Muller M, Gray NS, Jamieson CH, Weng AP, Staudt LM, Druker BJ, Look AT. TYK2-STAT1-BCL2 Pathway Dependence in T-Cell Acute Lymphoblastic Leukemia. Cancer *Discov*. 2013 Mar 7. [Epub ahead of print]. PMID:23471820

15. Ramos P, Casu C, Gardenghi S, Breda L, Crielaard BJ, Guy E, Marongiu MF, Gupta R, **Levine R.L.**, Abdel-Wahab O, Ebert BL, Van Roolien N, Ghaffari S, Grady RW, Giardina PJ, Rivella S. Macrophages support pathological erythropoiesis in polycythemia vera and β-thalassemia. *Nat Med.* 2013 Mar 17. doi: 10.1038/nm.3126. [Epub ahead of print]. PMID: 23502961

IAAO2013 Title of the Talk:

Role of Mutations in Epigenetic Regulators in Pathogenesis of Myeloid Malignancies

ABSTRACT:

Clinical, cytogenetic, and gene-based studies have been used to inform biology and improve prognostication for patients with acute myeloid leukemia (AML), myelodysplasia (MDS), and myeloroliferative neoplasms (MPN). Most recently, a series of candidate gene and whole genome studies have identified recurrent somatic mutations in AML patients including TET2, ASXL1, DNMT3A, and EZH2 mutations. We and others have shown these mutations are of prognostic relevance, and can be used to improve risk stratification in AML. We identified genetic predictors of outcome that improved risk stratification in AML independent of age, WBC count, induction dose, and post-remission therapy and validated their significance in an independent cohort. Importantly, these mutational predictors involved complex genotypes, suggesting combinations of mutations mark prognostically relevant groups and segregate AML into distinct, biologically significant subsets. Integrating mutational data with dose-intensity revealed that high-dose daunorubicin improved survival in patients with DNMT3A/NPM1 mutations or MLL translocations relative to treatment with standard dose daunorubicin, but not in patients wild-type for these alterations. These data provide important clinical implications of genetic alterations in AML by delineating mutation combination genotypes that predict outcome in AML and improve AML risk stratification. Of biologic importance, the TET family of proteins have been shown to place a hydroxyl mark on methylated DNA and lead to DNA demethylation. We and others have found that TET2 mutations leads to loss of DNA hydroxymethylation and a hypermethylation phenotype in leukemia patients. In addition, in vitro and in vivo studies show that TET2 loss leads to impaired hematopoietic differentiation, increased stem cell self-renewal, and myeloid transformation in vivo. These data demonstrate that novel mutations coopt the epigenetic state of hematopoietic stem/progenitor cells in order to contribute to transformation and that these mutations have biologic and prognostic relevance.

Session 3-1

Title: Immune Checkpoint Blockade in Cancer Therapy: New Insights & Opportunities

James P. Allison, PhD
Chairman, Department of Immunology, MD Anderson Cancer Center
Director, Immunology Platform, MD Anderson Cancer Center
Deputy Director, David H. Koch Center for Applied Research of Genitourinary Cancers, MD Anderson Cancer Center, USA

Speaker

Makoto Ogawa, MD
Emeritus President, Aichi Cancer Center, Japan

Chairman

James P. Allison, PhD

EDUCATION:

1969	BS, Microbiology, the University of Texas, Austin, Texas
1973	PhD, Biological Sciences, the University of Texas, Austin, Texas
1974 -1977	Post doctoral training, Molecular Immunology, Scripps Clinic and Research Foundation

POSTDOCTORAL TRAINING:

1974-1977	Postdoctoral Fellow, Department of Molecular Immunology, Scripps Clinic and Research Foundation, La Jolla, California

Positions and Honors.

Positions

1974-1977	Postdoctoral Fellow, Department of Molecular Immunology, Scripps Clinic and Research Foundation, La Jolla, CA
1977-1983	Assistant Biochemist and Assistant Professor Biochemistry, The University of Texas System Cancer Center, Science Park - Research Division, Smithville, TX
1979-1984	Adjunct Assistant Professor of Zoology, The University of Texas at Austin, Austin, TX
1980-1984	Special Associate Member of the Graduate Faculty, The University of Texas at Austin, Austin, TX
1983-1984	Associate Biochemist and Associate Professor of Biochemistry, The University of Texas System Cancer Center, Science Park - Research Division, Smithville, TX
1983-1984	Visiting Scholar, Department of Pathology, Stanford University School of Medicine, Stanford, CA
1985-2004	Professor, Division of Immunology, Department of Molecular and Cell Biology, University of California, Berkeley, CA
1985-2004	Director, Cancer Research Laboratory, University of California, Berkeley, CA
1987-1989	Interim Head, Division of Immunology, Department of Molecular and Cell Biology, University of California, Berkeley, CA
1989-1997	Head, Division of Immunology, Department of Molecular and Cell Biology, University of California, Berkeley, CA
1995	Merit Award, National Institutes of Health
1997	Member, National Academy of Sciences
1997	Fellow, American Academy of Microbiology
1997	Investigator, Howard Hughes Medical Institute
1997-2012	Investigator, Howard Hughes Medical Institute
1997-2004	Adjunct Professor, Division of Rheumatology, Department of Medicine, School of Medicine, UCSF
1998-2000	Co-Chair, Department of Molecular and Cell Biology, University of California, Berkeley, CA
2004-2012	Chairman, Immunology Program, Memorial Sloan-Kettering Cancer Center, New York, NY
2004-2012	David H. Koch Chair in Immunologic Studies, Memorial Sloan-Kettering Cancer Center, New York, NY
2004-2012	Attending Immunologist, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY
2004-2012	Co-Chair, Graduate Program in Immunology and Microbial Pathogenesis, Weill Graduate School of Medical Sciences of Cornell University, New York, NY
2004-2012	Professor, Weill Medical College of Cornell University, New York, NY
2006-2012	Director, Ludwig Center for Cancer Immunotherapy, New York, NY
2012-present	Chairman, Department of Immunology, MD Anderson Cancer Center, Houston, TX
2012-present	Director, Immunotherapy Platform, MD Anderson Cancer Center, Houston, TX
2012-present	Deputy Director, David H. Koch Center for Applied Research of Genitourinary Cancers, MD Anderson Cancer Center, Houston, TX

Honors

1986	Merit Award, National Institutes of Health
1997	Member, National Academy of Sciences
1997	Fellow, American Academy of Microbiology
1997	Investigator, Howard Hughes Medical Institute
2001	Centeon Award for Innovative Breakthroughs in Immunology

2002	Outstanding Alumnus Award, The University of Texas at Austin Graduate School
2005	William B. Coley Award for Distinguished Research in Basic and Tumor Immunology, Cancer Research Institute
2007	Fellow, American Association for the Advancement of Science
2007	Elected Member, Institute of Medicine
2008	C. Chester Stock Award, Memorial Sloan-Kettering Cancer Center
2008	Dana Foundation Award in Human Immunology Research, American Association of Immunologists
2010	Richard V. Smalley, MD, Memorial Lectureship Award, International Society for Biological Therapy of Cancer
2011	Lifetime Achievement Award, American Association of Immunologists
2011	Roche Award for Cancer Immunology and Immunotherapy
2011	Breakthrough Achievement in Translational Cancer Research, American Skin Association
2011	Jacob Heskel Gabbay Award in Biotechnology and Medicine, Brandeis University
2011	Advancement of Cancer Research Award, Gilda's Club

Selected peer-reviewed publications (in chronological order).

1. Leach DR, Krummel MF, Allison JP. Enhancement of antitumor immunity by CTLA-4 blockade. Science 271:1734-1736, 1996. PMID 8596936.
2. Hurwitz AA, Yu TF-Y, Leach DR, Allison JP. CTLA-4 blockade synergizes with tumor-derived GM-CSF for treatment of an experimental mammary carcinoma. Proc Natl Acad Sci USA 95:10067-10071, 1998.
3. van Elsas A, Hurwitz AA, Allison JP. Combination immunotherapy of B16 melanoma using anti-cytotoxic T lymphocyte—associated antigen 4 (CTLA-4) and granulocyte/macrophage colony-stimulating factor (GM-CSF)-producing vaccines induces rejection of subcutaneous and metastatic tumors accompanied by autoimmune depigmentation. J Exp Med 190:355-366, 1999. PMCID: PMC2195583.
4. Hurwitz AA, Foster BA, Kwon ED, Truong T, Choi EM, Greenberg NM, Burg MB, Allison JP. Combination immunotherapy of primary prostate cancer in a transgenic mouse model using CTLA-4 blockade. Cancer Res 60:2444-2448, 2000. PMID: 10811122.
5. van Elsas A, Sutmuller RPM, Hurwitz AA, Ziskin J, Villasenor J, Medema J-P, Overwijk WW, Restifo NP, Melief CJM, Offringa R, Allison JP. Elucidating the autoimmune and anti-tumor effector mechanisms of a treatment based on cytotoxic T lymphocyte antigen-4 (CTLA-4) blockade in combination with a B16 melanoma vaccine: Comparison of prophylaxis and therapy. J Exp Med 194:481-489, 2001. PMCID: PMC2193490.
6. Sutmuller RPM, van Duivenvoorde LM, van Elsas A, Schumacher TNM, Wildenberg ME, Allison JP, Toes REM, Offringa R, Melief CJM. Synergism of CTLA-4 blockade and depletion of CD25+ regulatory T cells in anti-tumor therapy reveals alternative pathways for suppression of auto-reactive CTL responses. J Exp Med 194:823-832, 2001. PMCID: PMC 2195955.
7. Quezada SA, Peggs KS, Curran MA, Allison JP. CTLA-4-blockade and GMCSF combination immunotherapy increases effector frequencies altering the intra-tumor balance of effector and regulatory T cells. J Clin Invest 7:1935-1945, 2006. PMCID: PMC1479425.
8. Small EJ, Tchekmedyian NS, Rini BI, Fong L, Lowy I, Allison JP. A pilot trial of CTLA-4 blockade with human anti-CTLA-4 in patients with hormone-refractory prostate cancer. Clin Cancer Res 13:1810-1815, 2007. PMID 17363537.
9. Fasso M, Waitz R, Hou Y, Rim T, Greenberg NM, Shastri N, Fong L, Allison JP. SPAS – (stimulator of prostatic adenocarcinoma-specific T cells)/SH3GLB2: A prostate tumor antigen identified by CTLA-4 Blockade. Proc Natl Acad Sci USA 105(9):3509-3514, 2008. PMCID: PMC2265147.
10. Segal NH, Parsons DW, Peggs KS, Velculescu V, Kinzler KW, Vogelstein B, Allison JP. Epitope landscape in breast and colorectal cancer. Cancer Res 68:889-892, 2008. PMID: 18245491.
11. Quezada SA, Peggs KS, Simpson TR, Shen Y, Littman DR, Allison JP. Limited tumor infiltration by activated T effector cells restricts the therapeutic activity of regulatory T cell depletion against established melanoma. J Exp Med 205(9):2125-2138, 2008. PMCID: PMC2526206.
12. Quezada SA, Simpson TR, Peggs KS, Merghoub T, Vider J, Fan X, Blasberg R, Yagita H, Muranski P, Antony PA, Restifo NP, Allison JP. Tumor-reactive CD4+ T cells develop cytotoxic activity and eradicate large established melanoma after transfer into lymphopenic hosts. J Exp Med 207(3):637-

650, 2010. PMCID: PMC2839156.

