Program

International Academy for Advanced Oncology

IAAO

国際フォーラム2012

The Dynamism of Therapeutic Strategy from the New Oncology Paradigm

2012年8月3日(金)・4日(土)
六本木アカデミーヒルズ49

CHAAO
Chugai
Academy for
Advanced Oncology

The Dynamism of Therapeutic Strategy from the New Oncology Paradigm

Friday, August 3, 2012 13:00~18:00

Opening Remarks P.3

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

1. New Molecular Targets P.4

13:10 **Immune Checkpoint Blockade in Cancer Immunotherapy**
Speaker: James P. Allison, PhD (Memorial Sloan-Kettering Cancer Center, USA)
Chair: Ryuzo Ueda, MD, PhD (Aichi Medical University, Japan)

13:50 **Chemokine Receptor 4 (CCR4) is a Promising Target for Development of New Tumor Immunotherapy**
Speaker: Ryuzo Ueda, MD, PhD (Aichi Medical University, Japan)
Chair: Makoto Ogawa, MD (Emeritus President, Aichi Cancer Center, Japan)

14:30 Break

14:50 **Targeting the Hedgehog Pathway in Medulloblastoma**
Speaker: Thomas Curran, PhD (The University of Pennsylvania, USA)
Chair: Nobuyuki Mizunuma, MD (Cancer Institute Hospital, JFCR, Japan)

2. Rationale for Combination of Molecular Targeted Agents P.26

15:30 **Acquired and Adaptive Resistance to Targeted Therapy**
Speaker: Neal Rosen, MD, PhD (Memorial Sloan-Kettering Cancer Center, USA)
Chair: Chikashi Ishioka, MD (Tohoku University, Japan)

16:10 Break

16:30 **Combinatorial Approaches against PI3 Kinase Pathway**
Speaker: José Baselga, MD, PhD (Massachusetts General Hospital, USA)
Chair: Masakazu Toi, MD, PhD (Kyoto University, Japan)

3. New Molecular Class P.46

17:10 **Antibody Drug Conjugates for Cancer Therapy**
Speaker: Paul Polakis, PhD (Genentech Inc, USA)
Chair: Mitsuaki Yoshida, PhD (Cancer Chemotherapy Center, JFCR, 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, August 4, 2012 9:00~15:45

4. Drug Resistances P.54

9:00 **Challenges with Drug Resistance**
Speaker: Jeffrey A. Engelman, MD, PhD (Massachusetts General Hospital, USA)
Chair: Nagahiro Saijo,MD, PhD (Japanese Society of Medical Oncology, Japan)

9:40 **Sensitivity and Resistance to Targeting FGFR in Cancer**
Speaker: Nicholas Turner, MD, PhD (The Royal Marsden, UK)
Chair: Kiyohiko Hatake, MD, PhD (Cancer Institute Hospital, JFCR, Japan)

10:20 **Break**

5. Advances and Challenges in Tumor Therapy P.70

10:40 **Prostate Cancer**
Speaker: Howard I . Scher, MD (Memorial Sloan-Kettering Cancer Center, USA)
Chair: Chikashi Ishioka, MD (Tohoku University, Japan)

11:20 **The Treatment of Colorectal Cancer in the Era of Molecular Characterization**
Speaker: Josep Tabernero, MD (Vall d'Hebron University Hospital, Spain)
Chair: Yuko Kitagawa, MD, PhD (Keio University, Japan)

12:00 **Lunch**

12:45 **The Evolution to Genomic Testing and Targeted Therapy as Standard of Care for Lung Cancer**
Speaker: Bruce E . Johnson, MD (Dana-Farber Cancer Institute, USA)
Chair: Hiroyuki Mano, MD, PhD (Jichi Medical University/The University of Tokyo, Japan)

6. Impact of Oncology New Paradigm on Patients P.92

13:25 **Drug Development and Approval in the Age of Molecular Targeting and "*Precision*" Therapy**
Speaker: Bruce A. Chabner, MD (Massachusetts General Hospital, USA)
Chair: Kiyohiko Hatake, MD, PhD (Cancer Institute Hospital, JFCR, Japan)

14:05 **Break**

14:25 **Strategy and Development in Asian Clinical Trials**
Speaker: Kiyohiko Hatake, MD, PhD (Cancer Institute Hospital, JFCR, Japan)
Chair: Patrick G. Johnston, MD, PhD (Queen's University of Belfast, UK)

15:05 **Value-based Medicine - a UK and European Perspective**
Speaker: Patrick G. Johnston, MD, PhD (Queen's University of Belfast, UK)
Chair: Bruce A. Chabner, MD (Massachusetts General Hospital, USA)

Opening Remarks

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

As Chairman of Chugai Academy for Advanced Oncology (CHAAO), I would like to express my great thanks to all the distinguished guests, experts, and investigators, both from overseas and Japan, for participating in the International Academy for Advanced Oncology 2012.

This is the third opportunity for us to organize IAAO. The number of participants has continued to increase each time, with more than 180 people in attendance this year. We are very happy to learn that more and more experts have become interested in IAAO and see it as a valuable chance to learn from their colleagues.

I would like to express my heartfelt appreciation to the IAAO Advisory Board members, Dr. Bruce Chabner of the United States, Dr. Patrick Johnston of the United Kingdom, and the six members from Japan: Dr. Hatake, Dr. Ishioka, Dr. Mano, Dr. Kitagawa, Dr. Toi and Dr. Mizunuma.

The title of this year's meeting is "The Dynamism of Therapeutic Strategy from the New Oncology Paradigm." In addition to the fields covered in previous meetings, such as lung, breast and colorectal cancers, we are also including topics on prostate and hematological cancers, which has enabled us to realize the participation of doctors from a broad range of specialties.

As one of the keynote presentations, we will be discussing the cutting-edge science on immune therapy, one of the most high-profile subjects these days. We will also take up the issue of regulatory matters in the US, Europe and Japan. As you can see from the program, a large number of fascinating sessions have been organized, and I am sure they will serve as excellent opportunities for all of you to share your knowledge and deep insights into a wide range of fields.

In closing, let me again say that our sincere wish is that the next two days will be a most informative and engaging time for everyone. Our goal is for CHAAO to provide a forum for researchers and academics from around the world and Japan to exchange valuable information, and ultimately, lead to the realization of cancer treatments which allow patients to confront cancer proactively and with hope.

Session 1

New Molecular Targets

1-1. Immune Checkpoint Blockade in Cancer Immunotherapy

Speaker: James P. Allison, PhD (Memorial Sloan-Kettering Cancer Center, USA)

1-2. Chemokine Receptor 4 (CCR4) is a Promising Target for Development of New Tumor Immunotherapy

Speaker: Ryuzo Ueda, MD, PhD (Aichi Medical University, Japan)

1-3. Targeting the Hedgehog Pathway in Medulloblastoma

Speaker: Thomas Curran, PhD (The University of Pennsylvania, USA)

Title: Beyond Immune Checkpoint Blockade: Manipulation of T Cell Regulatory Circuits in Cancer Therapy

Speaker

James P. Allison, Ph.D.
David H. Koch Chair in Immunologic Studies, Memorial Sloan-Kettering Cancer Center, New York, NY
Attending Immunologist, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY
Co-Chair, Graduate Program in Immunology and Microbial Pathogenesis, Weill Graduate School of Medical Sciences of Cornell University, New York, NY
Professor, Weill Medical College of Cornell University, New York, NY
Director, Ludwig Center for Cancer Immunotherapy, Memorial Sloan-Kettering Cancer Center, New York, NY

Chairman

Ryuzo Ueda, M.D., Ph.D.
Professor Emeritus, Senior Adviser, Nagoya City University
Professor, Dept. of Tumor Immunology, Aichi Medical University, Japan

James P. Allison, Ph.D.

EDUCATION:

1969	B.S. Microbiology, The University of Texas, Austin, Texas
1973	Ph.D. Biological Sciences, The University of Texas, Austin, Texas

POSTDOCTORAL TRAINING:

1974-1977.1.1.1	Postdoctoral Fellow, Department of Molecular Immunology, Scripps Clinic and Research Foundation, La Jolla, California

POSITIONS AND APPOINTMENTS:

2004-Present	David H. Koch Chair in Immunologic Studies, Memorial Sloan-Kettering Cancer Center, New York, NY
2004-Present	Attending Immunologist, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY
2004- Present	Co-Chair, Graduate Program in Immunology and Microbial Pathogenesis, Weill Graduate School of Medical Sciences of Cornell University, New York, NY
2004- Present	Professor, Weill Medical College of Cornell University, New York, NY
2006- Present	Director, Ludwig Center for Cancer Immunotherapy, Memorial Sloan-Kettering Cancer Center, New York, NY

RECENT HONORS AND AWARDS:

2010	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
2012	Lifetime Achievement Award, Molecular Targeted Therapy Group

LATEST PUBLICATIONS:

1. Corse E., Gottschalk R.A., Krogsgaard M., Allison J.P. Attenuated T cell responses to a high-potency ligand in vivo. PLoS Biol 8(9): e1000481. Doi:10.1371/journal.pbio.1000481; 2010.
2. Gottschalk R.A., Corse E., Allison J.P. TCR ligand density and affinity determine peripheral induction of Foxp3 in vivo. J Exp Med 207:1701-1711; 2010.
3. Pedicord, V.A., Montalvo W., Leiner I.M., Allison J.P. Single dose of anti-CTLA-4 enhances CD8+ T-cell memory formation, function and maintenance. Proc Natl Acad Sci USA. 108:266-71; 2011.
4. Yuan J., Ginsberg B., Page D., Li Y., Rasalan T., Gallardo HF., Xu Y., Adams S., Bhardwaj N., Busam K., Old L.F., Allison J.P., Wolchock J.D. CTLA-4 blockade increases antigen-specific CD8(+) T cells in prevaccinated patients with melanoma: three cases. Cancer Immunol Immunother. 60(8):1137-1146; 2011.
5. Donkor D.K., Sarkar A., Savage P.A., Franklin R.A., Johnson L.K., Jungbluth A.A., Allison J.P., Li M.O. T cell surveillance of oncogene-induced prostate cancer is impeded by T cell-derived TGF-β1 cytokine. Immunity 35:123-134; 2011.
6. Curran M.A., Kim M., Montalvo W., Al-Shamkhani A., Allison J.P. Combination CTLA-4 blockade and 4-1BB activation enhances tumor rejection by increasing T-cell infiltration, proliferation, and cytokine production. PLoS One. 29;6(4); 2011.
7. Wei J., Zang X., Loke P., Allison J.P. Tissue specific expression of B7x protects from T cell mediated autoimmunity. J Exp Med. 208(8):1683-94; 2011.
8. Balachandran V.P., Cavnar M.J., Zeng S., Bambout Z.M., Ocuin L.M., Obaid H., Sorenson E.C., Popow R., Ariyan C., Rossi F,, Besmer P., Guo T., Antonescu C.R., Taguchi T., Yuan J., Wolchok J.D., Allison J.P., Dematteo R.P. Imatinib potentiates antitumor T cell responses in gastrointestinal stromal tumor through the inhibition of Ido. Nat Med. 17(9):1094-100; 2011.
9. Krummel M.F., Allison J.P. Pillars article: CD28 and ctla-4 have opposing effects on the response of T cells to stimulation. The journal of experimental medicine. 1995. 182: 459-465. J Immunol. 1;187(7):3459-65; 2011.
10. Yuan J., Adamow M., Ginsberg B.A., Rasalan T.S., Ritter E., Gallardo H.F., Xu Y., Pogoriler E., Terzulli S.L., Kuk D., Panageas K.S., Ritter G., Sznol M., Halaban R., Jungbluth A.A., Allison J.P., Old L.J., Wolchok J.D., Gnjatic S. Integrated NY-ESO-1 antibody and CD8+ T-cell responses correlate with clinical benefit in advanced melanoma patients treated with ipilimumab. Proc Natl Acad Sci USA. 108(40):16723-8; 2011.
11. Curran M.A., Callahan M.K., Subudhi S.K., Allison J.P. Response to "Ipilimumab (Yervoy) and the TGN1412 catastrophe". Immunobiology; 2011.
12. Waitz R., Solomon S.B., Petre E.N., Trumble A.E., Fasso M., Norton L., Allison J.P. Induction of tumor immunity through cryoablation and cytotoxic T lymphocyte-associated antigen 4 blockade combination therapy. Cancer Res. Jan 15;72(2):430-9; 2012.
13. Gottschalk R.A., Hawthorn H.M., Beuneu H., Corse E., Dustin M.L., Altan-Bonnet G. Allison J.P. Distinct influences of peptide-MHC quality and quantity on in vivo T cell responses. Proc Natl Acad Sci. USA. Jan 17;109(3):881-6; 2012.

