Précis: Hematologic malignancy patients have intrinsic deficits in humoral immunity that are further compounded by cancer-directed therapies, resulting in attenuated antibody responses to COVID-19 vaccination.

Predictors of Humoral Response to SARS-CoV-2 Vaccination after Hematopoietic Cell Transplantation and CAR T-cell Therapy........... 577

Précis: Immune recovery post–cellular therapies is an important predictor of response to the anti-SARS-CoV-2 vaccine and can be used to guide timing of primary vaccination, as well as booster vaccine, after therapy.

Integrative Genomic Analysis of Pediatric Myeloid-Related Acute Leukemias Identifies Novel Subtypes and Prognostic Indicators ................. 586
M. Fornerod, J. Ma, S. Noort, Y. Liu, M.P. Walsh, L. Shi, S. Nance, Y. Liu, Y. Wang, G. Song, T. Lamprecht, J. Easton, H.L. Mulder, D. Yergeau, J. Myers, J.L. Kamens, E.A. Obeng, M. Pigazzi, M. Jarosova, C. Kelaidi, S. Polychronopoulou, J.K. Lamba, S.D. Baker, J.E. Rubnitz; D. Reinhardt; for the Berlin-Frankfurt-Munster Study Group (BFM); M.M. van den Heuvel-Eibrink; for the Dutch Children’s Oncology Group (DCOG); F. Locatelli; for the Associazione Italiana di Ematologia e Oncologia Pediatrica (AIEOP); H. Hasle; for the Nordic Society for Pediatric Hematology and Oncology (NOPHO); J.M. Klco, J.R. Downing, J. Zhang, S. Pounds; C.M. Zwaan; for the Dutch Children’s Oncology Group (DCOG); and T.A. Gruber; for St. Jude Children’s Research Hospital Study Group (SJCRH)

Précis: Integrating somatic mutation analysis and gene expression profiling distinguishes pediatric AML subtypes with differential prognoses and clinical risks.
Aberrant Extrafollicular B Cells, Immune Dysfunction, Myeloid Inflammation, and MyD88-Mutant Progenitors Precede Waldenstrom Macroglobulinemia .... 600

Précis: A distinct immune landscape marked by features across immune cell types, including nonmalignant B cells and early lymphoid progenitors, establishes an environment conducive to WM.

Phase II Trial of Pembrolizumab after High-Dose Cytarabine in Relapsed/Refractory Acute Myeloid Leukemia ......................... 616

Précis: Immune checkpoint blockade with pembrolizumab after high-dose cytarabine salvage chemotherapy is tolerable and leads to encouraging clinical outcomes in relapsed/refractory AML patients.

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Overcoming Acquired Epigenetic Resistance to BTK Inhibitors ............ 630

Précis: B-cell malignancies evolve early resistance to BTK inhibitors via epigenetic reprogramming of B-cell receptor–dependent NF-κB signaling, a mechanism that suggests therapeutic strategies to overcome the resistance.

See commentary, p. 555

NOT-Gated CD93 CAR T Cells Effectively Target AML with Minimized Endothelial Cross-Reactivity ............... 648

Précis: CD93 CAR T cells eliminate AML in preclinical models without targeting hematopoietic progenitor cells, and a NOT-gated CAR engineering strategy mitigates on-target, off-tumor toxicity to endothelial cells.

See commentary, p. 559

Blood cancer patients are among the most vulnerable to COVID-19 infection. In this issue, two clinical studies from Memorial Sloan Kettering Cancer Center show they may also be among the least protected by the vaccines. On page 568, Chung et al. report low antibody titers and even lower neutralizing activity among 551 patients with leukemia, lymphoma, and myeloma as compared to healthy controls. Venetoclax, kinase inhibitors, and B-cell antigen–targeting therapies further cripple vaccine-elicited immunity. On page 577, Tamari et al. show that immune recovery after cellular therapies of hematologic cancers correlates with response to COVID-19 vaccines. In a pooled data analysis of these and other studies, Ribas et al. (page 562) conclude that hematologic cancer patients have impaired antibody response to vaccination and boosters, and call for public health measures to protect this vulnerable group. Among the recommendations is to give booster vaccine doses to patient’s caregivers and household members. The cover image illustrates how this strategy can prevent viral spread to and from patients with blood cancer. Artwork by Katie Vicari.

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BLOOD CANCER DISCOVERY

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