13. Curran M, Montalvo W, Yagita H, Allison JP. PD-1 and CTLA-4 combination blockade expands infiltrating T-cells and reduces regulatory T and myeloid cells within B16 melanoma tumors. Proc Natl Acad Sci USA 107(9):4275-4280, 2010. PMCID: PMC2840093.

14. Curran MA, Kim M, Montalvo W, Al-Shamkhani A, Allison JP. Combination CTLA-4 blockade and 4-1BB activation enhances tumor rejection by incrasing T-cell infiltration, proliferation, and cytokine production. PLoS One 6(4):e19499, 2011. PMCID: PMC3085474.

15. Waitz R, Solomon SB, Petre EN, Trumble AE, Fasso M, Norton L, Allison JP. Induction of tumor immunity through cryoablation and cytotoxic T lymphocyte-associated antigen 4 blockade combination therapy. Cancer Res 72(2):430-439, 2012. PMID: 22108823.

Session 3-1

IAAO2013 Title of the Talk:

Immune Checkpoint Blockade in Cancer Therapy: New Insights & Opportunities

ABSTRACT:

Title: Immune Monitoring on Pre-surgical Clinical Trials with Anti-CTLA-4: Implicating the ICOS/ICOSL Pathway in Anti-tumor Immune Responses

Padmanee Sharma, MD, PhD
Scientific Director Immunotherapy Platform, The University of Texas MD Anderson Cancer Center, Houston, TX
Associate Professor, Department of Genitourinary Medical Oncology, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Speaker

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

Chairman

Padmanee Sharma, MD, PhD

Present Title & Affiliation

Primary Appointment

Member, Investigational Drug Steering Committee (IDSC) for the National Cancer Institute's Clinical Trials Working Group, Chelsea, MI

Scientific Director Immunotherapy Platform, The University of Texas MD Anderson Cancer Center, Houston, TX

Associate Professor, Department of Genitourinary Medical Oncology, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX

Dual/Joint/Adjunct Appointment

Associate Professor, Department of Immunology, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX

Member, The University of Texas Graduate School of Biomedical Sciences Faculty, Houston, TX

Director, Flow Cytometry Facility in Koch Center of GU Medical Oncology, Houston, TX

Education & Training

Degree-Granting Education

1998 Pennsylvania State University, College of Medicine, Hershey, PA, MD, Medicine

1998 Pennsylvania State University, College of Medicine, Hershey, PA, Ph.D., Immunology

1991 Boston University, Boston, MA, MA, Biotechnology

1990 Boston University, Boston, MA, BA, Biology

Postgraduate Training

6/2004 Clinical Fellowship, Medical Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY

6/2000 Clinical Residency, Internal Medicine, New York Hospital, Cornell Medical Center, New York, NY

Board Certifications

1/2003 Board Certified Medical Oncology

1/2000 Board Certified Internal Medicine

Experience/Service

Academic Appointments

Assistant Professor, Department of Immunology, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, 7/2005-2010

Assistant Professor, Department of Genitourinary Medical Oncology, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, 7/2004-2010

Fellow, Medical Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY, 7/2000-7/2004

Resident, New York Hospital, Cornell Medical Center, New York, NY, 7/1998-7/2000

Other Appointments/Responsibilities

Member, Executive Committee, Clinical Immunology Society, Milwaukee, WI, 2012-2015

Member, ASCO Scientific Program Committee on the Developmental Therapeutics-Clinical Pharmacology and Immunotherapy Track, Alexandria, VA, 2010-present

Board Member, Society for Immunotherapy of Cancer, Milwaukee, WI, 2010-present

Member, Cancer Research Institute Cancer Vaccine Acceleration Fund (CVAF) Global Sourcing Committee, New York, NY, 2010-present

Member, Stand Up to Cancer (SU2C) Innovative Research Grants (IRG) Scientific Review Committee, Philadelphia, PA, 2010

Associate Clinical Director, Ludwig Center for Cancer Immunotherapy at Memorial Sloan-Kettering Cancer Center, New York, NY, 7/2007-11/2012

Honors and Awards

2012 MD Anderson Cancer Center Faculty Scholar Award

2012 MD Anderson Women Faculty Programs "Woman Leading the Way"

2012 National Institute of Health R01 Award

2011 Cancer Prevention Research Institute of Texas Award

2010 DOD/CDMRP Idea Development Award

2009 American Cancer Society Mentored Research Scholar Grant

2008 Doris Duke Clinical Scientist Development Award

2008 Melanoma Research Alliance Young Investigator Award

2008 Prostate Cancer Foundation Challenge Award in Immunology
2007 Carl C. Anderson, Sr. & Marie Jo Anderson Charitable Foundation
2007 MD Anderson Cancer Center Bladder Cancer SPORE Development Award
2007 The Gillson Longenbaugh Foundation
2006 American Society of Clinical Oncology Career Development Award
2006 Cancer Research Institute Clinical Investigator Award
2006 Prostate Cancer Foundation Young Investigator Award
2005 MD Anderson Cancer Center Institutional Research Grant
2005 MD Anderson Cancer Center Physician Scientist Training Program Award
2005 National Institute of Health Renewal Clinical Loan Repayment Program Award
2003 American Society of Clinical Oncology, Young Investigator Award Recipient
2003 Award Recipient, GSK National Medical Oncology Fellows Forum
2002 Award for Abstract Presentation, Doris Duke Symposium
2001 Memorial Sloan-Kettering Cancer Center Institutional NIH T32 Grant
1998 Pennsylvania State University, Department of Medicine Scholarship for Excellence in Medicine
1995 Pennsylvania State University Student Clinician Research Award
1994 The Judy S. Finkelstein Memorial Award in Immunology
1990 Golden Key National Honor Society

Professional Memberships

American Association for Cancer Research (AACR)
Member, 2006-present

American Society of Clinical Oncology (ASCO)
Member, 2005-present

Anti-CTLA Clinical Trials, LICR/CRI/BMS Initiative
Member, 2006

ASCO Scientific Program Committee on the Developmental Therapeutics-Clinical Pharmacology and Immunotherapy Track
Member, 2011-present

Cancer Research Institute Cancer Vaccine Acceleration Fund (CVAF) Global Sourcing Committee
Member, 2010-present

Clinical Immunology Society, Milwaukee, IL
Councilor, 2012-2015

International Society for Biological Therapy of Cancer (iSBTc)
Member, Board of Directors, 2010
Member, 2005-present

International Society for Biological Therapy of Cancer Organizational Collaborations (now known as Society for Immunotherapy of Cancer, SITC)
Member, 2010

Investigational Drug Steering Committee (IDSC) Task Force
Member, 2012-present

SITC Program Committee
Member, 2010

SITC Strategic Planning Retreat
Member, 2010

Stand Up to Cancer (SU2C) Innovative Research Grants (IRG) Scientific Review Committee

Member, 2010-present

Women in Cancer Research (AACR), Philadelphia, PA

Member, 2009-present

Selected Publications

Peer-Reviewed Original Research Articles

1. Richey SL, Tamboli P, NG CS, Lim ZD, Araujo JC, Jonasch E, Sharma P, Pagliaro LC, Tannir NM. Phase II trial of Pemetrexed plus Gemcitabine in patients with locally advanced and metastatic non-clear cell renal cell carcinoma. Am J Clin Oncol, 6/2012. PMID: 22706175.
2. Sun JJ, Ng Tang D, Fu T,Sharma P. Identification of human regulatory T cells in the setting of T cell activation and anti-CTLA-4 immunotherapy based on expression of latency associated peptide (LAP). Cancer Discovery 2(2):122-30, 2012. PMID: 22585857.
3. Fox BA, Schendel DJ, Butterfield LH. . Sharma P, etal. Defining the critical hurdles in cancer immunotherapy. J Transl Med. 9(1):214, 12/2011. PMCID: PMC3338100.
4. Fu T, He Q, Sharma P. The ICOS/ICOSL pathway is required for optimal anti-tumor responses mediated by anti-CTLA-4 therapy. Cancer Res 71(16):5445-54, 8/2011. PMID: 21708958.
5. Carthon BC, Wolchok JD, Yuan J, Kamat A, Ng Tang DS, Sun J, Ku G, Troncoso P, Logothetis CJ, Allison JP, Sharma P. Preoperative CTLA-4 blockade: tolerability and immune monitoring in the setting of a presurgical clinical trial. Clin Cancer Res 16(10):2861-71, 5/2010. PMCID: PMC2919850.
6. Matin SF, Sharma P, Gill IS, Tannenbaum C, Hobart MG, Novick AC, Finke JH. Immunologic response to renal cryoablation in an in vivo orthotopic renal cell carcinoma murine model. J Urol 183(1):333-8, 1/2010. PMID: 19914660.
7. Gnjatic S, Altorki NK, Tang DN, Tu SM, Kundra V, Ritter G, Old LJ, Logothetis CJ, Sharma P. NY-ESO-1 DNA vaccine induces T cell responses that are suppressed by regulatory T cells. Clin Cancer Res 15(6):2130-9, 3/2009. PMID: 19276258.
8. Chen H, Liakou CI, Kamat A, Pettaway C, Ward JF, Tang DN, Sun J, Jungbluth AA, Troncoso P, Logothetis C, Sharma P. Anti-CTLA-4 therapy results in higher CD4+ICOShi T cell frequency and IFN-{gamma} levels in both nonmalignant and malignant prostate tissues. Proc Natl Acad Sci U S A 106(8):2729-34, 2/2009. PMCID: PMC2650334.
9. Sharma P, Bajorin DF, Jungbluth AA, Herr H, Old LJ, Gnjatic S. Immune responses detected in urothelial carcinoma patients after vaccination with NY-ESO-1 protein plus BCG and GM-CSF. J Immunother 31(9):849-57, 11/2008. PMID: 18833002.
10. Liakou CI, Kamat A, Tang DN, Chen H, Sun J, Troncoso P, Logothetis C, Sharma P. CTLA-4 blockade increases IFNgamma-producing CD4+ICOShi T cells to shift the ratio of effector to regulatory T cells in cancer patients. Proc Natl Acad Sci U S A 105(39):14987-92, 9/2008. PMCID: PMC2567480.
11. Sun J, Schiffman J, Raghunath A, Ng Tang D, Chen H, Sharma P. Concurrent decrease in IL-10 with development of immune-related adverse events in a patient treated with anti-CTLA-4 therapy. Cancer Immun 8:9, 5/2008. PMCID: PMC2935772.
12. Zang X, Thompson RH, Al-Ahmadie HA, Serio AM, Reuter VE, Eastham JA, Scardino PT, Sharma P, Allison JP. B7-H3 and B7x are highly expressed in human prostate cancer and associated with disease spread and poor outcome. Proc Natl Acad Sci U S A 104(49):19458-63, 12/2007. PMCID: PMC2148311.
13. Kopetz S, Jimenez CA, Tu SM, Sharma P. Pulmonary arteriovenous fistula in a patient with renal cell carcinoma. Eur Resp J 29(4):813-5, 4/2007. PMID: 17400880.
14. Sharma P, Shen Y, Wen S, Yamada S, Jungbluth AA, Gnjatic S, Bajorin DF, Reuter VE, Herr H, Old LJ, Sato E. CD8 tumor-infiltrating lymphocytes are predictive of survival in muscle-invasive urothelial carcinoma. Proc Natl Acad Sci U S A 104(10):3967-72, 3/2007. PMCID: PMC1820692.
15. Sharma P, Shen Y, Wen S, Bajorin DF, Reuter VE, Old LJ, Jungbluth AA. Cancer-testis antigens: expression and correlation with survival in human urothelial carcinoma. Clin Cancer Res 12(18):5442-7, 9/2006. PMID: 17000678.
16. Sharma P, Gnjatic S, Jungbluth AA, Williamson B, Herr H, Stockert E, Dalbagni G, Donat SM, Reuter VE, Santiago D, Chen YT, Bajorin DF, Old LJ. Frequency of NY-ESO-1 and LAGE-1 expression in bladder cancer and evidence of a new NY-ESO-1 T cell epitope in a patient with bladder cancer. Cancer Immun 3:19, 12/2003. PMID: 14680360.

