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REVIEW
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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 \textit{TMPRSS2–ERG} Fusion-Negative Prostate Cancers Implicate an EZH2-Dependent Mechanism with \textit{miR-26a} Hypermethylation .................. 1024
Précis: EZH2 overexpression is caused by \textit{miR-26a} hypermethylation in prostate cancers lacking the \textit{TMPRSS2–ERG} gene fusion, which have distinct DNA methylation profiles.

\textbf{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.

\textbf{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 \textit{BRCA1}-mutant breast tumors, revealing a role for PI3K in the DNA damage response.

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- 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.

\textbf{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.