

HIGHLIGHTS FROM THE LITERATURE

1057 What We're Reading

MEETING REPORT

1058 Report on the Third FDA–AACR Oncology Dose-Finding Workshop

Leisha A. Emens, Rene Bruno, Eric H. Rubin, Elizabeth M. Jaffee, and Amy E. McKee

RESEARCH ARTICLES

1062 Differential Expression of Homing Receptor Ligands on Tumor-Associated Vasculature that Control CD8 Effector T-cell Entry

Amber N. Woods, Ashley L. Wilson, Nithya Srivinisan, Jianhao Zeng, Arun B. Dutta, J. David Peske, Eric F. Tewalt, Randal K. Gregg, Andrew R. Ferguson, and Victor H. Engelhard

Homing receptor ligands on tumor-associated vasculature were found to vary with anatomical location and depend, in part, on intratumoral effectors. The required homing receptor/ligand interactions were identified that mediate effector CD8⁺ T cell entry into these tumors.

1074 Prostate Cancer Cells Express More Androgen Receptor (AR) Following Androgen Deprivation, Improving Recognition by AR-Specific T Cells

Brian M. Olson, Melissa Gamat, Joseph Seliski, Thomas Sawicki, Justin Jeffery, Leigh Ellis, Charles G. Drake, Jamey Weichert, and Douglas G. McNeel

Androgen deprivation therapy (ADT), used to treat recurrent prostate cancer, can lead to overexpression of the androgen receptor. ADT combined with vaccination targeted against the androgen receptor led to improved responses in murine prostate cancer models.

1086 Natural Killer T-cell Immunotherapy in Combination with Chemotherapy-Induced Immunogenic Cell Death Targets Metastatic Breast Cancer

Simon Gebremeskel, Lynnea Lobert, Kaitlyn Tanner, Brynn Walker, Tora Oliphant, Livia E. Clarke, Graham Dellaire, and Brent Johnston

Low-dose cyclophosphamide or gemcitabine treatments, in combination with natural killer T-cell activation therapy, modulated immune function and improved survival in a mouse model of metastatic breast cancer.

1098 Interleukin-12 from CD103⁺ Batf3-Dependent Dendritic Cells Required for NK-Cell Suppression of Metastasis

Deepak Mittal, Dipti Vijayan, Eva M. Putz, Amelia R. Aguilera, Kate A. Markey, Jasmin Straube, Stephen Kazakoff, Stephen L. Nutt, Kazuyoshi Takeda, Geoffrey R. Hill, Nicola Waddell, and Mark J. Smyth

Several host factors can affect cancer metastasis. Batf3⁺ dendritic cells were shown in mouse models to produce the IL12 that stimulates NK cells to produce IFN γ , which helped to control cancer metastasis.

1109 Combination of CD40 Agonism and CSF-1R Blockade Reconditions Tumor-Associated Macrophages and Drives Potent Antitumor Immunity



Karla R. Wiehagen, Natasha M. Girgis, Douglas H. Yamada, Addressa A. Smith, Szeman Ruby Chan, Iqbal S. Grewal, Michael Quigley, and Raluca I. Verona

This study demonstrates the advantage of combining agonist anti-CD40 with CSF-1R blockade for maximal antitumor benefit and survival in a preclinical mouse model. The results provide rationale for the combination of two distinct immunotherapies to improve clinical outcome.

1122 Complex Immune Evasion Strategies in Classical Hodgkin Lymphoma

Frederik Wein, Marc A. Weniger, Benedikt Höing, Judith Arnolds, Andreas Hüttmann, Martin-Leo Hansmann, Sylvia Hartmann, and Ralf Küppers

Classical Hodgkin lymphoma uses multiple strategies to evade the immune system. cHL cells promoted regulatory T-cell features in CD4⁺ T cells and invoked additional strategies, such as purinergic signaling, to suppress immune detection.


1133 Characterization of Thyroid Disorders in Patients Receiving Immune Checkpoint Inhibition Therapy

Hyunju Lee, F. Stephen Hodi, Anita Giobbie-Hurder, Patrick A. Ott, Elizabeth I. Buchbinder, Rizwan Haq, Sara Tolaney, Romualdo Barroso-Sousa, Kevin Zhang, Hilary Donahue, Meredith Davis, Maria E. Gargano, Kristina M. Kelley, Rona S. Carroll, Ursula B. Kaiser, and Le Min

Immune checkpoint inhibitor–induced thyroid disorders were assessed in patients with a variety of cancers. Guidance is provided on monitoring and managing thyroid disorders induced by anti–PD-1 monotherapy or in combination with anti–CTLA-4.

