Editorial

Eribulin: Rediscovering Tubulin as an Anticancer Target. Antonio Jimeno ................................................................. 3903
Commentary on Goel et al., p. 4207 and Tan et al., p. 4213

CCR Translations

Toward an Effective Targeted Chemotherapy for Multiple Myeloma. Andrew G. Polson and Mark X. Sliwkowski ................................................................. 3906
Commentary on Ikeda et al., p. 4028

CCR Practice of Translational Oncology


Molecular Pathways

Targeting NEDD8-Activated Cullin-RING Ligases for the Treatment of Cancer. Teresa A. Soucy, Peter G. Smith, and Mark Rolfe ................................................................. 3912

CCR Special Focus

From the Editor. Susan E. Bates ................................................................................................................................. 3917

Epigenetic Modifiers: Basic Understanding and Clinical Development. Richard L. Piekarz and Susan E. Bates ................................................................. 3918

Cancer DNA Methylation: Molecular Mechanisms and Clinical Implications. Michael T. McCabe, Johann C. Brandes, and Paula M. Vertino ................................................................. 3927

Targeting DNA Methylation. Jean-Pierre J. Issa and Hagop M. Kantarjian ........................................................................ 3938

Cytotoxicity Mediated by Histone Deacetylase Inhibitors in Cancer Cells: Mechanisms and Potential Clinical Implications. David S. Schrump ........................................................................ 3947

Clinical Studies of Histone Deacetylase Inhibitors. H. Miles Prince, Mark J. Bishton, and Simon J. Harrison ................................................................. 3958

Rational Combinations Using HDAC Inhibitors. Michael Bots and Ricky W. Johnstone ................................................................. 3970

Human Cancer Biology

Global Gene Expression Analysis of Reactive Stroma in Prostate Cancer. Olga Dakhova, Mustafa Ozen, Chad J. Creighton, Rile Li, Gustavo Ayala, David Rowley, and Michael Ittmann ........................................................................ 3979

GATA4 and GATA5 are Potential Tumor Suppressors and Biomarkers in Colorectal Cancer. Debby M.E.I. Hellebrekers, Marjolein H.F.M. Lentjes, Sandra M. van den Bosch, Veele Melotte, Kim A.D. Wouters, Kathleen L.J. Daenen, Kim M. Smits, Yoshimitsu Akiyama, Yasuhiro Yuasa, Silvia Sanduleanu, Carolina A.J. Khalid de Bakker, Daisy Jonkers, Matty P. Weijenberg, Joost Louwagie, Wil van Crikkinge, Beatriz Carvalho, Gerrit A. Meijer, Stephen B. Baylin, James G. Herman, Adriaan P. de Bruine, and Manon van Engeland ........................................................................ 3990

MiR-21 Indicates Poor Prognosis in Tongue Squamous Cell Carcinomas as an Apoptosis Inhibitor. Jinsong Li, Hongzhang Huang, Liujuan Sun, Mei Yang, Shaobin Pan, Weiliang Chen, Donghui Wu, Zhaoyu Lin, Chuxian Zeng, Yandan Yao, Peter Zhang, and Erwei Song ........................................................................ 3998

Locked Nucleic Acid In situ Hybridization Analysis of miR-21 Expression during Colorectal Cancer Development. Nobutake Yamamichi, Ryoichi Shimomura, Ken-ichi Inada, Kouhei Sakurai, Takeshi Haraguchi, Yuka Ozaki, Shuji Fujita, Taketoshi Mizutani, Chiiro Furukawa, Mitsuhito Fujishiro, Masao Ichinose, Kazuya Shiogama, Yutaka Tsutsumi, Masao Omata, and Hideo Iba ........................................................................ 4009
Fibroblast Growth Factor Receptor 2–Positive Fibroblasts Provide a Suitable Microenvironment for Tumor Development and Progression in Esophageal Carcinoma. Chunyu Zhang, Li Fu, Jianhua Fu, Liang Hu, Hong Yang, Tie-Hua Rong, Yan Li, Haibo Liu, Song-Bin Fu, Yi-Xin Zeng, and Xin-Yuan Guan

