SPECIAL FEATURES

CCR Translations

3 The Importance of Doing Trials Right While Doing the Right Trials
David M. Dilts and Steven K. Cheng
See article p. 256

6 Elusive Extraneurcule Estrogen Receptors in Breast Cancer
Ellis R. Levin
See article p. 118

CCR Drug Updates

9 Vemurafenib and BRAF Inhibition: A New Class of Treatment for Metastatic Melanoma
Jason J. Luke and F. Stephen Hodi

Molecular Pathways

15 Molecular Pathways: Targeting Proteasomal Protein Degradation in Cancer
Susan M. Molineaux

CCR Focus

22 On Drug Development, Chance, and the Prepared Mind
Susan E. Bates

23 Drug Development: Portals of Discovery
Susan E. Bates, Laleh Amiri-Kordestani, and Giuseppe Giacone

33 BRAF Inhibitors for the Treatment of Metastatic Melanoma: Clinical Trials and Mechanisms of Resistance
Alexander Marzuka Alcal and Keith T. Flaherty

40 The Insulin Receptor/Insulin-Like Growth Factor Receptor Family as a Therapeutic Target in Oncology
Michael Pollak

51 Inhibitors Targeting Mitosis: Tales of How Great Drugs against a Promising Target Were Brought Down by a Flawed Rationale
Edina Komlodi-Pasztor, Dan L. Sackett, and Antonio Tito Fojo

HUMAN CANCER BIOLOGY

77 Polycomb Repressor Complex-2 Is a Novel Target for Mesothelioma Therapy
Clinton D. Kemp, Mahadev Rao, Sichuan Xi, Suzanne Inchauste, Haresh Mani, Patricia Fetsch, Armando Filie, Mary Zhang, Julie A. Hong, Robert L. Walker, Yuelin J. Zhu, R. Taylor Ripley, Aarti Mathur, Fang Liu, Maosheng Yang, Paul A. Meltzer, Victor E. Marquez, Assunta De Rienzo, Raphael Bueno, and David S. Schrump

91 Eph-B2/Ephrin-B2 Interaction Plays a Major Role in the Adhesion and Proliferation of Waldenstrom’s Macroglobulinemia
Feda Azab, Abdel Kareem Azab, Patricia Maiso, Teresa Callimeri, Ludmila Flores, Yang Liu, Phong Quang, Aldo M. Rocco, Antonio Sacco, Hai T. Ngo, Yong Zhang, Brittany L. Morgan, Ruben D. Carrasco, and Irene M. Ghozrial

105 Costimulatory Protein 4IgB7H3 Drives the Malignant Phenotype of Glioblastoma by Mediating Immune Escape and Invasiveness
Dieter Lemke, Philipp-Niclas Pfennig, Felix Sahm, Ann-Catherine Klein, Tore Kempf, Uwe Warnken, Martina Schlozer, Ruxandra Tudoran, Michael Weller, Michael Platten, and Wolfgang Wick

118 STAT5A-Mediated SOCS2 Expression Regulates Jak2 and STAT3 Activity Following e-Src Inhibition in Head and Neck Squamous Carcinoma
Phenylarsine Oxide Induces Apoptosis in Bax- and Bak-Deficient Cells through Upregulation of Bim
Biyun Ni, Qi Ma, Baowei Li, Lixia Zhao, Yong Liu, Yushan Zhu, and Quan Chen

Synergistic Antitumor Activity of Anti-CD25 Recombinant Immunotoxin LMB-2 with Chemotherapy
Rajat Singh, Yujian Zhang, Ira Pastan, and Robert J. Kreitman

Modulation of the Tumor Microvasculature by Phosphoinositide-3 Kinase Inhibition Increases Doxorubicin Delivery In Vivo
Naseer Qayum, Jaehong Im, Michael R. Stratford, Eric J. Bernhard, W. Gillies McKenna, and Ruth J. Muschel

Antitumor Activity of NVP-BKM120—A Selective Pan Class I PI3 Kinase Inhibitor Showed Differential Forms of Cell Death Based on p53 Status of Glioma Cells
Dimpy Koul, Jun Fu, Ruijun Shen, Tiffany A. LaFortune, Shuzhen Wang, Ningyi Tiao, Yong-Wan Kim, Juinn-Lin Liu, Deepti Ramnarian, Ying Yuan, Carlos Garcia-Echeverria, Sauveur-Michel Maira, and W.K. Alfred Yung