17. Sharma P, Page MJ, Poritz LS, Koltun WA, Chorney MJ. An increased gamma delta T cell population in the intestine of thymus-leukemia antigen transgenic mice. Cell Immunol 176(2):153-7, 3/1997. PMID: 9073388.

18. Sharma P, Johnson CA, Bonneau RH, Lang CM, Chorney MJ. Transgenic mice expressing the thymus leukemia antigen fail to control cutaneous herpes simplex virus infection. Cell Immunol 174(1):84-9, 11/1996. PMID: 8929457.

19. Joyce S, Negishi I, Boestanu A, DeSilva DA, Sharma P , Chorney MJ, Loh DY, Van Kaer L. Expansion of natural (NK1+) T cells that express alpha/beta T-cell receptors in transporters associated with antigen presentation-1 null and thymus-leukemia antigen positive mice. J Exp Med 184(4):1579-84, 10/1996. PMCID: PMC2192848.

20. Venditti CP, Lawlor DA, Sharma P, Chorney MJ. Structure and content of the major histocompatibility complex (MHC) class I regions of the great anthropoid apes. H Immunol 49(2):71-84, 9/1996. PMID: 8872161.

21. Sharma P, Joyce S, Chorney K, Griffith J, Bonneau RH, Wilson F, Flavell R, Chorney MJ. Thymus-leukemia antigen, T18d, interacts with T cells and self peptides. J Immunol 156(3):987-96, 2/1996. PMID: 8558026.

Invited Articles

1. Gao JJ, Bernatchez C, Sharma P, Radvanyi LG, Hwu P. Advances in the development of cancer immunotherapies. Trends Immunol 34(2):90-8, 2/2013. PMCID: PMC3565019.

2. Lizee G, Overwij WW, Radvanyi L, Gao JJ, Sharma P, Hwu P. Harnessing the power of the immune system to target cancer. Annual Rev Med 64(71-90), 2013. e-Pub 10/2012. PMID: 23092383.

3. Sharma P, Logothetis C. Prostate cancer: Combination of vaccine plus ipilimumab-safety and toxicity. Nat Rev Urol 9(6):302-3, 5/2012. e-Pub 2012. PMID: 22565371.

4. Sharma P, Allison JP. Retrospective. Lloyd J. Old (1933-2011). Science 335(6064):49, 1/2012. PMID: 22223799.

5. Gerritsen WR, Sharma P. Current and emerging treatment options for castration-resistant prostate cancer: A focus on immunotherapy. Journal of Clinical Immunology 32(1):25-35, 11/2011. PMCID: PMC3276755.

6. Sharma P, Wagner K, Wolchok JD, Allison JP. Novel cancer immunotherapy agents with survival benefit: Recent successes and next steps. Nature Reviews Cancer 11(11):805-12, 10/2011. PMCID: PMC3426440.

7. Hammeerstrom A, Cauley D, Atkinson B, Sharma P. Cancer immunotherapy: Sipuleucel-T and beyond. Pharmacotherapy 31(8):813-28, 8/2011. PMID: 21923608.

8. Sharma P. Cancer immunotherapy: In vivo imaging of adoptively transferred T cells in an immunocompetent host. Proc Natl Acad Sci U S A 107(32):13977-8, 8/2010. PMCID: PMC2922614.

9. Mittendorf EA, Sharma P. Mechanisms of T cell inhibition: Implications for cancer immunotherapy. Expert Rev Vaccines 9(1):89-105, 1/2010. PMID: 20021308.

10. Carthon B, Sharma P. Advanced urothelial carcinoma: Current treatment strategies and novel agents in clinical trials. CML Urology 14:57-68, 2009. PMID: 20460488.

11. Aparicio A, Sharma P, Millikan RE. Experimental systemic therapy of metastatic urothelial cancer. In: UpToDate, Basow, DS (Ed), UpToDate, Waltham, MA, 2009.

12. Liakou CI, Narayanan S, Ng Tang D, Logothetis CJ, Sharma P. Focus on TILs: Prognostic significance of tumor infiltrating lymphocytes in bladder cancer. Cancer Immun 7:10, 6/2007. PMCID: PMC2935746.

13. Sharma P, Old LJ, Allison JP. Immunotherapeutic strategies for high risk bladder cancer. Semin Oncol 34(2):165-72, 4/2007. PMID: 17382800.

14. Pagliaro LC, Sharma P. Review of treatment strategies for metastatic bladder cancer. Minerva Urol Nefrol 58:53-71, 2006. PMID: 16760884.

15. Sharma P, Donat MS, Herr H, Bajorin D. Treatment of locally advanced bladder cancer. Princ Prac Oncol Updates 16:8, 2001.

IAAO2013 Title of the Talk:

Immune Monitoring on Pre-surgical Clinical Trials with Anti-CTLA-4: Implicating the ICOS/ICOSL Pathway in Anti-tumor Immune Responses

ABSTRACT:

Session 4-1

Title: Approaches to Hypothesis Based Combination Therapy for Cancer

Speaker

Neal Rosen, MD, PhD

Member, Departments of Medicine and Neurology; and Program in Molecular Pharmacology and Chemistry, Memorial Sloan-Kettering Cancer Center, New York, NY
Professor of Pharmacology, Cornell University Graduate School of Medical Sciences, New York, NY
Professor of Medicine, Joan and Sanford I. Weill Medical College, Cornell University, New York, NY
Director, Center for Mechanism-Based Cancer Therapeutics, Sloan-Kettering Institute, New York, NY
Vice Chair, Developmental Therapeutics, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

Chairman

Mitsuaki Yoshida, PhD

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

Neal Rosen, MD, PhD

EDUCATION:

1971	BA, Columbia College, New York, NY
1979	MD, PhD (Molecular Biology), Albert Einstein College of Medicine, New York, NY

ACADEMIC APPOINTMENTS:

1985-1988	Senior Investigator, Medicine Branch, National Cancer Institute, Bethesda, MD
1988-1991	Associate Professor of Medicine, Georgetown University Medical School, Washington, DC
1992-1998	Associate Member, Program in Cell Biology and Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY Associate Professor of Cell Biology, Cornell University Graduate School of Medical Sciences,New York, NY

1992-2000	Associate Professor of Medicine, Joan and Sanford I. Weill Medical College, Cornell University, New York, NY
1998-present	Member, Departments of Medicine and Neurology; and Program in Molecular Pharmacology and Chemistry, Memorial Sloan-Kettering Cancer Center, New York, NY Professor of Pharmacology, Cornell University Graduate School of Medical Sciences, New York, NY
2000-present	Professor of Medicine, Joan and Sanford I. Weill Medical College, Cornell University, New York, NY
2012-present	Director, Center for Mechanism-Based Cancer Therapeutics, Sloan-Kettering Institute Vice Chair, Developmental Therapeutics, Department of Medicine

HOSPITAL APPOINTMENTS:

1988-1991	Director, Gastrointestinal Oncology Clinic, Lombardi Cancer Center, Georgetown University Medical School, Washington, DC
1991-1998	Associate Attending Physician, Department of Medicine, Memorial Hospital for Cancer and Allied Diseases
1998-	Attending Physician, Department of Medicine, Memorial Hospital for Cancer and Allied Diseases (Breast, Gastroenterology, and Genitourinary Services)

PROFESSIONAL MEMBERSHIPS:

- American Association for Cancer Research
- American Society of Clinical Oncology
- American Association for the Advancement of Science
- The Harvey Society

REVIEWER:

- Melanoma Research Alliance Review Committee (MRA)
- Cancer Protection and Research Institute of Texas (CPRIT) Scientific Review Committee
- Prostate Cancer Foundation

ADVISORY BOARD; ACADEMIC/MEDICAL:

- Dana-Farber Cancer Institute
- Vanderbilt Breast SPORE
- Melanoma Research Alliance
- Prostate Cancer Foundation
- Pediatric Low Grade Astrocytoma Foundation (PLGA)

RESEARCH INTERESTS:

- Mechanism of transduction of the growth signal induced by activated tyrosine kinases in epithelial tumors, especially hormone-dependent malignancies (breast and prostate cancer)
- The Hsp90 chaperone machine (its role in normal physiology and malignant transformation)
- Development of signal transduction inhibitors as anti-cancer therapeutics
- Ansamycin antibiotics (mechanism of action, preclinical development, development of specific ansamycin derivatives as targeted inhibitors of specific proteins)

RESEARCH INTERESTS:

>180 publications in the peer reviewed journals.

