WHAT WE'RE READING

1223  A Sampling of Highlights from the Literature

CANCER IMMUNOLOGY AT THE CROSSROADS

1224  Lessons Learned from Checkpoint Blockade Targeting PD-1 in Multiple Myeloma
Alexander M. Lesokhin, Susan Bai, and Ashraf Z. Badros

CANCER IMMUNOLOGY MINIATURES

1230  Intrinsic Resistance to Immune Checkpoint Blockade in a Mismatch Repair–Deficient Colorectal Cancer

This case of PD-1 blockade resistance, despite microsatellite instability-high (MSI-H) molecular features, suggests that other biomarkers should be considered. Loss of \( \beta_2 \)-microglobulin expression and infiltration of NK cells and M2 macrophages may be informative in therapy selection.

PRIORITY BRIEF

1237  Systemic Interferon-\( \gamma \) Increases MHC Class I Expression and T-cell Infiltration in Cold Tumors: Results of a Phase 0 Clinical Trial
Shibong Zhang, Karan Kohli, R. Graeme Black, Lu Yao, Sydney M. Spadinger, Qianchuan He, Venu G. Pillarisetty, Lee D. Cranmer, Brian A. Van Tine, Cassian Yee, Robert H. Pierce, Stanley R. Riddell, Robin L. Jones, and Seth M. Pollack

Interferon-\( \gamma \), an FDA approved drug, can drive inflammation of non-inflamed cancers, potentially facilitating immunotherapy with PD-1 inhibitors. A multicenter trial sponsored by the Cancer Immunotherapy Trials Network is based on these results.

1258  IRF1 Inhibits Antitumor Immunity through the Upregulation of PD-L1 in the Tumor Cell

IFN signaling can mediate antitumor responses, with transcription factor IRF1 involved in tumor suppression. Tumor cell–expressed IRF1 was found to upregulate PD-L1, aiding tumor escape. Thus, tumor cell–specific targeting of IRF1 may be important in immunotherapy.

1267  An Improved Patient-Derived Xenograft Humanized Mouse Model for Evaluation of Lung Cancer Immune Responses
Ismail M. Meraz, Mourad Majidi, Feng Meng, RuPing Shao, Min Jin Ha, Shinya Neri, Bingliang Fang, Steven H. Lin, Peggy T. Tinkey, Elizabeth J. Shpall, Jeffrey Morris, and Jack A. Roth

Often drugs tested in preclinical models fail in the clinic. An improved humanized mouse model derived from nonexpanded CD34\(^+\) stem cells from cord blood allowed for robust engraftment and the testing of non-HLA–matched patient tumors with immune therapies.

RESEARCH ARTICLES

1244  Disrupting LILRB4/APOE Interaction by an Efficacious Humanized Antibody Reverses T-cell Suppression and Blocks AML Development
Xun Gui, Mi Deng, Hao Song, Yuanzhi Chen, Jingjing Xie, Zanling Li, Licaei He, Fangfang Huang, Xiyang Xu, Yasuaki Anami, Hai Yu, Chenyi Yu, Leike Li, Zihao Yuan, Xiaoying Xu, Qihui Wang, Yan Chai, Tao Huang, Yi Shi, Kyoji Tsuchikama, X. Charlene Liao, Ningshao Xia, George F. Gao, Ningyang Zhang, Cheng Cheng Zhang, and Zhiqiang An

When LILRB4 on acute myeloid leukemia cells (AML) binds to its ligand APOE, T-cell activation is suppressed. A humanized mAb to LILRB4 blocks LILRB4/APOE interaction and, through multiple modes of action, blocks AML development in mouse models.

1258  An Improved Patient-Derived Xenograft Humanized Mouse Model for Evaluation of Lung Cancer Immune Responses
Ismail M. Meraz, Mourad Majidi, Feng Meng, RuPing Shao, Min Jin Ha, Shinya Neri, Bingliang Fang, Steven H. Lin, Peggy T. Tinkey, Elizabeth J. Shpall, Jeffrey Morris, and Jack A. Roth

Often drugs tested in preclinical models fail in the clinic. An improved humanized mouse model derived from nonexpanded CD34\(^+\) stem cells from cord blood allowed for robust engraftment and the testing of non-HLA–matched patient tumors with immune therapies.
High Numbers of Circulating CD57⁺ NK Cells Associate with Resistance to HER2-Specific Therapeutic Antibodies in HER2⁺ Primary Breast Cancer

