

CANCER DISCOVERY CONTENTS

NOVEMBER 2012 ■ VOLUME 2 ■ NUMBER 11

IN THIS ISSUE Highlighted research articles 961

NEWS IN BRIEF Important news stories affecting the community 964

NEWS IN DEPTH Q&A: George Sledge on Trends in Clinical Trials 967

Emphasizing the Provocative 968

RESEARCH WATCH Selected highlights of recent articles of exceptional significance from the cancer literature 969

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

VIEWS In The Spotlight

The Potential of Circulating Tumor Cells as a Liquid Biopsy to Guide Therapy in Prostate Cancer 974

K. Pantel and C. Alix-Panabières

Commentary on Miyamoto et al., p. 995

Fingerprinting Acute Leukemia: DNA Methylation Profiling of B-Acute Lymphoblastic Leukemia 976

L. Cimmino and I. Aifantis

Commentary on Geng et al., p. 1004

Distinct Epigenetic Mechanisms Distinguish *TPR52-ERG* Fusion-Positive and -Negative Prostate Cancers 979

J.J. Alunkal and J.G. Herman

Commentary on Börno et al., p. 1024

The Promise of Combining Inhibition of PI3K and PARP as Cancer Therapy 982

F.L. Rehman, C.J. Lord, and A. Ashworth

Commentary on Ibrahim et al., p. 1036, and Juvekar et al., p. 1048

REVIEW Measuring Oncogenic Signaling Pathways in Cancer with PET: An Emerging Paradigm from Studies in Castration-Resistant Prostate Cancer 985

M.J. Evans

RESEARCH BRIEF Androgen Receptor Signaling in Circulating Tumor Cells as a Marker of Hormonally Responsive Prostate Cancer 995

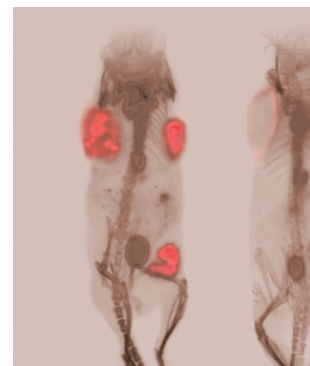
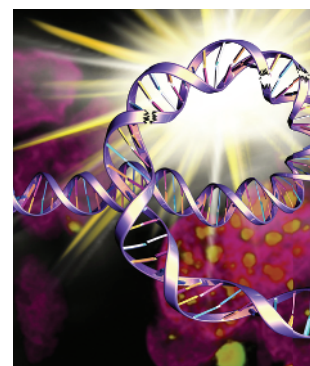
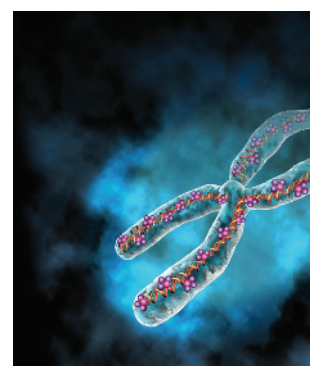
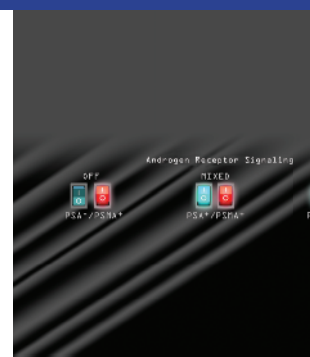
D.T. Miyamoto, R.J. Lee, S.L. Stott, D.T. Ting, B.S. Wittner, M. Ulman, M.E. Smas, J.B. Lord, B.W. Brannigan, J. Trautwein, N.H. Bander, C.-L. Wu, L.V. Sequist, M.R. Smith, S. Ramaswamy, M. Toner, S. Maheswaran, and D.A. Haber

Précis: Automated immunofluorescence imaging of circulating tumor cells can noninvasively detect androgen receptor activity in patients with metastatic prostate cancer.