Cancer Therapy: Preclinical

The Monoclonal Antibody nBT062 Conjugated to Cytotoxic Maytansinoids Has Selective Cytotoxicity Against CD138-Positive Multiple Myeloma Cells In vitro and In vivo. Hiroshi Ikeda, Teru Hideshima, Mariateresa Fulciniti, Robert J. Lutz, Hiroshi Yasui, Yutaka Okawa, Tanyel Kiziltepe, Sonia Vallet, Samantha Pozzi, Lovedana Santo, Giulia Perrone, Yu-Tzu Tai, Diana Cirstea, Noopur S. Raje, Christoph Uherek, Benjamin Dälken, Silke Aigner, Frank Osterroth, Nikhil Munshi, Paul Richardson, and Kenneth C. Anderson


CIUIC-305, a Novel Synthetic HSP90 Inhibitor with Unique Pharmacologic Properties for Cancer Therapy. Rudi Bao, Cheng-Jung Lai, Hui Qu, Dagon Wang, Ling Yin, Brian Zifcak, Ruzanna Atoyan, Jeng Wang, Maria Samson, Jeffrey Forrester, Steven DellaRocca, Guang-Xin Xu, Xu Tao, Hai-Xiao Zhai, Xiong Cai, and Changgeng Qian


High Efficacy of Panobinostat Towards Human Gastrointestinal Stromal Tumors in a Xenograft Mouse Model. Mitsuru Miyachi, Naoki Kazaku, Shigeki Yagyu, Yoshiki Katsumi, Satoko Tsubai-Shimizu, Ken Kikuchi, Kunihihiro Tsuchiya, Tomoko Ichara, and Hajime Hosoi

Restoration of p53 Pathway by Nutlin-3 Induces Cell Cycle Arrest and Apoptosis in Human Rhabdomyosarcoma Cells. Giuseppe Fiori, Maria Debic-Rychter, Raf Sciot, Cristiana Stefan, Steffen Fieuss, Kathleen Machiels, Peter Atadja, Agnieszka Wozniak, Gavino Faa, and Patrick Schöffski

Impaired STAT Phosphorylation in T Cells from Melanoma Patients in Response to IL-2: Association with Clinical Stage. Roberta Mortarini, Claudia Vegetti, Alessandra Molla, Flavio Arienti, Fernando Ravagnani, Andrea Maurichi, Roberto Patuzzo, Mario Santinami, and Andrea Anichini


MMP11: A Novel Target Antigen for Cancer Immunotherapy. Daniela Peruzzi, Federica Mori, Antonella Conforti, Domenico Lazzaro, Emanuele De Rinaldis, Gennaro Ciliberto, Nicola La Monica, and Luigi Aurisicchio


Extranuclear Coactivator Signaling Confers Insensitivity to Tamoxifen. Rakesh Kumar, Hao Zhang, Caroline Holm, Ratna K. Vadlamudi, Goran Landberg, and Suresh K. Rayala

Antitumor Effects and Biomarkers of Activity of AZD0530, a Src Inhibitor, in Pancreatic Cancer. N. V. Rajeshkumar, Aik Choon Tan, Elizabeth De Oliveira, Chris Womack, Helen Wombwell, Shethala Morgan, Madhuri V. Warren, Jill Walker, Tim P. Green, Antonio Jimeno, Wells A. Messersmith, and Manuel Hidalgo........................................................................................................................................4138

Suppression of HER2/HER3-Mediated Growth of Breast Cancer Cells with Combinations of GDC-0941 PI3K Inhibitor, Trastuzumab, and Pertuzumab. Evelyn Yao, Wei Zhou, Si Tuen Lee-Hoeflich, Tom Truong, Peter M. Haverty, Jeffrey Eastham-Anderson, Nicholas Lewin-Koh, Bert Gunter, Marcia Belvin, Lesley J. Murray, Lori S. Friedman, Mark X. Sliwowski, and Klaus P. Hoeflich........................................................................................................4147

Imaging, Diagnosis, Prognosis

High Expression of Mammalian Target of Rapamycin Is Associated with Better Outcome for Patients with Early Stage Adenocarcinoma. Valsamo K. Anagnostou, Gerold Bepler, Konstantinos N. Syrigos, Lynn Tanoue, Scott Gettinger, Robert J. Homer, Daniel Boffa, Frank Dettterbeck, and David L. Rimm................................................................................................................................4157


