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62 Mapping the MHC Class I–Spliced Immunopeptidome of Cancer Cells
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.

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, Qunxian Li, Shuqiong Wen, Liqun Luo, Jian Xia, Jun Cui, Gucheng Zeng, Lieping 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, Xiaqing Xu, Yuli Qian, Guikai Liang, Fengqji Yao, Zhangting Yao, Honghai Wu, Jieqiong Zhang, Qiaojun 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.

Correction: Stromal Cell PD-L1 Inhibits CD8+ T-cell Antitumor Immune Responses and Promotes Colon Cancer

Acknowledgment to Reviewers

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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.