RESEARCH ARTICLES Integrative Epigenomic Analysis Identifies Biomarkers and Therapeutic Targets in Adult B-Acute Lymphoblastic Leukemia 1004

H. Geng, S. Brennan, T.A. Milne, W.-Y. Chen, Y. Li, C. Hurtz, S.-M. Kweon, L. Zickl, S. Shojaaee, D. Neuberg, C. Huang, D. Biswas, Y. Xin, J. Racevskis, R.P. Ketterling, S.M. Luger, H. Lazarus, M.S. Tallman, J.M. Rowe, M.R. Litow, M.L. Guzman, C.D. Allis, R.G. Roeder, M. Müschen, E. Paietta, O. Elemento, and A.M. Melnick

Précis: Distinct DNA methylation profiles and gene expression patterns are associated with expression of leukemic fusion proteins in adult B-ALLs with poor outcome.



Genome-wide DNA Methylation Events in *TPMRSS2-ERG* Fusion-Negative Prostate Cancers Implicate an *EZH2*-Dependent Mechanism with *miR-26a* Hypermethylation 1024

S.T. Börno, A. Fischer, M. Kerick, M. Fälth, M. Laible, J.C. Brase, R. Kuer, A. Dahl, C. Grimm, B. Sayanjali, M. Isau, C. Röhr, A. Wunderlich, B. Timmermann, R. Claus, C. Plass, M. Graefen, R. Simon, F. Demichelis, M.A. Rubin, G. Sauter, T. Schlomm, H. Sultmann, H. Lehrach, and M.R. Schweiger

Précis: *EZH2* overexpression is caused by *miR-26a* hypermethylation in prostate cancers lacking the *TPMRSS2-ERG* gene fusion, which have distinct DNA methylation profiles.

PI3K Inhibition Impairs *BRCA1/2* Expression and Sensitizes *BRCA*-Proficient Triple-Negative Breast Cancer to PARP Inhibition 1036

Y.H. Ibrahim, C. García-García, V. Serra, L. He, K. Torres-Lockhart, A. Prat, P. Anton, P. Cozar, M. Guzmán, J. Grueso, O. Rodríguez, M.T. Calvo, C. Aura, O. Díez, I.T. Rubio, J. Pérez, J. Rodón, J. Cortés, L.W. Ellisen, M. Scaltriti, and J. Baselga

Précis: PI3K suppression represses *BRCA1/2* expression and increases the sensitivity of *BRCA*-wild-type breast cancer cells to PARP inhibitors via ERK activation.

Combining a PI3K Inhibitor with a PARP Inhibitor Provides an Effective Therapy for *BRCA1*-Related Breast Cancer 1048

A. Juvekar, L.N. Burga, H. Hu, E.P. Lunsford, Y.H. Ibrahim, J. Balmaña, A. Rajendran, A. Papa, K. Spencer, C.A. Lyssiotis, C. Nardella, P.P. Pandolfi, J. Baselga, R. Scully, J.M. Asara, L.C. Cantley, and G.M. Wulf

Précis: PI3K inhibition synergizes with PARP inhibitors *in vivo* to decrease the growth of *BRCA1*-mutant breast tumors, revealing a role for PI3K in the DNA damage response.

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

- A Megafund for Drug Development
- Clearing the Final Hurdles to the FDA
- Taking a Chance on Novelty
- Collaborating Against Blood Cancers
- Test Identifies Genetic Changes Preceding Cervical Cancer
- Cancer Drugs Cross Finish Line Faster in U.S.

ON THE COVER

Miyamoto and colleagues noninvasively assayed androgen receptor (AR) signaling activity in patients with prostate cancer by measuring levels of prostate-specific antigen (PSA) and prostate-specific membrane antigen (PSMA) in single circulating tumor cells (CTC). The CTCs of untreated patients showed an “AR-on” (PSA⁺/PSMA⁺) signature that switched to an “AR-off” (PSA[−]/PSMA⁺) signature after androgen deprivation therapy, but the CTCs of patients with castration-resistant prostate cancer (CRPC) were heterogeneous and had “AR-on,” “AR-off,” and “AR-mixed” (PSA⁺/PSMA⁺) signatures. The presence of “AR-mixed” CTCs was associated with a poor response to abiraterone acetate, suggesting that monitoring of AR signaling in CTCs may guide use of secondary hormonal therapies in patients with CRPC. For details, please see the article by Miyamoto and colleagues on page 995.