Representative and recent publications

1. ERK Pathway Inhibitors: How Low Should We Go? Nissan MH, Rosen N, Solit DB. Cancer Discov. 2013 Jul;3(7):719-21. doi: 10.1158/2159-8290.CD-13-0245.
2. Enhanced Inhibition of ERK Signaling by a Novel Allosteric MEK Inhibitor, CH5126766, That Suppresses Feedback Reactivation of RAF Activity. Ishii N, Harada N, Joseph EW, Ohara K, Miura T, Sakamoto H, Matsuda Y, Tomii Y, Tachibana-Kondo Y, Iikura H, Aoki T, Shimma N, Arisawa M, Sowa Y, Poulikakos PI, Rosen N, Aoki Y, Sakai T. Cancer Res. 2013 Jul 1;73(13):4050-60. doi: 10.1158/0008-5472.CAN-12-3937. Epub 2013 May 10.
3. CD44 regulates the apoptotic response and promotes disease development in chronic lymphocytic leukemia. Fedorchenko O, Stiefelhagen M, Peer-Zada AA, Barthel R, Mayer P, Eckei L, Breuer A, Crispatzu G,Rosen N, Landwehr T, Lilienthal N, Möllmann M, Montesinos-Rongen M, Heukamp L, Dürig J, Hallek M, Fingerle-Rowson G, Herling M. Blood. 2013 May 16;121(20):4126-36. doi: 10.1182/blood-2012-11-466250. Epub 2013 Apr 1.
4. Phase II trial of MEK inhibitor selumetinib (AZD6244, ARRY-142886) in patients with BRAFV600E/K-mutated melanoma. Catalanotti F, Solit DB, Pulitzer MP, Berger MF, Scott SN, Iyriboz T, Lacouture ME, Panageas KS, Wolchok JD, Carvajal RD, Schwartz GK, Rosen N, Chapman PB. Clin Cancer Res. 2013 Apr 15;19(8):2257-64. doi: 10.1158/1078-0432.CCR-12-3476. Epub 2013 Feb 26.
5. Relief of feedback inhibition of HER3 transcription by RAF and MEK inhibitors attenuates their antitumor effects in BRAF-mutant thyroid carcinomas. Montero-Conde C, Ruiz-Llorente S, Dominguez JM, Knauf JA, Viale A, Sherman EJ, Ryder M, Ghossein RA, Rosen N, Fagin JA. Cancer Discov. 2013 May;3(5):520-33. doi: 10.1158/2159-8290.CD-12-0531. Epub 2013 Jan 29.
6. Relief of profound feedback inhibition of mitogenic signaling by RAF inhibitors attenuates their activity in BRAFV600E melanomas. Lito P, Pratilas CA, Joseph EW, Tadi M, Halilovic E, Zubrowski M, Huang A, Wong WL, Callahan MK, Merghoub T, Wolchok JD, de Stanchina E, Chandarlapaty S, Poulikakos PI, Fagin JA, Rosen N. Cancer Cell. 2012 Nov 13;22(5):668-82. doi: 10.1016/j.ccr.2012.10.009.
7. Progression of RAS-mutant leukemia during RAF inhibitor treatment. Callahan MK, Rampal R, Harding JJ, Klimek VM, Chung YR, Merghoub T, Wolchok JD, Solit DB,Rosen N, Abdel-Wahab O, Levine RL, Chapman PB. N Engl J Med. 2012 Dec 13;367(24):2316-21. doi: 10.1056/NEJMoa1208958. Epub 2012 Nov 7.
8. Delayed development of chronic lymphocytic leukemia in the absence of macrophage migration inhibitory factor. Reinart N, Nguyen PH, Boucas J, Rosen N, Kvasnicka HM, Heukamp L, Rudolph C, Ristovska V, Velmans T, Mueller C, Reiners KS, von Strandmann EP, Krause G, Montesinos-Rongen M, Schlegelberger B, Herling M, Hallek M, Fingerle-Rowson G. Blood. 2013 Jan 31;121(5):812-21. doi: 10.1182/blood-2012-05-431452. Epub 2012 Nov 1.
9. Relief of profound feedback inhibition of mitogenic signaling by RAF inhibitors attenuates their activity in BRAFV600E melanomas. Lito P, Pratilas CA, Joseph EW, Tadi M, Halilovic E, Zubrowski M, Huang A, Wong WL, Callahan MK, Merghoub T, Wolchok JD, de Stanchina E, Chandarlapaty S, Poulikakos PI, Fagin JA, Rosen N. Cancer Cell. 2012 Nov 13;22(5):668-82. doi:10.1016/j.ccr.2012.10.009.
10. RAF inhibitor resistance is mediated by dimerization of aberrantly spliced BRAF(V600E). Poulikakos PI, Persaud Y, Janakiraman M, Kong X, Ng C, Moriceau G, Shi H, Atefi M, Titz B, Gabay MT, Salton M, Dahlman KB, Tadi M, Wargo JA, Flaherty KT, Kelley MC, Misteli T, Chapman PB, Sosman JA, Graeber TG, Ribas A, Lo RS, Rosen N, Solit DB. Nature. 2011 Nov 23;480(7377):387-90. doi:10.1038/nature10662.
11. mTOR kinase inhibition causes feedback-dependent biphasic regulation of AKT signaling. Rodrik-Outmezguine VS, Chandarlapaty S, Pagano NC, Poulikakos PI, Scaltriti M, Moskatel E, Baselga J, Guichard S, Rosen N. Cancer Discov. 2011 Aug;1(3):248-59. doi:10.1158/2159-8290.CD-11-0085. Epub 2011 Jun 17.
12. Reciprocal feedback regulation of PI3K and androgen receptor signaling in PTEN-deficient prostate cancer. Carver BS, Chapinski C, Wongvipat J, Hieronymus H, Chen Y, Chandarlapaty S, Arora VK, Le C, Koutcher J, Scher H, Scardino PT, Rosen N, Sawyers CL. Cancer Cell. 2011 May 17;19(5):575-86. doi: 10.1016/j.ccr.2011.04.008.
13. AKT inhibition relieves feedback suppression of receptor tyrosine kinase expression and activity. Chandarlapaty S, Sawai A, Scaltriti M, Rodrik-Outmezguine V, Grbovic-Huezo O, Serra V, Majumder PK, Baselga J, Rosen N. Cancer Cell. 2011 Jan 18;19(1):58-71. doi:10.1016/j.ccr.2010.10.031. Epub 2011 Jan 6.

14. 4E-BP1 is a key effector of the oncogenic activation of the AKT and ERK signaling pathways that integrates their function in tumors. She QB, Halilovic E, Ye Q, Zhen W, Shirasawa S, Sasazuki T, Solit DB, Rosen N. Cancer Cell. 2010 Jul 13;18(1):39-51. doi:10.1016/j.ccr.2010.05.023.

15. RAF inhibitors transactivate RAF dimers and ERK signalling in cells with wild-type BRAF. Poulikakos PI, Zhang C, Bollag G, Shokat KM, Rosen N. Nature. 2010 Mar 18;464(7287):427-30. doi: 10.1038/nature08902.

16. (V600E)BRAF is associated with disabled feedback inhibition of RAF-MEK signaling and elevated transcriptional output of the pathway. Pratilas CA, Taylor BS, Ye Q, Viale A, Sander C, Solit DB, Rosen N. Proc Natl Acad Sci U S A. 2009 Mar 17;106(11):4519-24. doi: 10.1073/pnas.0900780106. Epub 2009 Feb 27.

17. Basso AD, Solit DB, Munster PN, Rosen N. Ansamycin antibiotics inhibit Akt activation and cyclin D expression in breast cancer cells that overexpress HER2. Oncogene. 2002 Feb 14;21(8):1159-66.

18. Moasser MM, Basso A, Averbuch SD, Rosen N. The tyrosine kinase inhibitor ZD1839 (“Iressa”) inhibits HER2-driven signaling and suppresses the growth of HER2-overexpressing tumor cells. Cancer Res. 2001 Oct 1;61(19):7184-8.

19. Munster PN, Basso A, Solit D, Norton L, Rosen N. Modulation of Hsp90 function by ansamycins sensitizes breast cancer cells to chemotherapy-induced apoptosis in an RB- and schedule-dependent manner. Clin Cancer Res. 2001;7:2155-8.

20. Munster PN, Srethapakdi M, Moasser MM, Rosen N. Inhibition of heat shock protein 90 function by ansamycins causes the morphological and functional differentiation of breast cancer cells. Cancer Res. 2001 Apr 1;61(7):2945-52.

21. Chiosis G, Timaul MN, Lucas B, Munster PN, Zheng FF, Sepp-Lorenzino L, Rosen N. A small molecule designed to bind to the adenine nucleotide pocket of Hsp90 causes Her2 degradation and the growth arrest and differentiation of breast cancer cells. Chem Biol. 2001 Mar;8(3):289-99.

22. Moasser MM, Srethapakdi M, Sachar KS, Kraker AJ, Rosen N. Inhibition of Src kinases by a selective tyrosine kinase inhibitor causes mitotic arrest. Cancer Res. 1999 Dec 15;59(24):6145-52.

23. Zheng FF, Kuduk SD, Chiosis G, Munster PN, Sepp-Lorenzino L, Danishefsky SJ, Rosen N. Identification of a geldanamycin dimer that induces the selective degradation of HER-family tyrosine kinases. Cancer Res. 2000 Apr 15;60(8):2090-4.

24. Srethapakdi M, Liu F, Tavorath R, Rosen N. Inhibition of Hsp90 function by ansamycins causes retinoblastoma gene productdependent G1 arrest. Cancer Res. 2000 Jul 15;60(14):3940-6.

25. Muise-Helmericks RC, Grimes HL, Bellacosa A, Malstrom SE, Tsichlis PN, Rosen N. Cyclin D expression is controlled posttranscriptionally via a phosphatidylinositol 3-kinase/Akt-dependent pathway. J Biol Chem. 1998 Nov 6;273(45):29864-72.

26. Stebbins CE, Russo AA, Schneider C, Rosen N, Hartl FU, Pavletich NP. Crystal structure of an Hsp90-geldanamycin complex: targeting of a protein chaperone by an antitumor agent. Cell. 1997 Apr 18;89(2):239-50.

