WHAT WE'RE READING

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MASTERS OF IMMUNOLOGY

894 About the Masters

895 Immunological Mechanisms Underneath the Efficacy of Cancer Therapy
Lorenzo Galluzzi, Laurence Zitvogel, and Guido Kroemer

CANCER IMMUNOLOGY MINIATURES

903 Clinical Response of a Patient to Anti–PD-1 Immunotherapy and the Immune Landscape of Testicular Germ Cell Tumors
Shalin Shah, James E. Ward, Riyue Bao, Curtis R. Hall, Bruce E. Brockstein, and Jason J. Luke
A patient with testicular germ cell tumor (TGCT) responded to PD-1 blockade. A T-cell signature in the TGCT cohort of The Cancer Genome Atlas predicted benefit from immunotherapy and suggested an immunoinhibitory role for α-fetoprotein.

PRIORITY BRIEF

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

RESEARCH ARTICLES

917 Restoring Retinoic Acid Attenuates Intestinal Inflammation and Tumorigenesis in APCMin/+ Mice
Intestinal adenomas are driven by inflammation in familial adenomatous polyposis (FAP) and its APCMin/+ mouse model. FAP patients have reduced intestinal retinoic acid; restoring it in mice ameliorated inflammation and reduced tumor burden, suggesting therapeutic approaches for FAP.

927 MicroRNA let-7, T Cells, and Patient Survival in Colorectal Cancer
Ruoxu Dou, Reiko Nishihara, Yin Cao, Tsuyoshi Hamada, Kosuke Mima, Atsuhiro Masuda, Yohei Masugi, Yan Shi, Mancang Gu, Wanwan Li, Annacarolina da Silva, Katsuhiko Nisho, Xuehong Zhang, Jeffrey A. Meyerhardt, Edward L. Giovannucci, Andrew T. Chan, Charles S. Fuchs, Zhi Rong Qian, and Shuji Ogino
The population-based data presented in this study support a possible role for microRNA let-7a in the suppression of antitumor immunity in colorectal cancer patients. This may have implications for expanding the benefit of immunotherapy through targeting microRNAs.

936 Kinase Regulation of Human MHC Class I Molecule Expression on Cancer Cells
Elliott J. Brea, Claire Y. Oh, Eusebio Manchado, Sadna Budhu, Ron S. Gejman, George Mo, Patricia Mondello, James E. Han, Casey A. Jarvis, David Ullmer, Qing Xiang, Aaron Y. Chang, Ralph J. Garippa, Taha Menghoub, Jedd D. Wolchok, Neal Rosen, Scott W. Lowe, and David A. Scheinberg
Kinome screens revealed EGFR and MEK as key to reduced MHC-I expression on many tumors. FDA-approved inhibitors of these kinases increased surface MHC-I, providing a rationale for clinically testing similar kinase inhibitors with immunotherapies dependent on MHC-I.

948 Systemic GM-CSF Recruits Effector T Cells into the Tumor Microenvironment in Localized Prostate Cancer
Xiao X. Wei, Stephen Chan, Serena Kweek, Jera Lewis, Vinh Dao, Li Zhang, Matthew R. Cooperberg, Charles I. Ryan, Amy M. Lin, Terence W. Friedlander, Brian Rini, Christopher Kane, Jeffrey P. Simko, Peter R. Carroll, Eric J. Small, and Lawrence Fong
GM-CSF is a component of many combination immunotherapeutic strategies. This phase I clinical study investigated GM-CSF effects on circulating and intratumoral immune cells, and found that infiltration of antigen-presenting cells was unaffected, but intratumoral CD8+ T cells increased.
Targeted Next Generation Sequencing Identifies Markers of Response to PD-1 Blockade

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.

IL2 Variant Circumvents ICOS+ Regulatory T-cell Expansion and Promotes NK Cell Activation
Geok Choo Sim, Chengwen Liu, Hui Liu, Caitlin Creasy, Zhimin 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.

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.