14. Gottschalk R.A., Corse E., Allison J.P. Expression of Helios in Peripherally Induced Foxp3+ Regulatory T cells. J Immunol. Feb 1;188(3):976-80; 2012.
15. Matsushita H., Vesely M.D., Koboldt D.C., Rickert C.G., Uppaluri R., Magrini V.J., Arthur C.D., White J.M., Chen Y., Shea L.K., Hundal J., Wendl M.C., Demeter R., Wylie T. Allison J.P., Smyth M.J., Old L.J., Mardis E.R., Scheiber R.D. Cancer exome analysis reveals a T-cell-dependent mechanism of cancer immunoediting. Nature. Feb 8; 482(7385):400-4; 2012.
16. Postow M.A., Callahan M.K., Barker C.A., Yamada Y., Yuan J., Kitano S., Mu Z., Rasalan T., Adamow M., Ritter E., Sedrak C., Jungbluth A.A., Chua R., Yang A., Roman R.A., Rosner, S., Benson B., Allison J.P., Lesokhin A.M., Gnjatic S., Wolchok J.D. Immunologic Correlates of an Abscopal Effect in a Patient with Melanoma. N Engl J Med. Mar 8;366(1):923-31; 2012.
17. Yu P., Steel J.C., Zhang M., Morris J.C., Waitz R. Fasso M., Allison J.P., Waldermann T.A. Simultaneous inhibition of two regulatory T-cell subsets enhanced Interleukin-15 efficacy in a prostate tumor model. Proc Natl Acad Sci. USA. Apr 17;109(16):6187-6192; 2012.
18. Jenq R.R., Curran M.A., Goldberg G.L., Liu C., Allison J.P., van den Brink M.R. Repertoire enhancement with adoptively transferred female lyphocytes controls the growth of pre-implanted murine prostate cancer. PLoS One. Apr 6;7(4):e35222; 2012.
19. Zhang M., Ju W., Yao Z., Yu P., Wei B.R., Simpson R.M., Waitz R., Fasso M., Allison J.P., Waldmann T.A. Augmented IL-15Rα Expression by CD40 Actiation Is Critical in Synergistic CD8 T Cell-Mediated Antitumor Activity of Anti-CD40 Antibody with IL-15 in TRAMP-C2 Tumors in Mice. May 16: J Immunol; 2012.
20. Waitz R., Fasso M., Allison J.P. CTLA-4 blockade synergizes with cryoablation to mediate tumor rejection. Oncoimmunology. Jul 1;1(4):544-546; 2012

CURRENT INTEREST:

One of our major areas of current interest is in the mechanisms that regulate T cell responses and the development of strategies for manipulating the process in clinical situations, such as autoimmunity, allergy, vaccination, and tumor therapy. It is now well accepted that recognition of specific antigen by the TCR is not sufficient for activation but that a second antigen nonspecific “co-stimulatory” signal is required. We have demonstrated that this second signal is provided the co-stimulatory receptor CD28 upon recognition of its counter-receptors, members of the B7 family, on the antigen-presenting cell. CD28 engagement is required under most situations for IL-2 production and proliferation. The lack of a CD28-mediated co-stimulatory signal upon TCR engagement can result in the induction of a long-lived state of nonresponsiveness. We are studying the intracellular mechanisms of co-stimulatory signal transduction. We are also examining the relevance of this costimulatory model of T cell activation to immune responses in vivo with the goal of understanding the basis of self-tolerance and to develop means for regulating immune responses.

We have recently found that co-stimulation is more complex than previously thought. CTLA-4, a homolog of CD28, also binds members of the B7 family, and binds them with affinities much higher than CD28. A wealth of data accumulated in the past few years show that CTLA-4 is an important downregulator of T cell responses. We have proposed that CTLA-4 plays a critical role in both the initiation and termination of T cell responses. According to this view, T cell activation is a dynamic process that is determined by the strength of the TCR signal; the strength of co-stimulation provided by CD28; and the magnitude of inhibitory signals generated by CTLA-4. We have begun to analyze the mechanisms by which the signals generated by these different pathways are integrated in T cell activation. We have found that CTLA-4 and CD28 have distinct sites of localization in the T cell, and that both transit to the site of T cell receptor engagement upon the encounter of the T cell with an antigen presenting cell. We are currently studying this relocalization in the context of formation of the immunological synapse between the T cell and the APC.

IAAO2012 Title of the Talk:

Beyond Immune Checkpoint Blockade: Manipulation of T Cell Regulatory Circuits in Cancer Therapy

ABSTRACT:

We conducted extensive pre-clinical studies in mouse models which showed that blockade of the inhibitory signals mediated by CTLA-4 in T cells, either alone or in combination with a variety of immunologic and conventional therapies, led to tumor rejection and long-lived immunity. Ipilimumab, an antibody to human CTLA-4 developed (Bristol Meyers-Squibb) has been given to over 10,000 patients in clinical trials. Objective responses have been observed in melanoma, prostate, kidney, ovarian, and lung cancer. A randomized, placebo controlled trial of ipilimumab documented an increase in survival of patients with advanced melanoma, the first drug of any type to do so, with more than 20% of patients alive for over 4 years after treatment. In 2011 ipilimumab was approved for the treatment of patients with late stage melanoma and it is now a standard of care for this diseases. While CTLA-4 blockade can lead to durable responses in patients, there is clearly a need to increase the response rate. Recent trials have shown that blockade of another immune checkpoint mediated by the molecule PD-1 can also produce objective responses in several tumor types.

We have shown that administration of anti-CTLA-4 results in an increase of the frequency of CD4 T cells that express ICOS in both tumor tissue and blood of bladder cancer patients. The ICOS+ population contained tumor-specific effector CD4 T cells. We also showed that sustained elevation of ICOS+ CD4 T cells correlated with increase survival of advanced melanoma patients treated with Ipilimumab. Together, these data suggested to us that ICOS might play an important role in the therapeutic effects of CTLA-4 blockade. To test this we used a mouse model of melanoma. We found that the efficacy of anti-CTLA-4 was markedly diminished in mice that were deficient in either ICOS or ICOS ligand (ICOSL), confirming that the pathway plays a critical role in anti-CTLA-4 therapy.

These observations led us to test the possibility that engagement of ICOS could enhance the efficacy of anti-CTLA-4 therapy. We transduced mouse B16F10 melanoma cells with a cDNA encoding ICOSL or a control construct. B16ICOSL+ cells (IVAX) and control B16 cells were irradiated and used alone or in combination with anti-CTLA-4 to treat mice bearing established B16F10 tumors. We found that the combination of IVAX with anti-CTLA-4 was markedly more effective than the other combined or single treatments. The increase in therapeutic efficacy was accompanied by a marked in increase in the density and functionality of CD4 and CD8 T cells within the tumor.

These results suggest a novel strategy for manipulating the immune system to enhance anti-tumor responses: checkpoint blockade coupled with provision of agonist signals mediated by ICOS to enhance costimulation.

Title: Chemokine Receptor 4 (CCR4) is a Promising Target for Development of New Tumor Immunotherapy

Speaker

Ryuzo Ueda, M.D.,Ph.D.
Professor Emeritus, Senior Adviser, Nagoya City University
Professor, Dept. of Tumor Immunology, Aichi Medical University, Japan

Chairman

Makoto Ogawa, M.D.
Emeritus President, Aichi Cancer Center, Japan

Ryuzo Ueda, M.D.,Ph.D.

EDUCATION:

1969:	Nagoya University School of Medicine, M.D.
1969-1976:	Clinical Fellow, Nagoya University School of Medicine, Nagoya
1976-1980:	Research Fellow, Research Associate (1979), Memorial Sloan-Kettering Cancer Center, N.Y., USA

CURRENT POSITION:

2010-	Professor Emeritus, Senior Adviser, Nagoya City University
2012-	Professor, Dept. of Tumor Immunology, Aichi Medical University

SPECIALTIES AND FIELD OF INTEREST:
Specialty: Hematology and Medical Oncology
Field of Interest; Molecular Target Therapy for Cancer, Monoclonal Antibody Therapy

RECENT SELECTED ORIGINAL PAPER:

1. Nishikawa H, Maeda Y, Ishida T, Gnjatic S, Sato E, Mori F, Sugiyama D, Ito A, Fukumori Y, Utsunomiya A, Inagaki H, Old LJ, Ueda R, Sakaguchi S. Cancer/testis antigens are novel targets of immunotherapy for adult T-cell leukemia/lymphoma. Blood, 119: 3097-3104 2012.

2. Ishida T, Joh T, Uike N, Yamamoto K, Utsunomiya A, Yoshida S, Saburi Y, Miyamoto T, Takemoto S, Suzushima H, Tsukasaki K, Nosaka K, Fujiwara H, Ishitsuka K, Inagaki H, Ogura M, Akinaga S, Tomonaga M, Tobinai K, Ueda R. Defucosylated Anti-CCR4 Monoclonal Antibody (KW-0761) for Relapsed Adult T-Cell Leukemia-Lymphoma: A Multicenter Phase II Study. J Clin Onol., 30: 837-842, 2012.

3. Sugauchi F, Tanaka Y, Kusumoto S, Matsuura K, Sugiyama M, Kurbanov F, Ueda R, Mizokami M. Virological and clinical characteristics on reactivation of occult hepatitis B in patients with hematological malignancy. J Med Virol., 83: 412-418, 2011.

4. Ishida T, Ueda R. Immunopathogenesis of lymphoma: focus on CCR4. Cancer Sci., 102:44-50, 2011.

5. A complement-dependent cytotoxicity-enhancing anti-CD20 antibody mediating potent antitumor activity in the humanized NOD/Shi-scid, IL-2Rγ(null) mouse lymphoma model. Sato F, Ito A, Ishida T, Mori F, Takino H, Inagaki A, Ri M, Kusumoto S, Komatsu H, Iida S, Okada N, Inagaki H, Ueda R. Cancer Immunol Immunother. 59: 1791-1800, 2010

6. Phase I study of KW-0761, a defucosylated humanized anti-CCR4 antibody, in relapsed patients with adult T-cell leukemia-lymphoma and peripheral T-cell lymphoma. Yamamoto K, Utsunomiya A, Tobinai K, Tsukasaki K, Uike N, Uozumi K, Yamaguchi K, Yamada Y, Hanada S, Tamura K, Nakamura S, Inagaki H, Ohshima K, Kiyoi H, Ishida T, Matsushima K, Akinaga S, Ogura M, Tomonaga M, Ueda R. J Clin Oncol. 20: 1591-1598, 2010.

7. Defucosylated humanized anti-CCR4 monoclonal antibody KW-0761 as a novel immunotherapeutic agent for adult T-cell leukemia/lymphoma. Ishii T, Ishida T, Utsunomiya A, Inagaki A, Yano H, Komatsu H, Iida S, Imada K, Uchiyama T, Akinaga S, Shitara K, Ueda R. Clin Cancer Res., 16:1520-1531, 2010.

8. Ito A, Ishida T, Utsunomiya A, Sato F, Mori F, Yano H, Inagaki A, Suzuki S, Takino H, Ri M, Kusumoto S, Komatsu H, Iida S, Inagaki H, Ueda R. Defucosylated anti-CCR4 monoclonal antibody exerts potent ADCC against primary ATLL cells mediated by autologous human immune cells in NOD/Shi-scid, IL-2R gamma(null) mice in vivo. J Immunol.,183:4782-4791, 2009.

9. Defucosylated anti-CCR4 monoclonal antibody exercises potent ADCC-mediated antitumor effect in the novel tumor-bearing humanized NOD/Shi-scid, IL-2Rgamma(null) mouse model. Ito A, Ishida T, Yano H, Inagaki A, Suzuki S, Sato F, Takino H, Mori F, Ri M, Kusumoto S, Komatsu H, Iida S, Inagaki H, Ueda R. Caner Immunol Immunother., 58: 1195-1206, 2008.