Early [18F]Fluorodeoxyglucose Positron Emission Tomography at Two Days of Gefitinib Treatment Predicts Clinical Outcome in Patients with Adenocarcinoma of the Lung
Ryo Takahashi, Haruhiko Hirata, Isao Tachibana, Eku Shimosegawa, Atsuo Inoue, Izumi Nagatomo, Yoshiho Takeda, Hiroshi Kida, Sho Goya, Takashi Kijima, Mitsuhito Yoshida, Toru Kumagai, Atsushi Kumanogoh, Meinoshin Okumura, Jun Hatazawa, and Ichiro Kawase

Lymphatic Invasion Is Independently Prognostic of Metastasis in Primary Cutaneous Melanoma
Xiaowei Xu, Lianjun Chen, DuPont Guerry, Peter R. Dawson, Wei-ting Hwang, Patricia Vanelle, David E. Elder, Paul J. Zhang, Michael E. Ming, Lynn Schuchter, and Phyllis A. Gimotty

In Vivo Positron Emission Tomography Imaging of Protease Activity by Generation of a Hydrophobic Product from a Noninhibitory Protease Substrate

CANCER THERAPY: CLINICAL

A Phase I Weekly Dosing Study of Brentuximab Vedotin in Patients with Relapsed/Refractory CD30-Positive Hematologic Malignancies
Michelle A. Fanale, Andres Forero-Torres, Joseph D. Rosenblatt, Ranjana H. Advani, Anna R. Franklin, Dana A. Kennedy, Tae H. Han, Eric L. Sievers, and Nancy L. Bartlett

Achieving Sufficient Accrual to Address the Primary Endpoint in Phase III Clinical Trials from U.S. Cooperative Oncology Groups

See commentary p. 3
Skin Tumors Induced by Sorafenib; Paradoxic RAS–RAF Pathway Activation and Oncogenic Mutations of HRAS, TP53, and TGFBR1

Jean Philippe Arnault, Christine Mateus, Bernard Escudier, Gorana Tomasic, Janine Wechsler, Emilie Hollville, Jean-Charles Soria, David Malka, Alain Sarasin, Magalie Larcher, Jocehyne André, Nyam Kamou-Kom, Lise Boussenart, Ludovic Lacroix, Alain Spatz, Alexander M. Eggermont, Sabine Druiullenec, Stephan Vagner, Alain Eychene, Nicolas Dumaz, and Caroline Robert

Concurrent Temozolomide and Dose-Escalated Intensity-Modulated Radiation Therapy in Newly Diagnosed Glioblastoma

Christina I. Tsien, Doris Brown, Daniel Normolle, Matthew Schipper, Morand Piert, Larry Junck, Jason Heth, Diana Gomez-Hassan, Randall K. Ten Haken, Thomas Chenevert, Yue Cao, and Theodore Lawrence

Molecular Determinants of Retinoic Acid Sensitivity in Pancreatic Cancer

Sonal Gupta, Dipankar Pramanik, Radha Mukherjee, Nathaniel R. Campbell, Sathyarayanan Elumalai, Roeland F. de Wilde, Seung-Mo Hong, Michael G. Goggins, Ana De Jesus-Acosta, Daniel Laheru, and Anirban Maitra

TP53 Disruptive Mutations Lead to Head and Neck Cancer Treatment Failure through Inhibition of Radiation-Induced Senescence

Heath D. Skinner, Vlad C. Sandulache, Thomas J. Ow, Raymond E. Meyn, John S. Yordy, Beth M. Beadle, Alison L. Fitzgerald, Uma Giri, K. Kian Ang, and Jeffrey N. Myers

Prognostic Significance of Plasma Osteopontin in Patients with Locoregionally Advanced Head and Neck Squamous Cell Carcinoma Treated on TROG 02.02 Phase III Trial

A CDD Polymorphism as Predictor of Capecitabine-Induced Hand-Foot Syndrome—Letter

NKX3.1 Haploinsufficiency Is Prognostic for Prostate Cancer Relapse following Surgery or Image-Guided Radiotherapy

TP53 Disruptive Mutations Lead to Head and Neck Cancer Treatment Failure through Inhibition of Radiation-Induced Senescence

Correction: Lysosomal Sequestration of Sunitinib: A Novel Mechanism of Drug Resistance

Correction: ABCB1 (MDR1) Polymorphisms and Progression-Free Survival among Women with Ovarian Cancer following Paclitaxel/Carboplatin Chemotherapy

LETTER TO THE EDITOR

CORRECTIONS
ABOUT THE COVER

B7H3 represents a novel driver of gliomagenesis by mediating an immunosuppressive and proinvasive phenotype in glioblastoma. Immunofluorescence demonstrates the perivascularly (alpha-SMA staining; red) enhanced expression of B7H3 (vesicular distribution; green) in human glioblastoma tissue (nuclei staining; blue). For details, see the article by Lemke and colleagues on page 105 of this issue.