


WHAT WE'RE READING

- 1289** A Sampling of Highlights from the Literature

IN THE SPOTLIGHT

- 1290** Of Microbes and Microsatellites
Chloe E. Atreya and Alan P. Venook
[See related article, p. 1327.](#)


PRIORITY BRIEF


- 1292** Restoration of Endogenous Retrovirus Infectivity Impacts Mouse Cancer Models
 Eleonora Ottina, Prisca Levy, Urszula Eksmond, Julia Merckenschlager, George R. Young, Juliette Roels, Jonathan P. Stoye, Thomas Tüting, Dinis P. Calado, and George Kassiotis
Commonly used murine cancer models were affected by mouse-specific, reactivated endogenous retroviruses (ERVs). ERVs were shown to alter tumor progression and antitumor immunity, emphasizing that ERVs are a confounding variable and, if possible, should be avoided during investigations.

RESEARCH ARTICLES

- 1301** Nanoparticle Conjugation of Human Papillomavirus 16 E7-long Peptides Enhances Therapeutic Vaccine Efficacy against Solid Tumors in Mice
 Gabriele Galliverti, Mélanie Tichet, Sonia Domingos-Pereira, Sylvie Hauert, Denise Nardelli-Haeffliger, Melody A. Swartz, Douglas Hanahan, and Stephan Wullschlegel
A nanoparticle-based long peptide vaccine activates CD8⁺ T cells and improves therapeutic efficacy in mouse models of HPV-driven cancer. This strategy may be effective in enhancing responses in other solid tumors, suggesting its potential for clinical development.
- 1314** Selective Targeting of Glioblastoma with EGFRvIII/EGFR Bitargeted Chimeric Antigen Receptor T Cell
Hua Jiang, Huiping Gao, Juan Kong, Bo Song, Peng Wang, Bizhi Shi, Huamao Wang, and Zonghai Li
CAR T cells targeting EGFR- and EGFRvIII-overexpressing tumor cells exhibit antitumor activity without toxicity toward normal EGFR-expressing cells in mouse glioblastoma models. This strategy may provide an avenue for future therapeutic development in EGFR- and EGFRvIII-overexpressing cancers.

- 1327** *Fusobacterium nucleatum* in Colorectal Cancer Relates to Immune Response Differentially by Tumor Microsatellite Instability Status
Tsuyoshi Hamada, Xuehong Zhang, Kosuke Mima, Susan Bullman, Yasutaka Sukawa, Jonathan A. Nowak, Keisuke Kosumi, Yohei Masugi, Tyler S. Twombly, Yin Cao, Mingyang Song, Li Liu, Annacarolina da Silva, Yan Shi, Mancang Gu, Wanwan Li, Hideo Koh, Katsuhiko Noshio, Kentaro Inamura, NaNa Keum, Kana Wu, Jeffrey A. Meyerhardt, Aleksandar D. Kostic, Curtis Huttenhower, Wendy S. Garrett, Matthew Meyerson, Edward L. Giovannucci, Andrew T. Chan, Charles S. Fuchs, Reiko Nishihara, Marios Giannakis, and Shuji Ogino
In patients with colorectal cancer, the presence of Fusobacterium nucleatum may suppress immune responses for microsatellite instability (MSI)-high tumors and encourage immune responses for non-MSI-high tumors. F. nucleatum and MSI status interact to affect antitumor immune reactions.
[See related Spotlight, p. 1290.](#)

- 1337** The Protease-Dependent Mesenchymal Migration of Tumor-Associated Macrophages as a Target in Cancer Immunotherapy
 Philippe Gui, Myriam Ben-Neji, Ekaterina Belozertseva, Florence Dalenc, Camille Franchet, Julia Gilhodes, Arnaud Labrousse, Elisabeth Bellard, Muriel Golzio, Renaud Poincloux, Isabelle Maridonneau-Parini, and Véronique Le Cabec
Migration patterns of human and mouse tumor-associated macrophages (TAMs) were evaluated and compared with macrophage migration in nontumorous tissues. TAMs and other macrophage populations used differential modes of migration, highlighting TAM motility as a potential target for therapy.

- 1352** *lnc-C/EBPβ* Negatively Regulates the Suppressive Function of Myeloid-Derived Suppressor Cells
 Yunhuan Gao, Wei Sun, Wencong Shang, Yuanyuan Li, Dan Zhang, Tianze Wang, Xipeng Zhang, Shiwu Zhang, Yuan Zhang, and Rongcun Yang
A long noncoding RNA, lnc-C/EBPβ, regulated the differentiation and function of myeloid-derived suppressor cells (MDSCs) and was found to also bind and inhibit C/EBPβ activation. This finding provides insights into MDSC regulation and could enable more precise therapeutic targeting for tumors.

