Cancer Immunology Research

Table of Contents

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WHAT WE'RE READING

1741 A Sampling of Highlights from the Literature

CANCER IMMUNOLOGY AT THE CROSSROADS

1742 Harnessing Natural Killer Cell Antitumor Immunity: From the Bench to Bedside
Karrune V. Woan and Jeffrey S. Miller

CANCER IMMUNOLOGY MINIATURES

1748 Direct Detection and Quantification of Neoantigens
Qing Wang, Jacqueline Douglass, Michael S. Hwang, Emily Han-Chung Hsiue, Brian J. Mog, Ming Zhang, Nickolas Papadopoulos, Kenneth W. Kinzler, Shibin Zhou, and Bert Vogelstein
Methodology that accurately predicts if cancer-derived neoantigens are processed and bind to human leukocyte antigen molecules (HLA) has been a challenge. "Mutation-associated neoantigen-selected reaction monitoring" (MANA-SRM) is a novel technique that directly detects and quantifies HLA-binding MANA.

1755 Anti–PD-1–Induced Pneumonitis Is Associated with Persistent Imaging Abnormalities in Melanoma Patients
Douglas B. Johnson, Kevin B. Taylor, Justine V. Cohen, Noura Ayoubi, Alexandra M. Haugh, Daniel Y. Wang, Brian D. Schlick, Amber L. Voorhees, Kenneth L. Gage, Florian J. Fintelmann, Ryan J. Sullivan, Zeynep Eroglu, and Richard G. Abramson
Lung abnormalities, resulting from anti–PD-1–induced pneumonitis in melanoma patients, were visible by computerized tomography during follow-up, despite resolution of clinical symptoms following steroid treatment. This study underscores the need for further examination of long-term effects of immunotherapies.

RESEARCH ARTICLES

1760 Head and Neck Cancers Promote an Inflammatory Transcriptome through Coactivation of Classic and Alternative NF-κB Pathways
Xinping Yang, Hui Cheng, Jianhong Chen, Ru Wang, Anthony Saleh, Han Si, Steven Lee, Emine Guven-Maiorov, Ozlem Keskin, Attila Gursoy, Ruth Nussinov, Jugao Fang, Carter Van Waes, and Zhong Chen
Inflammation in the tumor microenvironment of HNSCC is induced by NF-κB signaling. The genes involved in the induction of the classical and alternative NF-κB signaling pathway were determined in HPV^+ and HPV^- HNSCC tumors.

1775 The Atypical Receptor CCRL2 Is Essential for Lung Cancer Immune Surveillance
Annalisa Del Prete, Francesca Sozio, Tiziana Schioppa, Andrea Ponzetta, William Vermi, Stefano Calza, Mattia Bugatti, Valentina Salvi, Giovanni Bernardini, Federica Benvenuti, Annunciata Vecchi, Barbara Bottazzi, Alberto Mantovani, and Silvano Sozzani
The migration of innate immune cells through tumors is necessary for cancer immunosurveillance. Chemokine receptor CCRL2 expression on nonhematopoietic cells in lung tumors controls NK-cell infiltration and their subsequent ability to limit tumor growth.

1789 AXL Targeting Overcomes Human Lung Cancer Cell Resistance to NK- and CTL-Mediated Cytotoxicity
Stéphane Terry, Abderemane Abdou, Agnete S.T. Engelsen, Stéphanie Buart, Philippe Dessen, Stéphanie Corgnac, Davi Collares, Guillaume Meurice, Gro Gausdal, Véronique Baud, Pierre Saintigny, James B. Lorens, Jean-Paul Thiery, Fathia Mami-Chouaib, and Salem Chouaib
Lung carcinoma cells that express AXL, a tyrosine kinase receptor associated with epithelial-to-mesenchymal transition, have intrinsic resistance to cytotoxic lymphocyte attacks. AXL protein may represent a therapeutic target to enhance cancer cell susceptibility to antitumor immunity.

1803 Blockade of CTLA-4 and PD-1 Enhances Adoptive T-cell Therapy Efficacy in an ICOS-Mediated Manner
Lewis Zhichang Shi, Sangeeta Goswami, Tihui Fu, Baoxiang Guan, Jianfeng Chen, Liangwen Xiong, Jan Zhang, Derek Ng Tang, Xuejun Zhang, Luis Vence, Jorge Blando, James P. Allison, Renata Collazo, Jianjun Gao, and Padmanee Sharma
Adoptive T-cell therapy (ACT) is ineffective in solid tumors due to lack of T-cell infiltration. Dual blockade of CTLA-4 and PD-1 enhances efficacy of ACT in melanoma, in an ICOS-dependent manner.

1813 Eradication of Hepatocellular Carcinoma by NKG2D-Based CAR-T Cells
Bin Sun, Dong Yang, Hongjiu Dai, Xiuyun Liu, Ru Jia, Xiaoyue Cui, Wenxuan Li, Changchun Cai, Jianming Xu, and Xudong Zhao
CAR T-cell therapies have shown little clinical success in hepatocellular carcinoma (HCC) due to ineffective killing. NKG2D-based CAR T cells robustly kill HCC cell lines and can clear HCC xenograft tumors.

