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## What We’re Reading

723  A Sampling of Highlights from the Literature

## In the Spotlight

724  **IL11: A Specific Repressor of Tumor-Specific CD4+ T Cells**  
Sjoerd H. van der Burg  
See related article, p. 735

725  **Characterizing the Complexities of Neutrophils with Suppressive Properties**  
Marco Antonio Cassatella  
See related article, p. 790

## Priority Brief

726  **Regulatory T-cell Transcriptomic Reprogramming Characterizes Adverse Events by Checkpoint Inhibitors in Solid Tumors**  
Regulatory T cells (Treg) maintain peripheral tolerance. The authors show a common inflammatory signature between Tregs from patients with solid tumors who develop immune-related adverse events and Tregs from patients with autoimmune diseases, suggesting shared underlying mechanisms.

## Research Articles

735  **Host IL11 Signaling Suppresses CD4+ T cell–Mediated Antitumor Responses to Colon Cancer in Mice**  
Jennifer Huynh, David Baloyan, David Chisanga, Wei Shi, Megan O’Brien, Shoukat Afshar-Sterle, Mariah Alorro, Lokman Pang, David S. Williams, Adam C. Parslow, Pathum Thilakasiri, Moritz F. Eissmann, Louis Boon, Frederick Masson, Ashwini L. Chand, and Matthias Ernst  
This study shows genetic ablation of IL11 signaling augments production of IFNγ and TNFα by antitumor CD4+ T cells, suppressing colon cancer development in vivo. The data suggest IL11 as a potential therapeutic target in colon cancer.  
See related Spotlight, p. 724

748  **MHC Class II Antigen Presentation by Lymphatic Endothelial Cells in Tumors Promotes Intratumoral Regulatory T cell–Suppressive Functions**  
Anastasia O. Gkountidi, Laure Garnier, Juan Dubrot, Julien Angelillo, Guillaume Harlé, Dale Brighouse, Ludovic J. Wrobel, Robert Pick, Christoph Scheiermann, Melody A. Swartz, and Stéphanie Hugues  
In this study, tumoral lymphatic endothelial cells are shown to present tumor antigens via MHC class II molecules, promoting a tumor-specific signature in regulatory T cells (Treg) and enhanced Treg suppressive functions, inhibiting antitumor immunity.

765  **Exercise Training Improves Tumor Control by Increasing CD8+ T-cell Infiltration via CXCR3 Signaling and Sensitizes Breast Cancer to Immune Checkpoint Blockade**  
Igor L. Gomes-Santos, Zohreh Amoozgar, Ashwin S. Kumar, William W. Ho, Kangsan Roh, Niles P. Talele, Hannah Curtis, Kosuke Kawaguchi, Rakesh K. Jain, and Dai Fukumura  
Optimized exercise therapy induces vessel normalization, boosts antitumor effector cell infiltration and function, and delays tumor growth in a CXCR3 pathway/CD8+ T-cell-dependent manner. This results in sensitization of refractory breast cancer to immune checkpoint blockade.

779  **The Chemokine CX3CL1 Improves Trastuzumab Efficacy in HER2 Low–Expressing Cancer In Vitro and In Vivo**  
Tobias F. Dreyer, Sabine Kuhn, Christoph Stange, Nadine Heithorst, Daniela Schilling, Jel Jelsma, Wolfgang Sievert, Stefanie Seitz, Stefan Stangl, Alexander Hapfelmeier, Aurelia Noske, Anja K. Wege, Wilko Weichert, Jürgen Ruland, Manfred Schmitt, Julia Dorn, Marion Kiechle, Ute Reuning, Viktor Magdolen, Gabriele Multhoff, and Holger Bronger  
CX3CL1 is demonstrated to modulate NK-cell recruitment into the tumor microenvironment of HER2+ cancer, increase NK-cell cytotoxicity against HER2+ targets, and synergize with trastuzumab therapy. The data highlight CX3CL1 as a potential target molecule to enable anti-HER2 treatment.
Mechanisms Driving Neutrophil-Induced T-cell Immunoparalysis in Ovarian Cancer


The ovarian cancer microenvironment induces suppressor neutrophils that inhibit T-cell signaling and metabolic function. Acquisition of the suppressor phenotype is dependent on several pathways including complement signaling, which can be targeted therapeutically to enhance antitumor immunity.

See related Spotlight, p. 725

Tumor-Associated Neutrophils Drive B-cell Recruitment and Their Differentiation to Plasma Cells

Merav E. Shaul, Asaf Zlotnik, Einat Tidhar, Asaf Schwartz, Ludovica Arpinati, Naomi Kaisar-Iluz, Sojod Mahroum, Inbal Mishalian, and Zvi G. Fridlender

Tumor-associated neutrophils (TAN) are shown to regulate TNFα-mediated B-cell migration into the TME and their differentiation into functional plasma cells, partially mediated by interaction of TAN BAFF and B-cell BAFF-R. The data highlight potential targets for cancer therapy.

838 Flightless I Homolog Reverses Enzalutamide Resistance through PD-L1-Mediated Immune Evasion in Prostate Cancer

Hailong Ruan, Lin Bao, Zhen Tao, and Ke Chen

This study reports a functional and biological interaction between enzalutamide resistance and immune evasion through a FLII/YBX1/PD-L1 cascade. The data suggest that combining FLII expression and endocrine therapy may benefit prostate cancer patients by preventing tumor immune evasion.