## IN THIS ISSUE
Highlighted research articles .......................... 539

## NEWS IN BRIEF
Important news stories affecting the community .......... 542

## NEWS IN DEPTH
Chromosome Instability Drives Tumor Evolution .......... 546

## RESEARCH WATCH
Selected highlights of recent articles of exceptional significance from the cancer literature ............... 547

## ONLINE
For more News and Research Watch, visit Cancer Discovery online at http://cancerdiscovery.aacrjournals.org/content/early/by/section.

## VIEWS
**In The Spotlight**

Quantifying the Benefits of Genome-Driven Oncology ..... 552
A.M. Schram and D.M. Hyman
See article, p. 586

Toward Molecularly Driven Precision Medicine in Lung Adenocarcinoma .......... 555
D. Liu, N.I. Vokes, and E.M. Van Allen
See article, p. 596

Targeting BRAF-Mutant Colorectal Cancer: Progress in Combination Strategies ..................... 558
R. Sundar, D.S. Hong, S. Kopetz, and T.A. Yap
See article, p. 610

## REVIEW
Neoadjuvant Trials in ER+ Breast Cancer: A Tool for Acceleration of Drug Development and Discovery ... 561
A.L. Guerrero-Zotano and C.L. Arteaga

## RESEARCH BRIEF
An Acquired HER2
Gatekeeper Mutation Induces Resistance to Neratinib in a Patient with HER2 Mutant-Driven Breast Cancer ............... 575

Précis: A patient with breast cancer with an activating HER2 mutation who initially responded to neratinib acquired a HER2 mutation that promoted neratinib resistance, but may retain sensitivity to afatinib.

## RESEARCH ARTICLES
High-Throughput Genomics and Clinical Outcome in Hard-to-Treat Advanced Cancers: Results of the MOSCATO 01 Trial .......... 586

Précis: In a prospective clinical trial of patients with advanced solid tumors, genomics analyses identified genomic alteration-matched therapies that extended progression-free survival in 33% of patients.

See commentary, p. 552

Prospective Comprehensive Molecular Characterization of Lung Adenocarcinomas for Efficient Patient Matching to Approved and Emerging Therapies .......... 596
Précis: Comprehensive profiling of somatic tumor alterations identifies actionable genomic alterations in the majority of patients with advanced lung adenocarcinoma, allowing for selection of clinically beneficial matched targeted therapies.

See commentary, p. 555

A Phase Ib Dose-Escalation Study of Encorafenib and Cetuximab with or without Alpelisib in Metastatic BRAF-Mutant Colorectal Cancer ..... 610
Précis: The RAF inhibitor encorafenib in combination with the EGFR inhibitor cetuximab is tolerable and achieves responses in patients with BRAF-mutant colorectal cancer with or without PI3Kα inhibition with alpelisib.
See commentary, p. 558

ON THE COVER
Qamra and colleagues characterized epigenetic promoter alterations in gastric cancer and identified unaltered promoters, somatic tumor-specific promoters gained in tumors, and normal-specific promoters lost in tumors. Overall, 18% of the gastric cancer somatic promoters were alternative promoters that resulted in overexpression of alternative transcript isoforms as well as proteins with altered N-terminal peptide sequences, which may allow for increased proteomic diversity in gastric cancer. Further, alternative somatic promoter usage was linked to decreased tumor immunity. The N-terminal peptides downregulated by gastric cancer somatic promoters elicited immune responses, suggesting that the tumor-specific promoters may decrease tumor immunogenicity. Altogether, these findings identify tumor-specific alternative promoters in gastric cancer that may produce tumor-specific isoforms to promote tumor immune evasion. For details, please see the article by Qamra and colleagues on page 630.
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7 (6)

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