### WHAT WE'RE READING

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A Sampling of Highlights from the Literature

### CANCER IMMUNOLOGY AT THE CROSSROADS

990  
Jonathan A. Trujillo, Randy F. Sweis, Riyue Bao, and Jason J. Luke

### CANCER IMMUNOLOGY MINIATURES

1001  
Response to Immune Checkpoint Inhibition in Two Patients with Alveolar Soft-Part Sarcoma  
Jeremy Lewin, Scott Davidson, Nathaniel D. Anderson, Beatrice Y. Lau, Jacalyn Kelly, Uri Tabori, Samer Salah, Marcus O. Butler, Kyaw L. Aung, Adam Shliefen, Brendan C. Dickson, and Albiniru R. Abdul Razak  
Two patients with ASPS responded to immune checkpoint inhibition. Genomic analysis of a larger group of patients demonstrated molecular mismatch repair deficiency signatures in 71% of patients. Immune checkpoint blockade may be a useful therapy for ASPS.

1008  
Siglec-6 on Chronic Lymphocytic Leukemia Cells Is a Target for Post-Allogeneic Hematopoietic Stem Cell Transplantation Antibodies  
Jing Chang, Haiyong Peng, Brian C. Shaffer, Sivasubramanian Baskar, Ina C. Wecken, Matthew G. Cyr, Gustavo J. Martinez, Jo Soden, Jim Freeth, Adrian Wiestner, and Christoph Rader  
Mining the antibody repertoire of patients responding well to allogeneic hematopoietic stem cell transplantation (alloHST) can unveil targets with therapeutic potential. Through the use of phage display, Siglec-6 was identified as a major antigenic target of such antibodies.

1014  
IL35 Hinders Endogenous Antitumor T-cell Immunity and Responsiveness to Immunotherapy in Pancreatic Cancer  
Bhalchandra Mirlekar, Daniel Michaud, Ryan Searsy, Kevin Greene, and Yuliya Pylaeva-Gupta  
IL35 was identified as a major regulator of T cell-mediated antitumor responses in pancreatic ductal adenocarcinoma. IL35 deficiency in vivo allowed for increased effector T-cell infiltration into tumors and improved the efficacy of anti–PD-1 therapy.

1025  
Enhancement of Peptide Vaccine Immunogenicity by Increasing Lymphatic Drainage and Boosting Serum Stability  
Jing Chang, Haiyong Peng, Brian C. Shaffer, Sivasubramanian Baskar, Ina C. Wecken, Matthew G. Cyr, Gustavo J. Martinez, Jo Soden, Jim Freeth, Adrian Wiestner, and Christoph Rader  
Augmented antitumor vaccines were synthesized by conjugating albumin-binding moieties to peptide antigens. This platform improved vaccine stability and lymphatic distribution, leading to augmented and extended antigen presentation in lymph nodes and enhanced CD8+ T-cell priming.

1039  
Improved Risk-Adjusted Survival for Melanoma Brain Metastases in the Era of Checkpoint Blockade Immunotherapies: Results from a National Cohort  
J. Bryan Iorgulescu, Maya Harary, Cheryl K. Zogg, Keith L. Ligon, David A. Reardon, F. Stephen Hodi, Ayal A. Aizer, and Timothy R. Smith  
Melanoma patients presenting with brain metastases have been mostly excluded from treatment trials. A large-scale analysis of these patients from a national cohort revealed that after immune checkpoint blockade, median and 4-year overall survival were significantly improved.

1046  
Circulating Tumor Microparticles Promote Lung Metastasis by Reprogramming Inflammatory and Mechanical Niches via a Macrophage-Dependent Pathway  
Huaifeng Zhang, Yuandong Yu, Li Zhou, Jingwei Ma, Ke Tang, Pingwei Xu, Tianran Ji, Xiaoyu Liang, Jia Li, Wenshan Dong, Tianzhen Zhang, Degao Chen, Jing Xie, Yuying Liu, and Bo Huang  
Lung macrophages are induced by tumor-derived microparticles to drive development of metastasis via mediators that promote immune, inflammatory, and mechanical reprogramming of the microenvironment. Elucidation of this pathway has implications for therapeutic prevention or treatment of lung metastasis.
Mechanisms by Which Dendritic Cells Present Tumor Microparticle Antigens to CD8⁺ T Cells

Dual PD-1 and CTLA-4 Checkpoint Blockade

Safety and Efficacy of Re-treating with Immunotherapy after Immune-Related Adverse Events in Patients with NSCLC

Reducing Ex Vivo Culture Improves the Antileukemic Activity of Chimeric Antigen Receptor (CAR) T Cells

Cytomegalovirus Serostatus Affects Autoreactive NK Cells and Outcomes of IL2-Based Immunotherapy in Acute Myeloid Leukemia

About the Cover

Although immunotherapy has shown success in treating a variety of cancers, patients with pancreatic ductal adenocarcinoma (PDA) remain unresponsive to treatment, and the lack of efficient antitumor responses is not yet well understood. Mirlekar et al. establish IL35 as a driver of PDA tumor growth via suppression of T cell–mediated responses. Comparison of mice with and without this cytokine show that IL35’s absence significantly reduces pancreatic tumor growth, increases tumor infiltration by CD8⁺ T cells, and improves anti-PD-1 efficacy. Thus, IL35 is a cytokine that may be targeted to improve antitumor responses in PDA, including responses to PD-1 blockade. Read more in this issue starting on page 1014. Original immunofluorescence image of human PDA from Supplementary Fig. S4C. Artwork by Lewis Long.