Cancer Research. on November 15, 2017. © 2017 American Association for Cancer Research.

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 RARα Dependency Targetable by SY-1425, a Potent and Selective RARα Agonist ...................... 1136


Précis: Characterization of enhancer landscapes in patients with AML identified a subset of non-APL AML with an RARA superenhancer that confers sensitivity to treatment with the selective RARα agonist SY-1425.

See commentary, p. 1065

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.

Loss of MutL Disrupts CHK2-Dependent Cell-Cycle Control through CDK4/6 to Promote Intrinsic Endocrine Therapy Resistance in Primary Breast Cancer ................. 1168


Précis: Dysregulation of the mismatch repair complex MutL promotes intrinsic resistance to endocrine therapy in ER+ breast cancer model systems and patients and may confer sensitivity to CDK4/6 inhibitors.

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.

See commentary, p. 1067

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.