27. Sepp-Lorenzino L, Ma Z, Lebwohl DE, Vinitsky A, Rosen N. Herbimycin A induces the 20 S proteasome- and ubiquitin-dependent degradation of receptor tyrosine kinases. J Biol Chem. 1995 Jul 14;270(28):16580-7.

Session 4-1

IAAO2013 Title of the Talk:

Approaches to Hypothesis Based Combination Therapy for Cancer

ABSTRACT:

Session 4-2

Title: Targeting Oncogenic Drivers in Lung Cancer

Pasi A. Jänne, MD, PhD
Director, Lowe Center for Thoracic Oncology,
Associate Professor of Medicine, Dana Farber Cancer Institute ,
Harvard Medical School, USA

Speaker

Nagahiro Saijo, MD, PhD
Executive Officer of Japanese Society of Medical Oncology, Japan

Chairman

Pasi A. Jänne, MD, PhD

EDUCATION

1989	B.A.	Chemistry, Vassar College, Poughkeepsie, NY
1996	M.D.	Medicine, University of Pennsylvania, School of Medicine, Philadelphia, PA
1996	Ph.D.	Genetics (advisor Dr. Robert Nussbaum), University of Pennsylvania, School of Medicine
2002	M.MSc.	Clinical investigation, Harvard University, Cambridge, MA

Personal Statement

My research program in thoracic oncology is focused on studying genomic abnormalities in lung cancer and translating the laboratory based observations into effective clinical treatments for patients with lung cancer. I am accomplishing this through laboratory based studies, by studying tumors from patients with thoracic malignancies, and by conducting clinical trials in patients with lung cancer. Our group was among the first in 2004 that identified epidermal growth factor receptor (EGFR) mutations and their association with sensitivity to EGFR kinase inhibitors *in vitro* and in lung cancer patients. In the ensuing nine years, this finding has transformed the care of non-small cell lung cancer (NSCLC) patients. Tumors from patients are now routinely screened for *EGFR* mutations, and EGFR inhibitors are used as initial treatment, instead of chemotherapy, for advanced *EGFR* mutant NSCLC and have become part of the most commonly used

guidelines in cancer (National Comprehensive Cancer Network). Similarly, we are studying and validating the therapeutic relevance of targeted therapies including kinase inhibitors in other genomic subsets of lung cancer such as those with alterations *ALK*, *ROS1* and *RET*. We have also begun to develop therapeutic strategies for *KRAS* mutant lung cancer detected in 25% of all lung cancer patients. We have identified the combination of the MEK inhibitor selumetinib and docetaxel as a promising therapy and are engaged in further understanding the biologic determinants of response and using the findings to further refine our therapeutic strategies.

Positions and Honors

Employment and Experience:

1996 – 1997	**Intern in Medicine**, Brigham and Women's Hospital, Boston, MA
1997 – 1998	**Resident in Medicine**, Brigham and Women's Hospital, Boston, MA
1998 – 2001	**Fellow in Medical Oncology**, Dana-Farber Cancer Institute, Boston, MA
2001 – 2004	**Instructor in Medicine**, Harvard Medical School; Assistant Physician, Dana-Farber Cancer Institute, Boston, MA
2004 – 2008	**Assistant Professor of Medicine**, Harvard Medical School; Dana-Farber Cancer Institute
2008 –	**Associate Professor of Medicine**, Harvard Medical School; Dana-Farber Cancer Institute
2009 -2012	**Director**, Translational Research Laboratory, Center for Clinical and Translational Research at the Dana-Farber Cancer Institute, Boston, MA
2011 -	**Co-Scientific Director**, Belfer Institute for Applied Cancer Science, Dana-Farber Cancer Institute, Boston, MA
2013-	**Director**, Lower Center for Thoracic Oncology, Dana Farber Cancer Institute
2013-	**Director**, Division of Thoracic and Head and Neck Oncology, Dana Farber Cancer Institute

Honors:

1985	Finalist, Westinghouse Science Talent Search
1989	Phi Beta Kappa, Vassar College, Poughkeepsie,
1996	Alpha Omega Alpha, University of Pennsylvania, School of Medicine, Philadelphia, PA
2001	Merit Award; American Society of Clinical Oncology
2002 – 2004	Dunkin Donuts Rising Star Award; Dana Farber Cancer Institute
2004	Tisch Family Award for Outstanding Achievement in Clinical Investigation; Dana Farber Cancer Institute
2005	George P. Canellos Award for Excellence in Clinical Investigation and Patient Care; Dana Farber Cancer Institute
2007	Hope Now Award for Lung Cancer Research; Joan's Legacy: The Joan Scarangello Foundation to Conquer Lung Cancer
2010	Team Science Award; American Association for Cancer Research
2010	Richard and Hinda Rosenthal Memorial Award; American Association for Cancer Research
2010	Research Excellence Award; Uniting Against Lung Cancer

Professional Society Involvement:

1999	American Society of Clinical Oncology
1999	American Association for Cancer Research
2001	International Association for the Study of Lung Cancer
2008	American Society of Clinical Investigation; elected member

Selected Peer-reviewed Publications (selected from 143 publications)

1. Paez, J.G., *__Jänne, P.A__., Lee, J.C., Tracy, S., Greulich, H., Gabriel, S., Herman, P., Kaye, F.J., Lindeman, N.Boggon, T.J., Naoki, K., Sasaki, H., Fujii, Y., Eck, M.J., Sellers, W.R., Johnson, B.E., and Meyerson, M. (2004) EGFR mutations in lung cancer: correlation with clinical response to gefitinib therapy. *Science*, **304** (5676):1497-1500. *co-first author.

2. Kobayashi, S., Boggon, T.J., Dayaram, T., **Jänne, P.A**., Kocher, O., Meyerson, M., Johnson, B.E., Eck, M.J., Tenen, D.G., and Halmos, B. EGFR mutation and resistance of non-small-cell lung cancer to gefitinib. New England Journal of Medicine; 2005; 352: 786-92.

3. Ji, H., Li, D., Chen, L., Shimamura, T., Kobayashi, S., McNamara, K., Mahmood, U., Mitchell, A., Sun,Y., Al-Hashem, R., Chirieac, L.R., Padera, R., Bronson, R.T., Kim, W., **Jänne, P.A**., Shapiro, G.I., Tenen, D., Johnson, B.E., Weissleder, R., Sharpless, N.E., and Wong, K. The impact of human EGFR kinase domain mutations on lung tumorigenesis and *in vivo* sensitivity to EGFR targeted therapies. Cancer Cell 2006; 9(6):485-95.

4. Engelman, J.A., Mukohara, T., Zejnullahu, K., Lifshits, E., Borrás, A.M., Gale, C.-M., Naumov, G.N., Yeap, B.Y., Jarrell, E., Sun, J., Tracy, S., Zhao, X., Heymach, J.V., Johnson, B.E., Cantley, L.C. and **Jänne, P.A.**

   Allelic dilution obscures detection of a biologically significant resistance mutation in EGFR-amplified lung cancer. J Clin Invest 2006;116(10):2695-2706. PMCID: PMC1570180

5. Engelman, J.A., Zejnullahu, K., Mitsudomi, T., Song, Y., Hyland, C., Park, J.O., Lindeman, N., Gale, C.-M., Zhao, X., Christensen, J., Kosaka, K., Holmes, A.J., Rogers, A.M., Cappuzzo, F., Mok, T., Lee, C., Johnson, B.E., Cantley, L.C., and **Jänne, P.A.** *MET* Amplification Leads to Gefitinib Resistance by Activating ERBB3 Signaling in Lung Cancer. Science 2007; 316(5827):1039-43.

6. Engelman, J.A., Zejnullahu, K, Gale, C.-M., Lifshits, E., Gonzales, A.J., Shimamura, T., Zhao, F., Vincent, P.W., Naumov, G.N., Bradner, J.E., Althaus, I.W., Gandhi, L., Shapiro, G.I., Nelson, J.M., Heymach, J.V., Meyerson, M., Wong, K.-K. and **Jänne, P.A**. PF00299804, an irreversible pan-ERBB inhibitor, is effective in lung cancer models with *EGFR* and *ERBB2* mutations that are resistant to gefitinib. Cancer Research 2007; 67:11924-32.

7. Zhou, W., Ercan, D., Chen, L., Yun, C.-H., Li, D., Capelletti, M., Cortot, A.B., Chirieac, L., Lacob, R.E., Padera, R., Engen, J.R., Wong, K.-K., Eck, M.J., Gray, N.S., and **Jänne, P.A.** Novel mutant-selective EGFR kinase inhibitors effective against EGFR T790M. Nature 2009; 462(7276):1070-4. PMCID: PMC2879581

8. Turke, A.,B., Zejnullahu, K., Wu, Y.-L., Song, Y., Dias-Santagata, D., Lifshits, E., Toschi, L., Rogers, A., Mok, T., Sequist, L., Lindeman, N.I., Murphy, c., Akhavanfard, S., Yeap, B.Y., Xiao, Y., Capelletti, M., Iafrate, A.J., Lee, C., Christensen, J.G., Engelman, J.A., and **Jänne, P.A.** Pre-existence and clonal selection of MET amplification in EGFR mutant NSCLC. Cancer Cell 2010; 17(1):77-88; PMCID: PMC2980857

9. Chen, Z., Sasaki, T., Tan, X., Carretero, J., Shimamura, T., Li, D., Xu, C., Wang, Y., Adelmant, G.O., Capelletti, M., Lee, H.J., Rodig, S., Borgman, C., Park, S.-I., Kim, H.R., Padera, R., Marto, J.A. , Gray, N.S., Kung, A.L., Shapiro, G.I., **Jänne, P.A*.,** and Wong, K.K. Inhibition of ALK, PI3K/MEK and HSP90 in Inducible EML4-ALK-driven Murine Lung Adenocarcinoma. Cancer Research 2010; 70(23):9827-9836. [*co-corresponding author] PMCID: PMC3043107

10. Sasaki T., Okuda K., Zheng W., Butrynski J., Capelletti M., Wang L., Gray N.S., Wilner K., Christensen J.G., Demetri G., Shapiro G.I., Rodig S.J., Eck M.J, and **Jänne PA.** The Neuroblastoma-Associated F1174L ALK Mutation Causes Resistance to an ALK Kinase Inhibitor in ALK-Translocated Cancers. Cancer Research. 2010;70(24):10038-10043. PMCID: PMC3045808

