WHAT WE'RE READING

1  A Sampling of Highlights from the Literature

CANCER IMMUNOLOGY AT THE CROSSROADS

2  Lighting a Fire: Can We Harness Pyroptosis to Ignite Antitumor Immunity?
   Zhibin Zhang, Ying Zhang, and Judy Lieberman

RESEARCH ARTICLES

8  The Prognostic Role of Macrophage Polarization in the Colorectal Cancer Microenvironment
   Juha P. Väyrynen, Koichiro Haruki, Mai Chan Lau, Sara A. Väyrynen, Rong Zhong, Andressa Dias Costa, Jennifer Borowsky, Melissa Zhao, Kenji Fujiyoshi, Kota Arima, Tyler S. Twombly, Junko Kishikawa, Simeng Gu, Sina Aminmoradifarre, Shanshan Shi, Yoshifumi Baba, Naohiko Akimoto, Tomotaka Ugai, Annacarolina Da Silva, Jennifer L. Guerriero, Mingyong Song, Kana Wu, Andrew T. Chan, Reiko Nishihara, Charles S. Fuchs, Jeffrey A. Meyerhardt, Marios Giannakis, Shuji Ogino, and Jonathan A. Nowak
   Macrophage polarization state, rather than overall density, in the colorectal cancer microenvironment is associated with cancer-specific survival independent of potential confounding factors, with M1-like and M2-like macrophage phenotypes exhibiting distinct prognostic roles.

20  Retinoic Acid Synthesis Deficiency Fosters the Generation of Polymorphonuclear Myeloid-Derived Suppressor Cells in Colorectal Cancer
   Hong-Wei Sun, Jing Chen, Wen-Chao Wu, Yan-Yan Yang, Yi-Tao Xu, Xing-Juan Yu, Hai-Tian Chen, Zilian Wang, Xiao-Jun Wu, and Limin Zheng
   A defect in ADH1-mediated retinoic acid synthesis contributes to the accumulation of polymorphonuclear (PMN)-MDSCs in colorectal cancer. The data highlight how restoring retinoic acid signaling could abrogate the generation of PMN-MDSCs and improve antitumor responses.

34  A CRISPR Screen Reveals Resistance Mechanisms to CD3-Bispecific Antibody Therapy
   Si-Qi Liu, Alyssa Grantham, Casey Landry, Brian Granda, Rajiv Chopra, Srinivas Chakravarty, Sabine Deutsch, Markus Vogel, Katie Russo, Katherine Seiss, William R. Tschantz, Tomas Rejtar, David A. Ruddy, Tiancen Hu, Kimberly Aardalen, Joel P. Wagner, Glenn Dranoff, and Joseph A. D’Alessio
   A genome-wide CRISPR screen was developed to understand cancer cell–derived resistance mechanisms to CD3-bispecific antibodies. The screen identifies IFNg signaling being pivotal for responsiveness to CD3 bispecifics, and deficiency in core fucosylation as causing resistance to the therapeutic flotetuzumab.

50  A Bispecific Antibody Antagonizes Prosurvival CD40 Signaling and Promotes Vγ9Vδ2 T cell–Mediated Antitumor Responses in Human B-cell Malignancies
   Iris de Weerdt, Roeland Lameris, George L. Scheffer, Jana Vree, Renate de Boer, Anita G. Stam, Rieneke van de Ven, Mark-David Levin, Steven T. Pals, Rob C. Roovers, Paul W.H.I. Parren, Tanja D. de Grujil, Arnon P. Kater, and Hans J. van der Vliet
   The generation of a CD40-specific Vγ9Vδ2 T-cell engager, which abrogates prosurvival CD40 signaling, is described. This bispecific antibody unleashes Vγ9Vδ2 T cell–mediated responses against both leukemia and multiple myeloma in vitro and in vivo.

62  CD28 Costimulatory Domain–Targeted Mutations Enhance Chimeric Antigen Receptor T-cell Function
   Justin C. Boucher, Gorgo Bi, Hiroshi Kotani, Maria L. Cabral, Dylan Morrissey, Sae Bom Lee, Kristen Spiteri, Nolan J. Beatty, Estelle V. Cervantes, Bishwas Shrestha,Bin Yu, Aslamuzzaman Kazi, Xuefeng Wang, Said M. Sebi, and Marco L. Davila
   CD28 mutations enhance CAR T-cell function by reducing expression of exhaustion-related genes. These data highlight considerations for CAR design that could improve antitumor responses.
The Cerebroventricular Environment Modifies CAR T Cells for Potent Activity against Both Central Nervous System and Systemic Lymphoma


In the clinic, CD19-CAR T cells are administered IV and are not used specifically to treat CNS lymphoma. The authors show a single ICV infusion of CD19-CAR T cells completely eradicates both CNS and systemic lymphoma in mice.

Activin A Promotes Regulatory T-cell–Mediated Immunosuppression in Irradiated Breast Cancer

Mara De Martino, Camille Daviaud, Julie M. Diamond, Jeffrey Kraynak, Amandine Alard, Silvia C. Formenti, Lance D. Miller, Sandra Demaria, and Claire Vanpouille-Box

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