WHAT WE'RE READING

1. A Sampling of Highlights from the Literature

MEETING REPORT

   Mustafa Diken, Srivani Ravoori, and Arthur N. Brodsky

CANCER IMMUNOLOGY MINIATURE

6. Autoantibody Development under Treatment with Immune-Checkpoint Inhibitors
   Emma C. de Moel, Elisa A. Rozeman, Ellen H. Kapiteijn, Els M.E. Verdegaal, Annette Grummels, Jaap A. Bakker, Tom W.J. Huizinga, John B. Haanen, Rene E.M. Toes, and Diane van der Woude
   Ipilimumab induced autoantibodies in a fifth of melanoma patients. Patients who developed autoantibodies, especially thyroid autoantibodies, experienced more irAEs and had a survival and response benefit, suggesting that breaking of B-cell tolerance could indicate therapy toxicity and efficacy.

RESEARCH ARTICLES

12. Collapse of the Plasmacytoid Dendritic Cell Compartment in Advanced Cutaneous Melanomas by Components of the Tumor Secretome
   Raffaella Vescovi, Matilde Monti, Daniele Moratto, Lucia Paolini, Francesca Consoli, Luisa Benerini, Laura Melocchi, Stefano Calza, Mariella Chiodinelli, Giulio Rossi, Mattia Bugatti, Michele Maio, Ester Fonsatti, Camillo Almici, Rosanna Verardi, Aldo Scarpa, Paolo Bergese, Ausilia Manganoni, Fabio Facchetti, and William Vermi
   Plasmacytoid dendritic cells (PDCs) can regulate anti-cancer immune responses. Factors in the melanoma secretome drive the PDC compartment to collapse during disease progression, and rescue of PDCs could aid existing spontaneous and drug-induced adaptive immune responses.

29. Batf3-Dependent Genes Control Tumor Rejection Induced by Dendritic Cells Independently of Cross-Presentation
   Derek J. Theisen, Stephen T. Ferris, Carlos G. Briseño, Nicole Kretzer, Arifumi Iwata, Kenneth M. Murphy, and Theresa L. Murphy
   In addition to stabilizing cDC1 dendritic cell lineage commitment, BATF3 controls a set of genes required for cDC1 cells to promote tumor rejection. These BATF3-controlled genes, which are independent of cross-presentation, may be targets in the development of immunotherapies.

40. Leveraging TCR Affinity in Adoptive Immunotherapy against Shared Tumor/Self-Antigens
   Aaron M. Miller, Milad Bahmanof, Dietmar Zehn, Ezra E.W. Cohen, and Stephen P. Schoenberger
   Adoptive cellular therapy (ACT) with a low-affinity T-cell receptor (TCR) that recognizes a self-antigen yields antitumor cytotoxicity but not autoimmune damage. A better understanding of TCR affinity could ultimately minimize autoimmunity while increasing ACT therapeutic efficacy.

50. High-Throughput Stability Screening of Neoantigen/HLA Complexes Improves Immunogenicity Predictions
   Dylan T. Blaha, Scott D. Anderson, Daniel M. Yoakum, Marlies V. Hager, Yuanyuan Zha, Thomas F. Gajewski, and David M. Kranz
   Using a rapid, high-throughput method, peptide/HLA thermal stability was determined for a variety of peptides and peptide variants. This approach allows for predicting neoantigens that can best serve as targets for a robust T-cell response against cancer.

62. Mapping the MHC Class I–Spliced Immunopeptidome of Cancer Cells
   Juliane Lirpe, John Sidney, Felix K.M. Lorenz, Alessandro Sette, and Michele Misho
   Unconventional spliced peptides can be presented by cancer cells. This survey of peptide characteristics in the immunopeptidome of colon and breast carcinoma cell lines may help to predict and identify an unforeseen pool of antigenic targets for immunotherapy.
Peripheral Blood TCR Repertoire Profiling May Facilitate Patient Stratification for Immunotherapy against Melanoma

Analysis of TCR repertoire clonality in blood samples collected from patients with melanoma before treatment may predict their eventual response to anti-PD1 and anti-CTLA4 therapy. Such a biomarker could help clinicians refine treatment courses for melanoma patients.

