CONTENTS

MAY 2014—VOLUME 4—NUMBER 5

IN THIS ISSUE
Highlighted research articles ................................. 495

NEWS IN BRIEF
Important news stories affecting the community .................. 500

NEWS IN DEPTH
Q&A: Mikala Egeblad on Tumor Microenvironment ............... 503
Tracking CTCs May Improve Cancer Treatment ................. 504

RESEARCH BRIEFS
Selected highlights of recent articles of exceptional significance from the cancer literature .............. 505

ONLINE
For more News and Research Watch, visit Cancer Discovery online at http://CDnews.aacrjournals.org.

VIEWS
In The Spotlight
Finding the Right Balance of BRAF Inhibition in Melanoma ...... 510
M.A. Davies
See article, p. 538

MTOR Mutations in the Crosshairs of Targeted Therapy ........... 513
PA. Rejto and R.T. Abraham
See article, p. 546
See article, p. 554

From Breaking Bad to Worse: Exploiting Homologous DNA Repair Deficiency in Cancer ... 516
M.T. Hemann
See article, p. 592

Paths of Resistance to EGFR Inhibitors: Is NF Enough? ......... 519
O. Maertens and K. Cichowski
See article, p. 606

In Focus
T-Cell and NK-Cell Infiltration into Solid Tumors: A Key Limiting Factor for Efficacious Cancer Immunotherapy ................. 522
I. Melero, A. Rouzaut, G.T. Motz, and G. Coukos

REVIEW
Promising SINEs for Embargoing Nuclear–Cytoplasmic Export as an Anticancer Strategy ........... 527

Efficacy of Intermittent Combined RAF and MEK Inhibition in a Patient with Concurrent BRAF- and NRAS-Mutant Malignancies .... 538
Précis: Intermittent combined use of the RAF inhibitor vemurafenib and the MEK inhibitor cobimetinib in a patient with BRAF-mutant melanoma and NRAS-mutant leukemia controlled both diseases.
See commentary, p. 510

Activating mTOR Mutations in a Patient with an Extraordinary Response on a Phase I Trial of Everolimus and Pazopanib ........ 546
Précis: The identification of two activating MTOR mutations in a patient who experienced a complete response to everolimus and pazopanib suggests an underlying mechanism of mTOR inhibitor sensitivity.
See commentary, p. 513

A Diverse Array of Cancer-Associated MTOR Mutations Are Hyperactivating and Can Predict Rapamycin Sensitivity ............... 554
B.C. Grabiner, V. Nardi, K. Birsoy, R. Possemato, M. Stewart, M.T. Hemann
Précis: Activating MTOR mutations are widespread in human cancers and correlate with hypersensitivity to mTOR pathway inhibition.
See commentary, p. 513

CONTACT
Editorial Office: 222 W. Miller Street, 13th Floor, Philadelphia, PA 19107
Phone: 215-625-3500; Fax: 215-625-3195
E-mail: cancerdiscovery@aacrjournals.org
Web: cancerdiscovery.aacrjournals.org

For more News and Research Watch, visit Cancer Discovery online at http://CDnews.aacrjournals.org.
Vemurafenib treatment was previously shown to uncover an NRAS-mutant chronic myelomonocytic leukemia (CMML) in a patient with BRAF-mutant metastatic melanoma. Abdel-Wahab and colleagues report that the combination of vemurafenib and the MEK inhibitor cobimetinib blocked vemurafenib-induced CMML proliferation and restored normal white blood cell counts in this patient. Intermittent administration of vemurafenib and cobimetinib has durably maintained a near-complete melanoma response and has prevented CMML progression in association with decreased levels of CMML-derived circulating tumor DNA and reduced ERK activation in monocytes. Intermittent combination RAF and MEK inhibitor therapy may thus be useful for treatment of RAS-driven malignancies arising due to paradoxical activation of wild-type RAF by RAF inhibitors in RAS-mutant cells. For details, please see the article by Abdel-Wahab and colleagues on page 538.