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Somatic HLA Class I Loss Is a Widespread Mechanism of Immune Evasion Which Refines the Use of Tumor Mutational Burden as a Biomarker of Checkpoint Inhibitor Response .......... 282

Précis: Across cancer types, loss of heterozygosity at the locus encoding HLA-I was an independent prognostic factor for response to immune checkpoint blockade, and its predictive power improved when combined with measures of tumor mutation burden.

Somatic HLA Class I Loss Is a Widespread Mechanism of Immune Evasion Which Refines the Use of Tumor Mutational Burden as a Biomarker of Checkpoint Inhibitor Response .......... 282

Précis: Across cancer types, loss of heterozygosity at the locus encoding HLA-I was an independent prognostic factor for response to immune checkpoint blockade, and its predictive power improved when combined with measures of tumor mutation burden.

Lower Airway Dysbiosis Affects Lung Cancer Progression .......... 293
Lower airway dysbiosis characterized by excessive colonization with oral commensal microbes, particularly Veillonella parvula, was a predictor of poor prognosis in lung cancer, and in vivo experiments supported a role for V. parvula colonization in decreasing survival.

See commentary, p. 224
The RNA m6A Reader YTHDF2 Maintains Oncogene Expression and Is a Targetable Dependency in Glioblastoma Stem Cells 480
Précis: In glioblastoma stem cells, YTHDF2 (which reads mRNA for the modified nucleotide N6-methyladenosine) stabilized MYC and VEGFA transcripts via an IGFBP3-mediated mechanism, and blocking IGF–IGF1R signaling in vivo hindered glioblastoma growth.

The Hepatic Microenvironment Uniquely Protects Leukemia Cells through Induction of Growth and Survival Pathways Mediated by LIPG 500
Précis: Liver-infiltrating leukemia stem cells in mice acquired a proliferative, chemotherapy-resistant phenotype characterized by overexpression of the gene encoding the lipase LIPG, which was sufficient to induce the same phenotype in non–liver-infiltrating leukemia cells.

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Correction: Impact of PD-1 Blockade on Severity of COVID-19 in Patients with Lung Cancers 520

The risk of skin cancers such as basal cell carcinoma and squamous cell carcinoma varies greatly across the body, and it is known that healthy aged skin cells often harbor cancer driver mutations, but whether these observations are connected has not been determined. Fowler and colleagues discovered that the mutation density in healthy human skin differed from location to location across the body. Common sites for skin cancer, such as the forearm, bore more mutations than uncommon sites, and the mutation profile suggested UV radiation as a cause. Interestingly, not only was there selection for cancer-associated mutations in healthy skin, but the DNA repair mechanisms used varied based on site. For more information, see the article by Fowler and colleagues on page 340.

ON THE COVER
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