Antitumor Activity Associated with Prolonged Persistence of Adoptively Transferred NY-ESO-1c259T Cells in Synovial Sarcoma


Précis: In a prospective clinical study of 12 patients with synovial sarcoma, adoptive transfer of autologous NY-ESO-1c259 cells resulted in a 50% objective response rate and long-term persistence of a clonally diverse, fully functional NY-ESO-1c259 cells.

See commentary, p. 914

Clinical and Biological Correlates of Neurotoxicity Associated with CAR T-cell Therapy in Patients with B-cell Acute Lymphoblastic Leukemia


Précis: Elevation of proinflammatory cytokines and disruption of blood–CSF barrier are associated with CAR T cell–driven neurotoxicity in patients with B-ALL who were treated with CD19 CAR 19-28ζ T cells.

See commentary, p. 918

Enhancing the Potency and Specificity of Engineered T Cells for Cancer Treatment


Précis: CAR T cells engineered to recognize three independent tumor antigens for activation, costimulation, and cytokine support limit on-target, off-tumor toxicity for enhanced antitumor efficacy and safety.

See commentary, p. 918
MACROD2 Haploinsufficiency Impairs Catalytic Activity of PARP1 and Promotes Chromosome Instability and Growth of Intestinal Tumors


Précis: Deletions of the mono-ADP-ribosylhydrolase gene MACROD2 enhance intestinal tumorigenesis in a haploinsufficient manner by suppressing PARP1 activity, leading to increased sensitivity to DNA damage and driving chromosome instability.

See commentary, p. 921

Adipocyte-Derived Lipids Mediate Melanoma Progression via FATP Proteins


Précis: Melanoma tumorigenesis is accelerated by the uptake of long-chain fatty acids from adipocytes via the FATP1 lipid transporter, and this adipocyte-melanoma cell cross-talk may be disrupted by FATP inhibitors.

YAP Is Essential for Treg-Mediated Suppression of Antitumor Immunity


Précis: YAP expression in Treg cells upregulates the activin receptor to enhance SMAD/TGFβ signaling, promote Treg differentiation, and suppress antitumor immunity, suggesting potential immunotherapeutic targets.

MACROD2 locus, which encodes a mono-ADP-ribosylhydrolase implicated in the regulation of PARP1, undergoes recurrent focal deletions in a subset of human colorectal cancers. Consistent with a tumor-suppressive role, loss of MACROD2 increased the growth of intestinal tumors in mice in a haploinsufficient manner. This effect was mediated at least in part via repression of PARP1 activity in response to MACROD2 deletion, leading to impaired DNA repair and enhanced sensitivity to genotoxic stress. MACROD2 loss recapitulated the phenotype of PARP1 inhibitor treatment, including mitotic chromosome missegregation and increased structural and numerical chromosome abnormalities, suggesting that MACROD2 loss promotes chromosome instability and aneuploidy. These results define MACROD2 as a haploinsufficient tumor suppressor essential for maintaining genome integrity in human colorectal cancer. For details, please see the article by Sakthianandeswaren, Parsons, Mouradov, and colleagues on page 988.