WHAT WE'RE READING

989  A Sampling of Highlights from the Literature

CANCER IMMUNOLOGY AT THE CROSSROADS

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 Shlieman, Brendan C. Dickson, and Albinur 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 antigentic 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 Pylayeva-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
Hualong Zhang, Yuandong Yu, Li Zhou, Jingwei Ma, Ke Tang, Pingwei Xu, Tianjian Ji, Xiaoyu Liang, Jiadi Lv, Wenqian 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.

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Mechanisms by Which Dendritic Cells Present Tumor Microparticle Antigens to CD8⁺ T Cells
Jingwei Ma, Keke Wei, Huafeng Zhang, Ke Tang, Fei Li, Tianchen Zhang, Junwei Liu, Pingwei Xu, Yuandong Yu, Weixi Sun, Lyvan Zhu, Jie Chen, Li Zhou, Xiaoyu Liang, Jiadi Yu, Roland Fiskesund, Yuying Liu, and Bo Huang

Dual PD-1 and CTLA-4 Checkpoint Blockade Promotes Antitumor Immune Responses through CD4⁺ Foxp3⁺ Cell–Mediated Modulation of CD103⁺ Dendritic Cells

RO8⁺/FoxP3⁺ Treg Tolerance to CD103⁺ Dendritic Cells
Angelamaria Rizzo, Martina Di Giovangiulio, Carmine Stolfi, Eleonora Franz Angelamaria Rizzo, Martina Di Giovangiulio, Carmine Stolfi, Eleonora Franz, Giovanni Monteleone, and Massimo C. Fantini

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
Elin Berenson, Alexander Hallner, Frida E. Sander, Malin Nicklason, Malin S. Nilsson, Karin Christenson, Ebru Aydin, Jan-Åke Liljeqvist, Mats Brune, Robin Foa, Johan Aurelius, Anna Martin, Kristoffer Hellstrand, and Fredrik Thoren

The efficacy of CAR T-cell therapy depends on the engraftment and persistence of T cells following adoptive transfer. Limiting ex vivo culture time of CD19-specific CAR T cells during manufacturing yields improved persistence and effector function in vivo.

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.