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 Merkenschlager, George R. Young, Juliette Roels,
Jonathan P. Stoying, Dinis T. 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, Melanie Tichet, Sonia Domingos-Pereira,
Sylvie Hauert, Denise Nardelli-Haefliger, Sylvie A. Schwartz,
Douglas Hanahan, and Stephan Wullschleger
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,
Bizi 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 Miina,
Susan Bullman, Yasutaka Sukawa, Jonathan A. Nowak,
Keisuke Kosumi, Yohei Masugi, Tyler S. Twombly, Yin Cao,
Mingsyang 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 Shuiji 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 Dalene, Camille Franchet, Julia Gilhodes,
Arnaud Labrousse, Elisabeth Bellard, Muriel Golzie,
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, Yuanxuan Li,
Dan Zhang, Tianzue 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, Vissia 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.
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

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

Somatic Mutations and Immune Alteration in Rectal Cancer Following Neoadjuvant Chemoradiotherapy
Dengbo Ji, Haizhao Yi, Dakui Zhang, Tiancheng Zhan, Zhaowei Li, Ming Li, Jinying Ia, Meng Qiao, Jinhong Xia, Zhifei Zhai, Can Song, and Jin Gu

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 Ruiu, Tatjana Wallmann, Helena Tufvesson-Stiller, Benedikt J. Chambers, Charlotte Rolny, Alvaro Lladser, Andreas Lundqvist, Federica Cavallo, and Rolf Kiessling

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

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.
Cancer Immunology Research

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