CANCER DISCOVERY CONTENTS

MAY 2012 • VOLUME 2 • NUMBER 5

IN THIS ISSUE
Highlighted research articles ............................. 377

NEWS IN BRIEF
Important news stories affecting the community ...................... 380

NEWS IN DEPTH
Q&A: Michael Pellini on Cancer Diagnostics ...................... 382

The States of Research .................................... 383

Cancer Stem Cells in the Crosshairs .............................. 384

RESEARCH WATCH
Selected highlights of recent articles of exceptional significance from the cancer literature .................... 385

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

RESEARCH BRIEFS

Preexisting MEK1 Exon 3 Mutations in \( V_{600E}\) BRAF Melanomas Do Not Confer Resistance to BRAF Inhibitors ................................. 414

Précis: Mutation of the downstream BRAF effector MEK1 is not a mechanism of innate resistance to targeted BRAF inhibitors.

Functional Characterization of an Isoform-Selective Inhibitor of PI3K-\( p_{110}\)β as a Potential Anticancer Agent ................................. 425

Précis: A selective small-molecule inhibitor of the \( p_{110}\)β isoform of PI3K is effective in a subset of PTEN-deficient tumor cell lines and xenografts.

In Focus


REVIEW
Emerging Epigenetic Targets and Therapies in Cancer Medicine ......................................... 405
R. Popovic and J.D. Licht

Occupy EGFR ...................... 398
J.H. Park and M.A. Lemmon
Commentary on Barkovich et al., p. 450 and Vivanco et al., p. 458

In The Spotlight

Making Sense of MEK1 Mutations in Intrinsic and Acquired BRAF Inhibitor Resistance ................................. 390
K.H.T. Paraiso and K.S.M. Smalley
Commentary on Shi et al., p. 414

Beta-Testing of PI3-Kinase Inhibitors: Is Beta Better? ........ 393
P.R. Shepherd and W.A. Denny
Commentary on Ni et al., p. 425

Circulating Endothelial Progenitors and Tumor Resistance to Vascular-Targeting Therapies ...................... 395
M. De Palma and S. Nucera
Commentary on Taylor et al., p. 434

Available online at www.aacrjournals.org
**RESEARCH ARTICLES**

**Reversing Resistance to Vascular-Disrupting Agents by Blocking Late Mobilization of Circulating Endothelial Progenitor Cells**


**Précis:** Vascular-disrupting agents induce a late surge in circulating endothelial progenitor cells that can be blocked by antiangiogenic agents.

**Kinetics of Inhibitor Cycling Underlie Therapeutic Disparities between EGFR-Driven Lung and Brain Cancers**


**Précis:** The glioma-derived EGFRVIII mutant releases erlotinib more quickly than non–small cell lung cancer–derived EGFR-mutant alleles.

**Differential Sensitivity of Glioma- versus Lung Cancer–Specific EGFR Mutations to EGFR Kinase Inhibitors**


**Précis:** Glioma cells with extracellular domain EGFR mutations are selectively sensitive to type II EGFR inhibitors that stabilize the inactive kinase conformation.

---

For more News and Research Watch, visit Cancer Discovery online at http://CDnews.aacrjournals.org. Online-only News stories include the following:

- Annotated Cell-Line Resources Speed Discovery
- Phase II Trial for Lymphoma Gives Promising Early Results
- Targeted Combo Effective for Refractory Ewing Sarcoma
- Novel PI3K Inhibitors Enter Human Studies
- An EMPaCT on Minority Recruitment
- MEK Inhibition Aids in Serous Ovarian Cancer

---

**ON THE COVER**

Vivanco and colleagues demonstrated that glioma-specific EGFR extracellular domain mutants were more sensitive to type II EGFR inhibitors (e.g., lapatinib) that stabilize an inactive kinase conformation than type I EGFR inhibitors (e.g., erlotinib) that target the active kinase conformation more commonly found in EGFR-mutant lung cancers. In a related article, Barkovich and colleagues found that the rapid release of erlotinib by glioma-specific EGFR mutants rendered them less sensitive to erlotinib than lung cancer–derived EGFR mutants. Together, these studies provide explanations for the limited success of first-generation EGFR inhibitors in treatment of EGFR-mutant gliomas and suggest alternative EGFR inhibition strategies may work best in these tumors. For details, please see the article by Vivanco and colleagues on page 458 and the article by Barkovich and colleagues on page 450.