

An AACR Special Conference on

# Molecularly Targeted Therapies: Mechanisms of Resistance

May 9-12, 2012 • Westin San Diego • San Diego, CA

## Wednesday, May 9

**7:00 p.m.-8:00 p.m.**      **Opening Keynote Session**  
Crystal Ballroom

**BRAF and RAS signaling in melanoma from basic to translational and clinical research**  
Richard M. Marais, Paterson Institute for Cancer Research, Manchester, United Kingdom

**8:00 p.m.-9:30 p.m.**      **Opening Reception**  
Emerald Ballroom

## Thursday, May 10

**7:00 a.m.-8:00 a.m.**      **Continental Breakfast**  
Ballroom Foyer

**8:00 a.m.-10:00 a.m.**      **Session 1: EGFR**  
Crystal Ballroom  
*Chairperson: Pasi A. Jänne, Dana-Farber Cancer Institute, Boston, MA*

**Challenges in overcoming resistance to targeted therapies**  
Jeffrey A. Engelman, Massachusetts General Hospital, Boston, MA

**Strategies to overcome resistance to EGFR tyrosine kinase inhibitors**  
Pasi A. Jänne

**Mechanisms of resistance to anti-EGFR therapies in colorectal cancers**  
Alberto Bardelli, University of Turin, Candiolo, Italy

**NKX2-1/TITF1/TTF-1-induced ROR1 is required to sustain EGFR survival signaling in lung adenocarcinoma\***  
Tomoya Yamaguchi, Nagoya University Graduate School of Medicine, Nagoya, Japan

**Stroma-derived matrix metalloproteinase 9 (MMP9) confers resistance to anti-EGFR therapy through cell-extrinsic activation of ERBB2/ERK/JUN pathway\***  
Janghee Woo, Dana-Farber Cancer Institute, Boston, MA

**10:00 a.m.-10:30 a.m.**      **Break**  
Ballroom Foyer

\*Short talks from proffered papers

**10:30 a.m.-12:30 p.m.      Session 2: Breast and Prostate Cancers**  
Crystal Ballroom  
*Chairperson: Carlos L. Arteaga, Vanderbilt-Ingram Cancer Center, Nashville, TN*

**Therapy response and resistance in mouse models of BRCA-associated breast cancer**  
Jos Jonkers, The Netherlands Cancer Institute, Amsterdam, The Netherlands

**PI3K inhibitors in ER+ breast cancer: Next steps**  
Matthew J. Ellis, Washington University Siteman Cancer Center, St. Louis, MO

**Presurgical studies as a tool for discovery of mechanisms of drug resistance in breast cancer**  
Carlos L. Arteaga

**Reciprocal feedback regulation of the PI3K and AR pathway in prostate cancer: A mechanism of innate resistance**  
Brett S. Carver, Memorial Sloan-Kettering Cancer Center, New York, NY

**12:30 p.m. - 2:00 p.m.      Lunch on Own/Free Time**

**2:00 p.m. - 4:30 p.m.      Poster Session A**  
Emerald Ballroom

**4:30 p.m.-6:30 p.m.      Session 3: Mouse Models**  
Crystal Ballroom  
*Chairperson: David A. Tuveson, CRI/Cancer Research UK, University of Cambridge, Cambridge, United Kingdom*

**Developing therapeutics in mice with ductal pancreatic cancer**  
David A. Tuveson

**Resistance to targeted therapies in mouse models of lung cancer**  
Katerina A Politi, Yale University, New Haven, CT

**Targeting PI3K in cancer: Mechanistic insights from genetic mouse models**  
Jean J. Zhao, Dana-Farber Cancer Institute, Boston, MA

**Patient-derived, BRCA1-deficient, triple-negative breast cancer xenografts develop resistance to DNA damaging agents via genetic and epigenetic mechanisms\***  
Petra ter Brugge, The Netherlands Cancer Institute, Amsterdam, The Netherlands

**Incomplete inhibition of phosphorylation of 4EBP1 is a mechanism for KRAS-driven resistance to the ATP-competitive mTOR inhibitor PP242 in colorectal cancer\***  
Gregory S. Ducker, University of California, Berkeley, CA

**6:30 p.m.                      Dinner on Own/Evening Off**

## Friday, May 11

**7:00 a.m.-8:00 a.m.**      **Continental Breakfast**  
Ballroom Foyer

**8:00 a.m.-10:00 a.m.**      **Session 4: Raf/MEK**  
Crystal Ballroom  
*Chairperson: Meenhard Herlyn, The Wistar Institute, Philadelphia, PA*

