

CANCER IMMUNOLOGY RESEARCH

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Analysis shows that TMB does not correlate with tumor immune infiltrates, including tumor-resident CD8⁺ T cells, in acral, mucosal, and cutaneous melanomas. The data indicate that TMB is not a significant driver of antitumor responses.

PRIORITY BRIEF

1354 **A DNA-Launched Nanoparticle Vaccine Elicits CD8⁺ T-cell Immunity to Promote *In Vivo* Tumor Control**
Ziyang Xu, Neethu Chokkalingam, Edgar Tello-Ruiz, Megan C. Wise, Mamadou A. Bah, Susanne Walker, Nicholas J. Tursi, Paul D. Fisher, Katherine Schultheis, Kate E. Broderick, Laurent Humeau, Daniel W. Kulp, and David B. Weiner
DNA nanoparticle vaccination plus electroporation robustly induces CD8⁺ CTL responses that are able to control, or protect from, melanoma growth in mice. The data demonstrate the utility of this platform and offer a strategy to boost antitumor responses.

RESEARCH ARTICLES

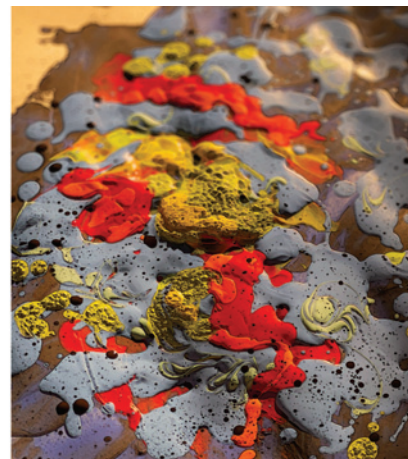
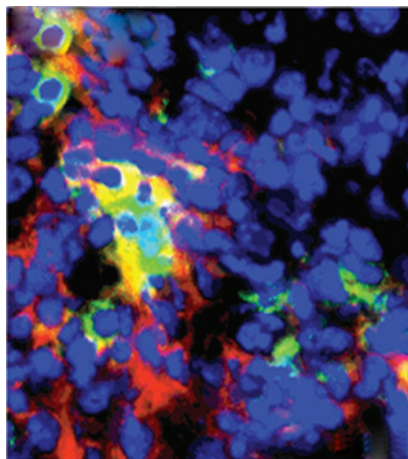
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Under immune pressure from T-cell checkpoint blockade, melanoma evolves a hypermetabolic phenotype conferring complete immunotherapy resistance. Key genes driving enhanced glycolysis and oxidative phosphorylation confer resistance when transferred to the parental melanoma or to a pancreatic cancer.1381 **Tumor-Derived IL33 Promotes Tissue-Resident CD8⁺ T Cells and Is Required for Checkpoint Blockade Tumor Immunotherapy**
Lujun Chen, Runzi Sun, Junchi Xu, Wensi Zhai, Dachuan Zhang, Min Yang, Cuihua Yue, Yichao Chen, Song Li, Heth Turnquist, Jingting Jiang, and Binfeng Lu
Despite the clinical efficacy of immune checkpoint blockade (ICB), much of its impact on the tumor microenvironment is unclear. IL33 mediated ICB efficacy by inducing the accumulation of tumor-resident CD103⁺CD8⁺ T cells and CD103⁺ dendritic cells.1393 **Tumor-Infiltrating Regulatory T-cell Accumulation in the Tumor Microenvironment Is Mediated by IL33/ST2 Signaling**
Jimin Son, Jae-Won Cho, Hyo Jin Park, Jihyun Moon, Seyeon Park, Hoyoung Lee, Jeewon Lee, Gamin Kim, Su-Myeong Park, Sergio A. Lira, Andrew N. McKenzie, Hye Young Kim, Cheol Yong Choi, Yong Taik Lim, Seong Yong Park, Hye Ryun Kim, Su-Hyung Park, Eui-Cheol Shin, Insuk Lee, and Sang-Jun Ha
Regulatory T cells (Treg) suppress antitumor immunity, yet the mechanism for how they accumulate in tumors is unclear. The IL33/ST2 signaling axis in Tregs is crucial for the accumulation of Tregs in the tumor microenvironment.

