IN THIS ISSUE
Highlighted research articles ......................... 521

NEWS IN BRIEF
Important news stories affecting the community ........524

NEWS IN DEPTH
What Biden’s Presidency Will Mean for Cancer ..........527

RESEARCH WATCH
Selected highlights of recent articles of exceptional significance from the cancer literature ...............529

ONLINE
For more News and Research Watch, visit Cancer Discovery online at http://cancerdiscovery.aacrjournals.org/CDNews.

RESEARCH BRIEFS
Genetic Ancestry Contributes to Somatic Mutations in Lung Cancers from Admixed Latin American Populations .......... 591

In The Spotlight
Genetic Ancestry Correlations with Driver Mutations Suggest Complex Interactions between Somatic and Germline Variation in Cancer ..........534
F. Gomez, M. Griffith, and O.L. Griffith
See article, p. 591

At the Heart of Immune Checkpoint Inhibitor–Induced Immune Toxicity .................537
A. Young and J.A. Bluestone
See article, p. 614

Poorer Clinical Outcomes for Black Patients with AML: A Wake-Up Call for Better Data and Greater Understanding of Cancer Outcomes in All Ethnic Groups ... 540
P. Vyas
See article, p. 626

In Focus
Maturation Block in Childhood Cancer ...............542
S. Behjati, R.J. Gilbertson, and S.M. Pfister

REVIEWS
Opportunities and Challenges in Drug Development for Pediatric Cancers ..........545
T.W. Laetsch, S.G. DuBois, J. Glade Bender, M.E. Macy, and L. Moreno

Applications of CRISPR Genome Editing to Advance the Next Generation of Adoptive Cell Therapies for Cancer ..........560
S.M. Fix, A.A. Jazaeri, and P. Hwu

Diffuse Glioma Heterogeneity and Its Therapeutic Implications .......... 575
J.G. Nicholson and H.A. Fine

Précis: Tumor sequencing data from patients with lung cancer from Latin America revealed that Native American ancestry significantly affected tumors' somatic mutation profiles; the observed disparities arose from germline differences rather than environmental exposures.
See commentary, p. 534

A Critical Role for Fas-Mediated Off-Target Tumor Killing in T-cell Immunotherapy ..........599

Précis: Apoptotic FAS–FASL signaling enabled CD8+ T cells to exert cytotoxic effects on antigen-negative “bystander” tumor cells in vivo, possibly explaining how antigen-specific chimeric antigen receptor T-cell therapies can eliminate tumors with heterogeneous antigen expression.
A Genetic Mouse Model Recapitulates Immune Checkpoint Inhibitor–Associated Myocarditis and Supports a Mechanism-Based Therapeutic Intervention .......... 614


Précis: A new mouse model of immune checkpoint inhibitor–induced myocarditis was developed, enabling the discovery that abatacept may be useful in inhibitor–induced myocarditis was developed, enabling the discovery that abatacept may be useful in

Cell of Origin Influences Pancreatic Cancer Subtype ................. 660


Précis: Pancreatic ductal adenocarcinomas in adult genetically engineered mice could arise from either ductal or acinar cells, and tumors arising from each cell type had distinct transcriptional profiles that matched those of defined human pancreatic cancer subtypes.

The Lipogenic Regulator SREBP2 Induces Transferin in Circulating Melanoma Cells and Suppresses Ferroptosis .... 678


Précis: Melanoma circulating tumor cells (CTC) prevented ferroptotic death by upregulating SREBP2-mediated lipogenic pathways and iron homeostatic pathways, and blocking this escape mechanism by knocking out the gene encoding transferin hindered CTC tumor formation.

An Empirical Antigen Selection Method Identifies Neoantigens That Either Elicit Broad Antitumor T-cell Responses or Drive Tumor Growth ... 696


Précis: An ex vivo bioassay, ATLAS, was able to identify stimulatory and inhibitory neoantigens for the design of personalized anticancer vaccines; this assay pinpointed anti- and protumorigenic antigens, as demonstrated via in vivo experiments.

Durable Suppression of Acquired MEK Inhibitor Resistance in Cancer by Sequestering MEK from ERK and Promoting Antitumor T-cell Immunity .... 714


Précis: Type II RAF inhibitors provided distinct advantages over Type I RAF inhibitors when used in combination with MEK inhibitors in models with MAPK pathway alterations.
ON THE COVER

The pattern of somatic mutations in lung cancers varies among populations, including in Latin America, where lung cancer is the primary cause of cancer death. Using tumor-sequencing data from 601 and 552 patients with lung cancer (43% of whom did not smoke) from Mexico and Colombia, respectively, Carrot-Zhang and colleagues identified relationships between Native American ancestry and several important tumor characteristics. For instance, EGFR mutations, particularly oncogenic ones, were more common in those with higher Native American ancestry. The identified differences in somatic mutation profiles arose from germline variation rather than disparate environmental exposures. This work highlights the importance of the finer details of ancestry in cancer genetics. For more information, see the article by Carrot-Zhang and colleagues on page 591.