CANCER DISCOVERY

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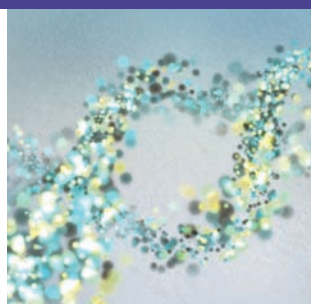
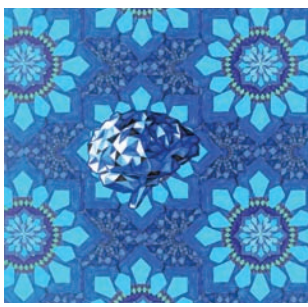

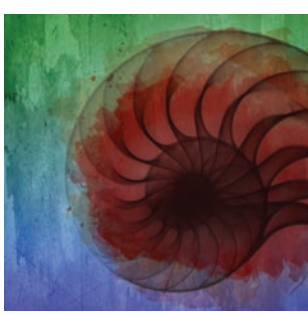
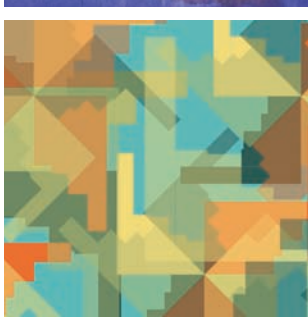
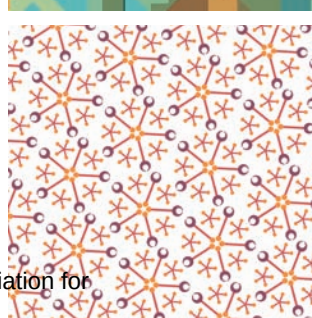

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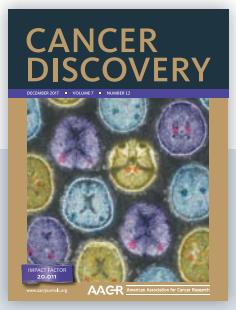

ON THE COVER Neurologic adverse events induced by autologous transfer of CD19-targeted chimeric antigen receptor-modified T (CAR-T) cells were investigated in 133 patients with B-cell acute lymphoblastic leukemia, chronic lymphocytic leukemia, or non-Hodgkin lymphoma who had received chemotherapy and 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.

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