Masters of Immunology

The Carcinoma-Associated Fibroblast Expressing Fibroblast Activation Protein and Escape from Immune Surveillance
Douglas T. Fearon

Cancer Immunology at the Crossroads: Experimental Immunotherapies

IL-10: Master Switch from Tumor-Promoting Inflammation to Antitumor Immunity
Martin Oft

Priority Brief

Transient Complement Inhibition Promotes a Tumor-Specific Immune Response through the Implication of Natural Killer Cells
Valérie Janelle, Marie-Pierre Langlois, Esther Tarrab, Pascal Lapierre, Laurent Poliquin, and Alain Lamarre
Synopsis: Using cobra venom factor to induce transient C3 molecule exhaustion in a mouse model of melanoma, Janelle and colleagues show that the antitumor immune response is NK dependent, uncovering a link between complement proteins and NK cells in tumor development.

Research Articles

Disruption of CD8⁺ Treg Activity Results in Expansion of T Follicular Helper Cells and Enhanced Antitumor Immunity
Diana A. Alvarez Arias, Hye-Jung Kim, Penghui Zhou, Tobias A.W. Holderried, Xuan Wang, Glenn Dranoff, and Harvey Cantor
Synopsis: Alvarez Arias, Kim, and colleagues show that disruption of CD8⁺ Tregs binding to Qa-1⁺ T follicular helper cells (Tfh) improves tumor vaccination-elicited immunity, a robust autoimmune antitumor response driven by enhanced Tfh activity and a strong antibody response.

Establishment of Tumor-Associated Immunity Requires Interaction of Heat Shock Proteins with CD91
Yu Jerry Zhou, Michelle Nicole Messmer, and Robert Julian Binder
Synopsis: Zhou and colleagues identify a mechanism by which immune responses are primed against a developing tumor: Disruption of the HSP-CD91 pathway abrogates cross-presentation of tumor-derived antigenic peptides and prevents antitumor immunity that characterizes tumor immunosurveillance.

Ex Vivo Assays of Dendritic Cell Activation and Cytokine Profiles as Predictors of In Vivo Effects in an Anti-Human CD40 Monoclonal Antibody Chilob 7/4 Phase I Trial
F. Chowdhury, P.W. Johnson, M.J. Glennie, and A.P. Williams
Synopsis: Chowdhury and colleagues use whole blood samples in ex vivo assays to show that Chilob 7/4 induces a pattern of DC activation and cytokine secretion matching the in vivo responses, providing a strategy to predict dosages and cytokine release syndromes.

Untreated Stage IV Melanoma Patients Exhibit Abnormal Monocyte Phenotypes and Decreased Functional Capacity
Rahul Chavan, Daniela Salvador, Michael P. Gustafson, Allan B. Dietz, Wendy Nevala, and Svetomir N. Markovic
Synopsis: Chavan and colleagues analyzed peripheral blood mononuclear cells from 18 patients with untreated stage IV melanoma; they found a decrease in the frequency of circulating myeloid dendritic cells and classical CD14⁺ CD16⁻ monocytes, and the latter also have decreased functional capacity.

Gene-Modified Human α/β-T Cells Expressing a Chimeric CD16-CD3ζ Receptor as Adoptively Transferable Effector Cells for Anticancer Monoclonal Antibody Therapy
Fumihiro Ochi, Hiroshi Fujiwara, Kazushi Tanimoto, Hiroaki Asai, Yukihiro Miyazaki, Sachiko Okamoto, Junichi Mineno, Kiyotaka Kuzushima, Hiroshi Shiku, John Barrett, Eiichi Ishii, and Masaki Yasukawa
Synopsis: Ochi and colleagues engineered T cells to express chimeric CD16 V158-CD3ζ receptors that mediate antibody-dependent tumoricidal activity; upon stimulation these T cells proliferate and differentiate into effector memory T cells, which could combine with and enhance clinical responses by anticancer monoclonal antibodies.

Influenza Virus Infection Elicits Protective Antibodies and T Cells Specific for Host Cell Antigens Also Expressed as Tumor-Associated Antigens: A New View of Cancer Immunosurveillance
Uzoma K. Iheagwara, Pamela L. Beatty, Phu T. Van, Ted M. Ross, Jonathan S. Minden, and Olivera J. Finn
Synopsis: Iheagwara and colleagues used a mouse model of influenza virus infection to validate a new cancer immunosurveillance hypothesis and show that viral infections elicit immunity against antigens abnormally expressed in infected cells and cancer cells that can provide effective anticancer control.
Polyamine-Blocking Therapy Reverses Immunosuppression in the Tumor Microenvironment

Candace S. Hayes, Allyson C. Shicora, Martin P. Keough, Adam E. Snook, Mark R. Burns, and Susan K. Gilmour

Synopsis: Hayes and colleagues report that polyamine elevation in cancer contributes significantly to tumor immunosuppression; they developed a novel polyamine-depletion strategy combining inhibitors of the polyamine transport system and ornithine decarboxylase to prevent tumor immune escape and promote antitumor immunity.

ABOUT THE COVER

The ability of T cells to accumulate among cancer cells is impaired in many cancers. T-cell exclusion from the “cancer cell nests” may account for the failure of systemic immunity to control tumor growth, and for the absence of a response to checkpoint antagonist anti–PD-1 in the murine model of pancreatic ductal adenocarcinoma (PDA). Recent studies have shown that fibroblast-like stromal cells, termed carcinoma-associated fibroblasts (CAF), in the tumor microenvironment exert an immune-suppressive function, and the depletion of CAF permits tumor infiltration of T cells and control of PDA tumors. PDA cancer cells are p53+ because they contain stable p53R172H proteins due to the loss of the wild-type p53 allele. The cover image is a confocal immunofluorescence photomicrograph of a mouse PDA containing epithelial cells (stained green for cytokeratin 19), p53+ cancer cells (silver), and CAF that express fibroblast-activating protein-1 (FAP; red). All nuclei are stained blue with DAPI. For details, see the Masters of Immunology article by Douglas T. Fearon on page 187 of this issue.