Highlights of This Issue 273

SPECIAL FEATURES

CCR Translations

275  Stressing the Development of Small Molecules Targeting HSP90
Len Neckers and Jane B. Trepel
See related article, p. 445

278  Pertuzumab Protects the Achilles’ Heel of Trastuzumab—Emtansine
William R. Gwin and Neil L. Spector
See related article, p. 456

CCR Perspectives in Drug Approval

281  Predictive Value of Phase I Trials for Safety in Later Trials and Final Approved Dose: Analysis of 61 Approved Cancer Drugs
Denis L. Jardim, Kenneth R. Hess, Patricia LoRusso, Razelle Kurzrock, and David S. Hong

Molecular Pathways

289  Molecular Pathways: Targeting Inhibitor of Apoptosis Proteins in Cancer—From Molecular Mechanism to Therapeutic Application
Simone Fulda

296  Molecular Pathways: Transcription Factories and Chromosomal Translocations
Cameron S. Osborne

Reviews

301  “Quitting Smoking Will Benefit Your Health”: The Evolution of Clinician Messaging to Encourage Tobacco Cessation
Benjamin A. Toll, Alana M. Rojewski, Lindsay R. Duncan, Amy E. Latimer-Cheung, Lisa M. Fucito, Julie L. Boyer, Stephanie S. O’Malley, Peter Salovey, and Roy S. Herbst

310  Deep Molecular Response in Chronic Myeloid Leukemia: The New Goal of Therapy?
François-Xavier Mahon and Gabriel Etienne

HUMAN CANCER BIOLOGY

323  IgG-Switched CLL Has a Distinct Immunogenetic Signature from the Common MD Variant: Ontogenetic Implications
Anna Vardi, Andreas Agathangelidis, Lesley-Ann Sutton, Maria Chatzouli, Lydia Scarfò, Larry Mansouri, Vassiliki Douka, Achilles Anagnostopoulos, Nikos Darzentas, Richard Rosenquistrate, Paolo Ghia, Chrysoula Belesi, and Kostas Stamatopoulos

331  Tumor-Reactive CD8+ T Cells in Metastatic Gastrointestinal Cancer Refractory to Chemotherapy
Simon Turcotte, Alena Gros, Eric Tran, Chyi-Chia R. Lee, John R. Wunderlich, Paul F. Robbins, and Steven A. Rosenberg

344  Altered Microenvironment Promotes Progression of Preinvasive Breast Cancer: Myoepithelial Expression of αvβ6 Integrin in DCIS Identifies High-risk Patients and Predicts Recurrence

358  The Activation of the WNT Signaling Pathway Is a Hallmark in Neurofibromatosis Type 1 Tumorigenesis

372  Oncogenic Function of SCCRO5/DCUN1D5 Requires Its Neddylation E3 Activity and Nuclear Localization
Claire C. Bommelje, Viola B. Weeda, Guochang Huang, Kushyap Shah, Sarina Bains, Elizabeth Buss, Manish Shaha, Mithat Gonen, Ronald Ghassemin, Suresh Y. Ramanathan, and Bhuvanesh Singh
CANCER THERAPY: PRECLINICAL

382 Integrative Genomic Analysis of Temozolomide Resistance in Diffuse Large B-Cell Lymphoma
Violetta V. Leshchenko, Pei-Yu Kuo, Zewei Jiang, Venu K. Thirukonda, and Samir Parekh

393 Antitumoral Activity of Lenalidomide in In Vitro and In Vivo Models of Mantle Cell Lymphoma Involves the Destabilization of Cyclin D1/p27KIP1 Complexes
Alexandra Moros, Sophie Bustany, Julie Cahu, Ifigenia Saborit-Villarroya, Antonio Martínez, Dolors Colomer, Brigitte Sola, and Gaël Roué

404 Proteomic Characterization of Breast Cancer Xenografts Identifies Early and Late Bevacizumab-Induced Responses and Predicts Effective Drug Combinations
Evita M. Lindholm, Marit Krohn, Sergio Iadevaia, Alexandr Kristian, Gordon B. Mills, Gunhild M. Mollandsmo, and Olav Engebraaten

Preclinical Activity Profile and Therapeutic Efficacy of the HSP90 Inhibitor Ganetespib in Triple-Negative Breast Cancer

