

CANCER DISCOVERY

CONTENTS

MAY 2012 ■ VOLUME 2 ■ NUMBER 5

IN THIS ISSUE Highlighted research articles377

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

NEWS IN DEPTH Q&A: Michael Pellini on Cancer Diagnostics382

The States of Research.....383

Cancer Stem Cells in the Crosshairs384

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>.

IEWS In The Spotlight

Making Sense of MEK1 Mutations in Intrinsic and Acquired BRAF Inhibitor Resistance390

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 Therapies395

M. De Palma and S. Nucera

Commentary on Taylor et al., p. 434

Occupy EGFR398

J.H. Park and M.A. Lemmon

Commentary on Barkovich et al., p. 450 and Vivanco et al., p. 458

In Focus

The cBio Cancer Genomics Portal: An Open Platform for Exploring Multidimensional Cancer Genomics Data401

E. Cerami, J. Gao, U. Dogrusoz, B.E. Gross, S.O. Sumer, B.A. Aksoy, A. Jacobsen, C.J. Byrne, M.L. Heuer, E. Larsson, Y. Antipin, B. Reva, A.P. Goldberg, C. Sander, and N. Schultz

REVIEW **Emerging Epigenetic Targets and Therapies in Cancer Medicine**405

R. Popovic and J.D. Licht

RESEARCH BRIEFS **Preexisting MEK1 Exon 3 Mutations in ^{V600E/K}BRAF Melanomas Do Not Confer Resistance to BRAF Inhibitors**414

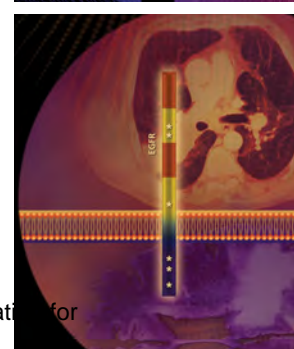
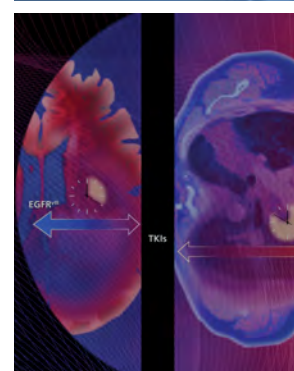
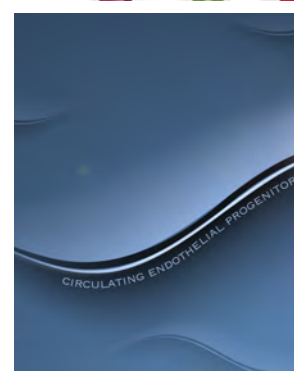
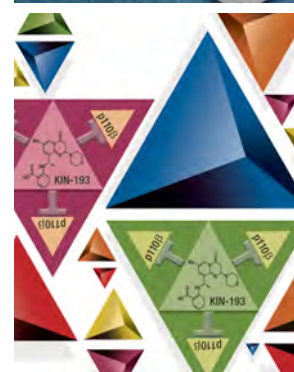
H. Shi, G. Moriceau, X. Kong, R.C. Koya, R. Nazarian, G.M. Pupo, A. Bacchiocchi, K.B. Dahlman, B. Chmielowski, J.A. Sosman, R. Halaban, R.F. Kefford, G.V. Long, A. Ribas, and R.S. Lo

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-p110 β as a Potential Anticancer Agent425

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 p110 β 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. Nicolaidis, 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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- 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.



CANCER DISCOVERY

2 (5)

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