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Précis: T-cell receptor sequencing of 45 tumor regions from 11 patients with NSCLC found T-cell repertoire intratumor heterogeneity that was associated with disease relapse and reduced disease-free survival.

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Précis: In-depth genetic characterization defines cholangiocarcinoma subtypes and identifies previously undescribed drivers, noncoding promoter mutations, and structural variants.

Superenhancer Analysis Defines Novel Epigenomic Subtypes of Non-APL AML, Including an RARA Dependency Targetable by SY-1425, a Potent and Selective RARα Agonist .......... 1136


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Overcoming the Immunosuppressive Tumor Microenvironment of Hodgkin Lymphoma Using Chimeric Antigen Receptor T Cells ..................... 1154


Précis: Anti-CD123 chimeric antigen receptor T cells overcome the immunosuppressive tumor microenvironment in Hodgkin lymphoma by targeting both malignant cells and tumor-associated macrophages.

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BLIMP1 Induces Transient Metastatic Heterogeneity in Pancreatic Cancer .................. 1184


Précis: Pancreatic ductal adenocarcinoma metastasis is promoted by hypoxia and HIF-driven upregulation of the prometastatic transcription factor BLIMP1.

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ON THE COVER

To determine how intratumor heterogeneity in the T-cell landscape correlates with the genomic landscape and with patient outcome in non–small cell lung cancer (NSCLC), Reuben and colleagues characterized the T-cell repertoire in a cohort of 11 patients with NSCLC who had previously been subject to whole-exome sequencing. T-cell receptor (TCR) sequencing profiled 45 tumor regions across the 11 tumors and revealed a high level of intratumor heterogeneity, with differences in T-cell density, clonality, and repertoire. TCR intratumor heterogeneity was linked to neoantigen heterogeneity and was correlated with disease relapse and reduced disease-free survival in patients with NSCLC. These findings link T-cell repertoire heterogeneity to genomic intratumor heterogeneity and relapse in NSCLC. For details, please see the article by Reuben and colleagues on page 1088.