10. Ishida, T, Utsunomiya, A, Iida, S, Inagaki, H, Takatsuka, Y, Kusumoto, S, Takeuchi, G, Shimizu, S, Ito, M, Komatsu, H, Wakita, A, Eimoto, T, Matsushima, K and Ueda R. Clinical significance of CCR4 expression in adult T-cell leukemia/lymphoma: its close association with skin involvement and unfavorable outcome. Clinical Cancer Res., 9:3625-3634, 2003.

IAAO2012 Title of the Talk:

Chemokine Receptor 4 (CCR4) is a Promising Target for Development of New Tumor Immunotherapy

Title: Targeting the Hedgehog Pathway in Medulloblastoma

Tom Curran, Ph.D., FRS
Professor of Pathology and Laboratory Medicine, University of Pennsylvania School of Medicine
Deputy Scientific Director, Children's Hospital of Philadelphia, Research Institute
Director, Basic Scientific Research, Center for Childhood Cancer Research, Children's Hospital of Philadelphia Research Institute
Professor of Cell and Developmental Biology, University of Pennsylvania School of Medicine (Secondary)
Member, Division of Cancer Pathobiology, CHOP

Speaker

Nobuyuki Mizunuma, M.D.
Director of Chemotherapy, Gastroenterology Center, Cancer Institute Hospital, Japanese Foundation for Cancer Research (JFCR), Japan

Chairman

Tom Curran, Ph.D., FRS

EDUCATION:

1978	BSc (Hons)	University of Edinburgh (Zoology)
1982	PhD	Imperial Cancer Research Fund Laboratories and University College London (Zoology and Anatomy)

POSTGRADUATE TRAINING AND FELLOWSHIP APPOINTMENTS:

1982-1984	Postdoctoral Fellow, Salk Institute, San Diego, CA

FACULTY APPOINTMENTS:

1991-1995	Associate Director, Roche Institute of Molecular Biology
1995-2006	Member and Chairman, Department of Developmental Neurobiology, St. Jude Children's Research Hospital, Memphis, TN
1995-2006	Professor, Department of Anatomy and Neurobiology, The University of Tennessee, College of Medicine, Memphis, TN
2006-present	Professor of Pathology and Laboratory Medicine, University of Pennsylvania School of Medicine
2006-present	Deputy Scientific Director, Children's Hospital of Philadelphia, Research Institute
2007-present	Director, Basic Scientific Research, Center for Childhood Cancer Research, Children's Hospital of Philadelphia Research Institute
2008-present	Professor of Cell and Developmental Biology, University of Pennsylvania School of Medicine (Secondary)
2010-present	Member, Division of Cancer Pathobiology, CHOP

OTHER APPOINTMENTS:

2006-present	Associate Director, Translational Genomics, Penn Genome Frontiers Institute (PGFI), University of Pennsylvania School of Medicine

AWARDS, HONORS AND MEMBERSHIP IN HONORARY SOCIETIES:

2000-2001	President, American Association for Cancer Research
2000-2005	National Cancer Institute Board of Scientific Advisors
2000	Highly Cited Scientist by Institute for Scientific Information (ISI) in three categories; Neuroscience, Molecular Biology & Genetics, and Microbiology
2001-2009	Javitz Neuroscience Investigator Award, National Institute of Neurological Disorders and Stroke, NIH
2001-2002	Past President, American Association for Cancer Research
2001	Presidential Address, American Association for Cancer Research, New Orleans, LA
2002	Peter M. Steck Memorial Award, Houston, Texas
2003	Martin Rodbell Lecture, Raleigh-Durham, NC
2004	LIMA International Award for Excellence in Pediatric Brain Tumor Research, Pediatric Brain Tumor FD, NY, NY
2005	Elected to The Royal Society, London, England, UK
2006	Marguerite Vogt Lecture Salk Institute, San Diego, CA
2006	21st Annual Colleen Giblin Memorial Lecture. Columbia University New York, NY
2009	W. W. Sutow Visiting Lecturer in Pediatric Oncology, University of Texas MD Anderson Cancer Center, Houston, TX
2009	Elected to the Institute of Medicine, of the National Academies
2012	Elected to the American Academy of Arts & Sciences, Cambridge, MA

BIBLIOGRAPHY:

Research Publications, peer reviewed (print or other media):

1. Kimura H, Ng JMY, Curran T.: Transient inhibition of the Hedgehog pathway in young micecauses permanent defects in bone structure. Cancer Cell 13: 249-60, 2008.

2. Park TJ, Curran T: Alternative Splicing Disabled by Nova2. Neuron Page: 66(6): 811-3, June 2010. PMCID: 20620865

3. Hallock Peter T, Xu Chong-Feng, Park Tae-Ju, Neubert Thomas A, Curran Tom, Burden Steven J: Dok-7 regulates neuromuscular synapse formation by recruiting Crk and Crk-L. Genes & development 24(21): 2451-61, Nov 2010. PMCID: PMC2964755

4. Seidel Kerstin, Ahn Christina P, Lyons David, Nee Alexander, Ting Kevin, Brownell Isaac, Cao Tim, Carano Richard A D, Curran Tom, Schober Markus, Fuchs Elaine, Joyner Alexandra, Martin Gail R, de Sauvage Frederic J, Klein Ophir D: Hedgehog signaling regulates the generation of ameloblast progenitors in the continuously growing mouse incisor. Development (Cambridge, England) 137(22): 3753-61, Nov 2010. PMCID: PMC3049275

5. Parsons D Williams, Li Meng, Zhang Xiaosong, Jones Siân, et al.: The Genetic Landscape of the Childhood Cancer Medulloblastoma. Science (New York, N.Y.) Dec 2010. PMCID: PMC 3110744

6. Brechbiel Jillian L, Ng Jessica M Y, Curran Tom: PTHrP treatment fails to rescue bone defects caused by Hedgehog pathway inhibition in young mice. Toxicologic pathology 39(3): 478-85, Apr 2011.

7. Austgen Kathryn, Johnson Emily T, Park Tae-Ju, Curran Tom, Oakes Scott A: The adaptor protein CRK is a pro-apoptotic transducer of endoplasmic reticulum stress. Nature cell biology 14(1): 87-92, 2011. PMCID: PMC3245775

8. George Britta, Verma Rakesh, Soofi Abdulsalam A, et al.: Crk1/2-dependent signaling is necessary for podocyte foot process spreading in mouse models of glomerular disease. The Journal of clinical investigation Jan 2012.

9. Romer J., Curran T.: Targeting medulloblastoma: small-molecule inhibitors of the Sonic Hedgehog pathway as potential cancer therapeutics. [Review] [23 refs] Cancer Research 65(12): 4975-8, Jun 15 2005.

10. Brumwell CL., Curran T.: Developmental mouse brain gene expression maps. [Review] [7 refs] Journal of Physiology 575(Pt 2): 343-6, Sep 1 2006.

11. Dellovade T., Romer JT., Curran T., Rubin LL.: The hedgehog pathway and neurological disorders. [Review] [115 refs] Annual Review of Neuroscience 29: 539-63, 2006.

12. Curran Tom, Ng Jessica M Y: Cancer: Hedgehog's other great trick. Nature 455(7211): 293-4, Sep 2008.

13. Curran Tom: Mouse models and mouse supermodels. EMBO molecular medicine 2(10): 385-6; author reply 386-7, Oct 2010.

14. Ng Jessica M Y, Curran Tom: The Hedgehog's tale: developing strategies for targeting cancer. Nature reviews. Cancer 11(7): 493-501, 2011.

Editorials, Reviews, Chapters, including participation in committee reports (print or other media):
Curran T, Christen Y. Eds: Targeting Children's Brain Tumors: Development of hedgehog Pathway Inhibitors for Medulloblastoma. In Two Faces of Evil: Cancer and Neurodegeneration; Research Perspectives in Alzheimer's Disease. Springer, 1: 57-71, 2010.

IAAO2012 Title of the Talk:

Targeting the Hedgehog Pathway in Medulloblastoma

ABSTRACT:

Children's brain tumors are quite distinct from adult brain tumors but, because of the limited market potential, they have received relatively little attention from the pharmaceutical industry. Traditionally, treatments were first developed for adult brain tumors then introduced at a lower dose in clinical trials for pediatric brain tumors. Fifteen years ago, we embarked on a long-term program to develop new therapeutic approaches for children's brain tumors based on the identification of specific molecular targets. Initially, we focused on medulloblastoma, a peripheral neuroectodermal tumor that arises in the cerebellum. Approximately 30% of medulloblastoma exhibit activation of the Hedgehog pathway and in approximately half of these cases this occurs a consequence of the loss of Patched-1 (Ptch1), the receptor for Sonic Hedgehog (Shh). This results in excess signaling through the hedgehog pathway. We utilized mouse models of medulloblastoma to test novel inhibitors of the hedgehog pathway in preclinical trials. The results obtained indicated remarkable efficacy and encouraged the development of Smoothened inhibitors as potential therapeutics. Recently, the first inhibitor was approved for the treatment of advanced basal cell carcinoma and it is currently in clinical trials for a range of other tumors including pediatric medulloblastoma. I will discuss the trials and tribulations involved in shepherding a novel therapy from mice to young humans.

Session 2

Rationale for Combination of Molecular Targeted Agents

2-1. Acquired and Adaptive Resistance to Targeted Therapy

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

2-2. Combinatorial Approaches against PI3 Kinase Pathway

Speaker: José Baselga, MD, PhD (Massachusetts General Hospital, USA)

Title: Acquired and Adaptive Resistance to Targeted Therapy

Neal Rosen, M.D., Ph.D.
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

Speaker

Chikashi Ishioka, M.D.
Professor, Institute of Development, Aging, and Cancer, Tohoku University, Japan

Chairman

Neal Rosen, M.D., Ph.D.

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.

Publications in 2011 and 2012

1. Bachleitner-Hofmann T, Sun MY, Chen CT, Liska D, Zeng Z, Viale A, Olshen AB, Mittlboeck M, Christensen JG, Rosen N, Solit DB, and Weiser MR. Antitumor activity of SNX-2112, a synthetic heat shock protein-90 inhibitor, in MET-amplified tumor cells with or without resistance to selective MET inhibition. Clin Cancer Res; 17(1): 122-33. 2011.
2. Chandarlapaty S, Sawai A, Scaltriti M, Rodrik-Outmezguine V, Grbovic-Huezo O, Serra V, Majumder PK, Baselga J, and Rosen N. AKT inhibition relieves feedback suppression of receptor tyrosine kinase expression and activity. Cancer Cell; 19(1):58-71. 2011. PMCID: PMC3025058
3. Franco AT, Malaguarnera R, Refetoff S, Liao XH, Lundsmith E, Kimura S, Pritchard C, Marais R, Davies TF, Weinstein LS, Chen M, Rosen N, Ghossein R, Knauf JA, Fagin JA. Thyrotrophin receptor signaling dependence of Braf-induced thyroid tumor initiation in mice. Proc Natl Acad Sci U S A; 108(4): 1615-20. 2011.
4. Poulikos PI, and Rosen N. Mutant BRAF melanomas: Dependence and resistance. Cancer Cell; 19(1): 11-5. 2011.
5. Solit DB, Rosen N. Resistance to BRAF inhibition in melanomas. N Engl J Med; 364(8): 772-4. 2011.
6. Xie Q, Wondergem R, Shen Y, Cavey G, Ke J, Thompson R, Bradley R, Daughtery-Holtrop J, Xu Y, Chen E, Omar H, Rosen N, Wenkert D, Xu HE, Vande Woude GF. Benzoquinone ansamycin 17AAG binds to mitochondrial voltage-dependent anion channel and inhibits cell invasion. Proc Natl Acad Sci U S A; 108(10): 4105-10. 2011.
7. Serra V, Scaltriti M, Prudkin L, Eichorn P, Ibrahim YH, Chandarlapaty S, Markman B, Rodriguez O, Guzman M, Rodriguez S, Gili M, Russillo M, Parra JL, Singh S, Arribas J, Rosen N, Baselga J. PI3K inhibition results in enhanced HER signaling and acquired ERK dependency in HER2-overexpressing breast cancer, Oncogene; 30(22): 2547-57. 2011.
8. Scaltriti M, Eichorn P, Cortes, J, Prudkin L, Aura C, Jimenez J, Chandarlapaty S, Serra V, Prat A, Ibrahim YH, Guzman M, Gili M, Rodriguez O, Rodriguez S, Perez J, Green SR, Mai S, Rosen N, Hudis C, Baselga J. Cyclin E amplification/overexpression is a mechanism of trastuzumab resistance in HER2-positive breast cancer patients. Proc Natl Acad Sci U S A; 108(9): 3761-6. 2011.
9. Carver BS, Chapinski C, Wongvipat J, Hieronymous 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; 19(5): 575-86. 2011.
10. Modi S, Stopeck AT, Linden HM, Solit DB, Chandarlapaty S, Rosen N, D'Andrea G, Dickler MN, Moynahan ME, Sugarman S, Ma W, Patil S, Norton L, Hannah AL, Hudis C. Hsp90 inhibition is effective in breast cancer: A phase 2 trial of Tanespimycin (17AAG) plus Trastuzumab in patients with Her2-positive metastatic breast cancer progressing on Trastuzumab. Clin Cancer Res; 2011 [Epub ahead of print]
11. 1Rodrik-Outmezguine V, Chandarlapaty S, Pagano NC, Poulikakos PI, Scaltriti M, Moskatel E, Baselga J, Guichard S, Rosen N. mTOR kinase inhibition causes feedback-dependent biphasic regulation of AKT signaling. Cancer Discovery, in press. Bachleitner-Hofmann T, Sun MY, Chen CT, Liska D, Zeng Z, Viale A, Olshen AB, Mittlboeck M, Christensen JG, Rosen N, Solit DB, and Weiser MR. Antitumor activity of SNX-2112, a synthetic heat shock protein-90 inhibitor, in MET-amplified tumor cells with or without resistance to selective MET inhibition. Clin Cancer Res; 17(1): 122-33. 2011.
12. Chandarlapaty S, Sawai A, Scaltriti M, Rodrik-Outmezguine V, Grbovic-Huezo O, Serra V, Majumder PK, Baselga J, and Rosen N. AKT inhibition relieves feedback suppression of receptor tyrosine kinase expression and activity. Cancer Cell; 19(1):58-71. 2011. PMCID: PMC3025058
13. Franco AT, Malaguarnera R, Refetoff S, Liao XH, Lundsmith E, Kimura S, Pritchard C, Marais R, Davies TF, Weinstein LS, Chen M, Rosen N, Ghossein R, Knauf JA, Fagin JA. Thyrotrophin receptor signaling dependence of Braf-induced thyroid tumor initiation in mice. Proc Natl Acad Sci U S A; 108(4): 1615-20. 2011.