Table of Contents

1824 **Single-Cell Transcriptome Analysis Reveals Gene Signatures Associated with T-cell Persistence Following Adoptive Cell Therapy**
Yong-Chen Lu, Li Jia, Zhili Zheng, Eric Tran, Paul F. Robbins, and Steven A. Rosenberg
Single-cell transcriptome analysis of clonotypes from a patient with metastatic colorectal cancer treated with adoptive cell therapy revealed distinctive gene expression profiles. Persistent and nonpersistent clonotype profiles are highlighted and include differences in surface markers and transcription factors.

1837 **STING Signaling in Melanoma Cells Shapes Antigenicity and Can Promote Antitumor T-cell Activity**
Rana Falahat, Patricio Perez-Villarroel, Adam W. Mailloux, Genyuan Zhu, Shari Pilon-Thomas, Glen N. Barber, and James J. Mulé
In some human melanoma cells, STING signaling can enhance antigenicity and susceptibility to lysis by tumor-infiltrating lymphocytes. Conversely, defective STING signaling protects melanoma cells, and this heterogeneity among tumor cells could therefore affect T cell–based immunotherapies.

1849 **Blockade of β-Adrenergic Receptors Improves CD8$^+$ T-cell Priming and Cancer Vaccine Efficacy**
Clara Daher, Lene Vimeux, Ralitsa Stoeva, Elisa Peranzoni, Georges Bismuth, Elisabeth Wieduwild, Bruno Lucas, Emmanuel Donnadieu, Nadège Bercovici, Alain Trautmann, and Vincent Feuillet
Immune-suppressive mechanisms of the tumor microenvironment limit the efficacy of anticancer vaccination. Targeting β-adrenergic receptor signaling improves the antitumor effects of antitumor vaccination by enhancing CD8$^+$ T-cell priming in the tumor-draining lymph node.

1864 **A Bispecific Molecule Targeting CD40 and Tumor Antigen Mesothelin Enhances Tumor-Specific Immunity**
Shiming Ye, Diane Cohen, Nicole A. Belmar, Donghee Choi, Siu Sze Tan, Mien Sho, Yoshiko Akamatsu, Han Kim, Ramesh Iyer, Jean Cabel, Marc Lake, Danying Song, John Harlan, Catherine Zhang, Yuni Fang, Alan F. Wahl, Patricia Culp, Diane Hollenbaugh, and Debra T. Chao
A bispecific molecule with conditional activity was engineered to target both an immune activator and a tumor-specific surface antigen. The strategy shows potential to enhance tumor-specific immune activation and reduce systemic toxicity.

1876 **Cyclophosphamide Enhances Cancer Antibody Immunotherapy in the Resistant Bone Marrow Niche by Modulating Macrophage FcγR Expression**
Ali Roghanian, Guangan Hu, Christopher Fraser, Maneesh Singh, Russell B. Foxall, Matthew J. Meyer, Emma Lees, Heather Huet, Martin J. Glennie, Stephen A. Beers, Sean H. Lim, Margaret Ashton-Key, Stephen M. Thirdborough, Mark S. Cragg, and Jianzhu Chen
Antibody therapies can engender resistance by the bone marrow (BM). Macrophages from multiple tissues in healthy, tumor-bearing NSG, or humanized NSG mice were assessed, and both tissue-intrinsic and tumor-induced BM resistance could be overcome using specific treatment modalities.

1891 **PD-1 and LAG-3 Dominate Checkpoint Receptor–Mediated T-cell Inhibition in Renal Cell Carcinoma**
Henning Zelba, Jens Bedke, Jörg Hennenlotter, Sven Mostböck, Markus Zettl, Thomas Zichner, Anoop Chandran, Arnulf Stenzl, Hans-Georg Rammensee, and Cécile Gouttefangeas
Despite the success of immune checkpoint blockade in renal cell carcinoma cancer, many patients do not respond. Through in vitro *analysis of immune checkpoints on intratumoral T cells, the efficacy of PD-1 antibody is improved by adding LAG3 antibody.*

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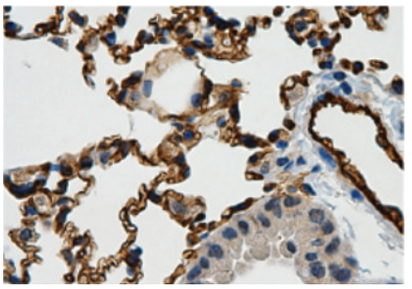
Table of Contents

ABOUT THE COVER

Chemokine and chemotactic receptor expression in nonhematopoietic cells can affect tumor formation, in part by altering the influx of innate immune cells into the tumor microenvironment (TME). Del Prete et al. investigate the link between mouse atypical chemotactic receptor CCRL2 expression in lung endothelial cells with immune surveillance of lung cancer and subsequent tumor formation. Knockout of CCRL2 in mice or antibody blockade of CCRL2 increases the establishment of lung cancer lesions, leading to poorer mouse survival, by inhibiting NK cell migration into the TME. CCRL2 expression is lower in patient lung tumor tissue compared to paired normal lung tissue, with low tumoral CCRL2 expression correlating to poorer patient survival. Read more starting on page 1775. Artwork is based on Figure 6D by the Sozzani laboratory. Artwork by Lewis Long.



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7 (11)

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