Adoptive T-cell transfer, but an inflammation-induced melanoma cell dedifferentiation resulted in loss of the MART1 tumor antigen and tumor relapse.

**Antitumor Activity Associated with Prolonged Persistence of Adoptively Transferred NY-ESO-1c259 T 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 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.

Corrections

Correction: Identifying and Targeting Sporadic Oncogenic Genetic Aberrations in Mouse Models of Triple-Negative Breast Cancer

Correction: Linking Tumor Mutations to Drug Responses via a Quantitative Chemical–Genetic Interaction Map.

ON THE COVER

Sakthianandeswaren, Parsons, Mouradov, and colleagues found that the 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.