WHAT WE’re READING

1443 A Sampling of Highlights from the Literature

IN THE SPOTLIGHT

1444 Seeking Synergy of Checkpoint Blockade through TGFβ Inhibition
Ellen Puré
See related article, p. 1459.

CANCER IMMUNOLOGY AT THE CROSSROADS

1445 The Balancing Act between Cancer Immunity and Autoimmunity in Response to Immunotherapy
Arabella Young, Zoe Quandi, and Jeffrey A. Bluestone

CANCER IMMUNOLOGY MINIATURE

1453 Clinical Significance of Pancreatic Atrophy Induced by Immune-Checkpoint Inhibitors: A Case-Control Study
Yael Ebet, Erez Nissim Baruch, Ronnie Shapira-Frommer, Yaël Steinberg-Silman, Teodor Kuznetsov, Guy Ben-Bzetale, Sameh Daher, Iris Gluck, Nethanel Asher, Sara Apter, Jacob Schachter, Jair Bar, Ben Boursi, and Gal Markel

1459 Stromal Fibroblasts Mediate Anti–PD-1 Resistance via MMP-9 and Dictate TGFβ Inhibitor Sequencing in Melanoma
Fei Zhao, Kathy Evans, Christine Xiao, Nicholas DeVito, Balamooyoran Thevasanthan, Alisha Holzhausen, Peter J. Siska, Gerard C. Clutter, and Brent A. Hanks

1463 FAP Delineates Heterogeneous and Functionally Divergent Stromal Cells in Immune-Excluded Breast Tumors

RESEARCH ARTICLES

1472 Phage-Based Anti-HER2 Vaccination Can Circumvent Immune Tolerance against Breast Cancer
Caterina Bartolacci, Cristina Andreani, Claudia Curcio, Sergio Occhipinti, Luca Massaccesi, Mirella Giovarelli, Roberts Galleazzi, Manuela Iezzi, Martina Tito, Valentina Gambini, Junhiao Wang, Cristina Marchini, and Augusto Amici

1486 Combination Therapy Using Ruxolitinib and Oncolytic HSV Renders Resistant MPNSTs Susceptible to Virotherapy
Mohammed G. Ghoum and Kevin A. Cassady

1499 A High-Throughput Immune-Oncology Screen Identifies EGFR Inhibitors as Potent Enhancers of Antigen-Specific Cytotoxic T-lymphocyte Tumor Cell Killing

See related Spotlight, p. 1444.
### 1524 Altered Binding of Tumor Antigenic Peptides to MHC Class I Affects CD8⁺ T Cell–Effector Responses

Influence of T-cell priming on effector antitumor responses was evaluated. Loss of secondary contacts between a peptide non-anchor residue and MHC skews effector functions to favor cytotoxicity over cytokine production in T cells specific for a melanoma self-antigen.

### 1537 NK Cell Education in Tumor Immune Surveillance: DNAM-1/KIR Receptor Ratios as Predictive Biomarkers for Solid Tumor Outcome
Concepción F. Guillamón, María V. Martínez-Sánchez, Lourdes Gimeno, Anna Mrowiec, Jerónimo Martínez-García, Gerardo Server-Pastor, Jorge Martínez-Escribano, Amparo Torroba, Belén Ferri, Daniel Abellán, José A. Campillo, Isabel Legaz, María R. López-Alvarez, María Rosa Moyá-Quiles, Manuel Muro, and Alfredo Minguela

Solid tumors modulate the expression of molecules induced by licensing interactions during NK-cell education and alter their function. Expression of these molecules can predict patient survival and have implications in the design of NK cell-based therapies.

### 1548 PD-L1 Mediates Dysfunction in Activated PD-1⁺ NK Cells in Head and Neck Cancer Patients
Fernando Concha-Benavente, Benjamin Kansy, Jessica Moskovitz, Jennifer Moy, Uma Chandran, and Robert L. Ferris

PD-1 expression and function were assessed in NK cells from patients with head and neck cancer. NK cell dysfunction was reversed by PD-1 blockade and improved responses to cetuximab therapy, thus, providing an approach to reverse tumor immune evasion.

### 1561 Entinostat Converts Immune-Resistant Breast and Pancreatic Cancers into Checkpoint-Responsive Tumors by Reprogramming Tumor-Infiltrating MDSCs

The HDAC inhibitor, entinostat, impairs myeloid immunosuppressive function, and in combination with immune checkpoint inhibitors, improves T-cell responses in models of breast and pancreatic cancers. These data provide rationale for combination therapy in patients to improve antitumor responses.

### 1578 Exosomes Released from Tumor-Associated Macrophages Transfer miRNAs That Induce a Treg/Th17 Cell Imbalance in Epithelial Ovarian Cancer
Jieru Zhou, Xiaoduan Li, Xiaoli Wu, Ting Zhang, Qinyi Zhu, Xining Wang, Husheng Wang, Kai Wang, Yingying Lin, and Xipeng Wang

The Treg/Th17 ratio is altered in epithelial ovarian cancer. Exosomal miRNAs from tumor-associated macrophages contribute to this T-cell imbalance, which promotes an immune suppressive tumor microenvironment and favors progression and metastasis of epithelial ovarian cancer cells.

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**ABOUT THE COVER**

Poor clinical outcome in cancer patients is associated with the presence of cancer-associated fibroblasts (CAFs). However, fibroblasts are heterogeneous and can have different functions, and whether CAFs directly interact with and impact T cells in the tumor microenvironment remains to be determined. Cremasco and Astarita et al. show that two populations of FAP⁺ mesenchymal stromal cells exist in breast cancer tumors from humans and mice: those that express podoplanin (PDPN⁺ CAFs) and those that do not (cancer-associated pericytes, CAPs). Each population has a distinctive gene signature and localization within tumors, and FAP⁺ PDPN⁺ CAFs were shown to suppress T cells, whereas FAP⁺ PDPN⁻ CAPs were not immunosuppressive. These data highlight how different FAP⁺ stromal cell populations can modulate the breast cancer tumor microenvironment. Read more in this issue on page 1472. Original image from Supplementary Fig. S1E. Artwork by Lewis Long.