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RESEARCH ARTICLES
Endothelial Activation and Blood–Brain Barrier Disruption in Neurotoxicity after Adoptive Immunotherapy with CD19 CAR-T Cells ...... 1404
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Impaired HLA Class I Antigen Processing and Presentation as a Mechanism of Acquired Resistance to Immune Checkpoint Inhibitors in Lung Cancer ...... 1420
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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.
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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.