11. Sasaki, T., Koivunen, J., Ogino, A., Yanagita, M., Nikiforow, S., Zheng, W., Lathan, C., Marcoux, J.P., Du, J., Okuda, K., Capelletti, M., Shimamura, T., Ercan, D., Stumpfova, M., Xiao, Y., Weremowicz, S., Butaney, M., Heon, S., Wilner, K., Christensen, J.G., Eck, M.J., Wong, K.-K., Lindeman, N., Gray, N.S., Rodig, S.J., and **Jänne, P.A**. A novel ALK secondary mutation and EGFR signaling cause resistance to ALK kinase inhibitors. Cancer Research 2011; 71(18):6051-60. NIHMSID: 337524

12. Yonesaka, K., Zejnullahu, K., Okamoto, I., Satoh, T., Cappuzzo, F., Souglakos, J., Ercan, D., Rogers, A., Roncalli, M., Takeda, M., Fujisaka, Y., Philips, J., Shimizu, T., Maenishi, O., Cho, Y., Sun, J., Destro, A., Taira, K., Takeda, K., Okabe, T., Swanson, J., Itoh, H., Takada, M., Lifshits, E., Okuno, K., Engelman, J.A., Shivdasani, R.A., Nishio, K., Fukuoka, M., Varella-Garcia, M., Nakagawa, K. and **Jänne, P.A**. Activation of ERBB2 signaling causes resistance to the EGFR-directed therapeutic antibody cetuximab. Science Translational Medicine 2011; 3(99):99ra86. NIHMSID: 337522

13. Lipson, D., Capelletti, M. Yelensky, R., Otto, G., Parker, A., Jarosz, M., Curran,

    J.A., Balasubramanian, S.,Bloom, T., Brennan, K.W., Donahue, A., Downing, S.R., Frampton, G.M., Garcia, L., Juhn, F., Mitchell, K.C., White, E., White, J., Zwirko, Z., Peretz, T., Nechushtan, H., Soussan-Gutman, L., Kim, J., Sasaki, H., Kim, H.R., Park, S., Ercan, D., Sheehan, C.E., Ross, J.S., Cronin, M.T., **Jänne, P.A***., and Stephens, P.J. Identification of novel *ALK* and *RET* gene fusions from colorectal and lung cancer biopsies. Nature Medicine 2012; Feb 12;18(3):382-4. doi: 10.1038/nm.2673. [*co-corresponding author] PMCID: In Process

14. **Jänne, P.A**., Shaw, A.T., Pereira, J.R., Jeannin, G., Vansteenkiste, J., Barrios, C., Franke, F.A., Grinsted, L., Zazulina, V., Smith, P., Smith, I. and Crino, L. Selumetinib plus docetaxel for KRAS-mutant advanced non-small cell lung cancer: a randomised, multicentre, phase 2 study. Lancet Oncology 2013; 14(1):38-47

15. Shaw A.T., Kim D.W., Nakagawa K., Seto T., Crinó L., Ahn M.J., De Pas T., Besse B., Solomon B.J., Blackhall F., Wu Y.L., Thomas M., O'Byrne K.J., Moro-Sibilot D., Camidge D.R., Mok T., Hirsh V., Riely, G.J., Iyer S., Tassell V., Polli A., Wilner K.D., and **Jänne P.A**. Crizotinib versus chemotherapy in advanced ALK-positive lung cancer. N Engl J Med. 2013 Jun 20;368(25):2385-94

NARRATIVE REPORT ON CAREER AND RESEARCH INTERESTS

Dr. Jänne is translational thoracic medical oncologist at the Dana Farber Cancer Institute and an Associate Professor of Medicine at Harvard Medical School. He is the Director of the Lowe Center for Thoracic Oncology and the Scientific co-director of the Belfer Institute for Applied Cancer Sciences. After earning his MD and PhD from the School of Medicine at the University of Pennsylvania, Dr Jänne completed his internship and residency in Medicine at Brigham and Women's Hospital, Boston. He subsequently completed fellowship training at Dana Farber Cancer Institute/Massachusetts General Hospital combined program in medical oncology in 2001. In 2002 he earned a Master's Degree in clinical investigation from Harvard University. He has been a member of IASLC since 2000.

Dr Jänne's research combines laboratory based studies, with translational research and clinical trials of novel therapeutic agents in patients with lung cancer. His main research interest centers around understanding and translating the therapeutic importance of oncogenic alterations in lung cancer. He has made seminal therapeutic discoveries, including being on one of the co-discoverers of EGFR mutations, and his work has led to the development of several clinical trials. Dr. Jänne has received several awards for his research including from Uniting Against Lung Cancer, American Lung Association and the Bonnie J. Addario Lung Cancer Foundation. In 2008 he was elected as a member to the American Society of Clinical Investigation. He is also the recipient of 2010 American Association of Cancer Research Richard and Hinda Rosenthal Memorial Award and a member of the 2010 AACR Team Science Award.

IAAO2013 Title of the Talk:

Targeting Oncogenic Drivers in Lung Cancer

ABSTRACT:

The treatment of advanced non-small cell lung cancer (NSCLC) has evolved from a “one-size fits all” therapeutic model to identification of therapies for subsets of NSCLC patients. These subsets are defined by oncogenic alterations including mutations in EGFR, KRAS, BRAF, ERBB2 and genomic rearrangements involving ALK, ROS1 and RET. For EGFR mutant and ALK rearranged NSCLC, kinase inhibitors, are now commonly used instead of chemotherapy, as initial systemic therapy for advanced NSCLC. For many of the other genomic subsets of NSCLC, testing of specific targeted therapies is currently underway.

An evolving challenge for the future of NSCLC is to identify new potential oncogenic alterations that can serve as therapeutic targets and to develop therapies for NSCLC patients harboring such alterations. This is particularly challenging as many of the recently identified genomic subsets are relatively rare. Thus the traditional approach of comparing a targeted therapy to chemotherapy within such a subset of NSCLC may not be feasible. Strategies to identify novel genomic alterations and potential means to accelerate their clinical development will be discussed.

Despite all of the success in targeted therapies for NSCLC, treatment of KRAS mutant NSCLC has been much more challenging. In Caucasian patients, KRAS mutant NSCLC is the most common subset of NSCLC. Therapeutic development of agents specifically targeting KRAS have been unsuccessful. However, recent preclinical and clinical studies suggest that targeting MEK may have some efficacy in KRAS mutant NSCLC. Strategies that are currently underway to target KRAS mutant NSCLC along with associated biomarkers in clinical development will be discussed.

Session 4-3

Title: Targeting Clinically Relevant Molecular Subtypes in Colorectal Cancer

Speaker

Patrick G. Johnston, MD, PhD
Dean, School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast
Director, Institute of Health & Life Sciences, Queen's University Belfast, UK

Chairman

Chikashi Ishioka, MD
Professor, Institute of Development, Aging, and Cancer, Tohoku University, Japan

Patrick Gerard Johnston, MD, PhD

Prof. Johnston is Dean of the School of Medicine, Dentistry and Biomedical Sciences and Director of the Institute of Health Sciences at Queen's University Belfast. Prof. Johnston has published over 250 research articles and 5 books, and holds over 25 patents. His research is focused on cellular signaling pathways in human cancer, primarily related to molecular targeted cancer, therapeutics, personalized cancer medicine and mechanisms of drug resistance. He received his medical degree with distinction from University College Dublin in 1982, followed by his PhD in Medicine in 1988. He obtained a fellowship at the National Cancer Institute (NCI USA) in 1987 where he pursued further clinical training in medical oncology and doctoral studies in molecular pharmacology, drug resistance and drug development. He was promoted to Senior Investigator at the NCI in 1991.

In 1997 he moved to Queen's University Belfast as Professor of Oncology and subsequently became Director of the Centre for Cancer Research and Cell Biology in 2004 at the same institution. He has been Dean of the Medical School since 2007. He has been awarded many national and international awards, is a Fellow of the Academy of Medical Sciences, and sits on a number of influential national and international scientific and government advisory boards. He is the Founder of the Society for Translational Oncology and the biotechnology company, Almac Diagnostics.

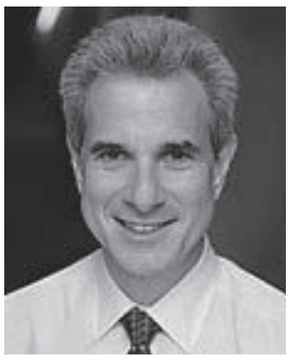
IAAO2013 Title of the Talk:

Targeting Clinically Relevant Molecular Subtypes in Colorectal Cancer

ABSTRACT:

Session 4-4

Title: Understanding and Targeting Mechanisms of Resistance to Next Generation AR and AR Signaling Inhibitors



Howard I . Scher, MD
Chief, Genitourinary Oncology Service;
D. Wayne Calloway Chair in Urologic Oncology
Memorial Sloan-Kettering Cancer Center, USA

Speaker

Patrick G. Johnston, MD, PhD
Dean, School of Medicine, Dentistry and Biomedical Sciences,
Queen's University Belfast
Director, Institute of Health & Life Sciences, Queen's University
Belfast

Chairman

Howard I . Scher, MD

EDUCATION

MD, New York University School of Medicine

CLINICAL EXPERTISE

Prostate Cancer and Other Genitourinary Malignancies; Immunotherapy

CURRENT ACTIVITIES AND RESEARCH INTEREST (from HP of MSKCC)

I am Chief of the Genitourinary Oncology Service at the Sidney Kimmel Center for Urologic and Prostate Cancers at Memorial Sloan-Kettering and a board-certified medical oncologist with special expertise in treating men with advanced prostate cancer. Under my leadership, the Genitourinary Oncology Service program is dedicated to the treatment of prostate cancer, testicular cancer, bladder and upper-tract urothelial cancer, and kidney cancer. Our objective is to foster synergy between scientific research and clinical practice, and to ensure that promising scientific discoveries are used to develop new diagnostic tests and treatments for patients.

My own research is focused on three critical areas: developing treatments that target specific signaling pathways that contribute to prostate cancer growth, developing non-invasive methods to determine whether these agents are working, and improving the way drugs are evaluated inthe clinic.

Targeted therapies, which attack specific cancer cells without harming normal cells, have the potential to treat cancers with fewer side effects than conventional therapies. Critical to the development of this approach, is to determine which treatment is most likely to be benefit anindividual patient. Currently, prostate-specific antigen (PSA) is the best routinely available biomarker providing diagnostic and prognostic information about prostate cancer. PSA testing is useful, but does not reliably determine whether or not a treatment is working, nor does not provide definitive guidance in selecting one therapy over another. My colleagues and I are evaluating a promising new blood test for circulating tumor cells. We are finding that the number of circulating tumor cells in a patient's blood helps determine a patient's prognosis and whether or not a treatment is working. Circulating tumor cells are also providing a biological snapshot of an individual patient's tumor, which may help determine the choice of therapy.

