RESEARCH BRIEF

V211D Mutation in MEK1 Causes Resistance to MEK Inhibitors in Colon Cancer


Précis: A previously uncharacterized mutation in mitogen-activated protein kinase 1 (MEK1) is activating and resistant to allosteric MEK inhibitors, but sensitive to ATP-competitive inhibitors.

RESEARCH ARTICLES

Immune Checkpoint Blockade Enhances Shared Neoantigen-Induced T-cell Immunity Directed against Mutated Calreticulin in Myeloproliferative Neoplasms

C. Cimen Bozkus, V. Roudko, J.P. Finnigan, J. Mascarenhas, R. Hoffman, C. Iancu-Rubin, and N. Bhardwaj

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


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 Reprograms BCAA Metabolism to Drive Leukemic Transformation

Précis: Knockout of the PRC2 component EZH2 and activating NRAS mutations cooperate to cause MPN progression to leukemia by upregulating the BCAA-metabolism enzyme BCAT1.
See commentary, p. 1158

Glioma Stem Cell–Specific Superenhancer Promotes Polysaturated Fatty-Acid Synthesis to Support EGFR Signaling

Précis: Glioma stem cells upregulate the polysaturated synthesis enzyme ELOVL2, which alters cell-membrane properties and composition to maintain EGFR signaling.
See commentary, p. 1161

Oncogenic KRAS Induces NIX-Mediated Mitophagy to Promote Pancreatic Cancer

Précis: Activating Kras mutations cause upregulation of the mitophagy-promoting protein NIX, which alters mitochondrial function and enhances redox capacity to support progression of pancreatic cancer.
See commentary, p. 1164

PTEN Methylation by NSD2 Controls Sensitivity to DNA Damage


Hundeyin, Kurz, and colleagues discovered that innate αβ T cells (iαβT) were a substantial part of the T-lymphocyte population in human and mouse pancreatic ductal adenocarcinoma (PDA) tumors. These tumor-infiltrating iαβTs 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 iαβTs led to conventional T-cell activation. The mechanism involved activation of CCR5, which induced immunogenic macrophage polarization. Collectively, these findings suggest that iαβT-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.
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