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16. Xie Q, Wondergem R, Shen Y, Cavey G, Ke J, Thompson R, Bradley R, Daughtery-Holtrop J, Xu Y, Chen E, Omar H, Rosen N, Wenkert D, Xu HE, Vande Woude GF. Benzoquinone ansamycin 17AAG binds to mitochondrial voltage-dependent anion channel and inhibits cell invasion. Proc Natl Acad Sci U S A; 108(10): 4105-10. 2011.
17. Serra V, Scaltriti M, Prudkin L, Eichorn P, Ibrahim YH, Chandarlapaty S, Markman B, Rodriguez O, Guzman M, Rodriguez S, Gili M, Russillo M, Parra JL, Singh S, Arribas J, Rosen N, Baselga J. PI3K inhibition results in enhanced HER signaling and acquired ERK dependency in HER2-overexpressing breast cancer, Oncogene; 30(22): 2547-57. 2011.
18. Scaltriti M, Eichorn P, Cortes, J, Prudkin L, Aura C, Jimenez J, Chandarlapaty S, Serra V, Prat A, Ibrahim YH, Guzman M, Gili M, Rodriguez O, Rodriguez S, Perez J, Green SR, Mai S, Rosen N, Hudis C, Baselga J. Cyclin E amplification/overexpression is a mechanism of trastuzumab resistance in HER2-positive breast cancer patients. Proc Natl Acad Sci U S A; 108(9): 3761-6. 2011.
19. Carver BS, Chapinski C, Wongvipat J, Hieronymous 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; 19(5): 575-86. 2011.
20. Modi S, Stopeck AT, Linden HM, Solit DB, Chandarlapaty S, Rosen N, D'Andrea G, Dickler MN, Moynahan ME, Sugarman S, Ma W, Patil S, Norton L, Hannah AL, Hudis C. Hsp90 inhibition is effective in breast cancer: A phase 2 trial of Tanespimycin (17AAG) plus Trastuzumab in patients with Her2-positive metastatic breast cancer progressing on Trastuzumab. Clin Cancer Res; 2011 [Epub ahead of print]
21. Rodrik-Outmezguine V, Chandarlapaty S, Pagano NC, Poulikakos PI, Scaltriti M, Moskatel E, Baselga J, Guichard S, Rosen N. mTOR kinase inhibition causes feedback-dependent biphasic regulation of AKT signaling. Cancer Discovery, Published OnlineFirst June 17, 2011; doi: 10.1158/2159-8290.CD-11-0085.
22. Jonathan H. Schatz, Elisa Oricchio, Andrew L. Wolfe, Man Jiang, Irina Linkov, Jocelyn Maragulia, Weiji Shi, Zhigang Zhang, Vinagolu K. Rajasekhar, Nen C. Pagano, John A. Porco Jr., Julie Teruya-Feldstein, Neal Rosen, Andrew D. Zelenetz, Jerry Pelletier and Hans-Guido Wendel. Targeting cap-dependent translation blocks converging survival signals by AKT and PIM kinases in lymphoma. JEM vol. 208 no. 9 1799-1807
23. Debyani Chakravarty, Elmer Santos, Mabel Ryder, Jeffrey A. Knauf, Xiao-Hui Liao, Brian L. West, Gideon Bollag, Richard Kolesnick, Tin Htwe Thin, Neal Rosen, Pat Zanzonico, Steven M. Larson, Samuel Refetoff, Ronald Ghossein, and James A. Fagin. Small-molecule MAPK inhibitors restore radioiodine incorporation in mouse thyroid cancers with conditional BRAF activation. J Clin Invest. 2011 December 1; 121(12): 4700–4711.
24. Gopa Iyer, Michael J. Morris, Dana Rathkopf, Susan F. Slovin, Macaulay Steers, Steven M. Larson, Laurence H. Schwarts, Tracy Curley, anthony DeLaCrus, Qing Ye, Glenn Heller, Merrill J. Egorin, S. Percy Ivy, Neal rosen, Howard I. Scher, David B. solit. A phase I trail of deoctaxel and pulse-dose 17-allylamino-127demethoxygeldanamaycin in adult patients with solid tumores. Cancer Chemother. Pharmacol (2012) 69;:1089-1097
25. Aphrothiti J. Hanrahan, Nikolaus Schultz, Maggie L. Westfal, Rita A. Sakr, Dilip D. Giri, Stefano Scarperi, Manickam Janikariman, Narciso Olvera, Ellen V. Stevens, Qing-Bai She, Carol Aghajanian, Tari A. King, Elisa de Stanchina, David R. Spriggs, Adriana Heguy, Barry S. Taylor, Chris Sander, Neal Rosen, Douglas A. Levine and David B. Solit. Genomic Complexity and AKT Dependence in Serous Ovarian Cancer. Published OnlineFirst November 3, 2011; doi: 10.1158/2159-8290.CD-11-0170
26. Mario E. Lacouture, Kathryn O'Reilly, Neal Rosen , David B. Solit. Induction of Cutaneous Squamous Cell Carcinomas by RAF Inhibitors: Cause for Concern? JCO January 20, 2012 vol. 30 no. 3 329-33
27. Guochang Huang, Gil Redelman-Sidi, Neal Rosen, Michael S. Glickman and Xuejun Jiang. Inhibition of Mycobacterial Infection by the Tumor Suppressor PTEN. Biological Chemistry, 287, 23196-23202.

IAAO2012 Title of the Talk:

Acquired and Adaptive Resistance to Targeted Therapy

Title: Combinatorial Approaches against PI3 Kinase Pathway

Jose Baselga, M.D., Ph.D.
Professor, Department of Medicine, Harvard Medical School
Associate Director, MGH Cancer Center, Medicine, Massachusetts General Hospital
Chief, Hematology/Oncology, Medicine, Massachusetts General Hospital
Associate Director, Clinical Sciences, Dana Farber/Harvard Cancer Center (DF/HCC)

Speaker

Masakazu Toi, M.D., Ph.D.
Professor, Department of Surgery, Graduate School of Medicine Kyoto University, Japan

Chairman

Jose Baselga, M.D., Ph.D.

EDUCATION:

9/76-6/82	MD	Medicine	Universitat Autonoma de Barcelona, Spain
11/92	Ph.D. Cum Laude and Extraordinary Award		Universitat Autonoma de Barcelona, Spain

FACULTY ACADEMIC APPOINTMENTS:

7/94-6/96 Instructor, Medical, Memorial Sloan-Kettering Cancer Center, Cornell University Medical College, New York, NY.
1/95-7/10 Professor, Medicine, Universitat Autonoma de Barcelona, Spain
2010- Professor, Medicine, Harvard Medical School, Boston, MA

APPOINTMENTS AT HOSPITALS/AFFILIATED INSTITUTIONS:

7/94-6/96 Clinical Assistant Physician, Breast/Gynecology Oncology Service, Department of Medicine
1/96-7/10 Chairman, Medical Oncology, Vall d'Hebron University Hospital, Barcelona, Spain
7/10 - Physician, Medicine, Massachusetts General Hospital, Boston, MA.

MAJOR ADMINISTRATIVE LEADERSHIP POSITIONS:

1996-2010 Chairman, Medical Oncology Service, Vall d'Hebron University Hospital, Barcelona, Spain
1996-2010 Director, Medical Oncology, Hematology and Radiation Oncology, Vall d'Hebron University Hospital, Barcelona, Spain
2007-2010 Director, Vall d'Hebron Institute of Oncology, Vall d'Hebron University Hospital, Barcelona, Spain
2010- Associate Director, MGH Cancer Center, Massachusetts General Hospital
2010- Division Chief, Division of Hematology/Oncology, Massachusetts General Hospital
2012- Associate Director Clinical Siences, Dana Farber/Harvard Cancer Center (DF/HCC)

PROFESSIONAL SOCIETIES:

1990 American Society of Clinical Oncology
- 2004-2006 Member, Board of Directors.
- 2008-2011 Member, Trials in Progress Track, Scientific Program Committee
- 2010-2013 Member, Special Awards Selection Committee

1990 American Association for Cancer Research
- 2008-2011 Member, Board of Directors
- 2012-2013 Chairperson, 2013 Annual Meeting Program Committee

1996 Spanish Cooperative Breast Cancer Group (SOLTI)
- 2009- President

1996 European Society for Medical Oncology
- 2008-2009 President
- 2006-2012 Member, Board of Directors

2002 European Cancer Organization
- 2010-2011 Member, Board of Directors, Re-elected

2006 Ludwing Institute for Cancer Research
- 2006- Member, Scientific Advisory Committee

2008 American-Italian Cancer Foundation
- 2008- Member, Board of Directors
- 2008-2011 Member, Scientific Advisory Board

2010 Breast International Group
- 2010- Member, Board of Directors

HONORS AND PRIZES:

1992-1993 Young Investigator Award, American Society of Clinical Oncology (ASCO)
1999 Young Investigator Award, American Association for Cancer Research (AACR)
2003 Honorary Membership Award, The European Society for Therapeutic Radiology and Oncology (ESTRO)
2004 Waun Ki Hong Visiting Professorship, UTMD Anderson Cancer Center
2004 Distinguished Alumni Award, 29th Annual Alumni Society Meeting, Memorial Sloan-Kettering Cancer Center

2005	Annual Award, European Society of Medical Oncology (ESMO), Career Recognition Award
2005	Professional Excellence Award in Biomedicine Research, Barcelona College of Physicians
2006	City Award “The Key to the City of Barcelona”, Francisco Godia Foundation, Civic leadership in Barcelona
2006	Michael Clavel Lecture Award, 18th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics, Contributions in early drug development
2006	San Salvatore Prize 2006, San Salvatore Foundation, Achievements in breast cancer research
2007	AICF Prize For Scientific Excellence in Medicine, American Italian Cancer Foundation
2008	Civil Order of Health – Commander with Plaque, Ministry of Health, Government of Spain; Contribution to the advanced of biomedical science in Spain
2008	Rosenthal Family Foundation Award, American Association for Cancer Research, Academic career in translational oncology
2008	Rey Jaime I Award in Medical Research, King Jaime I Foundation, Achievements in biomedical research in cancer
2010	Bruce A. Chabner Chair in Hematology Oncology, Massachusetts General Hospital Cancer Center, Academic career achievements in Hematology/Oncology
2010	Bob Pinedo Cancer Care Prize, The Society for Translational Oncology (STO), Exceptional contribution to improved care for cancer patients
2010	Gold Medal, Queen Sofia Spanish Institute, Achievements in biomedical research in cancer
2011	Honorary Doctoral Degree, Valencia University, Career excellence and innovation in biomedical research in cancer
2012	Joseph B. Martin Award, Massachusetts General Hospital, Best clinical paper published by MGH Investigators in 2011

PUBLICATIONS:
>280 publications in the peer reviewed journals.