As a member of the Prostate Cancer Clinical Trials Working Group, I led an international effort to standardize development of the design and analysis of phase 2 clinical trials, so we can better utilize prostate cancer therapeutics and imaging modalities. I also developed the Clinical States Model of Prostate Cancer Progression, which, in categorizing the clinical spectrum of prostate cancer from diagnosis to metastasis, provides a framework to access and reassess prognosis over time.

I am also the principal investigator of the Prostate Cancer Clinical Trials Consortium, a 13-center research collaborative headquartered at Memorial Sloan-Kettering and funded by the Department of Defense and the Prostate Cancer Foundation. A critical part of this effort is to design and conduct clinical trials of promising new approaches are available to patients as soon as possible. Since 2006, the consortium has facilitated 60 new studies related to prostate cancer. Ultimately, through these clinical trials, we seek to develop more effective treatments for prostate cancers of all stages and to discover means of prevention.

In addition to serving as Chief of the Genitourinary Oncology Service for the past 16 years, I am the incumbent of the D. Wayne Calloway Chair in Urologic Oncology and a Professor of Medicine at the Joan and Sanford Weill Medical College of Cornell University. I am a recipient of the Donald S. Coffey-Prostate Cancer Foundation Physician-Scientist Award, and the Distinguished Alumnus Award. I also serve on numerous editorial and scientific advisory boards and am a reviewer for many journals, including *The New England Journal of Medicine*, *Clinical Cancer Research*, the *Journal of Clinical Oncology*, the *Journal of Urology*, and the *Journal of the American Medical Association*. I have written extensively and published over 370 peerreviewed articles in scientific journals and coauthored the textbook *Principals and Practice of Genitourinary Oncology*.

PUBLICATIONS:

>400 publications

Publications in 2011 and 2012

1. Parkinson DR, Dracopoli N, Gumbs Petty B, Compton C, Cristofanilli M, Deisseroth A, Hayes DF, Kapke G, Kumar P, Lee JS, Liu MC, McCormack R, Mikulski S, Nagahara L, Pantel K, Pearson-White S, Punnoose EA, Roadcap LT, Schade AE, Scher HI, Sigman CC, Kelloff GJ. Considerations in the development of circulating tumor cell technology for clinical use.J Transl Med. 2012 Jul 2;10(1):138. [Epub ahead of print]
2. Ulmert D, Vickers AJ, Scher HI, Becker C, Iversen P, Frankel D, Jensen JK, Kold Olesen T, Lilja H. Rapid elimination kinetics of free PSA or human kallikrein-related peptidase 2 after initiation of gonadotropin-releasing hormone-antagonist treatment of prostate cancer: potential for rapid monitoring of treatment responses. Clin Chem Lab Med. 2012 May 30;0(0):1-6. doi: 10.1515/cclm-2011-0967.
3. Centenera MM, Gillis JL, Hanson AR, Jindal S, Taylor RA, Risbridger GP, Sutherland PD, Scher HI, Raj GV, Knudsen KE, Yeadon T; for the Australian Prostate Cancer BioResource, Tilley WD, Butler LM. Evidence for Efficacy of New Hsp90 Inhibitors Revealed by Ex Vivo Culture of Human Prostate Tumors. Clin Cancer Res. 2012 Jul 1;18(13):3562-3570. Epub 2012 May 9.
4. Morris MJ, Eisenberger MA, Pili R, Denmeade SR, Rathkopf D, Slovin SF, Farrelly J, Chudow JJ, Vincent M, Scher HI, Carducci MA. A phase I/IIA study of AGS-PSCA for castration-resistant prostate cancer. Ann Oncol. 2012 May 2. [Epub ahead of print]
5. Autio KA, Scher HI, Morris MJ. Therapeutic strategies for bone metastases and their clinical sequelae

in prostate cancer. Curr Treat Options Oncol. 2012 Jun;13(2):174-88.

6. Brown MS, Chu GH, Kim HJ, Allen-Auerbach M, Poon C, Bridges J, Vidovic A, Ramakrishna B, Ho J, Morris MJ, Larson SM, Scher HI, Goldin JG. Computer-aided quantitative bone scan assessment of prostate cancer treatment response. Nucl Med Commun. 2012 Apr;33(4):384-94.
7. Ulmert D, Kaboteh R, Fox JJ, Savage C, Evans MJ, Lilja H, Abrahamsson PA, Björk T, Gerdtsson A, Bjartell A, Gjertsson P, Höglund P, Lomsky M, Ohlsson M, Richter J, Sadik M, Morris MJ, Scher HI, Sjöstrand K, Yu A, Suurküla M, Edenbrandt L, Larson SM. A novel automated platform for quantifying the extent of skeletal tumour involvement in prostate cancer patients using the Bone Scan Index. Eur Urol. 2012 Jul;62(1):78-84. Epub 2012 Jan 27.
8. Thompson VC, Day TK, Bianco-Miotto T, Selth LA, Han G, Thomas M, Buchanan G, Scher HI, Nelson CC; Australian Prostate Cancer BioResource, Greenberg NM, Butler LM, Tilley WD A gene signature identified using a mouse model of androgen receptor-dependent prostate cancer predicts biochemical relapse in human disease. Int J Cancer. 2012 Aug 1;131(3):662-72. doi: 10.1002/ijc.26414. Epub 2012 Jan 24.
9. Clegg NJ, Wongvipat J, Joseph JD, Tran C, Ouk S, Dilhas A, Chen Y, Grillot K, Bischoff ED, Cai L, Aparicio A, Dorow S, Arora V, Shao G, Qian J, Zhao H, Yang G, Cao C, Sensintaffar J, Wasielewska T, Herbert MR, Bonnefous C, Darimont B, Scher HI, Smith-Jones P, Klang M, Smith ND, De Stanchina E, Wu N, Ouerfelli O, Rix PJ, Heyman RA, Jung ME, Sawyers CL, Hager JH. ARN-509: a novel antiandrogen for prostate cancer treatment. Cancer Res. 2012 Mar 15;72(6):1494-503. Epub 2012 Jan 20.
10. Chen Y, Scher HI. Prostate cancer in 2011: Hitting old targets better and identifying new targets. Nat Rev Clin Oncol. 2012 Jan 10;9(2):70-2. doi: 10.1038/nrclinonc.2011.213. Review.
11. Dennis ER, Jia X, Mezheritskiy IS, Stephenson RD, Schoder H, Fox JJ, Heller G, Scher HI, Larson SM, Morris MJ. Bone scan index: a quantitative treatment response biomarker for castration-resistant metastatic prostate cancer. J Clin Oncol. 2012 Feb 10;30(5):519-24. Epub 2012 Jan 9.
12. Danila DC, Pantel K, Fleisher M, Scher HI. Circulating tumors cells as biomarkers: progress toward biomarker qualification. Cancer J. 2011 Nov-Dec;17(6):438-50. Review Iyer G, Morris MJ, Rathkopf D, Slovin SF, Steers M, Larson SM, Schwartz LH, Curley T, DeLaCruz A, Ye Q, Heller G, Egorin MJ, Ivy SP, Rosen N, Scher HI, Solit DB. A phase I trial of docetaxel and pulse-dose 17-allylamino-17-demethoxygeldanamycin in adult patients with solid tumors. Cancer Chemother Pharmacol. 2012 Apr;69(4):1089-97. Epub 2011 Nov 29.
13. Armstrong AJ, Eisenberger MA, Halabi S, Oudard S, Nanus DM, Petrylak DP, Sartor AO, Scher HI. Biomarkers in the management and treatment of men with metastatic castrationresistant prostate cancer. Eur Urol. 2012 Mar;61(3):549-59. Epub 2011 Nov 12. Review Lowrance WT, Elkin EB, Yee DS, Feifer A, Ehdaie B, Jacks LM, Atoria CL, Zelefsky MJ, Scher HI, Scardino PT, Eastham JA. Locally advanced prostate cancer: a population-based Study of treatment patterns. BJU Int. 2012 May;109(9):1309-14. doi: 10.1111/j.1464-410X.2011.10760.x. Epub 2011 Nov 15.
14. Scher HI, Nasso SF, Rubin EH, Simon R. Adaptive clinical trial designs for simultaneous testing of matched diagnostics and therapeutics. Clin Cancer Res. 2011 Nov1;17(21):6634-40.
15. Antonarakis ES, Carducci MA, Eisenberger MA, Denmeade SR, Slovin SF, Jelaca-Maxwell K, Vincent ME, Scher HI, Morris MJ. Phase I rapid dose-escalation study of AGS-1C4D4, a human anti-PSCA (prostate stem cell antigen) monoclonal antibody, in patients with castration-resistant prostate cancer: a PCCTC trial. Cancer Chemother Pharmacol. 2012 Mar;69(3):763-71. Epub 2011 Oct 22.
16. Fox JJ, Autran-Blanc E, Morris MJ, Gavane S, Nehmeh S, Van Nuffel A, Gönen M, Schöder H, Humm JL, Scher HI, Larson SM. Practical approach for comparative analysis of multilesion molecular imaging using a semiautomated program for PET/CT. J Nucl Med. 2011 Nov;52(11):1727-32. Epub 2011 Oct 7.
17. Scher HI, Morris MJ, Basch E, Heller G. End points and outcomes in castration-resistant prostate cancer: from clinical trials to clinical practice. J Clin Oncol. 2011 Sep 20;29(27):3695-704. Epub 2011 Aug 22. Review.
18. Danila DC, Anand A, Sung CC, Heller G, Leversha MA, Cao L, Lilja H, Molina A, Sawyers CL, Fleisher M, Scher HI. TMPRSS2-ERG status in circulating tumor cells as a predictive biomarker of sensitivity in castration-resistant prostate cancer patients treated with abiraterone acetate. Eur Urol. 2011 Nov;60(5):897-904. Epub 2011 Jul 14.
19. Danila DC, Fleisher M, Scher HI. Circulating tumor cells as biomarkers in prostate cancer. Clin Cancer Res. 2011 Jun 15;17(12):3903-12. Review
20. de Bono JS, Logothetis CJ, Molina A, Fizazi K, North S, Chu L, Chi KN, Jones RJ, Goodman OB Jr, Saad F, Staffurth JN, Mainwaring P, Harland S, Flaig TW, Hutson TE, Cheng T, Patterson H, Hainsworth JD, Ryan CJ, Sternberg CN, Ellard SL, Fléchon A, Saleh M, Scholz M, Efstathiou E, Zivi A, Bianchini D, Loriot Y, Chieffo N, Kheoh T, Haqq CM, Scher HI; COU-AA-301 Investigators. Abiraterone and increased survival in metastatic prostate cancer. N Engl J Med. 2011 May 26;364(21):1995-2005.
21. Fox JJ, Morris MJ, Larson SM, Schöder H, Scher HI. Developing imaging strategies for castration

resistant prostate cancer. Acta Oncol. 2011 Jun;50 Suppl 1:39-48.

