Translational Activation of ATF4 through Mitochondrial Anaplerotic Metabolic Pathways Is Required for DLBCL Growth and Survival .......................... 50

Précis: ATF4 expression is required for DLBCL proliferation and is induced by rapid consumption of amino acids. Depletion of SIRT3 suppresses the TCA cycle and impairs ATF4 translation by increasing amino acid pools generated through autophagy, leading to cell death.

Next-Generation Sequencing of Minimal Residual Disease for Predicting Relapse after Tisagenlecleucel in Children and Young Adults with Acute Lymphoblastic Leukemia ............ 66

Précis: NGS-MRD >0 is highly predictive of relapse after tisagenlecleucel therapy for ALL. Serial monitoring of NGS-MRD and B-cell aplasia identifies high-risk patients with sufficient time for interventions to prevent relapse.

See commentary, p. 2

Correction: Tumor Burden Limits Bispecific Antibody Efficacy through T-cell Exhaustion Averted by Concurrent Cytotoxic Therapy .......................... 82

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ON THE COVER

Novel next-generation sequencing technologies are demystifying blood cancer patient prognosis and relapse risk. On page 66, Pulsipher et al. report minimal residual disease (MRD) detected by next-generation sequencing of bone marrow samples (BMNGS-MRD) and B-cell recovery in acute lymphoblastic leukemia (ALL) patients as strong predictors of relapse following CD19-targeting CAR T-cell therapy. BMNGS-MRD is more sensitive than multiparameter flow cytometry and identifies high-risk patients at an earlier time point prior to relapse. On page 2, Ghorashian and Bartram put Pulsipher et al. In The Spotlight, providing an overview of the current state of MRD detection in the clinic and the impact this research may have in treating relapsing patients. On page 5, Roschewski et al. review the utility and technical challenges to leveraging circulating tumor DNA (ctDNA) isolated from blood plasma for characterizing disease, assessing response, and detecting relapse in lymphoma patients. Though still in early stages and in need of validation, ctDNA analysis shows great promise as a sensitive, noninvasive biomarker for tumor genotyping and predicting patient outcomes.

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