Publications selected in the last 12 months:

1. Serra V, Scaltriti M, Prudkin L, Eichhorn PJ, Ibrahim YH, Chandarlapaty S, Markman B, Rodriguez O, Guzman M, Rodriguez S, Gili M, Russillo M, Parra JL, Singh S, Arribas J, Rosen N, Baselga J. PI3K inhibition results in enhanced HER signaling and acquired ERK dependency in HER2-overexpressing breast cancer. Oncogene. 2011 Jun 2;30(22):2547-57.
2. Lenihan D, Suter T, Brammer M, Neate C, Ross G, Baselga J. Pooled analysis of cardiac safety in patients with cancer treated with pertuzumab. Ann Oncol. 2012 Mar;23(3):791-800.

3. Bass AJ, Lawrence MS, Brace LE, Ramos AH, Drier Y, Cibulskis K, Sougnez C, Voet D, Saksena G, Sivachenko A, Jing R, Parkin M, Pugh T, Verhaak RG, Stransky N, Boutin AT, Barretina J, Solit DB, Vakiani E, Shao W, Mishina Y, Warmuth M, Jimenez J, Chiang DY, Signoretti S, Kaelin WG, Spardy N, Hahn WC, Hoshida Y, Ogino S, Depinho RA, Chin L, Garraway LA, Fuchs CS, Baselga J, Tabernero J, Gabriel S, Lander ES, Getz G, Meyerson M. Genomic sequencing of colorectal adenocarcinomas identifies a recurrent VTI1A-TCF7L2 fusion. Nat Genet. 2011 Oct;43(10):964-8.
4. Semiglazov V, Eiermann W, Zambetti M, Manikhas A, Bozhok A, Lluch A, Tjulandin S, Sabadell MD, Caballero A, Valagussa P, Baselga J, Gianni L. Surgery following neoadjuvant therapy in patients with HER2-positive locally advanced or inflammatory breast cancer participating in the NeOAdjuvant Herceptin (NOAH) study. Eur J Surg Oncol. 2011 Oct;37(10):856-63.
5. Serrano C, Cortés J, De Mattos-Arruda L, Bellet M, Gómez P, Saura C, Pérez J, Vidal M, Muñoz-Couselo E, Carreras MJ, Sánchez-Ollé G, Tabernero J, Baselga J, Di Cosimo S. Trastuzumab-related cardiotoxicity in the elderly: a role for cardiovascular risk factors. Ann Oncol. 2011 Aug 9.
6. Paz-Ares LG, Gomez-Roca C, Delord JP, Cervantes A, Markman B, Corral J, Soria JC, Berge Y, Roda D, Russell-Yarde F, Hollingsworth S, Baselga J, Umana P, Manenti L, Tabernero J. Phase I pharmacokinetic and pharmacodynamic dose-escalation study of RG7160 (GA201), the first glycoengineered monoclonal antibody against the epidermal growth factor receptor, in patients with advanced solid tumors. J Clin Oncol2011 Oct 1;29(28):3783-90.
7. Atzori F, Tabernero J, Cervantes A, Prudkin L, Andreu J, Rodriguez-Braun E, Domingo A, Guijarro J, Gamez C, Rodon J, Di Cosimo S, Brown H, Clark J, Hardwick J, Beckman RA, Hanley W, Hsu K, Calvo E, Rosello S, Langdon RB, Baselga J. A Phase I, Pharmacokinetic and Pharmacodynamic Study of Dalotuzumab (MK-0646), an Anti-IGF-1R Monoclonal Antibody, in Patients with Advanced Solid Tumors. Clin Cancer Res. 2011 Oct 1;17(19):6304-12.
8. Higgins MJ, Baselga J. Targeted therapies for breast cancer. J Clin Invest. 2011 Oct; 121(10):3797-803
9. Cortes J, Calvo V, Ramírez-Merino N, O'Shaughnessy J, Brufsky A, Robert N, Vidal M, Muñoz E, Perez J, Dawood S, Saura C, Di Cosimo S, González-Martín A, Bellet M, Silva OE, Miles D, Llombart A, Baselga J. Adverse events risk associated with bevacizumab addition to breast cancer chemotherapy: a meta-analysis. Ann Oncol. 2011 Oct 4.
10. Kostic AD, Gevers D, Pedamallu CS, Michaud M, Duke F, Earl AM, Ojesina AI, Jung J, Bass AJ, Tabernero J, Baselga J, Liu C, Shivdasani RA, Ogino S, Birren BW, Huttenhower C, Garrett WS, Meyerson M. Genomic analysis identifies association of Fusobacterium with colorectal carcinoma. Genome Res. 2012 Feb;22(2):292-8.
11. Sequist LV, Heist RS, Shaw AT, Fidias P, Rosovsky R, Temel JS, Lennes IT, Digumarthy S, Waltman BA, Bast E, Tammireddy S, Morrissey L, Muzikansky A, Goldberg SB, Gainor J, Channick CL, Wain JC, Gaissert H, Donahue DM, Muniappan A, Wright C, Willers H, Mathisen DJ, Choi NC, Baselga J, Lynch TJ, Ellisen LW, Mino-Kenudson M, Lanuti M, Borger DR, Iafrate AJ, Engelman JA, Dias-Santagata D. Implementing multiplexed genotyping of non-small-cell lung cancers into routine clinical practice. Ann Oncol. 2011 Dec; 22.
12. Rodrik-Outmezguine VS, Chandarlapaty S, Pagano NC, Poulikakos PI, Scaltriti M, Moskatel E, Baselga J, Guichard S, Rosen N. BIM expression in treatment naïve cancers predicts responsiveness to kinase inhibitors. Cancer Discov. 2011 Jun 17;1(3):248-59.
13. Baselga J, Campone M, Piccart M, Burris HA, Rugo HS, Sahmoud T, Noguchi S, Gnant M, Pritchard KI, Lebrun F, Beck JT, Ito Y, Yardley D, Deleu I, Perez A, Bachelot T, Vittori L, Xu Z, Mukhopadhyay P, Lebwohl D, Hortobagyi GN. Everolimus in Postmenopausal Hormone-Receptor-Positive Advanced Breast Cancer. N Engl J Med. 2012 366(6):520-9.
14. Bendell JC, Rodon J, Burris HA, de Jonge M, Verweij J, Birle D, Demanse D, De Buck SS, Ru QC, Peters M, Goldbrunner M, Baselga J. Phase I, Dose-Escalation Study of BKM120, an Oral Pan-Class I PI3K Inhibitor, in Patients With Advanced Solid Tumors. J Clin Oncol. 2012 30(3):282-90.

15. Baselga J, Cortés J, Kim SB, Im SA, Hegg R, Im YH, Roman L, Pedrini JL, Pienkowski T, Knott A, Clark E, Benyunes MC, Ross G, Swain SM; CLEOPATRA Study Group. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. N Engl J Med 2012 Jan 12;366(2):109-19.
16. Baselga J, Bradbury I, Eidtmann H, DeCosimo S, deAzambuja E, Aura C, Gomex H, Dinh P, Fauria K, Van Dooren V, Sktan G, Goldhirsch A, Chang TW, Horvath Z, Coccia-Portugal M, Dormont J, Tseng L, Kunz G, Sohn JH, Semiglazov V, Lerzo G, Palacova M, Probachai V, Pusztai L, Untch M, Gelber RD, Piccart M. Lapatinib with trastuzumab for HER2-positive early breast cancer (NeoALTTO): a randomized, open-label, multicentre, phase 3 trial. Lancet. 2012; Feb 18;379(9816):633-40
17. Eichhorn PJ, Rodon L, Gonzalez-Junca A, Dirac A, Gili M, Martinez-Saez E, Aura C, Barba I, Peg V, Prat A, Cuartas I, Jimenez J, Garcia-Dorado D, Sahuquillo J, Bernards R, Baselga J, Seoane J. USP15 stabilizes TGF-beta receptor I and promotes oncogenesis through the activation of TGF-beta signaling in glioblastoma. Nat Med 2012 Feb 19;18(3):429-35.
18. Markman B, Tabernero J, Krop I, Shapiro GI, Siu L, Chen LC, Mita M, Melendez Cuero M, Stutvoet S, Birle D, Anak O, Hackl W, Baselga J. Phase I safety, pharmacokinetic, and pharmacodynamic study of the oral phosphatidylinositol-3-kinase and mTOR inhibitor BGT226 in patients with advanced solid tumors. Ann Onco 2012 Feb 22.
19. Juric D, Baselga J. Tumor Genetic Testing for Patient Selection in Phase I Clinical Trials: The Case of PI3K Inhibitors. J Clin Oncol 2012 Mar 10;30(8):765-6
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NARRATIVE REPORT ON CAREER AND RESEARCH INTERESTS:

My career is focused towards the development of novel molecular targeted agents, with special emphasis in breast cancer. I have directed the pre-clinical and clinical development of therapies against the Epidermal Growth Factor Receptor (EGFR) and the closely related HER2 receptor. My current work has expanded towards the clinical development of mTOR and PI3Kinase inhibitors. In the process, I have been deeply involved in the creation of a new paradigm for translational and clinical research, generating hypotheses in the lab and moving them swiftly into clinical trials.

I have devoted 20 years to the development of anti-EGFR agents in the laboratory and in the clinic. I lead the initial clinical studies that identified the optimal dose and schedule of a series of EGFR agents. I was also the first one to report clinical activity with anti-EGFR (and anti-HER2) agents and have led the full clinical development of this class of agents. Our latest work is focused in triple negative breast cancer.

In the field of anti-HER2 therapies, I was the lead investigator in the first publication that demonstrated the clinical activity of the anti-HER2 monoclonal antibody trastuzumab (Herceptin) in patients with advanced HER2 over expressing breast cancer. I continue to lead state-of the art world-wide clinical trials with trastuzumab including in the neo-adjuvant and adjuvant setting. In the laboratory, I reported the synergy between paclitaxel and trastuzumab that lead to the registration clinical trial. We have also been able over the years to identify a number of mechanisms of resistance to anti-HER2 agents. Some of them including p95HER2 and hyper-activation of the PI3K-Akt-mTOR pathway are therapeutic targets themselves and we are exploring them. Our latest work includes the clinical development of novel anti-HER2 antibodies such as pertuzumab that have shown to improve the disease free survival and the overall survival in the first line setting. I am currently the principal investigator of the adjuvant clinical trial with pertuzumab.

I have pioneered the development of pharmacodynamic markers of target inhibition with signal transduction inhibitors in preclinical models and translated into early clinical trials where we sequentially interrogate tumors. Among a long list of findings, we observed that inhibition of mTOR induced intra-tumoral activation of compensatory feed back loops that resulted in activation of multiple pathways. In the lab and in the clinic we have established that the combined administration of rapamycin analogs and aromatase inhibitors results in improved outcome. We have also identified that the activation of compensatory pathways is mediated via the IGF-1R and clinical trials with anti-mTOR and anti-IGF-1R agents given combined have shown remarkable results in patients with Luminal B hormone refractory breast cancer. We have also led the conduct of clinical trials in patients with breast cancer harboring PI3K mutations.

On the administration front, I lead the transformation of the Vall d´Hebron Hospital in Barcelona from a small clinical service to a full cancer center with a large multidisciplinary research program and with the largest phase I program in Europe. I have recently moved to the Massachussets General Hospital Cancer Center where I am implementing a newly designed strategic plan that has lead to a robust growth of our patient volume, to the construction and acquisition of a number of satellites in Massachusetts, and to an unparallel expansion of our phase I program. In addition, I have been instrumental in raising the funds, in the design and in the construction of a new Center for Targeted Therapies that will be inaugurated in October 2012.

