

CANCER DISCOVERY CONTENTS

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

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B. Zhao, J.R. Pritchard, D.A. Lauffenburger, and M.T. Hemann

Précis: Computational modeling enables design and optimization of chemotherapeutic drug combinations that minimize tumor cell subpopulation outgrowth in heterogeneous tumors.

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Tolerance of Whole-Genome Doubling Propagates Chromosomal Instability and Accelerates Cancer Genome Evolution 175

S.M. Dewhurst, N. McGranahan, R.A. Burrell, A.J. Rowan, E. Grönroos, D. Endesfelder, T. Joshi, D. Mouradov, P. Gibbs, R.L. Ward, N.J. Hawkins, Z. Szallasi, O.M. Sieber, and C. Swanton

Précis: Genome doubling is an early event in colorectal cancer development that is associated with an increased tolerance for chromosomal instability and poor prognosis.

RESEARCH ARTICLES Epithelial-to-Mesenchymal Transition Rewires the Molecular Path to PI3K-Dependent Proliferation 186

M.B. Salt, S. Bandyopadhyay, and F. McCormick

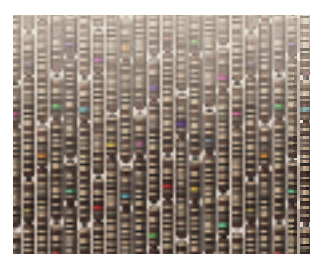
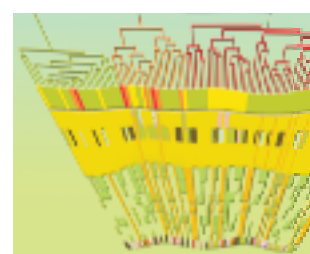
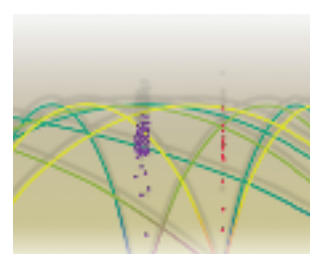
Précis: EMT removes an autocrine ERBB3 loop in NSCLC, leading to a reduction in proliferation that can be rescued by restoring PI3K signaling through divergent mechanisms.


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MEK-Dependent Negative Feedback Underlies BCR-ABL-Mediated Oncogene Addiction 200

J. Asmussen, E.A. Lasater, C. Tajon, J. Osés-Prieto, Y.-W. Jun, B.S. Taylor, A. Burlingame, C.S. Craik, and N.P. Shah

Précis: BCR-ABL activates a MEK-dependent negative feedback pathway that persistently inhibits growth factor receptor signaling and leads to apoptotic commitment upon BCR-ABL inhibition.





Comprehensive Genomic Analysis of Rhabdomyosarcoma Reveals a Landscape of Alterations Affecting a Common Genetic Axis in Fusion-Positive and Fusion-Negative Tumors 216

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Précis: Mutated genes in PAX fusion-negative rhabdomyosarcomas are enriched for PAX fusion protein targets.

Molecular Profiling of the Residual Disease of Triple-Negative Breast Cancers after Neoadjuvant Chemotherapy Identifies Actionable Therapeutic Targets 232

J.M. Balko, J.M. Giltane, K. Wang, L.J. Schwarz, C.D. Young, R.S. Cook, P. Owens, M.E. Sanders, M.G. Kuba, V. Sánchez, R. Kurupi, P.D. Moore, J.A. Pinto, F.D. Doimi, H. Gómez, D. Horiuchi, A. Goga, B.D. Lehmann, J.A. Bauer, J.A. Pietenpol, J.S. Ross, G.A. Palmer, R. Yelensky, M. Cronin, V.A. Miller, P.J. Stephens, and C.L. Arteaga

Précis: Genomic analysis of chemotherapy-resistant triple-negative breast cancer cells may guide use of adjuvant targeted therapies to prevent recurrence of metastatic disease.

Cell-Autonomous and Non-Cell-Autonomous Mechanisms of Transformation by Amplified *FGFR1* in Lung Cancer 246

F. Malchers, F. Dietlein, J. Schöttle, X. Lu, L. Nogova, K. Albus, L. Fernandez-Cuesta, J.M. Heuckmann, O. Gautschi, J. Diebold, D. Plenker, M. Gardizi, M. Scheffler, M. Bos, D. Seidel, F. Leenders, A. Richters, M. Peifer, A. Florin, P.S. Mainkar, N. Karre, S. Chandrasekhar, J. George, S. Silling, D. Rauh, T. Zander, R.T. Ullrich, H.C. Reinhardt, F. Ringeisen, R. Büttner, L.C. Heukamp, J. Wolf, and R.K. Thomas

Précis: FGFR dependency in *FGFR1*-amplified lung cancer is defined by multiple genetic factors including ligand-mediated FGFR signaling and MYC overexpression.

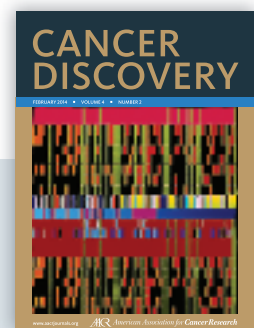
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For more News and Research Watch, visit *Cancer Discovery* online at <http://CDnews.aacrjournals.org>. Online-only News stories include the following:

- BCL-2 Inhibitor Yields High Response in CLL and SLL
- Anastrozole May Aid Breast Cancer Prevention
- *PIK3CA* Mutation Predicts Resistance to Breast Cancer Therapy
- Positive Results for Drug Combo in I-SPY 2 Trial
- Endoxifen Shows Promise in Breast Cancer

ON THE COVER

Patients with triple-negative breast cancer who do not experience a pathologic complete response following neoadjuvant chemotherapy have a poor prognosis due to a high rate of recurrence of metastatic disease. Balko and colleagues performed genomic analyses of residual triple-negative breast cancers after neoadjuvant chemotherapy to identify potential targets for adjuvant therapy and found that over 90% of residual triple-negative breast cancers harbored an actionable alteration in a targetable pathway. Molecular profiling of residual triple-negative breast cancers after neoadjuvant chemotherapy could thus potentially guide the use of adjuvant targeted therapies aimed at preventing disease recurrence. For details, please see the article by Balko and colleagues on page 232.



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