

CANCER IMMUNOLOGY RESEARCH

TABLE OF CONTENTS

WHAT WE'RE READING

- 797** **A Sampling of Highlights from the Literature**

IN THE SPOTLIGHT

- 798** **Do Not Forget the Granulocytic Compartment's Role in T cell-Mediated Antitumor Immunity**
Udo S. Gaipf
See related article, p. 822

REVIEW

- 800** **Spatial Dissection of the Immune Landscape of Solid Tumors to Advance Precision Medicine**
Francesco Di Mauro and Giuseppina Arbore

PRIORITY BRIEF

- 814** **Melanoma Clonal Heterogeneity Leads to Secondary Resistance after Adoptive Cell Therapy with Tumor-Infiltrating Lymphocytes**
David König, Michael T. Sandholzer, Sarp Uzun, Andreas Zingg, Reto Ritschard, Helen Thut, Katharina Glatz, Elisabeth A. Kappos, Dirk J. Schaefer, Christoph Kettelhack, Jakob R. Passweg, Andreas Holbro, Katharina Baur, Michael Medinger, Andreas Buser, Didier Lardinois, Lukas T. Jeker, Nina Khanna, Frank Stenner, Benjamin Kasenda, Krisztian Homicsko, Matthias Matter, Natalia Rodrigues Mantuano, Alfred Zippelius, and Heinz Läubli
Mechanisms of resistance to TIL-ACT are ill-defined. The authors report that transfer of TILs caused immune selection of a resistant melanoma cell clone in one patient. T-cell collection from multiple tumor sites could help overcome this issue.

RESEARCH ARTICLES

- 822** **IL3-Driven T Cell-Basophil Crosstalk Enhances Antitumor Immunity**
Jian Wei, Colleen L. Mayberry, Xiaoting Lv, Fangyan Hu, Taushif Khan, Natalie A. Logan, John J. Wilson, John D. Sears, Damien Chaussabel, and Chih-Hao Chang
The role of IL3 in antitumor immunity is ill-defined. The authors reveal that IL3 mediates crosstalk between CTLs and IL4-producing basophils, rejuvenating CTLs and amplifying their antitumor ability, suggesting new approaches to advance and optimize cancer immunotherapy.
See related Spotlight, p. 798
- 840** **Small Extracellular Vesicle piR-hsa-30937 Derived from Pancreatic Neuroendocrine Neoplasms Upregulates CD276 in Macrophages to Promote Immune Evasion**
Yuan Zhong, Ye Tian, Yan Wang, Jian'an Bai, Qin Long, Lijun Yan, Zhihui Gong, Wei Gao, and Qiyun Tang
The authors show that the piRNA piR-hsa-30937 in PNEN cell-derived small extracellular vesicles (sEV) promotes CD276 expression in macrophages to suppress T-cell immunity. The data indicate sEV piR-hsa-30937 and CD276 as potential immunotherapeutic targets in PNEN.
- 854** **Metabolic Reprogramming of Tumor-Associated Macrophages Using Glutamine Antagonist JHU083 Drives Tumor Immunity in Myeloid-Rich Prostate and Bladder Cancers**
Monali Praharaj, Fan Shen, Alex J. Lee, Liang Zhao, Thomas R. Nirschl, Debebe Theodoros, Alok K. Singh, Xiaoxu Wang, Kenneth M. Adusei, Kara A. Lombardo, Raekwon A. Williams, Laura A. Sena, Elizabeth A. Thompson, Ada Tam, Srinivasan Yegnasubramanian, Edward J. Pearce, Robert D. Leone, Jesse Alt, Rana Rais, Barbara S. Slusher, Drew M. Pardoll, Jonathan D. Powell, and Jelani C. Zarif
The authors show in myeloid-rich urologic tumors that glutamine antagonism in TAMs results in functional alterations including increased tumor-cell phagocytosis, inflammatory signaling, immune-proliferative pathways, and glycolysis. This promotes antitumor immunity, suggesting new therapeutic approaches for these immunotherapy-unresponsive tumors.

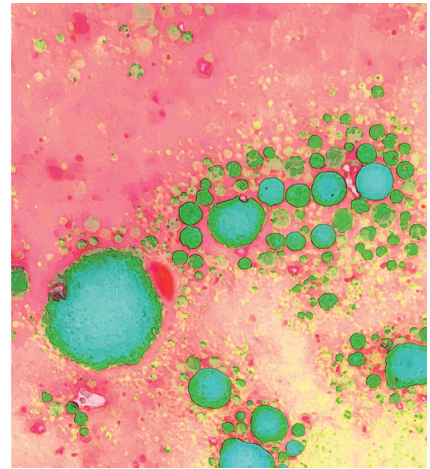
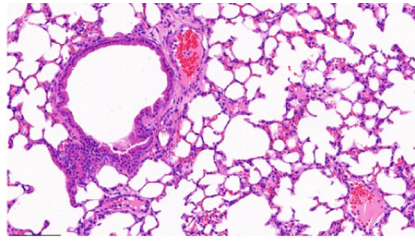
TABLE OF CONTENTS