Table of Contents

- 1141** **Cisplatin Alters Antitumor Immunity and Synergizes with PD-1/PD-L1 Inhibition in Head and Neck Squamous Cell Carcinoma**
Linda Tran, Clint T. Allen, Roy Xiao, Ellen Moore, Ruth Davis, So-Jin Park, Katie Spielbauer, Carter Van Waes, and Nicole C. Schmitt
The combination of cisplatin chemotherapy with anti-PD-1/PD-L1 immunotherapy is under investigation in clinical trials. Optimal doses of cisplatin were found to enhance the antitumor immune response, which was further improved by adding anti-PD-1/PD-L1 immunotherapy.

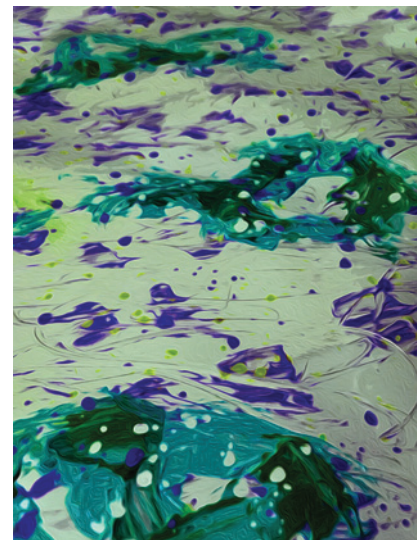
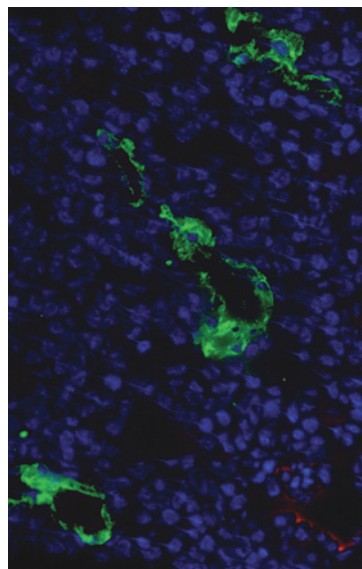
- 1152** **Safety and Efficacy of Intratumoral Injections of Chimeric Antigen Receptor (CAR) T Cells in Metastatic Breast Cancer**
 Julia Tchou, Yangbing Zhao, Bruce L. Levine, Paul J. Zhang, Megan M. Davis, Jan Joseph Melenhorst, Irina Kulikovskaya, Andrea L. Brennan, Xiaojun Liu, Simon F. Lacey, Avery D. Posey Jr., Austin D. Williams, Alycia So, Jose R. Conejo-Garcia, Gabriela Plesa, Regina M. Young, Shannon McGettigan, Jean Campbell, Robert H. Pierce, Jennifer M. Matro, Angela M. DeMichele, Amy S. Clark, Laurence J. Cooper, Lynn M. Schuchter, Robert H. Vonderheide, and Carl H. June
Transiently expressed chimeric antigen receptor T cells specific for c-Met, expressed in breast cancer, were injected into breast cancer tumors of six patients in a phase 0 clinical trial. Injections resulted in tumor necrosis and were well tolerated.

- 1162** **Acknowledgment to Reviewers**

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ABOUT THE COVER

Tissue and tumor vasculature needs to express appropriate "homing receptor ligands" to mediate the entry of T cells expressing "homing receptors" on their surfaces. The Engelhard laboratory investigated which homing receptors and tumor-expressed ligands are required for T-cell infiltration into tumors residing in different tissues. The tumor vasculature responded to the IFN γ produced by activated T cells, upregulating particular ligands that allowed the accumulation of T cells expressing the appropriate homing receptors. The altered expression of their homing receptors on T cells, based on site of activation, creates a receptor-ligand recognition system that may be exploitable for clinical practice. Read more in Woods et al. in this issue of *Cancer Immunology Research*, starting on p. 1062. Fluorescence micrograph of an intraperitoneal tumor from Fig. 5C, with green depicting the vasculature. Artwork by Lewis Long.



Cancer Immunology Research

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