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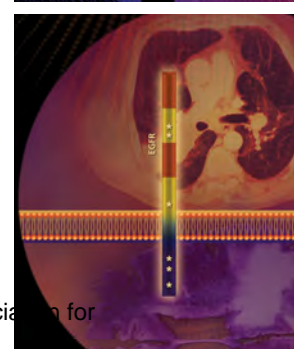
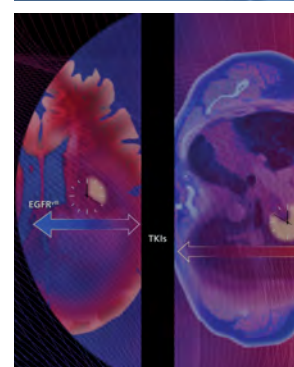
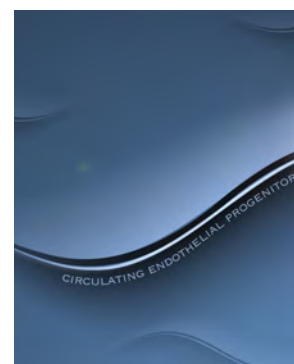
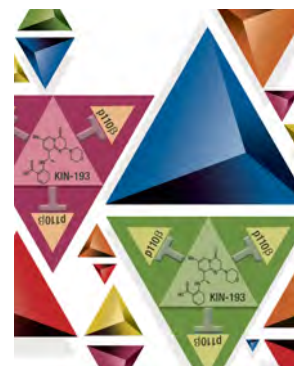
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**RESEARCH BRIEFS Preexisting MEK1 Exon 3 Mutations in <sup>V600E/K</sup>BRAF Melanomas Do Not Confer Resistance to BRAF Inhibitors** ..... 414  
*H. Shi, G. Moriceau, X. Kong, R.C. Koya, R. Nazarian, G.M. Pupo, A. Bacchiocchi, K.B. Dahlman, B. Chmielowski, J.A. Sosman, R. Halaban, R.F. Kefford, G.V. Long, A. Ribas, and R.S. Lo*

**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** .....425  
*J. Ni, Q. Liu, S. Xie, C. Carlson, T. Von, K. Vogel, S. Riddle, C. Benes, M. Eck, T. Roberts, N. Gray, and J. Zhao*

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



RESEARCH ARTICLES

Reversing Resistance to Vascular-Disrupting Agents by Blocking Late Mobilization of Circulating Endothelial Progenitor Cells. . . . . 434

M. Taylor, F. Billiot, V. Marty, V. Rouffiac, P. Cohen, E. Tournay, P. Opolon, F. Louache, G. Vassal, C. Laplace-Builhé, P. Vielh, J-C. Soria, and F. Farace

**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. . . . . 450

K.J. Barkovich, S. Hariono, A.L. Garske, J. Zhang, J.A. Blair, Q-W. Fan, K.M. Shokat, T. Nicolaides, and W.A. Weiss

**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. . . . . 458



I. Vivanco, H.I. Robins, D. Rohle, C. Campos, C. Grommes, P.L. Nghiemphu, S. Kubek, B. Oldrini, M.G. Chheda, N. Yannuzzi, H. Tao, S. Zhu, A. Iwanami, D. Kuga, J. Dang, A. Pedraza, C.W. Brennan, A. Heguy, L.M. Liao, F. Lieberman, W.K.A. Yung, M.R. Gilbert, D.A. Reardon, J. Drappatz, P.Y. Wen, K.R. Lamborn, S.M. Chang, M.D. Prados, H.A. Fine, S. Horvath, N. Wu, A.B. Lassman, L.M. DeAngelis, W.H. Yong, J.G. Kuhn, P.S. Mischel, M.P. Mehta, T.F. Cloughesy, and I.K. Mellinghoff

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

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- 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.



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