- 876** **PVRIG is Expressed on Stem-Like T Cells in Dendritic Cell-Rich Niches in Tumors and Its Blockade May Induce Immune Infiltration in Non-Inflamed Tumors**
 Zoya Alteber, Gady Cojocaru, Roy Z. Granit, Inbal Barbiro, Assaf Wool, Masha Frenkel, Amit Novik, Adi Shuchami, Yu Liang, Vered D. Carmi, Niv Sabath, Rob Foreman, Natalia Petrenko, Jiang He, Yossef Kliger, Adva Levy-Barda, Ram Eitan, Oded Raban, Eran Sadot, Omri Sulimani, Abraham Avi Nathan, Henry Adewoye, Pierre Ferre, Zurit Levine, and Eran Ophir
 Immune-excluded tumors rarely respond to immunotherapy. The authors show that blocking interactions between the T-cell checkpoint PVRIG on TSCM and its ligand PVRL2 on intratumoral DCs induces T-cell proliferation and infiltration, suggesting new therapeutic opportunities for immune-excluded tumors.
- 891** **SIRT3 Negatively Regulates T_{FH}-Cell Differentiation in Cancer**
 Yueru Hou, Yejin Cao, Ying He, Lin Dong, Longhao Zhao, Yingjie Dong, Ruiying Niu, Yujing Bi, and Guangwei Liu
 The mechanisms underlying T_{FH}-cell differentiation in tumors are unclear. The authors show that SIRT3 triggers NAD⁺-dependent glycolysis and an mTOR-HIF1 α -Bcl-6 pathway to reprogram T_{FH}-cell differentiation, which is meaningful for future immunotherapy approaches in cancer.
- 905** **Orchestrated Codelivery of Peptide Antigen and Adjuvant to Antigen-Presenting Cells by Using an Engineered Chimeric Peptide Enhances Antitumor T-Cell Immunity**
 Haifeng Pan, Siyuan Yu, Haoyun Zhuang, Han Yang, Jinlu Jiang, Haihui Yang, Shuling Ren, Guoxing Luo, Xuan Yu, Shuping Chen, Yanhua Lin, Roufang Sheng, Shiyin Zhang, Quan Yuan, Chenghao Huang, Tianying Zhang, Tingdong Li, Shengxiang Ge, Jun Zhang, and Ningshao Xia
 To address the pharmacokinetic challenges of traditional peptide-based cancer vaccines, the authors generate an engineered chimeric peptide-based orchestrated codelivery strategy, showing it enhances antitumor T-cell immunity. This approach may provide an avenue toward more effective cancer treatments.
- 921** **The CD33xCD123xCD70 Multispecific CD3-Engaging DARPIn MP0533 Induces Selective T Cell-Mediated Killing of AML Leukemic Stem Cells**
 Matteo Bianchi, Christian Reichen, Amelie Croset, Stefanie Fischer, Aline Eggenschwiler, Yvonne Gröbler, Rajlakshmi Marpakwar, Thamar Looser, Patricia Spitzli, Christel Herzog, Denis Villemagne, Dieter Schiegg, Liridon Abduli, Chloé Iss, Alexandra Neculcea, Marco Franchini, Tamara Lekishvili, Simone Ragusa, Christof Zitt, Yvonne Kaufmann, Alienor Auge, Martin Hänggi, Waleed Ali, Teresa M. Frasconi, Stephan Wullschleger, Iris Schlegel, Mirela Matzner, Ursina Lüthi, Bernd Schlereth, Keith M. Dawson, Vladimir Kirkin, Adrian F. Ochsenbein, Sebastian Grimm, Nina Reschke, Carsten Riether, Daniel Steiner, Nicolas Leupin, and Anne Goubier
 In preclinical studies on the T-cell engager MP0533, the authors show that targeting multiple tumor-associated antigens may lead to better selectivity and efficacy in eliminating leukemic stem cells and blasts, representing a promising therapeutic strategy for AML.

TABLE OF CONTENTS

ABOUT THE COVER

Pancreatic neuroendocrine neoplasms (PNEN) are largely unresponsive to current immunotherapies. Zhong, Tian, and Wang et al. provide new insight into why this might be, showing that macrophages expressing CD276 (B7H3) suppress T-cell immunity in the PNEN tumor microenvironment. CD276 expression in macrophages is induced by the PIWI-interacting RNA piR-hsa-30937 in PNEN cell-derived small extracellular vesicles (sEV) through the PTEN/AKT pathway. piR-hsa-30937 knockdown and anti-CD276 treatment enhance CD8⁺ T cell-mediated antitumor immunity in a preclinical model of PNEN, reducing tumor growth and metastasis, suggesting new approaches to consider for PNEN immunotherapy. Read more in this issue on page 840. Original image from Fig. 7C. Artwork by Lewis Long.



doi: 10.1158/2326-6066.CIR-12-7-CVR

NOTICE: This notice serves to inform the reader that, in 2023, AACR received a donation by Pfizer of the rights to royalties from the sale within the United States of Bavencio® (avelumab), a pharmaceutical owned by Merck. If any resulting funds are received, they would not be used to directly support any specific publication or author. If an individual article is published that deals with this particular drug, such article will include standard financial disclosures per AACR journal policy. For more detail regarding AACR's established policies for authors, please go to <https://aacrjournals.org/pages/editorial-policies#coi>.