**Novel mechanisms of resistance in BRAF-mutant melanoma**

Poulikos I. Poulikakos, Memorial Sloan-Kettering Cancer Center, New York, NY

**BRAF and MEK resistance in melanoma**

Meenhard Herlyn

**Selective BRAF inhibitors induce bypass mechanisms within the MAP kinase pathway and beyond**

Keith T. Flaherty, Massachusetts General Hospital, Boston, MA

**The MEK network as a target for combination therapies**

W. Michael Korn, UCSF Helen Diller Family Comprehensive Cancer Center, San Francisco, CA

**10:00 a.m.-10:30 a.m.**      **Break**  
Ballroom Foyer

**10:30 a.m.-12:30 p.m.**      **Session 5: Clinical Trial Design and Regulatory Issues**  
Crystal Ballroom  
*Chairperson: Mace L. Rothenberg, Pfizer, Inc., New York, NY*

**Preemptive or reactive? Drug development strategies in cancers resistant to targeted agents**

Mace L. Rothenberg

**Using molecular profiling strategies in clinical trials to understand resistance mechanisms in the era of personalized cancer medicine**

Lillian L. Siu, Princess Margaret Hospital, Toronto, ON, Canada

**Regulatory considerations in addressing resistance mechanisms**

Ramzi N. Dagher, Pfizer, Inc., Groton, CT

**Panel Discussion**

**12:30 p.m.-2:30 p.m.**      **Lunch on Own/Free Time**

\*Short talks from proffered papers

**2:30 p.m.-4:30 p.m.**      **Session 6: Strategies to Identify Mechanisms of Resistance: RNAi and ORFs**  
Crystal Ballroom  
*Chairperson: Thomas F. "Trey" Westbrook, Baylor College of Medicine, Houston, TX*

**Repositioning targeted therapies via forward genetics**  
Thomas F. "Trey" Westbrook

**Finding biomarkers of response to targeted cancer drugs through functional genetics**  
René Bernards, The Netherlands Cancer Institute, Amsterdam, The Netherlands

**Functional genomics to identify cancer targets and resistance**  
William C. Hahn, Dana-Farber Cancer Institute, Boston, MA

**Identifying mechanisms of drug resistance to MAPK pathway inhibition via genome-scale rescue screens\***  
Cory M. Johannessen, The Broad Institute of MIT and Harvard, Cambridge, MA

**Widespread potential for growth factor-driven resistance to anticancer kinase inhibitors\***  
Timothy R. Wilson, Genentech, Inc., South San Francisco, CA

**4:30 p.m.-7:00 p.m.**      **Poster Session B and Reception**  
Emerald Ballroom

**7:00 p.m.**      **Dinner on Own/Evening Off**

## Saturday, May 12

**7:00 a.m.-8:00 a.m.**      **Continental Breakfast**  
Ballroom Foyer

**8:00 a.m.-10:00 a.m.**      **Session 7: Immunology and Tumor Host Interactions**  
Crystal Ballroom  
*Chairperson: Joan S. Brugge, Harvard Medical School, Boston, MA*

**Spatial and mechanical considerations for tumor therapy**  
Valerie M. Weaver, UCSF Medical Center, San Francisco, CA

**Adaptive resistance of matrix-attached tumor cells**  
Joan S. Brugge

**Enhancing the efficacy of CTLA-4 blockade**  
Margaret Callahan, Memorial Sloan-Kettering Cancer Center, New York, NY

**Paracrine receptor activation by microenvironment triggers bypass survival signals and ALK inhibitor-resistance in EML4-ALK lung cancer cells\***  
Seiji Yano, Cancer Research Institute Kanazawa University, Kanazawa, Japan

**10:00 a.m.-10:15 a.m.**      **Break**  
Ballroom Foyer

**10:15 a.m.-12:15 p.m.**      **Session 8: Angiogenesis**  
Crystal Ballroom  
*Chairpersons: Lee M. Ellis, The University of Texas MD Anderson  
Cancer Center, Houston TX*

**VEGF-targeted therapies: Biomarkers, biology and understanding resistance**  
Lee M. Ellis

**Modeling intrinsic and acquired resistance of metastatic disease to antiangiogenic  
drugs**  
Robert S. Kerbel, University of Toronto Sunnybrook HSC, Toronto, ON, Canada

**Markers and mechanisms of resistance to VEGF inhibitors**  
John V. Heymach, The University of Texas MD Anderson Cancer Center, Houston, TX

**Insensitivity to RAF inhibition by vemurafenib in BRAF mutant colorectal cancer by  
EGFR-mediated reactivation of MAPK signaling\***  
Ryan B. Corcoran, Massachusetts General Hospital Cancer Center, Boston, MA

**Reactivation of oncogenic signaling through drug-induced feedback adaptations:  
Lessons from mTOR inhibitors\***  
Vanessa Rodrik-Outmezguine, Memorial Sloan-Kettering Cancer Center, New York, NY

**12:15 p.m.**                      **Closing Remarks/Departure**