WHAT WE’RE READING

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MILESTONES IN CANCER IMMUNOLOGY

814 2016 William B. Coley Awards

CANCER IMMUNOLOGY MINIATURES

815 Correlation of PD-L1 Surface Expression on Leukemia Cells with the Ratio of PD-L1 mRNA Variants and with Electrophoretic Mobility
Barbora Brodská, Petra Otevrellová, and Katerína Kuzelová
PD-L1 is a cell surface ligand negatively regulating immune responses. A simple PCR-based method that assesses PD-L1 surface expression is described that overcomes some obstacles to the use of PD-L1 as a prognostic marker and therapeutic target in leukemia.

820 Tumor Mutational Load and Immune Parameters across Metastatic Renal Cell Carcinoma Risk Groups
mRCC patients were assessed for mutational load and expression of active tumor microenvironment markers to find correlates with MSKCC risk prognostic classifications. No correlations were found; thus, patients who would benefit most from immunotherapy are not yet identifiable.

RESEARCH ARTICLES

823 Therapeutic HPV Cancer Vaccine Targeted to CD40 Elicits Effective CD8+ T-cell Immunity
In the U.S., HPV is responsible for more than 26,000 new cancer cases annually. A novel and effective immunotherapeutic vaccine against many types of HPV16-associated cancers was developed that supports targeting vaccines to dendritic cells via CD40.

835 Deep Sequencing of T-cell Receptor DNA as a Biomarker of Clonally Expanded TILs in Breast Cancer after Immunotherapy
Tumor cryoablation plus immune checkpoint blockade facilitates antitumor T-cell responses (TCRs) and improves survival in mice. Deep sequencing of TCRs in human early-stage breast cancer tumors revealed T-cell clonality and density and served as a biomarker after cryo-immunotherapy.

845 Response to Programmed Cell Death-1 Blockade in a Murine Melanoma Syngeneic Model Requires Costimulation, CD4, and CD8 T Cells
Although blockade of the PD-1 pathway has been successfully used to treat various cancers, how this modulates host-tumor interactions is not well understood. Additional mechanisms beyond licensing the final effector phase of killer T cells were identified.

858 VEGF Neutralization Plus CTLA-4 Blockade Alters Soluble and Cellular Factors Associated with Enhancing Lymphocyte Infiltration and Humoral Recognition in Melanoma
Xinqi Wu, Anita Giobbie-Hurder, Xiaoyun Liao, Donald Lawrence, David McDermott, Jun Zhou, Scott Rodig, and F. Stephen Hodi
Inhibiting both CTLA-4 and VEGF can lead to favorable clinical outcomes. This treatment increased the expression of IL1α, TNFα, IFN-γ, and PD-L1, and the adhesion receptors associated with increased tumor lymphocyte infiltration, and augmented humoral immune responses recognizing tumor targets.
Reduction of MDSCs with All-trans Retinoic Acid Improves CAR Therapy Efficacy for Sarcomas
Adrienne H. Long, Steven L. Highfill, Yongzhi Cui, Jillian P. Smith, Alec J. Walker, Sneha Ramakrishna, Rana El-Etriby, Susana Galli, Maria G. Tsokos, Rimas J. Orentas, and Crystal L. Mackall

The efficacy of chimeric antigen receptor (CAR)-modified T cells against solid tumors is not proven. Retinoids are clinically accessible and were found to modulate tumor myeloid-derived suppressor cells, enhancing the efficacy of CAR therapies targeting solid tumors.

Tn-MUC1 DC Vaccination of Rhesus Macaques and a Phase I/II Trial in Patients with Nonmetastatic Castrate-Resistant Prostate Cancer
Elizabeth Scheid, Pierre Major, Alain Bergeron, Olivera J. Finn, Russell D. Salter, Robin Eady, Bader Yassine-Diab, David Favre, Yoav Peretz, Claire Landry, Sebastien Hotte, Som D. Mukherjee, Gregory A. Dekaban, Corby Fink, Paula J. Foster, Jeffery Gaudet, Jean Gariepy, Rafick-Pierre Sekaly, Louis Lacombe, Yves Fradet, and Ronan Foley

Tumor-associated Tn-MUC1 glycosylated, but not unglycosylated, peptides, induce strong murine immunity. Tn-MUC1 vaccination in macaques and a clinical trial with a Tn-MUC1-DC vaccine confirmed the safety and the superiority of Tn-MUC1 vaccination for induction of cellular immune responses.

ABOUT THE COVER
Cancer treatments have traditionally worked best in combination, either by combining multiple chemotherapies or by combining treatment modalities (for example, chemotherapy plus radiation therapy). Immunotherapies have had some spectacular successes, but usually work well in only a small percentage of patients. A combination strategy, cryoablation plus anti–CTLA-4 blockade was tested for its safety as a pre-operative therapy in early stage breast cancer, and Page et al. used deep sequencing of T-cell receptors (TCRs) to measure the quantity and diversity of immune responses. They found that DNA sequencing could be more sensitive than histological stains in determining intratumoral T cell presence, and that the combination of cryo-immunotherapy, rather than either therapy alone, induced more T-cell clones to expand dramatically within the tumor bed. Read more in Page et al., starting on page 835 of this issue. The high-resolution multispectral immunofluorescence image on the right shows immune cell infiltration in an early stage breast cancer specimen (photo from Carmen Ballesteros-Merino of the Bernard Fox lab, in collaboration with David Page). Artwork by Lewis Long.