Computational Immune Monitoring Reveals Abnormal Double-Negative T Cells Present across Human Tumor Types

An analysis toolkit was developed for characterizing immunological changes over time in clinical samples. Use of this toolkit revealed the presence of a double-negative T-cell subset in melanoma, glioblastoma, and renal cell carcinoma but not in healthy tissues.

Phase I Trial of Autologous CAR T Cells Targeting NKG2D Ligands in Patients with AML/MDS and Multiple Myeloma

NKG2D-CAR T-cell therapy is safe and feasible. Infused cells were transiently detected and exhibited in vitro responses to autologous tumors. However, objective responses to low doses were only seen in lymphodepleted patients, warranting studies to improve efficacy.

Reduced Breast Tumor Growth after Immunization with a Tumor-Restricted MUC1 Glycopeptide Conjugated to Tetanus Toxoid
Natasha Stergiou, Nikolai Gaidzik, Anne-Sophie Heimes, Sarah Dietzen, Pol Besenius, Jörg Jäkel, Walburgis Bennner, Marcus Schmidt, Horst Kunz, and Edgar Schmitt

Tumor-associated MUC1 is a target for the development of breast cancer vaccines due to its tumor-specific overexpression and aberrant glycosylation. Immunization with synthetically produced tumor-associated MUC1 glycopeptides conjugated to tetanus toxoid resulted in reduced tumor burden in mice.

Calnexin Impairs the Antitumor Immunity of CD4⁺ and CD8⁺ T Cells
Yichen Chen, Da Ma, Xi Wang, Juan Fang, Xiangqi Liu, Jingjing Song, Xinye Li, Xianyue Ren, Qiusheng Li, Quansheng Li, Shuqiong Wen, Liqun Luo, Jian Xia, Jun Cui, Guancheng Zeng, Liqing Chen, Bin Cheng, and Zhi Wang

T-cell numbers and effector functions are diminished by calnexin, an ER chaperone protein, possibly through PD-1 upregulation, in OSCC patients and in a mouse melanoma model. These results suggest calnexin could be targeted to improve immunotherapy responses.

PARP1 Suppresses the Transcription of PD-L1 by Poly(ADP-Ribosyl)ating STAT3
Ling Ding, Xi Chen, Xiaqiong Xu, Yuli Qian, Guikai Liang, Fengqi Yao, Zhangting Yao, Honghai Wu, Jieqiong Zhang, Qiaojuan He, and Bo Yang

PARP1-mediated poly(ADP-ribosyl)ation of STAT3 drives its dephosphorylation, leading to the inhibition of PD-L1 transcription across multiple cancer types. In patients, PARP1 and PD-L1 expression are inversely correlated. These data highlight a conserved regulatory mechanism for PD-L1 expression.

PD-L1 microSPECT/CT Imaging for Longitudinal Monitoring of PD-L1 Expression in Syngeneic and Humanized Mouse Models for Cancer

PD-L1 microSPECT/CT is a technique to detect PD-L1 expression in syngeneic murine models and humanized mice, allowing the monitoring of therapy-induced changes in tumor PD-L1 expression. In the future, this technique could enable patient selection for PD-1/PD-L1-targeted therapies.
ABOUT THE COVER

Although T cells infiltrate melanomas, they usually fail to clear the tumor. Plasmacytoid DCs (PDCs) can regulate T-cell function and, in addition, can eliminate melanomas by TLR-mediated mechanisms. Vescovi et al. show that infiltration by PDCs occurs early in primary cutaneous melanoma and their localization is at the invasive margin, where the PDCs can interact with CD8+ T cells. However, in advanced and metastatic disease, PDCs do not infiltrate into tumor tissues and PDCs in circulation are reduced. This is due to a collapse of the PDC compartment during cancer progression, caused by soluble factors in the melanoma secretome that lead to PDC death and impaired differentiation from progenitor cells. These data highlight that rescuing PDCs could help in inducing antitumor responses. Read more in this issue on page 12. Original image is a primary cutaneous melanoma with little infiltration of PDCs from Fig. 1H. Artwork by Lewis Long.
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