In addition to my research and administrative functions described above, I have also been deeply involved in teaching. I established the first elective in oncology at the medical school in Barcelona in 1996 and I have also been involved in teaching of residents and fellows. At the European level, I created a number of International Fellowships during my ESMO presidency from which a large number of oncologists have benefited. At the societal level, I have been president of ESMO and a member of the board of director of both ASCO and AACR.

IAAO2012 Title of the Talk:

Combinatorial Approaches against PI3 Kinase Pathway

Session 3

New Molecular Class

3-1. Antibody Drug Conjugates for Cancer Therapy

Speaker: Paul Polakis, PhD (Genentech Inc, USA)

Title: Antibody Drug Conjugates for Cancer Therapy

Paul G. Polakis, Ph.D.
Staff Scientist and Director, Cancer Targets, Genentech, Inc.

Speaker

Mitsuaki Yoshida, Ph.D.
Director, The Cancer Chemotherapy Center of Japanese Foundation of Cancer Research (JFCR)
Professor Emeritus, The University of Tokyo, Japan

Chairman

Paul G. Polakis, Ph.D.

CURRENT POSIOTION:

2005-present Staff Scientist and Director, Cancer Targets, Genentech, Inc.

EDUCATION:

Ph.D., 1984, Biochemistry, Department of Biochemistry, Michigan State University

PUBLICATIONS:

1. Identification and immunotherapeutic targeting of antigens induced by chemotherapy. Nat. Biotechnol. 2006 24:205-9.
2. Shulewitz M, Soloviev I, Wu T, Koeppen H, Polakis P, Sakanaka C. 2006. Repressor roles for TCF-4 and Sfrp1 in Wnt signaling in breast cancer. Oncogene. 25:4361-9. Polakis, P. The many ways of Wnt in cancer. 2007. Curr Opin Genet Dev. 17; 45-
3. Chen Y, Clark S, Wong T, Chen Y, Chen Y, Dennis MS, Luis E, Zhong F, Bheddah S, Koeppen H, Gogineni A, Ross S, Polakis P, Mallet W. 2007. Armed antibodies targeting the mucin repeats of the ovarian cancer antigen, MUC16, are highly efficacious in animal tumor models.Cancer Res. 67:4924-32.

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7. Polakis P, Mallet W. 2008. Site-specific conjugation of a cytotoxic drug to an antibody improves the therapeutic index. Nat Biotechnol. 26:925-32.
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14. Asundi J, Reed C, Arca J, McCutcheon K, Ferrando R, Clark S, Luis E, Tien J, Firestein R, Polakis P. 2011. An antibody-drug conjugate targeting the endothelin B receptor for the treatment of melanoma. Clin Cancer Res. 17:965-75.
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20. Polakis P. Drugging wnt signaling in cancer. 2012. EMBO J. 2012 May 22..126. [Epub ahead of print]

IAAO2012 Title of the Talk:

Antibody Drug Conjugates for Cancer Therapy

ABSTRACT:

Antibody drug conjugates share the common feature of targeting internalizing cell surface proteins with an antibody covalently linked to a highly potent cytotoxic compound. In principal, this enables higher local exposure of the tumor to the drug than that permissible by systemic delivery of the free drug. Recent advances in this technology have resulted in some very encouraging objective clinical responses and numerous ADCs are now in various stages of development. I will discuss some of the challenges associated with research and development of antibody drug conjugates including target selection, the impact of linker chemistry, target- independent toxicity and drug resistance. In addition, I will present some evidence for the potential benefit of combining ADCs targeting melanocytic antigens with MAP kinase pathway inhibitors in the treatment of melanoma.

Session 4

Drug Resistances

4-1. Challenges with Drug Resistance

Speaker: Jeffrey A. Engelman, MD, PhD (Massachusetts General Hospital, USA)

4-2. Sensitivity and Resistance to Targeting FGFR in Cancer

Speaker: Nicholas Turner, MD, PhD (The Royal Marsden, UK)

Title: Challenges with Drug Resistance

Speaker

Jeffrey A. Engelman, M.D., Ph.D.
Principal Investigator, Research Laboratory, Massachusetts General Hospital (MGH) Cancer Center
Co-Leader, DFHCC Thoracic Program, Dana-Farber/Harvard Cancer Center
Director, Thoracic Oncology, MGH Cancer Center
Director, Molecular Therapeutics, MGH Cancer Center

Chairman

Nagahiro Saijo, M.D., Ph.D.
Executive Officer of Japanese Society of Medical Oncology, Japan

Jeffrey A. Engelman, M.D., Ph.D.

EDUCATION:

1993	B.A.	Chemistry	Northwestern University with honors
2000	M.D.	Medicine	Albert Einstein College of Medicine
2000	Ph.D.	Molecular Pharmacology (Dr. Michael Lisanti)	Albert Einstein College of Medicine

CURRENT POSITION:l

04/2012-	Associate Professor	Medicine	Harvard Medical School

MAJOR ADMINISTRATIVE LEADERSHIP POSITIONS: LOCAL

2008-	Principal Investigator, Research Laboratory	MGH Cancer Center
2009-	Co-Leader, DFHCC Thoracic Program	Dana-Farber/Harvard Cancer Center
2009-	Director, Thoracic Oncology	MGH Cancer Center
2012-	Director, Molecular Therapeutics	MGH Cancer Center

HONORS AND PRIZES:

2005	Young Investigator Award	American Society of Clinical Oncology
2005	Fellowship in Translational Lung	AACR-AstraZeneca Cancer Research and

	Cancer Research	Prevention Foundation
2007	Ellison Scholar Award	Massachusetts General Hospital
2008	Member of the One Hundred	Massachusetts General Hospital
2010	Team Science Award	AACR
2011	Stephen Krane Award	Massachusetts General Hospital Dept. of Medicine

LATEST PUBLICATIONS:

1 Chakrabarty A, Rexer BN, Wang SE, Cook RS, Engelman JA, Arteaga CL. H1047R phosphatidylinositol 3-kinase mutant enhances HER2-mediated transformation by heregulin production and activation of HER3. *Oncogene*. (2010). Jun 28. [Epub ahead of print]

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4 Qi J, McTigue M, Rogers A, Lifshits E, Christensen J, Jänne P, Engelman JA. Acquisition of mutations and development of bypass tracks cause acquired resistance to MET inhibitors. *Cancer Research*. (2011). Published OnlineFirst January 25, 2011; doi:10.1158/0008-5472.CAN-10-1623.

5 Jänne PA, Boss DS, Camidge DR, Britten CD, Engelman JA, Garon EB, Guo F, Wong S, Liang J, Letrent S, Millham R, Taylor I, Eckhardt SG, Schellens JH. Phase I Dose-Escalation Study of the Pan-HER Inhibitor, PF299804, in Patients with Advanced Malignant Solid Tumors. *Clin Cancer Res*. (2011). Mar 1;17(5):1131-1139. Epub 2011 Jan 10.

6 Corcoran RB, Contino G, Desphpande V, Tzatsos A, Conrad C, Benes CH, Settleman J, Engelman A, Bardeesy N. STAT3 plays a critical role in KRAS-induced pancreatic tumorigenesis. *Cancer Research*. (2011). Jul 15;71(14):5020-9. Epub 2011 May 17.

7 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 JA, Shivdasani RA, Nishio K, Fukuoka M, Varella-Garcia M, Nakagawa K, Jänne PA. Activation of ERBB2 Signaling Causes Resistance to the EGFR-Directed Therapeutic Antibody Cetuximab. *Science Translational Medicine*. (2011). Sep 7;3(99):99ra86

8 Shaw AT, Yeap BY, Solomon BJ, Riely GJ, Gainor J, Engelman JA, Shapiro GI, Costa DB, Ou SH, Butaney M, Salgia R, Maki RG, Varella-Garcia M, Doebele RC, Bang YJ, Kulig K, Selaru P, Tang Y, Wilner KD, Kwak EL, Clark JW, Iafrate AJ, Camidge DR. Effect of crizotinib on overall survival in patients with advanced non-small-cell lung cancer harbouring ALK gene rearrangement: a retrospective analysis. *Lancet Oncology*. (2011) Oct;12(11):1004-12. Epub 2011 Sep 18.

9 Ramalingam SS, Spigel DR, Chen D, Steins MB, Engelman JA, Schneider CP, Novello S, Eberhardt WE, Crino L, Habben K, Liu L, Jänne PA, Brownstein CM, Reck M. Randomized Phase II Study of Erlotinib in Combination With Placebo or R1507, a Monoclonal Antibody to Insulin-Like Growth Factor-1 Receptor, for Advanced-Stage Non-Small-Cell Lung Cancer. *J Clin Oncol.* (2011). Dec 1;29 (34):4574-80. Epub 2011 Oct 24.

10 Sequist LV, Heist RS, Shaw AT, Fidias P, Rosovsky R, Temel JS, Lennes IT, Digumarthy S, Waltman BA, Bast E, Tammireddy S, Morrissey L, Muzikansky A, Goldberg SB, Gainor J, Channick CL, Wain JC, Gaissert H, Donahue DM, Muniappan A, Wright C, Willers H, Mathisen DJ, Choi NC, Baselga J, Lynch TJ, Ellisen LW, Mino-Kenudson M, Lanuti M, Borger DR, Iafrate AJ, Engelman JA, Dias-Santagata D. Implementing multiplexed genotyping of non-small-cell lung cancers into routine clinical practice. *Ann Oncol*. (2011). Dec;22(12):2616-24. Epub 2011 Nov 9.

11 Ebi H, Corcoran RB, Singh A, Chen Z, Song Y, Lifshits E, Ryan DP, Meyerhardt J, Benes C, Settleman J, Wong K, Cantley L, Engelman JA. Receptor tyrosine kinases exert dominant control over PI3K signaling in human KRAS mutant colorectal cancers. *Journal of Clinical Investigation*. (2011). Oct 10. pii: 57909. doi: 10.1172/JCI57909. [Epub ahead of print]

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13 Bergethon K, Shaw AT, Ignatius Ou SH, Katayama R, Lovly CM, McDonald NT, Massion PP, Siwak-Tapp C, Gonzalez A, Fang R, Mark EJ, Batten JM, Chen H, Wilner KD, Kwak EL, Clark JW, Carbone DP, Ji H, Engelman JA, Mino-Kenudson M, Pao W, Iafrate AJ. ROS1 Rearrangements Define a Unique Molecular Class of Lung Cancers. *Journal of Clinical Oncology*. (2012). Jan 3. [Epub ahead of print]

14 Corcoran RB, Ebi H, Turke AB, Coffee EM, Nishino M, Cogdill AP, Brown RD, Delle Pelle P, Dias-Santagata D, Hung KE, Flaherty KT, Piris A, Wargo JA, Settleman J, Mino-Kenudson M, and Engelman JA. EGFR-mediated re-activation of MAPK signaling contributes to insensitivity of BRAF mutant colorectal cancers to RAF inhibition. *Cancer Discovery*. (2012). Published OnlineFirst January 16, 2012; doi: 10.1158/2159-8290.CD-11-0341

15 Katayama R, Shaw AT, Khan TM, Mino-Kenudson, M, Solomon BJ, Halmos B, Jessop N, Wain JC, Yeo AT, Benes C, Drew L, Saeh JC, Crosby K, Sequist LV, Iafrate AJ, Engelman JA. Mechanisms of acquired crizotinib resistance in ALK-rearranged lung cancers. *Science Translational Medicine*. (2012). Sci Transl Med. 2012 Feb 8;4(120):120ra17. Epub 2012 Jan 25.

16 Garnett MJ, Edelman EJ, Heidorn SJ, Greenman CD, Dastur A, Lau KW, Greninger P, Thompson IR, Luo X, Soares J, Liu Q, Iorio F, Surdez D, Chen L, Milano RJ, Bignell GR, Tam AT, Davies H, Stevenson JA, Barthorpe S, Lutz SR, Kogera F, Lawrence K, McLaren-Douglas A, Mitropoulos X, Mironenko T, Thi H, Richardson L, Zhou W, Jewitt F, Zhang T, O'Brien P, Boisvert JL, Price S, Hur W, Yang W, Deng X, Butler A, Choi HG, Chang JW, Baselga J, Stamenkovic I, Engelman JA, Sharma SV, Delattre O, Saez-Rodriguez J, Gray NS, Settleman J, Futreal PA, Haber DA, Stratton MR, Ramaswamy S, McDermott U, Benes CH. Systematic identification of genomic markers of drug sensitivity in cancer cells. *Nature*. (2012). Mar 28;483(7391):570-5. doi: 10.1038/nature11005.

