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Cancer Immunology Research

Illuminating the Interplay of Cancer and the Immune System

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Hiroto Nakahara, Brantley R. Herrin, Matthew N. Alder, Rosa CATERA, Xiao-Jie Yan, Nicholas Chiorazzi, and Max D. Cooper
- Synopsis:* Using B cells from patients with chronic lymphocytic leukemia (CLL), Nakahara and colleagues have produced a lamprey monoclonal antibody with CLL idiotope specificity that can be used for early detection of leukemia recurrence. Lamprey antibodies can be generated rapidly and offer a complementary approach to the use of classical Ig-based anti-idiotope antibodies in the monitoring and management of patients with CLL.

PRIORITY BRIEF

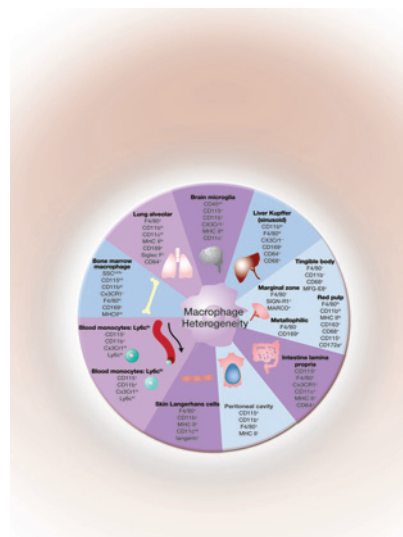
- 229 **Increased Frequency of ICOS⁺ CD4 T Cells as a Pharmacodynamic Biomarker for Anti-CTLA-4 Therapy**
Derek Ng Tang, Yu Shen, Jingjing Sun, Sijin Wen, Jedd D. Wolchok, Jianda Yuan, James P. Allison, and Padmanee Sharma
- Synopsis:* In a retrospective study, Tang and colleagues identified an increase in ICOS⁺ CD4 T cells following anti-CTLA-4 therapy and proposed its use as a pharmacodynamic biomarker for anti-CTLA-4 immunotherapy.

RESEARCH ARTICLES

- 235 **Enhancement of Tumor-Reactive Cytotoxic CD4⁺ T-cell Responses after Ipilimumab Treatment in Four Advanced Melanoma Patients**
Shigehisa Kitano, Takemasa Tsuji, Caillian Liu, Daniel Hirschhorn-Cymerman, Chrisann Kyi, Zhenyu Mu, James P. Allison, Sacha Gnjatich, Jianda D. Yuan, and Jedd D. Wolchok
- Synopsis:* Using archived blood samples from 4 NY-ESO-1-seropositive patients with advanced melanoma who were treated with the CTLA-4-blocking monoclonal antibody ipilimumab, Kitano and colleagues analyzed changes in antigen-specific CD4⁺ T cells during cancer immunotherapy. They characterized a novel consequence of the CTLA-4 blockade, the induction or expansion of tumor-reactive cytotoxic CD4⁺ T cells after ipilimumab treatment.
- 245 **Lysophosphatidic Acid Inhibits CD8 T-cell Activation and Control of Tumor Progression**
Shannon K. Oda, Pamela Strauch, Yuko Fujiwara, Amin Al-Shami, Tamas Oravec, Gabor Tigyi, Roberta Pelanda, and Raul M. Torres
- Synopsis:* Oda and colleagues show that lysophosphatidic acid (LPA) suppression of T-cell activation and proliferation is mediated by the LPA₅ receptor expressed by CD8 T cells, and that LPA₅-deficient CD8 T cells are more efficient in controlling the growth of established tumors in a murine melanoma model. These data suggest that LPA₅ blockade may provide an additional strategy to promote tumor immunity.
- 256 **Phosphatidylserine-Targeting Antibody Induces M1 Macrophage Polarization and Promotes Myeloid-Derived Suppressor Cell Differentiation**
Yi Yin, Xianming Huang, Kristi D. Lynn, and Philip E. Thorpe
- Synopsis:* Through their treatment of mouse models of human prostate cancer with the combined regimen of docetaxel and 2aG4, the mouse IgG2a version of bavituximab, a humanized antiphosphatidylserine (anti-PS)-targeting chimeric antibody (Ab) currently being tested in clinical trials for cancer, Yin and colleagues explored potential strategies by which anti-PS-targeting Ab alter the tumor microenvironment to restore tumor immunity.

ABOUT THE COVER

Macrophages are a heterogeneous population of tissue resident hematopoietic cells. This figure illustrates key cell surface markers of mouse macrophage and monocyte populations. Macrophages can be identified by a combination of cell surface markers, including the hematopoietic lineage marker CD45, the integrin CD11b, and the GPCR F4/80, among other markers. However, macrophages in different organs have different compositions and expression levels of these cell surface proteins, reflecting their inherent diversity. CD169, sialoadhesin, is an important marker in certain macrophage populations such as the bone marrow, spleen, and lung. CX3CR1 helps to identify macrophages in the intestine and to differentiate the blood monocyte subsets. For details, see the Masters of Immunology article by Lavin and Merad on page 201 of this issue.



ABOUT THE MASTER

Miriam Merad, MD, PhD, is Professor of Oncological Science in the Department of Medicine and Immunology and a member of the Immunology Institute and The Tisch Cancer Institute at the Mount Sinai School of Medicine in New York. Dr. Merad received her MD from the University of Algiers, Algeria. She did her residency in hematology and oncology in Paris, France, and obtained her PhD in immunology in collaboration between Stanford University and University of Paris VII. She was recruited to Mount Sinai School of Medicine in 2004 and was promoted to the rank of associate professor with tenure in 2007 and to full professor in 2010.

In 2010, Dr. Merad became the program leader of the Cancer Immunology Immunotherapy Group at The Tisch Cancer Institute and the director of the Human Immunomonitoring Center. Dr. Merad also serves as the associate director for the MD/PhD Program at Mount Sinai Medical School.

Dr. Merad's laboratory studies the mechanisms that regulate the development and function of innate myeloid cells, including dendritic cells, Langerhans cells, and macrophages. The Merad laboratory has made seminal discoveries in Langerhans cells and macrophage biology revealing their embryonic origin and their local maintenance *in situ*. Dr. Merad's laboratory has also extensively studied the mechanisms that control dendritic cells and macrophage homeostasis and function in barrier tissues such as the skin, lung, and gut. More recently she joined the ImmGen Consortium to help decipher the transcriptional regulation of the tissue dendritic cell and macrophage lineage. Currently, one of the major goals of the Merad laboratory is to identify the contribution of innate myeloid cells to disease outcome, including cancer and microbial immunity.

Dr. Merad has authored more than 100 primary papers and reviews in high-profile journals and obtained extensive NIH funding for her studies on dendritic cells and macrophage biology in mice and humans.



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