

MILESTONES IN CANCER IMMUNOLOGY

- 1193** James P. Allison Receives the 2015 Lasker-DeBakey Award in Clinical Medical Research

CANCER IMMUNOLOGY AT THE CROSSROADS: EXPERIMENTAL IMMUNOTHERAPIES

- 1195** Reducing Toxicity of Immune Therapy Using Aptamer-Targeted Drug Delivery
Eli Gilboa, Alexey Bereznoy, and Brett Schrand

CANCER IMMUNOLOGY MINIATURES

- 1201** Intrathecal Administration of Tumor-Infiltrating Lymphocytes Is Well Tolerated in a Patient with Leptomeningeal Disease from Metastatic Melanoma: A Case Report
Isabella C. Glitza, Cara Haymaker, Chantale Bernatchez, Luis Vence, Michelle Rohlfis, Jessie Richard, Carol Lacey, Rahmatu Mansaray, Orenthial J. Fulbright, Renjith Ramachandran, Christopher Toth, Seth Wardell, Sapna P. Patel, Scott E. Woodman, Wen-Jen Hwu, Laszlo G. Radvanyi, Michael A. Davies, Nicholas E. Papadopoulos, and Patrick Hwu
One treatment for metastatic melanoma is systemic IL2 with infusion of tumor-infiltrating lymphocytes (TILs). Intrathecal TIL administration, along with intrathecal IL2, briefly stabilized disease in this case, suggesting that such an approach might benefit a select patient population.

RESEARCH ARTICLES

- 1207** Loss of Host Type-I IFN Signaling Accelerates Metastasis and Impairs NK-cell Antitumor Function in Multiple Models of Breast Cancer
Jai Rautela, Nikola Baschuk, Clare Y. Slaney, Krishnath M. Jayatilake, Kun Xiao, Bradley N. Bidwell, Erin C. Lucas, Edwin D. Hawkins, Peter Lock, Christina S. Wong, Weisan Chen, Robin L. Anderson, Paul J. Hertzog, Daniel M. Andrews, Andreas Möller, and Belinda S. Parker
Type-I interferon immune signaling plays a critical role during the antimetastatic immune response. The authors show that loss of this pathway can promote bone metastasis in three different breast cancer models, revealing its importance across different models.

- 1218** Neutrophils Increase Oral Squamous Cell Carcinoma Invasion through an Invadopodia-Dependent Pathway
Judah E. Glogauer, Chun X. Sun, Grace Bradley, and Marco A.O. Magalhaes
The presence of neutrophils in oral squamous cell carcinoma correlates with poor prognosis. The TNF α and IL8 secreted by neutrophils were found to increase the invasiveness of cancer cells through invadopodia formation and matrix degradation.


- 1227** IL10R2 Overexpression Promotes IL22/STAT3 Signaling in Colorectal Carcinogenesis
Vineeta Khare, Gregor Paul, Oliver Movadat, Adrian Frick, Manuela Jambrich, Anita Krnjic, Brigitte Marian, Friedrich Wrba, and Christoph Gasche
Colon cancers exhibit an increased IL22:IL10 ratio. The two cytokines share one receptor subunit, but their second receptor subunits are distinct. Colorectal cancer shows overexpression of both receptor subunits for IL22, which triggers STAT3 signaling and promotes carcinogenesis.

- 1236** Inhibition of Fatty Acid Oxidation Modulates Immunosuppressive Functions of Myeloid-Derived Suppressor Cells and Enhances Cancer Therapies
Fokhrul Hossain, Amir A. Al-Khami, Dorota Wyczechowska, Claudia Hernandez, Liqin Zheng, Krzysztof Reiss, Luis Del Valle, Jimena Trillo-Tinoco, Tomasz Maj, Weiping Zou, Paulo C. Rodriguez, and Augusto C. Ochoa
Myeloid-derived suppressor cells in tumors, but not in the spleen, activated fatty acid uptake and oxidation (FAO) and increased their immunosuppressive pathways. Blocking FAO with inhibitors induced T-cell-mediated antitumor activity, which provides a novel approach for treatment.

