CANCER IMMUNOLOGY AT THE CROSSROADS: TUMOR MICROENVIRONMENT

83  The Complex Role of Neutrophils in Tumor Angiogenesis and Metastasis
Wei Liang and Napoleone Ferrara

CANCER IMMUNOLOGY MINIATURES

92  The Trojan Horse Tale Revisited: An Eye on Metastatic Spread of Carcinoma Cells
Rafael S. Grajewski, Jacobus J. Bosch, Heiko Bruns, Claus Cursiefen, and Ludwig M. Heindl

Macrophages expressing tumor markers were detected in the blood and eye of a patient with parotid gland carcinoma. These "Trojan horses" may transport tumor cells to distant organs, where carcinomas could grow and establish metastases in new environments.

PRIORITY BRIEF

95  Vaccines Combined with Immune Checkpoint Antibodies Promote Cytotoxic T-cell Activity and Tumor Eradication
Omar A. Ali, Sarah A. Lewin, Glenn Dranoff, and David J. Mooney

Despite dramatic clinical successes for cancer vaccines and immune checkpoint blockade, disease usually progresses. In a mouse model that combined vaccines with checkpoint blockade, significant CTL activation, tumor eradication, and long-term survival was achieved.

RESEARCH ARTICLES

101  MIF Is Necessary for Late-Stage Melanoma Patient MDSC Immune Suppression and Differentiation
Kaviha Yaddanapudi, Beatriz E. Rendon, Gwyneth Lamont, Eun Jung Kim, Numan Al Rayyan, Jamaal Richie, Sabrin Albeituni, Sabine Waigel, Ashley Wise, and Robert A. Mitchell

Macrophage migration inhibitory factor (MIF) is produced by monocytes in cancer-bearing mice and humans. MIF was found to be critical for suppressive monocyctic cells in melanoma patients, and when inhibited, the monocyctic cells acquire antitumor phenotypes.

113  Retuning of Mouse NK Cells after Interference with MHC Class I Sensing Adjusts Self-Tolerance but Preserves Anticancer Response
Arnika Kathleen Wagner, Stina Linnea Wickström, Rossana Tallerico, Sadia Salam, Tadepally Lalakshminarayana, Hanna Brauner, Petter Högland, Ennio Carbone, Maria Helena Johansson, and Klas Kärre

NK cell-based immunotherapy may be hampered by adaptation to reduced inhibitory input from MHC molecules on surrounding cells. However, while such readjustment of responsiveness leads to tolerance to healthy cells, reactivity to cancer cells remains.

124  Glioblastoma Eradication Following Immune Checkpoint Blockade in an Orthotopic, Immunocompetent Model

Glioblastoma has been especially challenging to treat. In a systematic analysis of combinations of checkpoint therapies in a murine model, some single and dual immunotherapies increased intratumoral effectors, reduced suppressors, and eliminated the tumors.

136  Hypomethylation of the Treg-Specific Demethylated Region in FOXP3 Is a Hallmark of the Regulatory T-cell Subtype in Adult T-cell Leukemia
Yayoi Shimazu, Yutaka Shimazu, Masahide Hamaguchi, Yuya Nagai, Noriko Sugino, Sumie Fujii, Masahiro Kawahara, Norimitsu Kadowaki, Hirooishii Nishikawa, Shimon Sakaguchi, and Akifumi Takaori-Kondo

A subtype of adult T-cell leukemia cells can be distinguished based on the hypomethylated state of their FOXP3 gene. These cells have Treg properties, and the patients have a poor prognosis.

146  Intratumoral Delivery of TriMix mRNA Results in T-cell Activation by Cross-Presenting Dendritic Cells
Sandra Van Lint, Dries Renmans, Katrijn Broos, Lode Goethals, Sarah Maenhout, Daphné Benteyn, Cleo Goyvaerts, Stephanie Du Four, Kevin Van der Jeught, Lukasz Bialkowski, Véronique Flmand, Carlo Heirman, Kris Thielenmans, and Karine Breckpot

Intratumoral injection of CTL-stimulatory agents could provide another avenue for immunotherapy. TriMix mRNA, comprising three DC-oriented stimulatory mRNAs, was examined in mouse models and provides a rationale for clinical testing in solid and accessible tumors.
Identification of Anti-CA125 Antibody Responses in Ovarian Cancer Patients by a Novel Deep Sequence–Coupled Biopanning Platform

Kathryn M. Frietze, Richard B.S. Roden, Ji-Hyun Lee, Yang Shi, David S. Peabody, and Bryce Chackerian

Ovarian cancer would benefit from the identification of early biomarkers of prognostic value. Deep sequence–coupled biopanning identified autoantibody responses to a CA125 epitope in a subset of ovarian cancer patients that correlated with extended survival.

Survivin Autoantibodies Are Not Elevated in Lung Cancer When Assayed Controlling for Specificity and Smoking Status

Ingrid Broodman, Martijn M. VanDuijn, Christoph Stingl, Lennard J.M. Dekker, Anastasios E. Germenis, Harry J. de Koning, Rob J. van Klaveren, Joachim G. Aerts, Jan Lindemans, and Theo M. Luider

Reports of autoantibodies to survivin in lung cancer sera lead to suggestions of roles as biomarkers. The authors tested patient serum with two approaches, controlling for specificity and using controls stratified for smoking habits. No autoreactivity was found.

Correction: Human Leukocyte Antigen (HLA) A*1101-Restricted Epstein-Barr Virus–Specific T-cell Receptor Gene Transfer to Target Nasopharyngeal Carcinoma

ABOUT THE COVER

Tumors create havoc by making their own rules. How cancer cells may travel and seed a new site, such as the immune-privileged eye, is not always clear. A case of "Trojan horse" travel is described by Grajewski and colleagues starting on p. 92 in this issue of Cancer Immunology Research. A covert parotid carcinoma may have traveled to the aqueous humor of the eye by fusing with migratory phagocytic cells to create monocyte–macrophage Trojan horses. The eye's trabecular network trapped these cells (the yellow section, lower left, of the iris), and they proliferated, causing a rare type of carcinoma in the aqueous humor. Artwork is by Lewis Long.