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Précis: Myeloproliferative neoplasm–associated calreticulin mutations elicit T-cell responses that can be promoted by immune checkpoint blockade with pembrolizumab.

Interferon Signaling Is Diminished with Age and Is Associated with Immune Checkpoint Blockade Efficacy in Triple-Negative Breast Cancer ............... 1208
Précis: Immune dysfunction associated with age in a mouse model of TNBC leads to lack of response to immune checkpoint blockade treatment that can be rescued by the addition of a STING agonist.

Loss of EZH2 Repograms BCAA Metabolism to Drive Leukemic Transformation ............... 1228
ON THE COVER

Hundeyin, Kurz, and colleagues discovered that innate αβ T cells (αβT) were a substantial part of the T-lymphocyte population in human and mouse pancreatic ductal adenocarcinoma (PDA) tumors. These tumor-infiltrating αβTs were highly activated, had a phenotype markedly different from those in the periphery, and were protective against PDA progression in mice. Demonstrating the relevance of these findings to human disease, treatment of patient-derived organotypic PDA tumor spheroids with autologous αβTs led to conventional T-cell activation. The mechanism involved activation of CCR5, which induced immunogenic macrophage polarization. Collectively, these findings suggest that αβT-based cell therapies should be investigated for the treatment of PDA. For details, please see the article by Hundeyin, Kurz, and colleagues on page 1288.
CANCER DISCOVERY

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