

CANCER IMMUNOLOGY RESEARCH

TABLE OF CONTENTS

WHAT WE'RE READING

1281 **A Sampling of Highlights from the Literature**

EDITORIAL

1282 **The AACR Journals: Advancing Progress Toward the AACR's 115-Year Mission**
Kenneth C. Anderson, Lewis C. Cantley, Riccardo Dalla-Favera, Chi Van Dang, Luis A. Diaz, Raymond N. DuBois, Keith T. Flaherty, Philip D. Greenberg, Massimo Loda, Elaine R. Mardis, Elizabeth A. Platz, Michael N. Pollak, Robert D. Schreiber, Lillian L. Siu, and Beverly A. Teicher

OBITUARY

1289 **Hiroshi Shiku, MD, PhD: In Memoriam (1943–2022)**
Hiroyoshi Nishikawa, Alexander Knuth, and Ryuzo Ueda

RISING STARS IN CANCER IMMUNOLOGY

1291 **About the Rising Star**
See related article, p. 1292

1292 **Harnessing Microbiota to Improve Immunotherapy for Gastrointestinal Cancers**
Jeremy Goc and Gregory F. Sonnenberg
See related article, p. 1291

PRIORITY BRIEF

1299 **PD-1/PD-L1 Inhibition Enhances Chemotherapy-Induced Neuropathic Pain by Suppressing Neuroimmune Antinociceptive Signaling**
Carlos Wagner S. Wanderley, Alexandre G.M. Maganin, Beatriz Adjafre, Atlante S. Mendes, Conceição Elidianne Anibal Silva, Andreza Urba Quadros, João Paulo Mesquita Luiz, Camila Meirelles S. Silva, Nicole R. Silva, Francisco Fabio Bezerra Oliveira, Francisco Isaac F. Gomes, Jeferson Leandro J. Restrepo, Cesar A. Speck-Hernandez, Fernanda Turaça, Gabriel Victor Lucena Silva, Glauce R. Pigatto, Helder I. Nakaya, Jose Mauricio Mota, Romualdo Barroso-Sousa, José C. Alves-Filho, Thiago M. Cunha, and Fernando Q. Cunha
Peripheral neuropathy has been reported in the context of combination treatment with checkpoint inhibitors and chemotherapeutic agents. The authors show that PD-1/PD-L1 checkpoint inhibition can enhance paclitaxel-induced neuropathic pain by inhibiting neuroimmune PD-1/PD-L1 antinociceptive signaling.

RESEARCH ARTICLES

1309 **Reciprocal Interactions Between the Gut Microbiome and Mammary Tissue Mast Cells Promote Metastatic Dissemination of HR⁺ Breast Tumors**
Tzu-Yu Feng, Francesca N. Azar, Sally A. Dreger, Claire Buchta Rosean, Mitchell T. McGinty, Audrey M. Putelo, Sree H. Kolli, Maureen A. Carey, Stephanie Greenfield, Wesley J. Fowler, Stephen D. Robinson, and Melanie R. Rutkowski
The role of mammary tissue-associated mast cells during breast cancer is poorly defined. Here, the authors uncover a novel gut microbiome–mast cell axis in mammary tissue that enhances early metastatic spread of HR⁺ tumors.

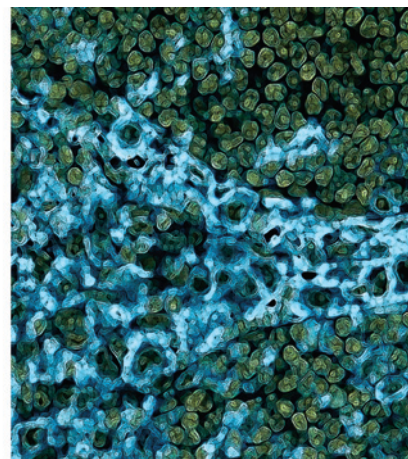
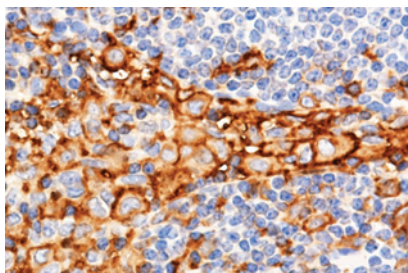
1326 **The Tumor Microenvironment of Clear-Cell Ovarian Cancer**
Michael-John Devlin, Rowan Miller, Florian Laforets, Panoraia Kotantaki, Dale W. Garsed, Rebecca Kristeleit, David D. Bowtell, Jacqueline McDermott, Eleni Maniati, and Frances R. Balkwill
The tumor microenvironment (TME) of clear cell ovarian cancer is characterized. Immune infiltration and collagen deposition differ based on disease stage, TME localization, and ARID1A status, highlighting the necessity of evaluating multiple features when determining treatment strategy.