Methylation of RASSF1A, RASSF2A, and HIN-1 Is Associated with Poor Outcome after Radiotherapy, but not Surgery, in Oral Squamous Cell Carcinoma. Kuo-Hao Huang, Shiang-Fu Huang, I-How Chen, Chun-Tao Liao, Hung-Ming Wang, and Ling-Ling Hsieh................................................................................................................................4174

Local Recurrence after Breast-Conserving Therapy in Relation to Gene Expression Patterns in a Large Series of Patients. Bas Kreike, Hans Halfwerk, Nicola Armstrong, Peter Bult, John A. Foekens, Sanne C. Veltkamp, Dimitry S.A. Nuyten, Harry Bartelink, and Marc J. van de Vijver................................................................................................................................4181

Cell Cycle/Apoptosis Molecule Expression Correlates with Imatinib Response in Patients with Advanced Gastrointestinal Stromal Tumors. Salvatore Romeo, Maria Debiec-Rychter, Martine Van Glabbeke, Heidi Van Paassen, Paola Comite, Ronald Van Eijk, Jan Oosting, Jaap Verweij, Philippe Terrier, Ulrike Schneider, Raf Sciot, Jean Yves Blay, and Pancras C.W. Hogendoorn on behalf of the European Organization for Research and Treatment of Cancer Soft Tissue and Bone Sarcoma Group................................................................................................................................4191

Changes in Gene Expression Predicting Local Control in Cervical Cancer: Results from Radiation Therapy Oncology Group 0128. Joanne B. Weidhaas, Shu-Xia Li, Kathryn Winter, Janice Ryu, Anuja Jhingran, Bridgette Miller, Adam P. Dicker, and David Gaffney................................................................................................................................4199

Cancer Therapy: Clinical

A Phase I Study of Eribulin Mesylate (E7389), a Mechanistically Novel Inhibitor of Microtubule Dynamics, in Patients with Advanced Solid Malignancies. Sanjay Goel, Alain C. Mita, Monica Mita, Eric K. Rowinsky, Quincy S. Chu, Nancy Wong, Christopher Desjardins, Fang Fang, Mendel Jansen, Dale E. Shuster, Sridhar Mani, and Chris H. Takimoto................................................................................................................................4207


Phase I Trial of Pazopanib in Patients with Advanced Cancer. Herbert I. Hurwitz, Afshin Dowlati, Shermin Saini, Shawna Savage, A. Benjamin Suttle, Diana M. Gibson, Jeffrey P. Hodge, Elmar M. Merkle, and Lini Pandite................................................................................................................................4220

Coadministration of Ritonavir Strongly Enhances the Apparent Oral Bioavailability of Docetaxel in Patients with Solid Tumors. Roos L. Oostendorp, Alwin Huitema, Hilde Rosing, Robert S. Jansen, Rob ter Heine, Marianne Keessen, Jos H. Beijnen, and Jan H.M. Schellens................................................................................................................................4228
Association of Breast Cancer Stem Cells Identified by Aldehyde Dehydrogenase 1 Expression with Resistance to Sequential Paclitaxel and Epirubicin-Based Chemotherapy for Breast Cancers. Tomonori Tanei, Koji Morimoto, Kenzo Shimazu, Seung Jin Kim, Yoshio Tanji, Tetsuya Taguchi, Yasuhiro Tamaki, and Shinzaburo Noguchi

Susceptibility and Prevention


About the Cover

Reactive stroma from prostate cancer and normal prostatic stroma was laser captured, RNAs were amplified and gene expression analyzed using expression microarrays. A total of 1141 genes were differentially expressed in reactive compared with normal stroma. The Human Protein Reference Database catalogue of over 35,000 known physical protein-protein interactions was queried to determine how the reactive stroma-associated genes relate to each other in terms of interactions between their associated proteins. A total of 292 interactions were visualized as a graphical network. A view of the central node is shown. For further details, please see Dakhova and colleagues on page 3979 in this issue.