

CANCER IMMUNOLOGY AT THE CROSS-ROADS: COMPLEMENTARY THERAPEUTIC MODALITIES

- 377** Old-School Chemotherapy in Immunotherapeutic Combination in Cancer, A Low-cost Drug Repurposed
Rasha Abu Eid, Ghazaleh Shoja E. Razavi, Mikayel Mkrtychyan, John Janik, and Samir N. Khleif

CANCER IMMUNOLOGY MINIATURES

- 383** Autoimmune Bullous Skin Disorders with Immune Checkpoint Inhibitors Targeting PD-1 and PD-L1
Jarushka Naidoo, Katja Schindler, Christiane Querfeld, Klaus Busam, Jane Cunningham, David B. Page, Michael A. Postow, Alyona Weinstein, Anna Skripnik Lucas, Kathryn T. Ciccolini, Elizabeth A. Quigley, Alexander M. Lesokhin, Paul K. Paik, Jamie E. Chaft, Neil H. Segal, Sandra P. D'Angelo, Mark A. Dickson, Jedd D. Wolchok, and Mario E. Lacouture
Bullous pemphigoid is a rare immune-related adverse event after anti-PD-1/PD-L1 immune checkpoint treatment and may be mediated by both T-cell and B-cell responses. Early referral to dermatology for accurate diagnosis and management is recommended.

RESEARCH ARTICLES

- 390** Expression of the MHC Class II Pathway in Triple-Negative Breast Cancer Tumor Cells Is Associated with a Good Prognosis and Infiltrating Lymphocytes
Andres Forero, Yufeng Li, Dongquan Chen, William E. Grizzle, Katherine L. Updike, Natalie D. Merz, Erinn Downs-Kelly, Todd C. Burwell, Christos Vakilavas, Donald J. Buchsbaum, Richard M. Myers, Albert F. LoBuglio, and Katherine E. Varley
The MHC II pathway is usually turned off in tumor cells. Expression in triple-negative breast tumors was correlated with antitumor responses and reduced relapse risk. MHC II expression may predict good prognosis, and inducing it may have therapeutic benefits.

- 400** IFN γ -Dependent Interactions between ICAM-1 and LFA-1 Counteract Prostaglandin E₂-Mediated Inhibition of Antitumor CTL Responses
Fatemah Salem Basingab, Maryam Ahmadi, and David John Morgan
Robust antitumor CTL responses require adhesion of the killer cell to tumor cells. PGE₂ suppresses CTL function, but this could be overcome by the IFN γ -induced upregulation of ICAM-1, which drove CTL generation and limited tumor growth in vivo.

- 412** TCR Sequencing Can Identify and Track Glioma-Infiltrating T Cells after DC Vaccination
Melody S. Hsu, Shaina Sedighim, Tina Wang, Joseph P. Antonios, Richard G. Everson, Alexander M. Tucker, Lin Du, Ryan Emerson, Erik Yusko, Catherine Sanders, Harlan S. Robins, William H. Yong, Tom B. Davidson, Gang Li, Linda M. Liao, and Robert M. Prins
A clinically translatable platform was developed to track T-cell populations without prior knowledge of their specificity. TCR sequencing data could be used to distinguish patients with glioblastoma who will benefit and are benefitting from immunotherapy.

- 419** Intratumoral CD3 and CD8 T-cell Densities Associated with Relapse-Free Survival in HCC
Andrew Gabrielson, Yunan Wu, Hongkun Wang, Jiji Jiang, Bhaskar Kallakury, Zoran Gatalica, Sandeep Reddy, David Kleiner, Thomas Fishbein, Lynt Johnson, Eddie Island, Rohit Satoskar, Filip Banovac, Reena Jha, Jaydeep Kachhela, Perry Feng, Tiger Zhang, Anteneh Tesfaye, Petra Prins, Christopher Loffredo, John Marshall, Louis Weiner, Michael Atkins, and Aiwu Ruth He
Tumor immune infiltration is a prognostic marker for relapse in patients with colorectal cancer. The Immunoscore methodology was extended to patients with hepatocellular carcinoma. The Immunoscore could predict the risk of postsurgical relapse and duration of relapse-free survival.

- 431** Broadening Specificity and Enhancing Cytotoxicity of Adoptive T Cells for Nasopharyngeal Carcinoma Immunotherapy
Damiana Antonia Faè, Debora Martorelli, Katy Mastorci, Elena Muraro, Jessica Dal Col, Giovanni Franchin, Luigi Barzan, Elisa Comaro, Emanuela Vaccher, Antonio Rosato, and Riccardo Dolcetti
Adoptive T-cell immunotherapy induces some responses in patients with nasopharyngeal carcinoma, but specificities are limited. A simple protocol is described that generates highly effective specific T cells, which could make adoptive immunotherapy more widely applicable.

