**RESEARCH BRIEFS**

**In Focus**


---

**Recent articles at Watch,**

**Emerging Epigenetic Targets and Therapies in Cancer Medicine**

R. Popovic and J.D. Licht

---

**Preexisting MEK1 Exon 3 Mutations in V600E/BRAF Melanomas Do Not Confer Resistance to BRAF Inhibitors**


**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-p110β as a Potential Anticancer Agent**


**Précis:** A selective small-molecule inhibitor of the p110β isofrom of PI3K is effective in a subset of PTEN-deficient tumor cell lines and xenografts.

---

**Circulating Endothelial Progenitors and Tumor Resistance to Vascular-Targeting Therapies**

M. De Palma and S. Nucera

**Commentary on Taylor et al., p. 434**

---

**Beta-Testing of PI3-Kinase Inhibitors: Is Beta Better?**

P.R. Shepherd and W.A. Denny

**Commentary on Ni et al., p. 425**

---

**Making Sense of MEK1 Mutations in Intrinsic and Acquired BRAF Inhibitor Resistance**

K.H.T. Paraizo and K.S.M. Smalley

**Commentary on Shi et al., p. 414**

---

**Occupy EGFR**

J.H. Park and M.A. Lemmon

**Commentary on Borkovich et al., p. 450 and Vivanco et al., p. 458**
**RESEARCH ARTICLES**


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


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


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 EMPerCT 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.