WHAT WE'RE READING

579  A Sampling of Highlights from the Literature

CANCER IMMUNOLOGY MINIATURES

580  Previous Infection Positively Correlates to the Tumor Incidence Rate of Patients with Cancer
Shinako Inaida and Shigeo Matsuno
Determining links to tumor formation is critical for combating cancer. A 7-year study of over 50,000 patients indicates that certain previous infections are linked to the formation of various cancers.

PRIORITY BRIEF

587  Remodeling Translation Primes CD8⁺ T-cell Antitumor Immunity
Katie E. Hurst, Kiley A. Lawrence, Rob A. Robino, Lauren E. Ball, Dongjun Chung, and Jessica E. Thaxton
Altering protein translation in T cells can affect their antitumor function. IL15-conditioned T cells have diminished protein translation in vitro but reinvigorate translation in tumors, a property that is attributed to T cells that produce superior tumor control.

RESEARCH ARTICLES

596  A PSMA-Targeting CD3 Bispecific Antibody Induces Antitumor Responses that Are Enhanced by 4-1BB Costimulation
Danica Chiu, Richard Tavaré, Laurie Haber, Oululu H. Aina, Kristin Vazzana, Priyanka Ram, Makenzie Danton, Jennifer Finney, Priyanka Ram, Makenzie Danton, Jennifer Finney, Alison Crawford
A CD3 bispecific antibody that targets a prostate tumor antigen elicits effective antitumor responses against smaller, but not larger, solid tumors. Addition of 4-1BB controls tumors through enhanced T-cell responses, T-cell memory formation, and response persistence.

609  Single-Cell Immune Competency Signatures Associate with Survival in Phase II GVAX and CRS-207 Randomized Studies in Patients with Metastatic Pancreatic Cancer
Nitya Nair, Shih-Yu Chen, Ed Lennmens, Serena Chang, Dung T. Le, Elizabeth M. Jaffee, Aimee Murphy, Richard Tavaré, David A. Berlin, Ali A. Al-Osaimi, Chuan-Ming Huang, Mark B. Osten, Peter S. Aas, Benjamin M. Kashi, and William A. Parilla
Circulating immune subsets that associate with survival in pancreatic cancer patients treated with GVAX pancreas and/or CRS-207 immunotherapy are identified. These immune subsets can potentially be used as biomarkers to stratify patients most likely to respond to treatment.

618  Deciphering the Immunomodulatory Capacity of Oncolytic Vaccinia Virus to Enhance the Immune Response to Breast Cancer
Brittany A. Umer, Ryan S. Noyce, Brian C. Franchak, Mira M. Shenouda, Rees G. Kelly, Nicole A. Favis, Megan Desaulniers, Troy A. Baldwin, Mary M. Hitt, and David H. Evans
Genomic alterations of oncolytic viruses can improve their antitumor efficacy. Various genomic alterations of VACV are tested “head-to-head” in order to determine their impact on antitumor efficacy and immunity in murine tumor models.

632  Intratumoral Delivery of a PD-1–Blocking scFv Encoded in Oncolytic HSV-1 Promotes Antitumor Immunity and Synergizes with TIGIT Blockade
Chao Long Lin, Wenfeng Ren, Yong Luo, Shaopeng Li, Yating Chang, Li Li, Dan Xiong, Xiaoxuan Huang, Zilong Xu, Zeng Yu, Yingbin Wang, Jun Zhang, Chenghao Huang, and Ninghao Xia
Oncolytic virus activity is often limited by an immunosuppressive tumor microenvironment. The antitumor efficacy of oncolytic herpes simplex virus is improved by delivering a single-chain variable fragment specific for PD-1. Pairing this with TIGIT blockade enhances antitumor responses.

648  Prevalent and Diverse Intratumoral Oncoprotein-Specific CD8⁺ T Cells within Polyomavirus-Driven Merkel Cell Carcinomas
Lichen Jing, Marilis Ott, Candice D. Church, Rima M. Kulikauskas, Dafina Ibrani, Jayasi G. Iyer, Olga K. Afanasiev, Ari Colunga, Maclean M. Cook, Hong Xie, Alexander L. Greninger, Kelly G. Paulson, Aude G. Chapuis, Shailender Bhatia, Paul N. Ghiem, and David M. Koelle
Merkel cell carcinoma is frequently associated with Merkel cell polyomavirus infection. Most patients' tumors contain virus-specific CD8⁺ T cells restricted by specific HLAs, highlighting the potential of using vaccination as part of immunotherapy strategies for this cancer.

660  IL1α Antagonizes IL1β and Promotes Adaptive Immune Rejection of Malignant Tumors
Tian Tian, Serena Lofftus, Youdong Pan, Claire A. Stingley, Sandra L. King, Jingxia Zhao, Timothy Y. Pan, Rebecca Lock, Jacob W. Marglous, Kevin Liu, Hans R. Widlund, Robert C. Fuhlbrigge, Karen Cichowski, and Thomas S. Kupper
Antibodies to IL1β can enhance antitumor immunity, but inhibiting IL1α reduces antitumor effects. Thus, antagonists that block the shared IL1R1 do not improve antitumor immunity and are not equivalent to blocking IL1β alone.
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### ABOUT THE COVER

Evidence for bispecific antibody efficacy against solid tumors is limited, and additional approaches may be required in the clinic to achieve the success seen with hematologic tumors. Chiu et al. address this by designing a CD3 bispecific antibody that also targets a major prostate cancer tumor antigen, prostate-specific membrane antigen (PSMA). Preclinical models show positive responses to bispecific antibody treatment that is dependent on tumor size, with smaller tumors being more sensitive than larger tumors. However, by combining the bispecific antibody with 4-1BB costimulation, larger tumors are more readily reduced due to boosted, durable T-cell responses and the generation of immune memory. The data highlight that tumor size matters and that 4-1BB costimulation can be used to increase the potency of bispecific antibody treatment in solid tumors. Read more in this issue on page 596. Original image from Supplementary Fig. S5A. Artwork by Lewis Long.