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441 Inhibition of Soluble Tumor Necrosis Factor Prevents Chemically Induced Carcinogenesis in Mice

Andrea Sobo-Vujanovic, Lazar Vujanovic, Albert B. DeLeo, Fernando Concha-Benavente, Robert L. Ferris, Yan Lin, and Nikola L. Vujanovic

The role of soluble TNF in tumorigenesis, distinct from transmembrane TNF, was delineated. Soluble TNF promoted chemically induced carcinogenesis and mediated the expansion of myeloid-derived suppressor cells. This pathway could serve as a potential target for cancer prevention and therapy.

452 Systemic Immunotherapy of Non-Muscle Invasive Mouse Bladder Cancer with Avelumab, an Anti-PD-L1 Immune Checkpoint Inhibitor

Amanda J. Vandevener, Jonathan K. Fallon, Robert Tighe, Helen Sabzevari, Jeffrey Schlom, and John W. Greiner

In an orthotopic model of non-muscle invasive bladder cancer, in which BCG had minimal activity, systemic administration of the anti-PD-L1 checkpoint inhibitor avelumab demonstrated durable antitumor responses and long-term survival mediated by CD4 and CD8 T cells.

463 Neoantigen Load, Antigen Presentation Machinery, and Immune Signatures Determine Prognosis in Clear Cell Renal Cell Carcinoma

Hirokazu Matsushita, Yusuke Sato, Takahiro Karasaki, Tohru Nakagawa, Haruki Kume, Seishi Ogawa, Yukio Homma, and Kazuhiro Kakimi

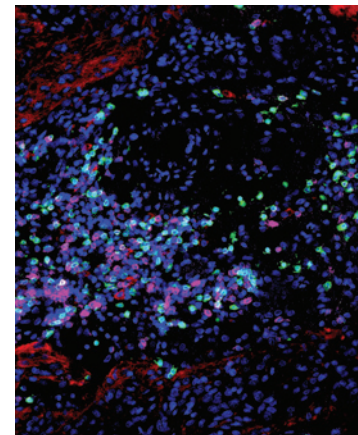
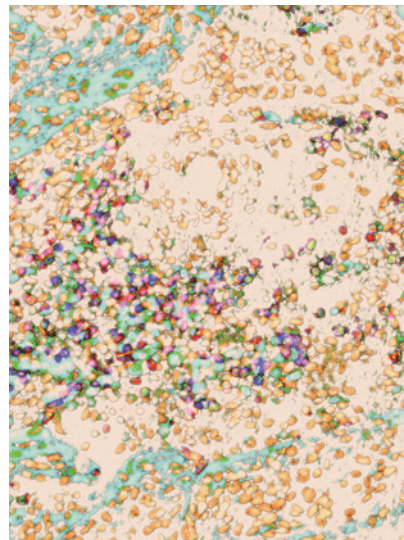
In ccRCC the abundant neoepitopes associated with more effective antitumor immune responses were counterbalanced by a strongly immunosuppressive microenvironment. Therefore, combining blockade of immunosuppressive molecular pathways with immunotherapies targeting neoantigens may achieve synergistic antitumor activity.

CORRECTION

472 Correction: Using Quantitative Seroproteomics to Identify Antibody Biomarkers in Pancreatic Cancer

ABOUT THE COVER

Cancer patients are often treated with immunotherapy; yet it is difficult to readily track the immune response to these treatments. Hsu, Sedighim, and colleagues have developed a clinically translatable platform that allows tracking of individual T-cell clones without prior knowledge of their specificity. By comparing sequences found in glioblastoma tumors to those found in the peripheral blood, the authors verified that the blood samples reflected the same specific T cells infiltrating into the tumors. T-cell receptor sequencing data could help distinguish glioblastoma patients that benefited, or could potentially benefit, from immunotherapy (specifically dendritic cell vaccination). The micrograph (right) upon which the cover this month is based shows, by multiplex immunohistochemistry, a tumor derived from one of the patients in this study. It is heavily infiltrated with T cells, which are critical for the immune response within the microenvironment. Photo by Shaina Sedighim. Artwork by Lewis Long. Read more starting on page 412 of this issue of *Cancer Immunology Research*.



Cancer Immunology Research

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Cancer Immunol Res 2016;4:377-472.

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