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Distinct Epigenetic Mechanisms Distinguish TMPRSS2-ERG Fusion-Positive and -Negative Prostate Cancers ............... 979
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### 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

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

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 TMPRSS2–ERG Fusion-Negative Prostate Cancers Implicate an EZH2-Dependent Mechanism with miR-26a Hypermethylation .......................... 1024
Précis: EZH2 overexpression is caused by miR-26a hypermethylation in prostate cancers lacking the TMPRSS2–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
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
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.

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.