Xuedong Liu, and Jing H. Wang

Enriched HLA-E and CD94/NKG2A Interaction Limits Antitumor CD8⁺ T Lymphocyte Infiltrating Tumor Responses

Megat Abul Hamid, Ruo-Zheng Wang, Xuan Yao, Peiwen Fan, Xi Li, Xue-Mei Chang, Yaning Feng, Stephanie Jones, David Maldonado-Perez, Craig Waugh, Clare Verrill, Alison Simmons, Vincenzo Cernudolo, Andrew McMichael, Christopher Conlon, Xiyan Wang, Yanchun Peng, and Tao Dong

Activating KIRs on Educated NK Cells Support Downregulation of CD226 and Inefficient Tumor Immunossurveillance

Concepción F. Guillamón, María V. Martínez-Sánchez, Lourdes Gimeno, José A. Campillo, Gerardo Server-Pastor, Jerónimo Martínez-García, Jorge Martínez-Escribano, Amparo Torroba, Belén Ferri, Daniel J. Abellán, Isabel Legaz, María R. López-Alvarez, María R. Moyá-Quiles, Manuel Muro, and Alfredo Minguela

Histone Deacetylase Inhibition Sensitizes PD1 Blockade-Resistant B-cell Lymphomas

Xiaoguang Wang, Brittany C. Waschke, Rachel A. Woolaver, Zhangguo Chen, Can Zhang, Anthony D. Piscopio, Xuedong Liu, and Jing H. Wang

The E3 Ubiquitin Ligase Asb2γ in T Helper 2 Cells Negatively Regulates Antitumor Immunity in Colorectal Cancer

Camille A. Spinner, Isabelle Lamsoul, Arnaud Métais, Chanaëlle Febrissy, Christel Moog-Lutz, and Pierre G. Lutz

Corrected Analysis of Lymphocytic Infiltration, Tumor Budding, and Their Spatial Relationship Improves Prognostic Accuracy in Colorectal Cancer

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Tumor Lympathic Function Regulates Tumor Inflammatory and Immunosuppressive Microenvironments

Raghu P. Katara, Catherine L. Ly, Jinyeon Shin, Hyeung Ju Park, Jung Eun Baik, Sonia Rehal, Sagrario Ortega, David Lyden, and Babak J. Mehrara

Efficient Tumor Clearance and Diversified Immunity through Neoepitope Vaccines and Combinatorial Immunotherapy


Anti–CTLA-4 Activates Infratmural NK Cells and Combined with IL15/IL15Ra Complexes Enhances Tumor Control

Emilio Sanseviero, Erin M. O'Brien, Jenna R. Karras, Tamer B. Shabaneh, Bulent Arman Aksoy, Wei Xu, Cathy Zheng, Xiangfan Yin, Xiaowei Xu, Giorgos C. Karakousis, Ravi K. Amaravadi, Brian Nam, Mary Jo Turk, Jeff Hammerbacher, Mark P. Rubinstein, Lynn M. Schuchter, Tara C. Mitchell, Qin Liu, and Erica L. Stone

Correction: Automated Analysis of Lymphocytic Infiltration, Tumor Budding, and Their Spatial Relationship Improves Prognostic Accuracy in Colorectal Cancer

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Camille A. Spinner, Isabelle Lamsoul, Arnaud Métais, Chanaëlle Febrissy, Christel Moog-Lutz, and Pierre G. Lutz
Primary breast cancer biopsy tissue is not always available to assess the degree of immune-cell infiltration into HER2⁺ breast cancer tumors. Thus, one goal for cancer diagnostics is to find reliable measures based on circulating immune cells. Muntasell and Servitja et al. measure the absolute number of circulating CD57⁺ NK cells before treatment with HER2-specific antibodies and find that the higher the number of NK cells before treatment, the worse the patient's response to treatment. High amounts of CD57⁺ NK cells in the blood inversely correlate with their density in tumors, suggestive of a tumor-homing or proliferative deficiency. Indeed, the authors find that CD57⁺ NK cells in the peripheral blood have both reduced tumor-homing chemokine receptor expression and low proliferation upon activation. The amount of these circulating cells could be used as a diagnostic marker of response to HER2 antibodies. Read more in this issue on page 1280. Original image from Fig. 3B. Artwork by Lewis Long.