WHAT WE'RE READING

1109  A Sampling of Highlights from the Literature

IN THE SPOTLIGHT

1110  Putting On the Gas and Taking Off the Brakes: A Novel Combinatorial Strategy to Enhance Tumor-Infiltrating Lymphocytes
  Martin Felices and Jeffrey S. Miller
  See related article, p. 1141

RESEARCH ARTICLES

1111  A. Muciniphila Suppresses Colorectal Tumorigenesis by Inducing TLR2/NLRP3-Mediated M1-Like TAMs
  Lina Fan, Chaochao Xu, Qiwei Ge, Yifeng Lin, Chi Chun Wong, Yadong Qi, Bin Ye, Qingwu Lian, Wei Zhuo, Jianmin Si, Shujie Chen, and Liangjing Wang
  The authors show that A. muciniphila can induce M1-like macrophages through a TLR2/NF-κB/NLRP3 pathway to suppress colorectal cancer progression, suggesting a new potential therapeutic strategy for colorectal cancer prevention and treatment.

1125  The Ratio of Exhausted to Resident Infiltrating Lymphocytes Is Prognostic for Colorectal Cancer Patient Outcome
  Momeneh Foroutan, Ramyar Molania, Aline Pfefferle, Corina Behrenbruch, Sebastian Scheer, Axel Kallies, Terence P. Speed, Joseph Carsons, and Nicholas D. Huntington
  The authors identify tumor mutations and tumor microenvironmental factors that drive residency programs in infiltrating lymphocytes, impairing their antitumor function and patient outcomes. Understanding how tumor lymphocyte residency is regulated might offer new approaches for therapeutic intervention.

1141  An Engineered IL15 Cytokine Mutein Fused to an Anti-PD1 Improves Intratumoral T-cell Function and Antitumor Immunity
  To overcome challenges associated with cytokine-based immunotherapies, the authors engineered a fusion protein of a single, potency-reduced, IL15 mutein and a PD1-specific antibody. The agent preferentially activates intratumoral CD8⁺ T cells and demonstrates potent preclinical antitumor efficacy.
  See related Spotlight, p. 1110

1158  Bispecific CAR T Cells against EpCAM and Inducible ICAM-1 Overcome Antigen Heterogeneity and Generate Superior Antitumor Responses
  Yanping Yang, Jaclyn E. McCloskey, Huan Yang, Janusz Puc, Yago Alcaina, Yoguianda Vediya, Angel A. Gomez Gallegos, Elizabeth Ortiz-Sánchez, Elisa de Stanchina, Irene M. Min, Eric von Hufe, and Moonsuoo J. Jin
  Generation of EpCAM/ICAM-1 dual CAR T cells improves the efficacy of single-targeting EpCAM CAR T cells in multiple tumor models. The data highlight a broadly applicable strategy to boost the activity of single antigen-specific CAR T-cell therapy.
ABOUT THE COVER

The identity and frequency of immune cells in the tumor microenvironment impact outcomes for patients with colorectal cancer. Using single-cell RNA sequencing data, Foroutan et al. identify signatures of residency and exhaustion for tumor-infiltrating CD8⁺, CD4⁺, and natural killer (NK) cells. Different signature combinations associated with distinct patient outcomes; for example, signatures of high NK-cell exhaustion and low NK-cell residency were associated with improved survival. The data provide new insight into the characteristics of tumor-infiltrating lymphocytes and suggest that preventing tumor residency by NK cells may enhance antitumor immunity and patient outcomes. Read more in this issue on page 1125. Artwork by Momeneh Foroutan inspired by several figures in the article, including the CD8 residency panel of Fig. 1B, shown here.

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