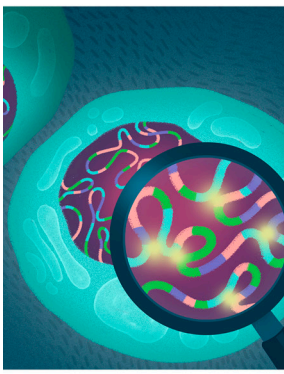
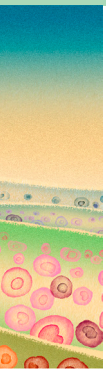
BLOOD CANCER DISCOVERY

JULY 2025 ■ VOLUME 6 ■ NUMBER 4

CONTENTS







Précis: Systematic discovery of enhancer hijacking in complex karyotype acute myeloid leukemia via the new tool Pyjacker identifies MNX1 activation, a novel leukemogenic event that can result from 7q deletion, among other events.

Précis: Double-hit Myc/Bcl-2 lymphomas lacking surface BCR evolve from *BCL2*-translocated dark zone–like state via reactivating RAG, followed by *MYC* translocation into unproductively recombined Ig-lambda locus.

See commentary, p. 284

ON THE COVER The surface of a healthy B lymphocyte is covered with Y-shaped B-cell receptors (BCR), which transmit signals as vital for B-cell survival as sunlight is for trees (left). In this issue, Varano and colleagues shed light on the biology of high-grade B-cell lymphomas with "double-hit" *MYC* and *BCL2* rearrangements (HGBCL-DH), which resemble a germinal center's dark zone cells and survive without detectable BCR on the surface. HGBCL-DH linger in a dark zone state, reactivating RAG recombinases, which then translocate oncogenes into immunoglobulin light-chain loci in a futile attempt to revise BCR specificity. In this setting, lymphoma cells survive without light (chain) and functional surface BCR, sustained instead by a residual signal ("glow") of the intracellular immunoglobulin heavy chain. For more information, see article on page 364 and a Spotlight by Shevchenko and Hodson on page 284.

doi: 10.1158/2643-3230.BCD-6-4-CVR