17 Chen Z, Cheng K, Walton Z, Wang Y, Ebi H, Shimamura T, Liu Y, Tupper T, Ouyang J, Li J, Gao P, Woo MS, Xu C, Yanagita M, Altabef A, Wang S, Lee C, Nakada Y, Peña CG, Sun Y, Franchetti Y, Yao C, Saur A, Cameron MD, Nishino M, Hayes DN, Wilkerson MD, Roberts PJ, Lee CB, Bardeesy N, Butaney M, Chirieac LR, Costa DB, Jackman D, Sharpless NE, Castrillon DH, Demetri GD, Jänne PA, Pandolfi PP, Cantley LC, Kung AL, Engelman JA, Wong KK. A murine lung cancer co-clinical trial identifies genetic modifiers of therapeutic response. *Nature*. (2012) Mar 18;483(7391):613-7. doi: 10.1038/nature10937.

18 Nardi V, Song Y, Santamaria-Barria JA, Cosper AK, Lam Q, Faber AC, Boland GM, Yeap BY, Bergethon K, Scialabba VL, Tsao H, Settleman J, Ryan DP, Borger DR, Bhan AK, Hoang MP, Iafrate AJ, Cusack JC, Engelman JA, Dias-Santagata D. Activation of PI3K signaling in Merkel cell carcinoma. *Clinical Cancer Research*. (2012) Mar 1;18(5):1227-36. Epub 2012 Jan 18.

CURRENT INTEREST:

The overarching aim of research in the Engelman laboratory is to develop new and more effective therapeutic strategies for the treatment of cancer, with a particular emphasis on lung cancer. Cancer therapies are changing from general chemotherapeutic agents to drugs that target specific proteins and signaling pathways (i.e. targeted therapies). My laboratory aims to understand the biological underpinnings of cancer sensitivity and resistance to this emerging class of therapies. We are particularly interested in the regulation of the PI3K pathway, a signaling network that is crucial for the growth and survival of many epithelial cancers. The ultimate goal of our research is to develop therapies that are more effective and less toxic for patients with cancer.

IAAO2012 Title of the Talk:

Challenges with Drug Resistance

Title: Sensitivity and Resistance to Targeting FGFR in Cancer

Nicholas Turner, M.D., Ph.D.
Senior Lecturer and Honorary Consultant in Medical Oncology
The Institute of Cancer Research and Royal Marsden Hospital

Speaker

Kiyohiko Hatake, M.D., Ph.D.
Cancer Chemotherapy Center Clinical Chemotherapy
Chief, Cancer Institute Hospital, JFCR, Japan

Chairman

Nicholas Turner, M.D., Ph.D.

EDUCATION

The Institute of Cancer Research, University of London - PhD	2007
Membership of the Royal College of Physicians (Lond)	2000
University of Oxford Medical School - BM BChir	1997
University of Cambridge Tripos - MA (Hons) Class I	1994

CURRENT APPOINTMENT

Senior Lecturer and Honorary Consultant in Medical Oncology	9/2008-
The Institute of Cancer Research and Royal Marsden Hospital	

PREVIOUS APPOINTMENTS

Specialist Registrar Medical Oncology	3/2007-9/2008
Royal Free Hospital and University College Hospitals	
Clinical Research Fellow	9/2003-3/2007
Breakthrough Breast Cancer Research Centre, The Institute of Cancer Research	
Specialist Registrar Medical Oncology	9/2001-9/2003

Middlesex Hospital and Royal Free Hospitals

Senior House Officer Royal Marsden Hospital, London	4/2001-9/2001
Senior House Officer St Thomas' Hospital, London	8/2000-2/2001
Senior House Officer Whittington Hospital, London	2/1999-8/2000
Senior House Officer Hammersmith Hospital, London	2/1999-8/1999
Senior House Officer Royal Brompton Hospital, London	8/1998-2/1999
House Physician, John Radcliffe Hospital, Oxford	2/1998-8/1998
House Surgeon, Northampton General Hospital	8/1997-2/1998

PROFESSIONAL ACTIVITY

Deputy Editor *Breast Cancer Research*
Programme Committee *IMPAKT breast cancer conference 2012*
San Antonio Breast Cancer Symposium 2012
ESMO 2012
ESMO 2013
Invited speaker *ESMO 2012*
Invited discussant *ASCO 2012*

SELECTED PUBLICATIONS

1. Jain VK, Turner NC. Challenges and opportunities in the targeting of fibroblast growth factor receptors in breast cancer. *Breast Cancer Res.* 2012 Jun 19;14(3):208. [Epub ahead of print] PMID: 22731805 [PubMed - as supplied by publisher]
2. Aarts M, Sharpe R, Garcia-Murillas I, Gevensleben H, Hurd MS, Shumway SD, Toniatti C, Ashworth A, Turner NC. Forced mitotic entry of S-phase cells as a therapeutic strategy induced by inhibition of WEE1. *Cancer Discovery* 2012 Jun;2(6):524-39. Epub 2012 Apr 23.
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IAAO2012 Title of the Talk:

Sensitivity and Resistance to Targeting FGFR in Cancer

ABSTRACT:

Activation of fibroblast growth factors through mutation or amplification is a common oncogenic event, and multiple FGFR inhibitors have entered clinical trials, yet the mechanisms of activation of signaling are diverse. In breast cancer *FGFR1* amplification is present in 8% unselected cancers, *FGFR2* amplification in 1-2% unselected cancers, and autocrine FGF2 expression in <5% cancers. Clinical development requires robust screening strategies targeted to the breast cancer subtypes that are associated with each aberration, and an understanding of how FGFR signaling affects response to standard therapies.

To identify mechanisms of resistance to FGFR inhibitors we have performed functional siRNA screens on a panel of 11 *FGFR* mutant and amplified cancer cell lines, including cell lines with amplification of *FGFR1* and *FGFR2*, and activating mutation of *FGFR2* and *FGFR3*. Screens were analysed to identify siRNA that that modulated sensitivity to the FGFR inhibitor, identifying both shared pathways that mediate resistance, and mutation specific resistance mechanisms.

Session 5

Advances and Challenges in Tumor Therapy

5-1. Prostate Cancer

Speaker: Howard I. Scher, MD (Memorial Sloan-Kettering Cancer Center, USA)

5-2. The Treatment of Colorectal Cancer in the Era of Molecular Characterization

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

5-3. The Evolution to Genomic Testing and Targeted Therapy as Standard of Care for Lung Cancer

Speaker: Bruce E. Johnson, MD (Dana-Farber Cancer Institute, USA)

Title: Prostate Cancer

Speaker

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

Chairman

Chikashi Ishioka, M.D.

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

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 in the clinic.

more…

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 an individual 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 peer-reviewed articles in scientific journals and coauthored the textbook *Principals and Practice of Genitourinary Oncology*.

PUBLICATIONS:
>400 publications

Publications in 2011 and 2012

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IAAO2012 Title of the Talk:

Prostate Cancer

Title: The Treatment of Colorectal Cancer in the Era of Molecular Characterization

Speaker

Josep Tabernero, M.D.
Head of the Medical Oncology Department at the Vall d'Hebron University Hospital, Spain

Chairman

Yuko Kitagawa, MD, Ph.D.
Professor, Department of Surgery, Graduate School of Medicine, Keio University, Japan

Josep Tabernero, M.D.

Josep Tabernero received his medical degree from the Universitat Autònoma de Barcelona, Spain. Afterwards, he completed his specialist training in medical oncology and has had appointments in Barcelona.

Dr. Tabernero is currently the Head of the Medical Oncology Department at the Vall d'Hebron University Hospital in Barcelona, Spain. He is also the head of the Gastrointestinal Tumors and Phase I Unit and is actively involved in translational research and pharmacodynamic phase I studies with molecular targeted therapies and related translational research, with a special focus on EGFR-family inhibitors and IGFR-PI3K-Akt-mTOR pathway inhibitors, and also in phase II and III studies with new chemotherapy agents in gastrointestinal tumors.

In addition, Dr. Tabernero is a member of the European Society for Medical Oncology (ESMO) and the American Society of Clinical Oncology (ASCO), and different Editorial Boards including the *Journal of Clinical Oncology, Clinical Cancer Research, Clinical Colorectal Cancer* and *Annals of Oncology*. He has (co)authored approximately 150 peer-reviewed papers. He has also been member of the Educational and Scientific Committees of the ESMO, ECCO, ASCO, AACR/NCI/EORTC, ASCO Gastrointestinal, and WCGIC meetings.

IAAO2012 Title of the Talk:

The Treatment of Colorectal Cancer in the Era of Molecular Characterization

Title: The Evolution to Genomic Testing and Targeted Therapy as Standard of Care for Lung Cancer

Speaker

Bruce E. Johnson, M.D.
Director of the Lowe Center for Thoracic Oncology at Dana-Farber Cancer Institute and Brigham and Women's Hospital
Professor of Medicine at Harvard Medical School

Chairman

Hiroyuki Mano, M.D., Ph.D.
Professor of Medicine, Department of Medical Genomics, Graduate School of Medicine, The University of Tokyo, Tokyo
Professor of Medicine, Division of Functional Genomics, Jichi Medical University, Tochigi

Bruce E. Johnson, M.D.

Bruce E. Johnson, MD is Director of the Lowe Center for Thoracic Oncology at Dana-Farber Cancer Institute and Brigham and Women's Hospital, and Professor of Medicine at Harvard Medical School. He is the leader of the Dana-Farber/Harvard Cancer Center Lung Cancer Program and the Principal Investigator of the Dana-Farber/Harvard Cancer Center Specialized Program of Research Excellence (SPORE) in Lung Cancer.

Dr. Johnson was elected to the ASCO Board of Directors and received the ASCO Cancer Foundation's Translational Research Professorship in 2008. In 2010 he received the IASLC (International Association for the Study of Lung Cancer) Scientific Award, given to an IASLC scientist for "life-time scientific contribution in thoracic malignancy research and who has also contributed to the organization's development". In 2010 he was one of the leaders of the team that was awarded the AACR (American Association for Cancer Research) Team Science Award. This "recognizes an outstanding interdisciplinary research team for its innovative and meritorious science that has advanced or likely will advance our fundamental knowledge of cancer or a team that has applied existing knowledge to advance the detection, diagnosis, prevention, or treatment of cancer".

Dr. Johnson received his MD from the University of Minnesota and did his postgraduate training at the University of Chicago and the National Cancer Institute. He came to the Lowe Center in 1998, after serving for six years as the head of the Lung Cancer Biology section of the NCI's Medicine Branch.

INTERESTS:
Non-small cell lung cancer, Small cell lung cancer, Genomic characterization, Mesothelioma

AREA OF RESEARCH:
The impact of genomic changes on the targeted treatment of thoracic malignancies:

DF/HCC Program Affiliation
Lung Cancer, Leader
Translational Pharmacology and Early Therapeutic Trials

DF/HCC Associations
Principal Investigator, Lung Cancer SPORE
Member, Center Scientific Council

SELECTED LATEST PAPERS:

1. Tumoral cavitation in patients with non-small-cell lung cancer treated with antiangiogenic therapy using bevacizumab. Nishino M, Cryer SK, Okajima Y, Sholl LM, Hatabu H, Rabin MS, Jackman DM, Johnson BE. Cancer Imaging. 2012 Jun 29;12:225-35.
2. The impact of initial gefitinib or erlotinib versus chemotherapy on central nervous system progression in advanced non-small cell lung cancer with EGFR mutations. Heon S, Yeap BY, Lindeman N, Joshi VA, Butaney M, Britt GJ, Costa DB, Rabin MS, Jackman DM, Johnson BE. Clin Cancer Res. 2012 Jun 25
3. The BATTLE trial: personalizing therapy for lung cancer. Kim ES, Herbst RS, Wistuba II, Lee JJ, Blumenschein GR Jr, Tsao A, Stewart DJ, Hicks ME, Erasmus J Jr, Gupta S, Alden CM, Liu S, Tang X, Khuri FR, Tran HT, Johnson BE, Heymach JV, Mao L, Fossella F, Kies MS, Papadimitrakopoulou V, Davis SE, Lippman SM, Hong WK. Cancer Discov. 2011 Jun;1(1):44-53.
4. Adjuvant chemotherapy for surgically resected non-small cell lung cancer. Heon S, Johnson BE. J Thorac Cardiovasc Surg. 2012 Apr 12.
5. Making personalized cancer medicine a reality: challenges and opportunities in the development of biomarkers and companion diagnostics. Parkinson DR, Johnson BE, Sledge GW. Clin Cancer Res. 2012 Feb 1;18(3):619-24.
6. CT tumor volume measurement in advanced non-small-cell lung cancer: Performance characteristics of an emerging clinical tool. Nishino M, Guo M, Jackman DM, DiPiro PJ, Yap JT, Ho TK, Hatabu H, Jänne PA, Van den Abbeele AD, Johnson BE. Acad Radiol. 2011 Jan;18(1):54-62. Epub 2010 Oct 30.
7. CT tumor volume measurement in advanced non-small-cell lung cancer: Performance characteristics of an emerging clinical tool. Nishino M, Guo M, Jackman DM, DiPiro PJ, Yap JT, Ho TK, Hatabu H, Jänne PA, Van den Abbeele AD, Johnson BE. Acad Radiol. 2011 Jan;18(1):54-62. Epub 2010 Oct 30.