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- 1407 Glycans as Immune Checkpoints: Removal of Branched N-glycans Enhances Immune Recognition Preventing Cancer Progression**
Mariana C. Silva, Ângela Fernandes, Maria Oliveira, Carlos Resende, Alexandra Correia, Julio C. de-Freitas-Junior, Aonghus Lavelle, Jéssica Andrade-da-Costa, Magdalena Leander, Helena Xavier-Ferreira, José Bessa, Carina Pereira, Rui M. Henrique, Fátima Carneiro, Mário Dinis-Ribeiro, Ricardo Marcos-Pinto, Margarida Lima, Bernd Lepenies, Harry Sokol, José C. Machado, Manuel Vilanova, and Salomé S. Pinho
Complex branched N-glycans are identified as glyco-immune checkpoints that are used by colorectal cancer cells to evade immune recognition. The data highlight how inhibiting this glycosylation could be a strategy to improve antitumor responses.
- 1426 Blocking P2X7-Mediated Macrophage Polarization Overcomes Treatment Resistance in Lung Cancer**
Juliang Qin, Xiaoyu Zhang, Binghe Tan, Su Zhang, Chengcong Yin, Qi Xue, Zhen Zhang, Hua Ren, Jinlian Chen, Mingyao Liu, Min Qian, and Bing Du
P2X7 is expressed in tumor-associated macrophages (TAM), yet its role in lung cancer progression is unknown. Blockade of P2X7 induces antitumor TAMs and rescues the efficacy of anti-PD-1 and chemotherapy against lung cancer.
- 1440 Lactate-Modulated Immunosuppression of Myeloid-Derived Suppressor Cells Contributes to the Radioresistance of Pancreatic Cancer**
Xuguang Yang, Yun Lu, Junjie Hang, Junfeng Zhang, Tiening Zhang, Yanmiao Huo, Jun Liu, Songtao Lai, Dawei Luo, Liwei Wang, Rong Hua, and Yuli Lin
Pancreatic cancer tends to be radioresistant, but the immune-mediated mechanisms behind this resistance are unclear. Lactate secretion from pancreatic tumor cells leads to immune-suppressive MDSCs via HIF-1 α signaling in MDSCs, limiting radiotherapy efficacy in pancreatic cancer.
- 1452 Infiltration by IL22-Producing T Cells Promotes Neutrophil Recruitment and Predicts Favorable Clinical Outcome in Human Colorectal Cancer**
Nadia Tosti, Eleonora Cremonesi, Valeria Governa, Camilla Basso, Venkatesh Kancharla, Mairene Coto-Llerena, Francesca Amicarella, Benjamin Weixler, Silvio Däster, Giuseppe Sconocchia, Pietro Edoardo Majno, Dimitri Christoforidis, Luigi Tornillo, Luigi Terracciano, Charlotte K.Y. Ng, Salvatore Piscuoglio, Markus von Flüe, Giulio Spagnoli, Serenella Eppenberger-Castori, Giandomenica Iezzi, and Raoul Andre Droeser
IL22-producing immune cells are involved in inflammatory gut diseases, yet their role in colorectal cancer (CRC) remains unclear. IL22-secreting T cells recruit neutrophils to CRC tumors, leading to enhanced patient survival.

ABOUT THE COVER

Although immune checkpoint blockade (ICB) has shown success in prolonging the survival of patients with cancer, the mechanisms behind this are not fully elucidated. Chen et al. find that tumor-derived IL33, whose expression increases after ICB treatment, and ST2 signaling in nontumor cells are key to inducing antitumor responses. IL33 increases functional CD103⁺CD8⁺ T cells and CD103⁺ dendritic cells (DC) in the tumor microenvironment (TME), and the CD103⁺ DCs are essential for the recruitment of tumor-infiltrating CD8⁺ T cells into the TME. By treating tumor-bearing mice with IL33 in combination with dual ICB, survival was extended, highlighting the important role of IL33 in mediating the efficacy of ICB. Read more in this issue on page 1381. Original image from Fig. 4F. Artwork by Lewis Long.



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