

EDITORIAL

- 1 Fresh Beginnings

MEETING REPORT

- 3 Translating Science into Survival: Report on the Inaugural International Cancer Immunotherapy Conference
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 Böhm, Dagmar Hess, Lotta von Boehmer, Alexander Knuth, Adrian Ochsenbein, Ulrike Gnad-Vogt, 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 Gyölvésvi, Christian Gorzelanny, Ari Waisman, Lubor Borsig, and Burkhard Becher
IL17A and T_H17 cells have been implicated in both tumor promotion and tumor protection. In this preclinical mouse study the IL17 produced by tumor-invading $\gamma\delta$ 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, Atsuhiko Masuda, Juhong Yang, Ruoxu Dou, Katsuhiko Noshio, Hideo Baba, Edward L. Giovannucci, Michaela Bowden, 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 Pinnaduwege, 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

Peter R. Rhode, Jack O. Egan, Wenxin Xu, Hao Hong, Gabriela M. Webb, Xiaoyue Chen, Bai Liu, Xiaoyun Zhu, Jinghai Wen, Lijing You, Lin Kong, Ana C. Edwards, Kaiping Han, Sixiang Shi, Sarah Alter, Jonah B. Sacha, Emily K. Jeng, Weibo Cai, and Hing C. Wong
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.

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61 T-cell Exhaustion in Multiple Myeloma Relapse after Autotransplant: Optimal Timing of Immunotherapy

David J. Chung, Katherine B. Pronschinske, Justin A. Shyer, Sneha 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.

72 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.

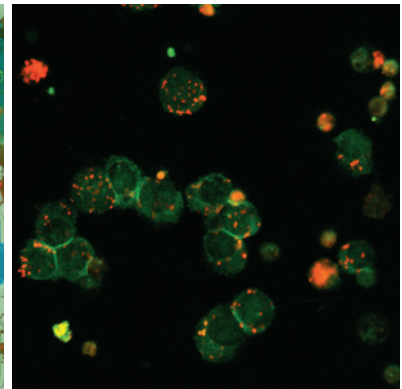
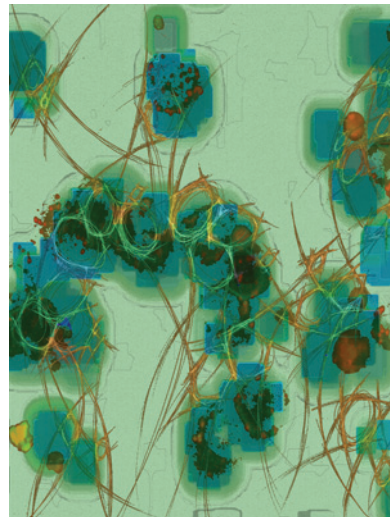


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ABOUT THE COVER

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.



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