IAAO2012 Title of the Talk:

The Evolution to Genomic Testing and Targeted Therapy as Standard of Care for Lung Cancer

RESEARCH ABSTRACT:

The translational research on patients with adenocarcinoma of the lung here at the Dana- Farber/Harvard Cancer Center has helped identify patient subsets that respond differently to targeted agents. Women, patients with adenocarcinoma, and those who do not smoke cigarettes are more likely to have a favorable response to gefitinib and erlotinib therapy (Iressa and Tarceva) than patients with other types of lung cancer and men respectively. This prompted my laboratory to assemble tumor cell lines from women with adenocarcinoma who either did or did not smoke cigarettes to characterize their response to gefitinib. A team composed of our laboratory and the laboratory led by Dr. Sellers and Meyerson at the Dana-Farber Cancer Institute discovered that most patients who have a clinical response to gefitinib treatment have either point mutations or deletion of amino acids from the tyrosine kinase domain of the epidermal growth factor receptor. Our laboratory showed lung cancer cell lines with epidermal growth factor cell lines with these point mutations or deletions are 100 fold more sensitive to treatment gefitinib than cell lines with wild type sequence of the epidermal growth factor receptor. The lung cancer cell lines with mutations in the epidermal growth factor receptor treated with 100 nM of gefitinib have downregulation of phosphorylated epidermal growth factor receptor. This also leads to downregulation of the downstream targets including phospho-Akt and phospho-Erk1/2 kinase. Treatment of lung cancer cells with mutated epidermal growth factor receptor with 1 micromolar gefitinib leads to apoptosis while the cells with wild type epidermal growth factor receptor undergo a G1/S arrest. Future studies will study the relationship between different mutations in the epidermal growth factor receptor, their susceptibility to different epidermal growth factor receptor inhibitors, and the signaling pathways. Prospective trials will test the impact of these epidermal growth factor receptor mutations on the treatment of patients with non-small cell lung cancer. The studies will include erlotinib treatment in previously untreated elderly patients with advanced non-small cell lung cancer (older than 70) and women with adenocarcinoma who are either never smokers or former smokers. These patients will have their tumor DNA studied for the epidermal growth factor receptor sequence, and their response, response duration, subsequent response to other chemotherapy, and survival will be recorded. This will be done to determine if there is a relationship between the epidermal growth factor receptor sequence and the outcome of patients with non-small cell lung cancer after treatment with erlotinib.

Session 6

Impact of Oncology New Paradigm on Patients

6-1. Drug Development and Approval in the Age of Molecular Targeting and "*Precision*" Therapy

Speaker: Bruce A. Chabner, MD (Massachusetts General Hospital, USA)

6-2. Strategy and Development in Asian Clinical Trials

Speaker: Kiyohiko Hatake, MD, PhD (Cancer Institute Hospital, JFCR, Japan)

6-3. Value-based Medicine - a UK and European Perspective

Speaker: Patrick G. Johnston, MD, PhD (Queen's University of Belfast, UK)

Title: Drug Development and Approval in the Age of Molecular Targeting and "Precision" Therapy

Speaker

Bruce A. Chabner, M.D.
Director of Clinical Research Cancer Center, Massachusetts General Hospital, Boston Massachusetts

Chairman

Kiyohiko Hatake, M.D., Ph.D.
Chief, Department of Hematology, Cancer Institute Hospital, Japanese Foundation for Cancer Research (JFCR), Japan

Bruce A. Chabner, M.D.

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, National Cancer Institute 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 Special Achievement	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.

IAAO2012 Title of the Talk:

Drug Development and Approval in the Age of Molecular Targeting and "Precision" Therapy

Title: Strategy and Development in Asian Clinical Trials

Speaker

Kiyohiko Hatake, M.D., Ph.D.
Chief, Department of Hematology, Cancer Institute Hospital, Japanese Foundation for Cancer Research (JFCR), Japan

Chairman

Patrick Gerard Johnston, M.D., Ph.D.
Queen's University of Belfast, UK
Dean, School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast
Director, Institute of Health & Life Sciences, Queen's University Belfast

Kiyohiko Hatake, M.D., Ph.D.

Graduated from Jichi Medical School in March 1978. Certified with national medical board.(M.D.)
Residency in Fukui Prefectural Hospital in 1978 to 1980.
Department of Internal Medicine, in 1980 to 1982.
Worked for two years in Natasho public clinic, in 1980.
In 1987, Graduated from Ph.D. course, and obtained degree of Ph.D.
Thesis is Purification and biological significance of Macrophage colony-stimulating factor (published in J. Chromatography and Experimental Hematology)
Assistant professor in Jichi Medical School, department of Hematology, and selected as a postdoctoral fellowship program in Japan Promotion of Science, Ministry of Culture and Science in 1987.
Postdoctoral fellow, in DNAX Research Institute, Palo Alto, CA, USA, in 1987 to 1989.
Associate professor, in department of Hematology, Jichi Medical School, in 1994.
Chief and director, in Department of Medical Oncology and Hematology, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, in 2000 and Director in division of Clinical Chemotherapy, Cancer Chemotherapy Center, JFCR, Director of Ambulatory Therapy Center, Director of New Drug Development Clinical Center, and Director of Olympus Bio-Imaging Lab.
Board member of Japanese Society of Medical Oncology, President elect 2010 in Japanese Society of Medical Oncology,
Journal editor: Associate editor in Cancer Science, Ann. Oncology, Cancer Science, and several Japanese journals.

Special interests: Molecular targeting therapy, Apoptosis, Lymphoma, Myeloma, Leukemia, Breast cancer, Colorectal cancer, Translational research.

Session 6-2

IAAO2012 Title of the Talk:

Strategy and Development in Asian Clinical Trials

Title: Value-based Medicine - a UK and European Perspective

Patrick Gerard Johnston, M.D., Ph.D.
Dean, School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast
Director, Institute of Health & Life Sciences, Queen's University Belfast

Speaker

Bruce A. Chabner, M.D.
Director of Clinical Research Cancer Center, Massachusetts General Hospital, Boston Massachusetts

Chairman

Patrick Gerard Johnston, M.D., Ph.D.

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 signalling pathways in human cancer, primarily related to molecular targeted cancer, therapeutics, personalised cancer medicine and mechanisms of drug resistance. He received his medical degree with distinction from University College Dublin in 1982, followed by his PhD in Medicine in 1988. He obtained a fellowship at the National Cancer Institute (NCI USA) in 1987 where he pursued further clinical training in medical oncology and doctoral studies in molecular pharmacology, drug resistance and drug development. 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

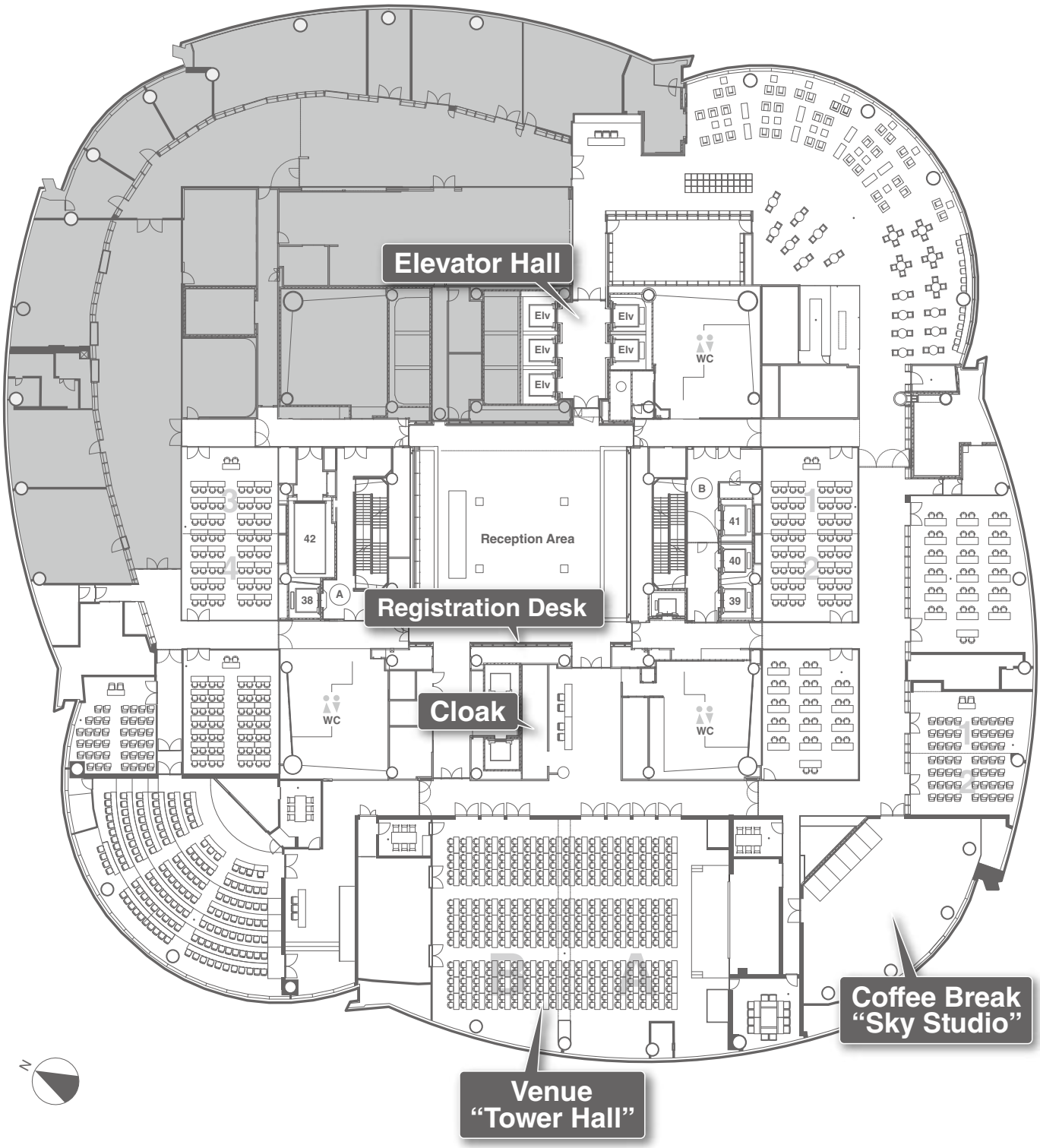
been awarded many national and international awards, is a Fellow of the Academy of Medical Sciences, and sits on a number of influential national and international scientific and government advisory boards. He is the Founder of the Society for Translational Oncology and the biotechnology company, Almac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

Session 6-3

IAAO2012 Title of the Talk:

Value-based Medicine - a UK and European Perspective

国際フォーラム2012 講演会場：六本木アカデミーヒルズ49（49階）



ウエルカム レセプション（8月3日18:00 ～）：六本木ヒルズクラブ（51階）
51階へはエレベーターをご利用ください。

アクセスマップ

会　場：六本木アカデミーヒルズ49

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

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

宿泊地：グランドハイアット東京

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

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

http://www.academyhills.com/

CHAAO Chugai Academy for Advanced Oncology

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