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Précis: Comparing scRNA-seq data of >1 million cells from 318 patients to a reference atlas of >260K normal human bone marrow cells revealed diverse ways in which differentiation can be disrupted in AML.

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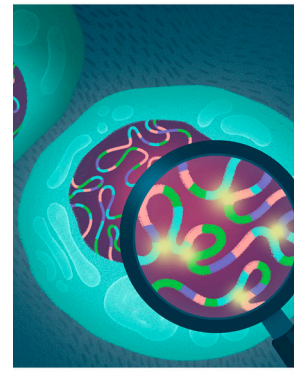
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Précis: Systematic discovery of enhancer hijacking in complex karyotype acute myeloid leukemia via the new tool Pyjacker identifies MNX1 activation, a novel leukemogenic event that can result from 7q deletion, among other events.

B-cell Receptor Silencing Reveals the Origin and Dependencies of High-Grade B-cell Lymphomas with MYC and BCL2 Rearrangements.....364

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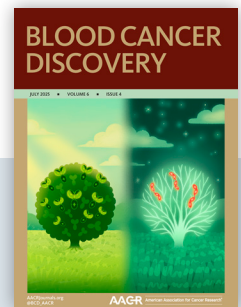
Précis: Double-hit Myc/Bcl-2 lymphomas lacking surface BCR evolve from BCL2-translocated dark zone-like state via reactivating RAG, followed by MYC translocation into unproductively recombined Ig-lambda locus.

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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.

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