IMAGING, DIAGNOSIS, PROGNOSIS

425 Prognostic Relevance of Circulating Tumor Cells in Blood and Disseminated Tumor Cells in Bone Marrow of Patients with Squamous Cell Carcinoma of the Oral Cavity
Alexander Gröbe, Marco Blessmann, Henning Hanken, Reinhard E. Friedrich, Gerhard Schön, Johannes Wilker, Katharina E. Effenberg, Lan Kluge, Max Heiland, Klaus Pantel, and Sabine Riethdorf

434 Tumor-Infiltrating Lymphocytes Expressing the Tissue Resident Memory Marker CD103 Are Associated with Increased Survival in High-Grade Serous Ovarian Cancer
John R. Webb, Katy Milne, Peter Watson, Ronald J. deLeeuw, and Brad H. Nelson

CANCER THERAPY: CLINICAL

445 A Phase 1, Dose-Escalation, Pharmacokinetic and Pharmacodynamic Study of BIIB021 Administered Orally in Patients with Advanced Solid Tumors
Muhammad Wasif Saif, Chris Takimoto, Monica Mita, Udai Banerji, Nicole Lamanna, Januario Castro, Susan O’Brien, Christopher Stogard, and Daniel Von Hoff
See related article, p. 275

456 Dual Targeting of HER2-Positive Cancer with Trastuzumab Emtansine and Pertuzumab: Critical Role for Neuregulin Blockade in Antitumor Response to Combination Therapy
Gail D. Lewis Phillips, Carter T. Fields, Guangmin Li, Donald Dowbenko, Gabriele Schaefer, Kathy Miller, Fabrice Andre, Howard A. Burris III, Kathy S. Albain, Nadia Harbeck, Veronique Dieras, Diana Crivellari, Liang Fang, Ellie Guarino, Steven R. Olsen, Lisa M. Crocker, and Mark X. Slivkowsk
See related article, p. 278

469 The High-Affinity CXCR4 Antagonist BKT140 is Safe and Induces a Robust Mobilization of Human CD34+ Cells in Patients with Multiple Myeloma
Amnon Peled, Michael Abraham, Irit Avivi, Jacob M. Rowe, Katia Beider, Hanna Wald, Lena Tjomkin, Lena Ribakovskiy, Yossi Riback, Yaron Ramati, Sigal Aviel, Ethan Galun, Howard Laurence Shaw, Orly Eizenberg, Izhar Hardan, Avichai Shimoni, and Amon Nagler

480 Safety, Pharmacokinetics, Pharmacodynamics, and Antitumor Activity of Dalantercept, an Activin Receptor–like Kinase-1 Ligand Trap, in Patients with Advanced Cancer

490 Phase II Study of the Oral MEK Inhibitor Selumetinib in Advanced Acute Myelogenous Leukemia: A University of Chicago Phase II Consortium Trial
Neoadjuvant Imatinib in Advanced Primary or Locally Recurrent Dermatofibrosarcoma Protuberans: A Multicenter Phase II DeCOG Trial with Long-term Follow-up
Selma Ugurel, Thomas Mentzel, Jochen Utikal, Peter Helmbold, Peter Mohr, Claudia Pfoehler, Meinhard Schiller, Axel Hauschild, Rüdiger Hein, Eckhardt Käppgen, Ivonne Kellner, Martin Leverkus, Jürgen C. Becker, Philip Ströbel, and Dirk Schadendorf

PREDICTIVE BIOMARKERS AND PERSONALIZED MEDICINE
Research-Based PAM50 Subtype Predictor Identifies Higher Responses and Improved Survival Outcomes in HER2-Positive Breast Cancer in the NOAH Study
Aleix Prat, Giampaolo Bianchini, Marlene Thomas, Anton Belousov, Maggie C.U. Cheang, Astrid Koehler, Patricia Gómez, Vladimir Semiglazov, Wolfgang Eiermann, Sergei Tjulandin, Mikhail Byakhow, Begoña Bermejo, Milvia Zambetti, Federico Vazquez, Luca Gianni, and José Baselga

ABOUT THE COVER
The cover shows a section of a lymph node biopsy from a patient with mantle cell lymphoma. Hematoxylin and eosin staining shows typical monomorphic small-to-medium-sized lymphoid cells with irregular nuclei. For details, see the article by Moros and colleagues on page 393 of this issue.