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Illuminating the Interplay of Cancer and the Immune System
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158 **Ipilimumab Treatment Results in an Early Decrease in the Frequency of Circulating Granulocytic Myeloid-Derived Suppressor Cells as well as Their Arginase1 Production**
Yago Pico de Coaña, Isabel Poschke, Giusy Gentilcore, Yumeng Mao, Maria Nyström, Johan Hansson, Giuseppe V. Massucci, and Rolf Kiessling

Synopsis: *Pico de Coaña and colleagues analyzed peripheral blood from patients undergoing ipilimumab treatment at weeks 0, 3, and 9 and found a sequential decrease in the frequencies of granulocytic MDSC and arginase1-producing CD3-negative cells. At week 9, they found a lower number of Tregs and reduced PD-1 surface expression in CD3-positive cells.*

PRIORITY BRIEF

163 **Human Regulatory T Cells Kill Tumor Cells through Granzyme-Dependent Cytotoxicity upon Retargeting with a Bispecific Antibody**
Bryan D. Choi, Patrick C. Gedeon, James E. Herndon II, Gary E. Archer, Elizabeth A. Reap, Luis Sanchez-Perez, Duane A. Mitchell, Darell D. Bigner, and John H. Sampson

Synopsis: *Regulatory T cells play a central role in tumor escape from immune-mediated rejection. Using a bispecific antibody targeting the tumor-specific mutation of the EGF receptor, EGFRvIII, Choi and colleagues describe a new mechanism they identified by which regulatory T cells can be redirected to elicit potent antitumor activity.*

RESEARCH ARTICLES

168 **Chemoimmunotherapy Using Pegylated Liposomal Doxorubicin and Interleukin-18 in Recurrent Ovarian Cancer: A Phase I Dose-Escalation Study**
Fiona Simpkins, Aurea Flores, Christina Chu, Jonathan S. Berek, Joseph Lucci III, Sharon Murray, John Bauman, Herbert Struemper, Fiona Germaschewski, Zdenka Jonak, Olivia Gardner, John Toso, and George Coukos

Synopsis: *Simpkins and colleagues found that the combination of FDA-approved dose and schedule of pegylated liposomal doxorubicin (PLD) with human recombinant IL-18 (SB-485232) in patients with recurrent advanced ovarian cancer induced minimal toxicity across the IL-18 dose range studied and did not reach a maximum tolerated dose. The concomitant and repeat administration of PLD did not attenuate the immunostimulatory effects of IL-18, providing a rationale for a future phase II trial to further evaluate this combination regimen.*

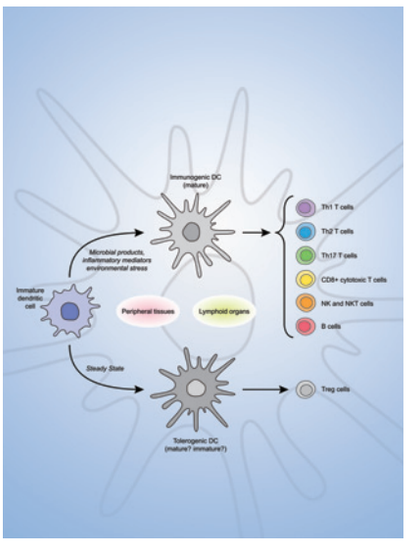
179 **Highly Optimized DNA Vaccine Targeting Human Telomerase Reverse Transcriptase Stimulates Potent Antitumor Immunity**
Jian Yan, Panyupa Pankhong, Thomas H. Shin, Nyamekye Obeng-Adjei, Matthew P. Morrow, Jewell N. Walters, Amir S. Khan, Niranjan Y. Sardesai, and David B. Weiner

Synopsis: *Yan and colleagues evaluated the efficacy of a synthetic, optimized, electroporation-delivered DNA vaccine targeting hTERT in overcoming tolerance and inducing hTERT-specific antitumor immunity in murine and nonhuman primate models.*

190 **Alternative Variants of Human *HYDIN* Are Novel Cancer-Associated Antigens Recognized by Adaptive Immunity**
Karoline Laske, Yuriy V. Shebzukhov, Ludger Grosse-Hovest, Dmitry V. Kuprash, Svetlana V. Khlgatian, Ekaterina P. Koroleva, Alexey Y. Sazykin, Dmitry N. Penkov, Pavel V. Belousov, Stefan Stevanović, Verona Vass, Steffen Walter, David Eisel, Barbara D. Schmid-Horch, Sergei A. Nedospasov, Hans-Georg Rammensee, and Cécile Gouttefangeas

Synopsis: *Using sera from patients with colorectal cancer, Laske and colleagues identified a novel alternative* HYDIN *transcript from a testis-derived cDNA expression library with reactivity to patient IgG, and defined two* HYDIN *variants as novel tumor-associated antigens recognized by both antibodies and CD8 cytotoxic T cells.*

ABOUT THE COVER



Depending on the type of signals encountered, a resting dendritic cell is converted into either a tolerogenic or an immunogenic state that programs the development of subsets of T cells, each with distinct functions adapted to the signal detected by the dendritic cell. Different arrays of cytokines released by these differentially matured dendritic cells play an important role in determining T-cell development outcomes. The cover image is a schematic diagram of the functional consequences of dendritic cell maturation. For details see the Masters of Immunology article by Ira Mellman on page 145 of this issue. [The cover image was rendered by Allison Bruce (Genentech).]

ABOUT THE MASTER

Ira Mellman received his AB degree from Oberlin College and his PhD degree in genetics from Yale University School of Medicine. He was a postdoctoral fellow and later assistant professor at The Rockefeller University, working with the late Ralph M. Steinman, the 2011 Nobel Prize winner in Physiology or Medicine. Dr. Mellman joined the Yale Department of Cell Biology, which was then headed by Nobel Laureate Dr. George E. Palade, whom he eventually succeeded as chair. Dr. Mellman has been a long-time member of the Ludwig Institute for Cancer Research and served as Scientific Director of the Yale Comprehensive Cancer Center. He is a member of the U.S. National Academy of Sciences, a fellow of the American Academy of Arts and Sciences, and an elected foreign member of the European Molecular Biology Organization. Dr. Mellman is the founder of CGI Pharmaceuticals, Inc. (now owned by Gilead) and Athersys, Inc., and an advisor to research institutes and foundations around the world.

Dr. Mellman's work has contributed numerous fundamental concepts to our current understanding of cell biology and immunology, beginning with the discovery, definition, and naming of a "new" organelle, the endosome. Extending this work, his laboratory helped to elucidate the mechanisms by which epithelial cells polarize to form tissues and initiate cancer and revealed the various specializations responsible for the ability of dendritic cells to initiate immune responses.

Dr. Mellman joined Genentech in 2007 as the Vice President of Research Oncology. Placed in charge of the largest therapeutic area in Genentech's research organization, Dr. Mellman is responsible for leading all aspects of oncology research and advancing both antibody and small-molecule drug candidates into the clinic. The development of immunotherapeutic approaches to cancer is now a key feature of Genentech's activities. Dr. Mellman also serves as Professor of Biochemistry and Biophysics at the University of California, San Francisco.

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