22. Diamandis EP, Pantel K, Scher HI, Terstappen L, Lianidou E. Circulating cancer cells and their clinical applications. Clin Chem. 2011 Nov;57(11):1478-84. doi: 10.1373/clinchem.2011.166678. Epub 2011 May 17. No abstract available.
23. Carver BS, Chapinski C, Wongvipat J, Hieronymus H, Chen Y, Chandarlapaty S, Arora VK, Le C, Koutcher J, Scher H, Scardino PT, Rosen N, Sawyers CL. Reciprocal feedback regulation of PI3K and androgen receptor signaling in PTEN-deficient prostate cancer. Cancer Cell. 2011 May 17;19(5):575-86.
24. International Collaboration of Trialists; Medical Research Council Advanced Bladder Cancer Working Party (now the National Cancer Research Institute Bladder Cancer Clinical Studies Group); European Organisation for Research and Treatment of Cancer Genito-Urinary Tract Cancer Group; Australian Bladder Cancer Study Group; National Cancer Institute of Canada Clinical Trials Group; Finnbladder; Norwegian Bladder Cancer Study Group; Club Urologico Espanol de Tratamiento Oncologico Group, Griffiths G, Hall R, Sylvester R, Raghavan D, Parmar MK. International phase III trial assessing neoadjuvant cisplatin, methotrexate, and vinblastine chemotherapy for muscle-invasive bladder cancer: long-term results of the BA06 30894 trial. J Clin Oncol. 2011 Jun 1;29(16):2171-7. Epub 2011 Apr 18.
25. Scher HI, Jia X, Chi K, de Wit R, Berry WR, Albers P, Henick B, Waterhouse D, Ruether DJ, Rosen PJ, Meluch AA, Nordquist LT, Venner PM, Heidenreich A, Chu L, Heller G. Randomized, open-label phase III trial of docetaxel plus high-dose calcitriol versus docetaxel plus prednisone for patients with castration-resistant prostate cancer. J Clin Oncol. 2011 Jun 1;29(16):2191-8. Epub 2011 Apr 11.
26. Rajasekhar VK, Studer L, Gerald W, Socci ND, Scher HI. Tumour-initiating stem-like cells in human prostate cancer exhibit increased NF-κB signalling. Nat Commun. 2011 Jan 18;2:162.

Session 4-4

IAAO2013 Title of the Talk:

Understanding and Targeting Mechanisms of Resistance to Next Generation AR and AR Signaling Inhibitors

ABSTRACT:

Session 5-1

Title: Changing the Regulatory Pathway for Targeted Drugs

Speaker

Bruce A. Chabner, MD
Director of Clinical Research Cancer Center, Massachusetts General Hospital, Boston Massachusetts, USA

Chairman

Isao Kamae, MD, ScD
Project Professor, Health Technology Assessment and Public Policy, Graduate School of Public Policy, The University of Tokyo
Adjunct Professor, Meiji Institute for Global Affairs
Adjunct Professor, Graduate School of Medicine, Kobe University
Adjunct Professor, Peking University

Bruce A. Chabner, MD

EDUCATION:

1961	BA Summa cum laude	Biology	Yale College
1965	MD Cum laude	Medicine	Harvard Medical School

FACULTY ACADEMIC APPOINTMENTS:

1995-	Professor of Medicine	Medicine	Harvard Medical School
1999-2002	Adjunct Professor	Institute of Health Professions	Massachusetts General Hospital, Boston

APPOINTMENTS AT HOSPITALS/AFFILIATED INSTITUTIONS:

1995-	Physician	Department of Medicine	Massachusetts General

			Hospital, Boston
1996-2001	Chief Medical Officer		Dana Farber/Partners Cancer Care, Boston
2010-	Director of Clinical Research	Cancer Center	Massachusetts General Hospital, Boston

MAJOR ADMINISTRATIVE LEADERSHIP POSITIONS:

Local

1999-	Associate Director	Clinical Science	Dana-Farber/Harvard Cancer Center, Boston
2010-	Director of Clinical Research	Cancer Center	Massachusetts General Hospital, Boston

National and International

1982-1995	Director	Division of Cancer Treatment	National Cancer Institute

COMMITTEE SERVICE:

Local

1995-	Chairman, Executive Committee of the Clinical Operations Team	Massachusetts General Hospital

NATIONAL AND INTERNATIONAL:

1997-	Advisory Board	Al Amal Cancer Center, Amman, Jordan
2006-	Member, USA-Japanese Foundation for Cancer Research Collaboration	MGHCC/JFCR
2006-2012	Member, National Cancer Advisory Board	National Cancer Institute
2010-	Acting Chair, National Cancer Advisory Board	National Cancer Institute
2010-	Co-Chair, working Group, Review, National Cancer Advisory Board	National Cancer Institute

PROFESSIONAL SOCIETIES:

1971-	American Association for Cancer Research	Board of Directors
1982-	American Society for Clinical Investigation	Member
1985-	American Society of Hematology	Member
1985-	Association of American Physicians	Member
1990-	American Clinical and Climatological Association	Member
1991-	American Society of Clinical Oncology	Board of Directors
1995-	Massachusetts Society of Clinical Oncology	Member
2003-	Society for Translational Oncology	Member

EDITORIAL ACTIVITIES:

1994-	Editor-in-Chief	The Oncologist
2001-2006	Senior Editor	Clinical Cancer Research

HONORS AND PRIZES:

1961	Phi Beta Kappa	Yale College
1965	Alpha Omega Alpha	Harvard Medical School
1976	Commendation Medal	Public Health Service
1983	Outstanding Service Medal	Public Health Service
1984	Unit Citation	Public Health Service
1986	Melville Jacobs Award	The American Radium Society
1986	Distinguished Oncologist for 1986	Dayton Oncology Society
1987	Meritorious Service Medal	Public Health Service
1990	Equal Employment Opportunity Achievement	Special National Cancer Institute
1990	Equal Opportunity Officer's Recognition Award	National Cancer Institute
1991	Awarded the flag rank of Rear Admiral	Public Health Service
1993	The Steven Beering Award	Indiana University Awarded for Advancement of Biomedical Science
1994	Distinguished Medal	Public Health Service
1996	Kantor Family Prize	For Cancer Research Excellence
1998	Bruce F. Cain Memorial Award	
2005	Paul Calabresi Award	
2005	Timothy Gee Humanity in Medicine Award	The Lauri Strauss Leukemia Foundation
2006	Bob Pinedo Award	The Society for Translational Oncology For Contributions to Improvement in the Care of Cancer Patients (First recipient)
2009	George S. Mitchell Award	Queens University, Belfast For Distinguished Contributions to Cancer Research
2010	Bloch Award Ohio State	University Cancer Center For Distinguished Contributions to Cancer Research

REPORT OF SCHOLARSHIP:

>180 Peer reviewed publications in print or other media

> 280 Reviews, Chapters, Monographs, and Editorials

NARRATIVE REPORT ON CAREER AND RESEARCH INTERESTS:

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

Dr. Chabner graduated *summa cum laude* from Yale College in 1961. He received his M.D. from Harvard University *cum laude* in 1965 following which he completed an internship and junior residency in internal medicine at Peter Bent Brigham Hospital in Boston and a senior residency in internal medicine at Yale-New Haven Medical Center.

Dr. Chabner has had extensive experience in the field of cancer drug discovery and development. After joining the National Cancer Institute (NCI) as a Senior Investigator in the Laboratory of Chemical Pharmacology 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 its fellowship programs in medical, pediatric, radiation, and surgical oncology; and, in 1981, one year as Acting Director, and for 13 years as permanent Director of the Division of Cancer Treatment, NCI.

During the period from 1971 to 1989, he maintained an active laboratory program in cancer pharmacology, focusing on the mechanism of action, and resistance of antifolates and other antimetabolites, and led the development of Taxol. His research contributed significantly to the development of high dose chemotherapy regimens, and to standard therapies for lymphoma.

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 standard text, Principles and Practice of Cancer Chemotherapy and Biological Response Modifiers, now in its fourth edition, has contributed the chapter on Antineoplastics in Goodman and Gilman's textbook of Pharmacology and has authored chapters for numerous other textbooks of internal medicine, hematology, oncology and pharmacology.

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

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

Session 5-1

IAAO2013 Title of the Talk:

Changing the Regulatory Pathway for Targeted Drugs

ABSTRACT:

Title: Health Technology Assessment: Changing Landscape in Asia and Japan

Isao Kamae, MD, ScD
Project Professor, Health Technology Assessment and Public Policy, Graduate School of Public Policy, The University of Tokyo
Adjunct Professor, Meiji Institute for Global Affairs
Adjunct Professor, Graduate School of Medicine, Kobe University
Adjunct Professor, Peking University

Speaker

Yasuhiro Fujiwara, MD, PhD
Strategic Planning Bureau, Department of Breast and Medical Oncology, National Cancer Center, Japan

Chairman

Isao Kamae, MD, ScD

RESEARCH THEMES

Challenges for the incorporation of health technology assessment into policymaking and an analysis of its impact

Research on social security finance (British medical reform since the Blair administration)

EXPERTISE

Health Policy and Technology Assessment

EDUCATION

1995	Harvard University, Doctor of Public Health in health decision sciences
1988	Harvard School of Public Health, Master in Biostatistics
1985	Kobe University School of Medicine, M.D.

1979	Kyoto University, M.S., Information Science

CAREER

2012	Project Professor, Health Technology Assessment and Public Policy, Graduate School of Public Policy, The University of Tokyo
2012	Adjunct Professor, Meiji Institute for Global Affairs
2011	Research Director, The Canon Institute for Global Studies
2007	Professor, Graduate School of Health Management, Keio University
1997	Professor, Research Center for Urban Safety and Security, Kobe University, and Professor, Medical Statistics, Kobe University Graduate School of Medicine
1994	Associate Professor, General Medicine and Clinical Epidemiology, Kyoto University Hospital
1993	Associate Professor, Medical Informatics, Shimane Medical University

Session 5-2

IAAO2013 Title of the Talk:

Health Technology Assessment: Changing Landscape in Asia and Japan

ABSTRACT: