893  What We’re Reading

894  Masters of Immunology

895  Immunological Mechanisms Underneath the Efficacy of Cancer Therapy

903  Clinical Response of a Patient to Anti–PD-1 Immunotherapy and the Immune Landscape of Testicular Germ Cell Tumors

910  Classical Hodgkin Lymphoma with Reduced β2M/MHC Class I Expression Is Associated with Inferior Outcome Independent of 9p24.1 Status

917  Restoring Retinoic Acid Attenuates Intestinal Inflammation and Tumorigenesis in APCMin/þ Mice

927  MicroRNA let-7, T Cells, and Patient Survival in Colorectal Cancer

936  Kinase Regulation of Human MHC Class I Molecule Expression on Cancer Cells

948  Systemic GM-CSF Recruits Effector T Cells into the Tumor Microenvironment in Localized Prostate Cancer
Targeted Next Generation Sequencing Identifies Markers of Response to PD-1 Blockade
Douglas B. Johnson, Garrett M. Frampton, Matthew J. Rith, Erik Yusko, Yaomin Xu, Xingyi Guo, Riley C. Ennis, David Fabrizio, Zachary R. Chalmers, Joel Greenhowe, Siraj M. Ali, Sohail Balasubramanian, James X. Sun, Yutung He, Dennie T. Frederick, Igor Puzanov, Justin M. Balko, Justin M. Cates, Jeffrey S. Ross, Catherine Sanders, Harlan Robins, Yu Shyr, Vincent A. Miller, Philip I. Stephens, Ryan J. Sullivan, Jeffrey A. Sosman, and Christine M. Lovly

Mutational load, by whole exome sequencing, can correlate with immunotherapy responses. Assessing melanoma mutational load of a fraction of the genome, by hybrid capture–based NGS, provided an accurate surrogate for WES determinations, and predicted response to anti–PD-1.

CXCR2-Dependent Accumulation of Tumor-Associated Neutrophils Regulates T-cell Immunity in Pancreatic Ductal Adenocarcinoma
Timothy Chao, Emma E. Furth, and Robert H. Vonderheide

Tumor-associated neutrophils found in pancreatic tumors were dependent on CXCR2 ligands. The signaling pathways that induce CXCR2 ligand expression were identified, and preventing neutrophil accumulation allowed activated T cells access to the tumor, making CXCR2 a potential therapeutic target.

ABOUT THE COVER

Patients with familial adenomatous polyposis (FAP) have inflamed colons and have a high risk of colon cancer. These patients have defective retinoic acid (RA) metabolism that produces a local deficit of RA in the tumor milieu. Using a mouse model of FAP, decreased or absent RA encouraged disease progression, but inhibiting an enzyme that catabolizes RA ameliorated disease. One of the effects of increasing RA was to dampen the inflammatory phenotype of gut dendritic cells, and these cells were found to be crucial for adenoma formation. Read more in the article by Penny and colleagues starting on page 917 of this issue. The confocal microscopy image is of an FAP polyp, with red labeling an inhibitor of the RA metabolic pathway, CTBP1, and green denoting dendritic cells labeled with DC-SIGN (photo by HL Penny, of the Edgar G Engleman lab). Artwork by Lewis Long.

IL2 Variant Circumvents ICOS\(^+\) Regulatory T-cell Expansion and Promotes NK Cell Activation
Geok Choo Sim, Chengwen Liu, Ena Wang, Hui Liu, Caitlin Creasy, Zhirnin Dai, Willem W. Overwijk, Jason Roszik, Francesco Marincola, Patrick Hwu, Elizabeth Grimm, and Laszlo Radvanyi

IL2 is not commonly used as immunotherapy due to its induction of regulatory T cells and dangerous cytokine storms. The IL2 variant, F42K, promoted the expansion and activation of antitumor NK cells without inducing highly suppressive Tregs.