EDITORIAL

1  Fresh Beginnings

MEETING REPORT

Vanessa M. Hubbard-Lucey and Matthew J. Tontonoz

CANCER IMMUNOLOGY MINIATURES

12  Radiologic Heterogeneity in Responses to Anti–PD-1/PD-L1 Therapy in Metastatic Renal Cell Carcinoma
Guillermo de Velasco, Katherine M. Krajewski, Laurence Albiges, Mark M. Awad, Joaquim Bellmunt, F. Stephen Hodi, and Toni K. Choueiri

The management of mRCC is being revolutionized by immune checkpoint inhibition. Patient response to anti–PD-1/PD-L1 agents is heterogeneous, and misleading CT scans might be common. Examples of five classes of patient responses and their images are presented and interpreted.

18  Short Peptide Vaccine Induces CD4⁺ T Helper Cells in Patients with Different Solid Cancers
Stefanie Gross, Volker Lennerz, Elisa Gallerani, Nicolas Mach, Steffen Büüm, Dagmar Hess, Lotta von Boehmer, Alexander Knuth, Adrian Ochsenbein, Adrian Ochsenbein, Ulf Forssmann, Thomas Woelfel, and Eckhart Kaempgen

The possibility that short peptide vaccines induce antitumor CD4⁺ T-cell responses has been widely ignored. Peripheral blood from vaccinated patients revealed that short peptides often activate specific T helper cells, facilitating a strong combined CD4⁺ and CD8⁺ T-cell response.

PRIORITY BRIEF

26  IL17A-Mediated Endothelial Breach Promotes Metastasis Formation
Paulina Kulig, Sara Burkhard, Joanna Mikita-Geoffroy, Andrew L. Croxford, Nadine Hövelmeyer, Gabor Gyulveszli, Christian Gorzelanny, Ari Waismian, Lubor Borsig, and Burkhard Becher

IL17A and Tgα17 cells have been implicated in both tumor promotion and tumor protection. In this preclinical mouse study the IL17 produced by tumor-invasive αβ T cells was found to promote transendothelial tumor invasion and lung metastasis.

RESEARCH ARTICLES

33  MicroRNA MIR21 and T Cells in Colorectal Cancer
Kosuke Mima, Reiko Nishihara, Jonathan A. Nowak, Sun A. Kim, Mingyang Song, Kentaro Inamura, Yasutaka Sukawa, Atsushi Masuda, Juhyong Yang, Ruoxu Dou, Katsuhiko Nosho, Hideo Baba, Edward L. Giovannucci, Michaela Bowlden, Massimo Loda, Marios Giannakis, Adam J. Bass, Glenn Dranoff, Gordon J. Freeman, Andrew T. Chan, Charles S. Fuchs, Zhi Rong Qian, and Shuji Ogino

Colon and rectal cancer cases in two U.S. nationwide prospective cohort studies were examined for an association of microRNA MIR21 (miR-21) and T-cell infiltration. MIR21 expression was inversely associated with densities of CD3⁺ and CD45RO⁺ T cells.

41  Validation of Intratumoral T-bet⁺ Lymphoid Cells as Predictors of Disease-Free Survival in Breast Cancer
Anna Marie Mulligan, Dushanthi Pinnaduwage, Sandrine Tchatchou, Shelley B. Bull, and Irene L. Andrulis

T-bet⁺ lymphoid cells are associated with adverse clinicopathologic features like the basal subgroup, yet confer a favorable outcome in invasive breast cancer. Thus, T-bet may prove to be an important prognostic and/or predictive marker for use in immunotherapy trials.

49  Comparison of the Superagonist Complex, ALT-803, to IL15 as Cancer Immunotherapeutics in Animal Models

IL15 stimulates T-cell and NK-cell responses, but not Tregs. The antitumor efficacy, biodistribution, and toxicity of an IL15-based superagonist, ALT-803, was examined in animal models and was superior, supporting its clinical development for advanced hematologic or solid tumors.
T-cell Exhaustion in Multiple Myeloma Relapse after Autotransplant: Optimal Timing of Immunotherapy
David J. Chung, Katherine B. Pronschinske, Justin A. Shyer, Sneh Sharma, Samantha Leung, Shane A. Curran, Alexander M. Lesokhin, Sean M. Devlin, Sergio A. Giralt, and James W. Young
Autologous transplantation prolongs disease-free survival in multiple myeloma but is not curative. Regulatory T cells decline early after transplant, and T-cell exhaustion/senescence signals imminent relapse, providing therapeutic opportunities to revive antimyeloma immunity and counteract relapse.

Dietary Consumption of Black Raspberries or Their Anthocyanin Constituents Alters Innate Immune Cell Trafficking in Esophageal Cancer
Daniel S. Peiffer, Li-Shu Wang, Noah P. Zimmerman, Benjamin W.S. Ransom, Steven G. Carmella, Chieh-Ti Kuo, Jo-Hsin Chen, Kiyoko Oshima, Yi-Wen Huang, Stephen S. Hecht, and Gary D. Stoner
Black raspberries and their constituents effectively reduce carcinogen-induced tumorigenesis in the rat esophagus through the reduction of inflammation. Current findings show that these changes are associated with altered immune cell trafficking within the esophagus tissue as well.

ABOUT THE COVER
T cells and NK cells are important components of antitumor responses against many cancers. Unlike some other interleukins, IL15 will stimulate and promote proliferation of these immune cells, but not regulatory T cells. A superagonist called ALT-803, based on an IL15 variant complexed to a dimeric IL15 receptor α-Fc fusion protein, was found to be a powerful antitumor agent in multiple models, as described in the Research Article by Rhode and colleagues that begins on p. 49 of this issue of Cancer Immunology Research. Original micrograph (right) shows CD8+ T cells binding and internalizing ALT-803. Photo credit: Samantha Suriano of the Mark Rubinstein laboratory at the Medical University of South Carolina and used with permission. Artwork: Lewis Long.