# 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

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

383  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.

# Expression of the MHC Class II Pathway in Triple-Negative Breast Cancer Tumor Cells Is Associated with a Good Prognosis and Infiltrating Lymphocytes

390  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.

# Intratumoral CD3 and CD8 T-cell Densities Associated with Relapse-Free Survival in HCC

395  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.

# Broadening Specificity and Enhancing Cytotoxicity of Adoptive T Cells for Nasopharyngeal Carcinoma Immunotherapy

400  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. Vandeveer, 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.