- 1364** TLR Stimulation during T-cell Activation Lowers PD-1 Expression on CD8⁺ T Cells
Christopher D. Zahm, Viswa T. Colluru, Sean J. McIlwain, Irene M. Ong, and Douglas G. McNeel
Ligands for TLR1/2, TLR7, and TLR9 led to decreased expression of PD-1 on activated CD8⁺ T cells, an effect mediated by IL12 from professional antigen-presenting cells. This effect resulted in improved antitumor immunity when combined with antigen-specific vaccination.

Table of Contents

- 1375** **PPAR-Induced Fatty Acid Oxidation in T Cells Increases the Number of Tumor-Reactive CD8⁺ T Cells and Facilitates Anti-PD-1 Therapy**
Partha S. Chowdhury, Kenji Chamoto, Alok Kumar, and Tasuku Honjo
PPAR signal activation enhanced the efficacy of PD-1 blockade cancer immunotherapy. The PPAR signal boosts fatty acid oxidation to rescue T cells from apoptosis by upregulating anti-apoptotic genes including bcl2, thus increasing the number of killer T cells.

- 1388** **Immune Cell Gene Signatures for Profiling the Microenvironment of Solid Tumors**
Ajit J. Nirmal, Tim Regan, Barbara B. Shih, David A. Hume, Andrew H. Sims, and Tom C. Freeman
ImSig is a resource of gene signatures for the quantitative and qualitative assessment of immune cells in the tumor microenvironment. It can be used on other tissue pathologies and identifying the immune component of single-cell transcriptomics data.

- 1401** **Somatic Mutations and Immune Alteration in Rectal Cancer Following Neoadjuvant Chemoradiotherapy**
Dengbo Ji, Haizhao Yi, Dakui Zhang, Tiancheng Zhan, Zhaowei Li, Ming Li, Jinying Jia, Meng Qiao, Jinhong Xia, Zhiwei Zhai, Can Song, and Jin Gu
Patients with locally advanced rectal cancer treated with neoadjuvant chemoradiotherapy (nCRT) exhibited induced immune activation, which improved immune checkpoint blockade efficacy in an in vivo model. Patient tumor mutation burden and neoantigen landscape also associated with nCRT responses.

- 1417** **Cripto-1 Plasmid DNA Vaccination Targets Metastasis and Cancer Stem Cells in Murine Mammary Carcinoma**
Kristina Witt, Maarten A. Ligtenberg, Laura Conti, Stefania Lanzardo, Roberto Ruij, Tatjana Wallmann, Helena Tufvesson-Stiller, Benedict J. Chambers, Charlotte Rolny, Alvaro Lladser, Andreas Lundqvist, Federica Cavallo, and Rolf Kiessling
A DNA vaccine targeting tumor-associated antigen Cripto-1 slowed tumor growth and reduced metastases in mouse models of breast cancer. The vaccine may have potential use as an immunotherapeutic for the treatment of metastatic breast cancer.

- 1426** **Stromal Cell PD-L1 Inhibits CD8⁺ T-cell Antitumor Immune Responses and Promotes Colon Cancer**
Grace O'Malley, Oliver Treacy, Kevin Lynch, Serika D. Naicker, Niamh A. Leonard, Paul Lohan, Philip D. Dunne, Thomas Ritter, Laurence J. Egan, and Aideen E. Ryan
Mesenchymal stromal cells (MSCs) present in colorectal cancer (CRC) were found to suppress antitumor responses in vitro and in vivo via PD-1/PD-L1. The results emphasize that PD-L1 on tumor MSCs can impact the efficacy of treatments for CRC.

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ABOUT THE COVER

Infiltration by tumor-associated macrophages (TAMs) can promote the progression of cancer. It is thought that macrophages use a similar mode of migration as other leukocytes (i.e. amoeboid motility). However, the mechanism of macrophage migration in tumoral tissues has not been elucidated. Gui et al. determined that TAM migration differs from the migration patterns of other leukocytes, including other macrophage populations in nontumor tissues. TAMs use the protease-dependent mesenchymal mode to migrate into mouse and human tumor tissues. Inhibiting TAM migration without inhibiting macrophage migration in nontumor tissues reduces their accumulation in tumors and results in reduced tumor growth. This highlights how targeting the migration of detrimental cell types could be used to help in controlling tumor growth in cancer patients. Read more in this issue on page 1337. Original image from Figure 6C. Artwork by Lewis Long.

