CANCER IMMUNOLOGY AT THE CROSSROADS: 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 Mkrtichyan, John Janik, and Samir N. Khleif

CANCER IMMUNOLOGY MINIATURES

383 Autoimmune Bullous Skin Disorders with Immune Checkpoint Inhibitors Targeting PD-1 and PD-L1

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, Erin Downsville-Kelly, Todd C. Burwell, Christos Vaklavas, 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 IFNγ-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 IFNγ-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
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
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 Faut, Debora Martorelli, Katy Mastorci, Elena Muzarco, Jessica Dal Col, Giovanni Franchin, Luigi Barzan, Elisa Comaro, Emanuela Vacher, 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.
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.

Systemic Immunotherapy of Non-Muscle Invasive Mouse Bladder Cancer with Avelumab, an Anti–PD-L1 Immune Checkpoint Inhibitor
Amanda J. Vandeveer, Jonathan K. Fallon, Robert Tighe, Helen Sabzevari, Jeffrey Schlam, 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.

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: Using Quantitative Seroproteomics to Identify Antibody Biomarkers in Pancreatic Cancer
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.