- 1248** Phase I Trial of a Yeast-Based Therapeutic Cancer Vaccine (GI-6301) Targeting the Transcription Factor Brachyury
Christopher R. Heery, B. Harpreet Singh, Myrna Rauckhorst, Jennifer L. Marté, Renee N. Donahue, Italia Grenga, Timothy C. Rodell, William Dahut, Philip M. Arlen, Ravi A. Madan, Jeffrey Schlom, and James L. Gully
Carcinomas can overexpress brachyury, a transcription factor not expressed in most adult tissues. A therapeutic yeast vaccine targeting brachyury was tested in phase I clinical trials. It induced T-cell responses with no autoimmunity and showed preliminary clinical activity.

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- 1257** **CTLA-4 Blockade Synergizes Therapeutically with PARP Inhibition in BRCA1-Deficient Ovarian Cancer**
Tomoe Higuchi, Dallas B. Flies, Nicole A. Marjon, Gina Mantia-Smaldone, Lukas Ronner, Phyllis A. Gimotty, and Sarah F. Adams
PARP inhibitors improve progression-free survival in BRCA1-deficient ovarian cancer. In a mouse model, checkpoint blockade with anti-CTLA-4, but not anti-PD-1, synergized with PARP inhibition to establish protective immune memory and achieve long-term survival.

- 1269** **Extracellular Vesicles Present in Human Ovarian Tumor Microenvironments Induce a Phosphatidylserine-Dependent Arrest in the T-cell Signaling Cascade**
 Raymond J. Kelleher Jr, Sathy Balu-Iyer, Jenni Loyall, Anthony J. Sacca, Gautam N. Shenoy, Peng Peng, Vandana Iyer, Anas M. Fathallah, Charles S. Berenson, Paul K. Wallace, Joseph Tario, Kunle Odunsi, and Richard B. Bankert
Ovarian tumor ascites fluid contains an immunosuppressive element identified as phosphatidylserine from nanovesicle membranes, originating from the tumor milieu. Suppression was disrupted by addition of diacylglycerol kinase inhibitors, suggesting that blocking these vesicles may enhance patient antitumor activity.

- 1279** **Rational Combination of Immunotherapies with Clinical Efficacy in Mice with Advanced Cancer**
Ali Bransi, Oscar Camilo Salgado, Michal Beffinger, Karim Milo, Karina Silina, Hideo Yagita, Burkhard Becher, Alexander Knuth, and Maries van den Broek
An efficacious combination of immunomodulatory treatments was identified in a late-stage prostate cancer model that prevented tolerance, promoted a sustained tumor-specific CD8⁺ T cells response, and cured tumors when given with adoptively transferred tumor-specific T cells.

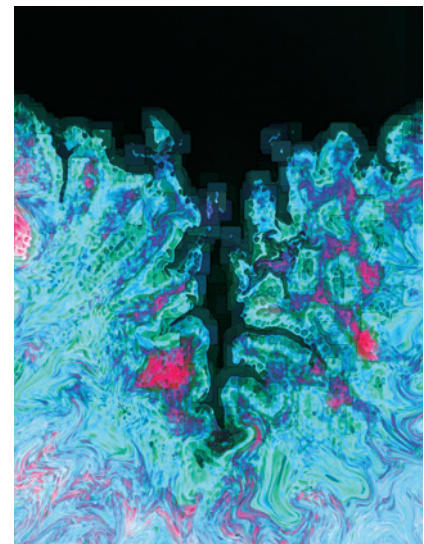
CORRECTION

- 1289** **Correction: Therapeutic Peptide Vaccine-Induced CD8 T Cells Strongly Modulate Intratumoral Macrophages Required for Tumor Regression**

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ABOUT THE COVER

In their article in the current issue, Khare and colleagues report that the receptor subunit shared by IL10 and IL22 is a key factor in the development of colorectal cancer. This "satellite image"-like rendition of the colon is based on a panel from their Fig. 4. Read more about the complex interplay between the shared and unique receptor subunits that generate the signals necessary for tumorigenesis in this research article on pages 1227–1235 in this issue of *Cancer Immunology Research*. Original micrograph from Gregor Paul, artwork by Lewis Long.



Cancer Immunology Research

3 (11)

Cancer Immunol Res 2015;3:1193-1289.

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