

## WHAT WE'RE READING

- 893 What We're Reading

## 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  $\alpha$ -fetoprotein.*

## PRIORITY BRIEF

- 910 Classical Hodgkin Lymphoma with Reduced  $\beta_2M$ /MHC Class I Expression Is Associated with Inferior Outcome Independent of 9p24.1 Status  
Margaretha G.M. Roemer, Ranjana H. Advani, Robert A. Redd, Geraldine S. Pinkus, Yasodha Natkunam, Azra H. Ligon, Courtney F. Connelly, Christine J. Pak, Christopher D. Carey, Sarah E. Daadi, Bjoern Chapuy, Daphne de Jong, Richard T. Hoppe, Donna S. Neuberg, Margaret A. Shipp, and Scott J. Rodig  
*Analysis of Hodgkin lymphomas revealed frequent reduction/loss of antigen-presentation proteins and 9p24.1/PD-L1/PD-L2 alterations. These immune evasion mechanisms had independent prognostic value after frontline therapy and prompt speculation regarding alternative mechanisms of action of PD-1 blockade.*

## RESEARCH ARTICLES

- 917 Restoring Retinoic Acid Attenuates Intestinal Inflammation and Tumorigenesis in APC<sup>Min/+</sup> Mice  
Hweixian Leong Penny, Tyler R. Prestwood, Nupur Bhattacharya, Fionna Sun, Justin A. Kenkel, Matthew G. Davidson, Lei Shen, Luis A. Zuniga, E. Scott Seeley, Reetesh Pai, Okmi Choi, Lorna Tolentino, Jinshan Wang, Joseph L. Napoli, and Edgar G. Engleman  
*Intestinal adenomas are driven by inflammation in familial adenomatous polyposis (FAP) and its APC<sup>Min/+</sup> 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, Atsuhiko Masuda, Yohei Masugi, Yan Shi, Mancang Gu, Wanwan Li, Annacarolina da Silva, Katsuhiko Noshio, 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, Patrizia Mondello, James E. Han, Casey A. Jarvis, David Ulmert, Qing Xiang, Aaron Y. Chang, Ralph J. Garippa, Taha Merghoub, 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 Kwek, Jera Lewis, Vinh Dao, Li Zhang, Matthew R. Cooperberg, Charles J. 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<sup>+</sup> T cells increased.*

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## 959 Targeted Next Generation Sequencing Identifies Markers of Response to PD-1 Blockade

Douglas B. Johnson, Garrett M. Frampton, Matthew J. Rioth, Erik Yusko, Yaomin Xu, Xingyi Guo, Riley C. Ennis, David Fabrizio, Zachary R. Chalmers, Joel Greenbowe, Siraj M. Ali, Sohail Balasubramanian, James X. Sun, Yuting 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 J. 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.*

## 968 CXCR2-Dependent Accumulation of Tumor-Associated Neutrophils Regulates T-cell Immunity in Pancreatic Ductal Adenocarcinoma

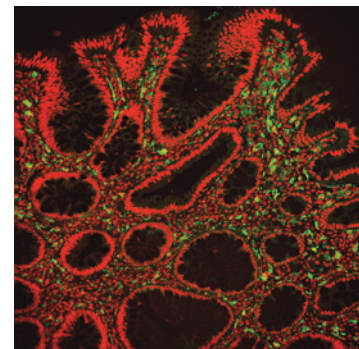
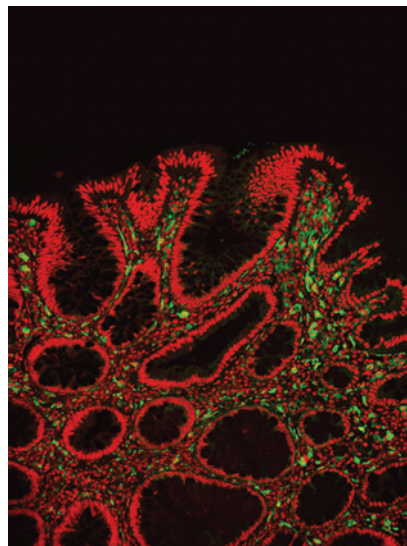
Timothy Chao, Emma E. Furth, and Robert H. Vonderheide  
*Tumor-associated neutrophils found in pancreatic tumors were dependent on CXCR2 ligands. The signaling pathways that induce CXCR2 ligand expression were identified, and preventing neutrophil accumulation allowed activated T cells access to the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

## 983 IL2 Variant Circumvents ICOS<sup>+</sup> Regulatory T-cell Expansion and Promotes NK Cell Activation

Geok Choo Sim, Chengwen Liu, Ena Wang, 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.



# Cancer Immunology Research

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*Cancer Immunol Res* 2016;4:893-994.

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