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## RESEARCH BRIEF
**Early Detection of Molecular Residual Disease in Localized Lung Cancer by Circulating Tumor DNA Profiling** ........ 1394

Précis: ctDNA profiling of pre- and post-treatment samples from patients with localized lung cancer identifies the presence of minimal residual disease earlier than standard imaging.
See commentary, p. 1368

**Endothelial Activation and Blood–Brain Barrier Disruption in Neurotoxicity after Adoptive Immunotherapy with CD19 CAR T Cells** ...... 1404

Précis: Endothelial activation and vascular disruption were associated with a high risk of severe neurotoxicity in 133 patients with B-cell malignancies treated with CD19-targeted CAR-T cell therapy.
See commentary, p. 1371

**Impaired HLA Class I Antigen Processing and Presentation as a Mechanism of Acquired Resistance to Immune Checkpoint Inhibitors in Lung Cancer** ...... 1420

Précis: Analysis of immune checkpoint inhibitor–resistant lung tumors revealed that loss of B2M expression may impair antigen processing to promote acquired resistance in patients with lung cancer.
A Transposon Screen Identifies Loss of Primary Cilia as a Mechanism of Resistance to SMO Inhibitors ...... 1436
X. Zhao, E. Pak, K.J. Ornell, M.F. Pazyra-Murphy, E.L. MacKenzie, E.J. Chadwick, T. Ponomaryov, J.F. Kelleher, and R.A. Segal
Précis: Mutations that result in loss of primary cilia promote resistance to SMO inhibitors by eliminating formation of the GLI2 repressor form, allowing persistent low-level activation of hedgehog signaling.
See commentary, p. 1374

mTOR and HDAC Inhibitors Converge on the TXNIP/Thioredoxin Pathway to Cause Catastrophic Oxidative Stress and Regression of RAS-Driven Tumors .................1450
Précis: Combined treatment with mTOR and HDAC inhibitors cooperatively suppresses thioredoxin to trigger excessive oxidative stress and induce cell death in NF1- and KRAS-mutant tumors.

Galectin-3, a Druggable Vulnerability for KRAS-Addicted Cancers ......... 1464
Précis: Inhibiting galectin-3 disrupts its interaction with integrin αβ3, preventing the association with mutant KRAS to reduce macropinocytosis, increase ROS, and suppress KRAS-mutant tumor growth and progression.

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ON THE COVER
Neurologic adverse events induced by autologous transfer of CD19-targeted chimeric antigen receptor-modified T (CAR-T) cells were investigated in 133 patients with B-cell acute lymphoblastic leukemia, chronic lymphocytic leukemia, or non-Hodgkin lymphoma who had received chemotherapy and CD19 CAR-T cell infusion. Cytokine release syndrome (CRS) preceded neurotoxicity in all 28 patients who developed grade 3+ neurotoxicity, and severe neurotoxicity was linked to endothelial activation and increased blood–brain barrier permeability. Signs of endothelial activation and vascular disruption were observed in the brain of a patient who died of CRS-induced neurotoxicity, and endothelial activation prior to treatment was linked to an increased risk of high-grade neurotoxicity. Altogether, these results identify risk factors for CD19 CAR-T cell therapy–induced neurotoxicity, and suggest that endothelial activation may serve as a biomarker for severe neurotoxicity. For details, please see the article by Gust, Hay, Hanafi, and colleagues on page 1404.