Highlights of This Issue 339

CHEMICAL THERAPEUTICS

341 The HSP70 and Autophagy Inhibitor Pifithrin-μ Enhances the Antitumor Effects of TRAIL on Human Pancreatic Cancer
Hiroyuki Monma, Nanae Harashima, Touko Inao, Shinnji Okano, Yoshitsugu Tajima, and Mamoru Harada

352 Tenovin-D3, a Novel Small-Molecule Inhibitor of Sirtuin SirT2, Increases p21 (CDKN1A) Expression in a p53-Independent Manner
Anna R. McCarthy, Marijke C.C. Sachweh, Maureen Higgins, Johanna Campbell, Catherine J. Drummond, Ingeborg M.M. van Leeuwen, Lisa Pirrie, Marcus J.G.W. Ladds, Nicholas J. Westwood, and Sonia Lain
See article, p. 471

361 Gossypin as a Novel Selective Dual Inhibitor of v-raf Murine Sarcoma Viral Oncogene Homolog B1 and Cyclin-Dependent Kinase 4 for Melanoma

373 Novel Inhibitors of Rad6 Ubiquitin Conjugating Enzyme: Design, Synthesis, Identification, and Functional Characterization
Matthew A. Sanders, Ghali Brahemi, Pratima Nangia-Makker, Vitaly Balan, Matteo Morelli, Hend Kothayer, Andrew D. Westwell, and Malathy P.V. Shekhar

SMALL MOLECULE THERAPEUTICS

384 HER2-Targeted Hybrid Peptide That Blocks HER2 Tyrosine Kinase Disintegrates Cancer Cell Membrane and Inhibits Tumor Growth In Vivo
Megumi Kawamoto, Tomohisa Horibe, Masayuki Kohno, and Koji Kawakami

LARGE MOLECULE THERAPEUTICS

394 Targeting IGF-IR with Ganitumab Inhibits Tumorigenesis and Increases Durability of Response to Androgen-Deprivation Therapy in VCaP Prostate Cancer Xenografts
Cale D. Fahrenholtz, Pedro J. Beltran, and Kerry L. Burnstein

395 Poly(β-amino ester) Nanoparticle Delivery of TP53 Has Activity against Small Cell Lung Cancer In Vitro and In Vivo
Chandrashokhar D. Kamat, Ron B. Shmueli, Nick Connis, Charles M. Rudin, Jordan J. Green, and Christine L. Hann

405 Downregulation of HER3 by a Novel Antisense Oligonucleotide, EZN-3920, Improves the Antitumor Activity of EGFR and HER2 Tyrosine Kinase Inhibitors in Animal Models
Yaming Wu, Yixian Zhang, Maoliang Wang, Qi Li, Zhengxing Qu, Victoria Shi, Patricia Kraft, Steve Kim, Ying Gao, Jenny Pak, Stephen Youngster, Ivan D. Horak, and Lee M. Greenberger

CANCER THERAPEUTICS INSIGHTS

438 Transient Exposure to Quizartinib Mediates Sustained Inhibition of FLT3 Signaling while Specifically Inducing Apoptosis in FLT3-Activated Leukemia Cells
Ruwanthi N. Gunawardane, Ronald R. Nepomuceno, Allison M. Rooks, Jeremy P. Hunt, Jill M. Ricono, Barbara Belli, and Robert C. Armstrong
GX15-070 (Obatoclax) Induces Apoptosis and Inhibits Cathepsin D- and L–Mediated Autophagosomal Lysis in Antiestrogen-Resistant Breast Cancer Cells
Jessica L. Schwartz-Roberts, Ayesha N. Shajahan, Katherine L. Cook, Anni Warri, Mones Abu-Asab, and Robert Clarke

Biological Characterization of TAK-901, an Investigational, Novel, Multitargeted Aurora B Kinase Inhibitor
Pamela Farrell, Lihong Shi, Jennifer Matuszkiewicz, Deepika Balakrishna, Takashi Hoshino, Lilly Zhang, Sarah Elliott, Robyn Falbrey, Bumsup Lee, Petro Halkowycz, BiChing Sang, Seigo Ishino, Toshiyuki Nomura, Mika Teratani, Yoshikazu Ohta, Charles Grimshaw, Bheema Parasseli, Takashi Satou, and Ron de Jong

Modulation of p53 C-Terminal Acetylation by mdm2, p14ARF, and Cytoplasmic SirT2
Ingerborg M.M. van Leeuwen, Maureen Higgins, Johanna Campbell, Anna R. McCarthy, Marijke C.C. Sachweh, Ana Marin Navarro, and Sonia Lain
See article, p. 352

Efficacy of Low-Dose Oral Metronomic Dosing of the Prodrug of Gemcitabine, LY2334737, in Human Tumor Xenografts
Susan E. Pratt, Sara Durland-Busbice, Robert L. Shepard, Gregory P. Donoho, James J. Starling, Enaksha R. Wickremsinhe, Everett J. Perkins, and Anne H. Dantzig

Tumor-Initiating Cells and FZD8 Play a Major Role in Drug Resistance in Triple-Negative Breast Cancer

Antitumor Effect of SIRT1 Inhibition in Human HCC Tumor Models In Vitro and In Vivo
Simone Portmann, René Fahrner, Antje Lechleiter, Adrian Keogh, Sarah Overney, Alexander Laemmle, Kei Mikami, Matteo Montani, Mario P. Tschan, Daniel Candinas, and Deborah Stroka

Inhibition of HSP90 with AU922 Induces Synergy in HER2-Amplified Trastuzumab-Resistant Breast and Gastric Cancer

COMPANION DIAGNOSTICS & CANCER BIOMARKERS

Quantitative Chemical Proteomics Profiling Differentiates Erlotinib from Gefitinib in EGFR Wild-Type Non–Small Cell Lung Carcinoma Cell Lines
Angélache Augustin, Jens Lamerz, Hélène Meistermann, Sabrina Golling, Stefan Scheiblich, Johannes C. Hermann, Guillemete Duchateau-Nguyen, Manuel Tzouros, David W. Avila, Hanno Langen, Laurent Essioux, and Barbara Klughammer

Analysis of DNA Repair–Related Genes in Breast Cancer Reveals CUL4A Ubiquitin Ligase as a Novel Biomarker of Trabectedin Response
María J. García, Laura Paula Sucreo-Cuevas, Iván Muñoz-Repeto, Victoria Fernández, Maria J. Robles, Samuel Domingo, José Palacios, Miguel Aracil, Antonio Nieto, Juan Carlos Tercero, and Javier Benítez

Use of Molecular Biomarkers to Quantify the Spatial Distribution of Effects of Anticancer Drugs in Solid Tumors
Jasdeep K. Saggar, Andrea S. Fung, Krupa J. Patel, and Ian F. Tannock
ABOUT THE COVER

The yeast Rad6 human homologues HHR6A and HHR6B (or Rad6A and Rad6B) encode ubiquitin-conjugating enzymes (or E2) that play a central role in substrate ubiquitination and E3 ligase selection. The ubiquitin-conjugating activity of Rad6 is essential for its function in postreplication DNA repair, damage-induced mutagenesis, and proteolysis. Using virtual screening of ZINC database against a pharmacophore model for consensus, E2-ubiquitin binding sites followed by biological evaluation of virtual hits, two small molecule compounds with a triazine core structure, and possessing Rad6 ubiquitin conjugation inhibitory activity were identified. These small molecules inhibit breast cancer cell proliferation, migration, and colony formation by blocking G2–M progression. For details, see article by Sanders and colleagues on page 373.