TABLE OF CONTENTS

- 1340** **A Population of TIM4⁺FOLR2⁺ Macrophages Localized in Tertiary Lymphoid Structures Correlates to an Active Immune Infiltrate Across Several Cancer Types**
Mattia Bugatti, Marco Bergamini, Francesco Missale, Matilde Monti, Laura Ardighieri, Irene Pezzali, Sara Picinoli, Nicoletta Caronni, Yoann Missolo-Koussou, Julie Helft, Federica Benvenuti, and William Vermi
Two distinct populations of TIM4-expressing tumor-associated macrophages localize to tertiary lymphoid structures or body cavities and either promote T-cell responses or induce immunosuppression, respectively, suggesting novel treatment approaches and relevance for selection of immune therapy.
- 1354** **Targeting Macrophages with CAR T Cells Delays Solid Tumor Progression and Enhances Antitumor Immunity**
Alfonso R. Sánchez-Paulete, Jaime Mateus-Tique, Gurkan Mollaoglu, Sebastian R. Nielsen, Adam Marks, Ashwitha Lakshmi, Jalal A. Khan, C. Matthias Wilk, Luisanna Pia, Alessia Baccharini, Miriam Merad, and Brian D. Brown
CAR T cells targeting tumor-associated macrophages are found to stimulate IFN γ -dependent endogenous T cell-mediated antitumor activity in mouse models of solid tumors. CAR T cell depletion of macrophages shows promise as a strategy for tumor antigen-agnostic immunotherapy.
- 1370** **Secreted Fas Decoys Enhance the Antitumor Activity of Engineered and Bystander T Cells in Fas Ligand-Expressing Solid Tumors**
Pradip Bajgain, Alejandro G. Torres Chavez, Kishore Balasubramanian, Lindsey Fleckenstein, Premal Lulla, Helen E. Heslop, Juan Vera, and Ann M. Leen
Tumors expressing FasL can kill antitumor T cells. The enhanced antitumor effects of CAR T cells armed with secreted Fas decoys reported here suggest a way to improve clinical efficacy of cellular therapies in solid tumors.
- 1386** **Treg-Dominant Tumor Microenvironment Is Responsible for Hyperprogressive Disease after PD-1 Blockade Therapy**
Hiroaki Wakiyama, Takuya Kato, Aki Furusawa, Ryuhei Okada, Fuyuki Inagaki, Hideyuki Furumoto, Hiroshi Fukushima, Shuhei Okuyama, Peter L. Choyke, and Hisataka Kobayashi
The mechanisms underlying hyperprogressive disease (HPD) associated with PD-1 blockade are unclear. The authors develop a way to reproduce HPD by partially eliminating CD8⁺ T cells with NIR-PIT, creating a regulatory T cell-dominant tumor microenvironment permissive of tumor growth.
- 1398** **ICBAtlas: A Comprehensive Resource for Depicting Immune Checkpoint Blockade Therapy Characteristics from Transcriptome Profiles**
Mei Yang, Ya-Ru Miao, Gui-Yan Xie, Mei Luo, Hui Hu, Hang Fai Kwok, Jian Feng, and An-Yuan Guo
ICBAtlas provides search, browse, and visualization functions for integrated and reanalyzed results based on large-scale transcriptome data from immune checkpoint blockade (ICB)-treated patient samples. This resource serves as a one-stop solution for transcriptome data-related research on ICB therapy.
- 1407** **Immune Phenotypes and Target Antigens of Clonally Expanded Bone Marrow T Cells in Treatment-Naive Multiple Myeloma**
Carlotta Welters, María Fernanda Lammoglia Cobo, Christian Alexander Stein, Meng-Tung Hsu, Amin Ben Hamza, Livius Penter, Xiaojing Chen, Christopher Buccitelli, Oliver Popp, Philipp Mertins, Kerstin Dietze, Lars Bullinger, Andreas Moosmann, Eric Blanc, Dieter Beule, Armin Gerbitz, Julian Strobel, Holger Hackstein, Hans-Peter Rahn, Klaus Dornmair, Thomas Blankenstein, and Leo Hansmann
Bone marrow T-cell clonal expansion, immune phenotypes, and specificities at the single-cell level were determined in treatment-naïve multiple myeloma. Dominant T-cell clones rarely recognize antigens presented on myeloma cells, are not neoantigen-specific, and show low immune checkpoint expression.

ABOUT THE COVER

The phosphatidylserine receptor TIM4 is expressed on the surface of antigen-presenting cells and is involved in antigen uptake and T-cell priming, but its expression on pleural/peritoneal cavity and omentum-resident macrophages is associated with protumor activity. Bugatti, Bergamini, Missale et al. have identified a novel class of TIM4⁺ macrophages found in the T-cell zone of tertiary lymphoid structures (TLS) across diverse cancer types. TIM4⁺ TLS-associated macrophages express a gene signature associated with tumor immunogenicity and positive patient prognosis, whereas TIM4⁺ cavity macrophages coexpress immunosuppressive genes, such as those encoding IL10 and TREM2. These data highlight spatially and phenotypically distinct TIM4⁺ TLS-macrophage populations with potential clinical implications across solid tumors. Read more in this issue on page 1340. Original image from Fig. 1B. Artwork by Lewis Long.



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