HIGHLIGHTS FROM THE LITERATURE

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347 Human Tumor Antigens Yesterday, Today, and Tomorrow
Olivia J. Finn

IN THE SPOTLIGHT

355 Rational Combination Immunotherapy: Understand the Biology
Howard L. Kaufman
See related article, p. 363.

PRIORITY BRIEF

357 Clinical Features of Acquired Resistance to Anti–PD-1 Therapy in Advanced Melanoma
Acquired resistance to checkpoint therapy is a growing clinical issue. This large retrospective study of anti-PD-1–treated progressing patients found that isolated disease treated with localized therapy or anti-PD-1 resumption often produced durable benefits, which may guide clinical management.

385 Lack of STAT6 Attenuates Inflammation and Drives Protection against Early Steps of Colitis-Associated Colon Cancer
Sonia A. Leon-Cabrera, Emmanuel Molina-Guzman, Yael G. Delgado-Ramirez, Armando Vázquez-Sandoval, Yadiza Ledesma-Soto, Carlos G. Pérez-Plascencia, Yolanda I. Chirino, Norma L. Delgado-Buenrostro, Miriam Rodríguez-Sosa, Felipe Vaca-Paniagua, Federico Ávila-Moreno, Emma B. Gutierrez-Cirlos, Luis E. Arias-Romero, and Luis A. Terrazas
STAT6 plays a role in inflammation and in some malignancies. It was found to fuel colitis-related colorectal cancer in a mouse model. Its absence decreased the number of tumors by inhibiting early steps in the progression to colon cancer.

397 Squamous Cell Tumors Recruit γδ T Cells Producing either IL17 or IFNγ Depending on the Tumor Stage
Elena Lo Presti, Francesca Toia, Sebastiano Oieni, Simona Bucheri, Alice Turdo, Laura Rosa Mangiapane, Giuseppe Campusi, Valentina Caputo, Matilde Todaro, Giorgia Stassi, Adriana Cordova, Francesco Moschella, Gaetana Rinaldi, Serena Meraviglia, and Francesco Dieli
Tumor-infiltrating lymphocytes contain γδ T cells. In early-stage SCC tumors, γδ T cells had antitumor properties, such as production of IFNγ. However, clinically advanced tumors contained many more γδ T cells that produced IL-17 and promoted tumor growth.

376 Identification of Glycopeptides as Posttranslationally Modified Neoantigens in Leukemia
Stacy A. Malaker, Sarah A. Penny, Lora G. Steadman, Paisley T. Myers, Justin C. Locke, Manoj Raghavan, Dina L. Bai, Jeffrey Shabanowitz, Donald F. Hunt, and Mark Cobbold
The identification of neotopes expressed by tumors will aid the effectiveness of antitumor therapies. Four classes of posttranslationally modified tumor neoantigens were identified on primary tumors. Healthy donors had detectable natural immunity to a subset of these.

408 Increased PD-1⁺ and TIM-3⁺ TILs during Cetuximab Therapy Inversely Correlate with Response in Head and Neck Cancer Patients
Hyun-Bae Jei, Raghavendra M. Srivastava, Athanasios Argiris, Julie E. Bauman, Lawrence P. Kane, and Robert L. Ferris
Cetuximab tumor-specific monotherapy for head and neck cancers is effective in less than 20% of cases. Cytolytic T cells were found to be increased, yet expressed PD-1 and TIM-3. Addition of checkpoint blockade could potentially improve clinical outcomes.

Targeting CD47 and Autophagy Elicited Enhanced Antitumor Effects in Non–Small Cell Lung Cancer
Xuyao Zhang, Jiajun Fan, Shaofei Wang, Yubin Li, Yichen Wang, Song Li, Jingyun Luan, Ziyu Wang, Ping Song, Qicheng Chen, Wenzhi Tian, and Dianwen Ju
Blocking CD47 interactions was a potent antitumor therapy for NSCLC. Cells resist death by increasing autophagy; simultaneously inhibiting autophagy provided a synergistic antitumor effect, providing a scientific basis for enhancing the efficacy of immune checkpoint inhibitors.
See related Spotlight, p. 355.

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Liver Metastasis and Treatment Outcome with Anti-PD-1 Monoclonal Antibody in Patients with Melanoma and NSCLC
The association between metastatic site and responses to anti-PD-1 immunotherapy was explored in both melanoma and lung cancer. Liver metastasis was associated with worse outcome and CD8⁺ T cell-poor tumors, suggesting a potential mechanism for the outcomes.

ABOUT THE COVER
A close relationship exists between colonic inflammation and the development of colon cancer. Inflammation is driven by IL4’s activation of the signaling protein STAT6 in immune cells. It is also known that STAT6 can be expressed in cancer cells, but its role in colon cancer is unclear. Leon-Cabrera and colleagues have found that STAT6 helps to promote survival in cancer cells in the early stages of progression from colitis to colon cancer, in addition to its role in maintaining an inflammatory environment. Read more in the Research Article by Leon-Cabrera on page 385 in this issue of Cancer Immunology Research. The histology is Alcian blue-stained diseased colon from Fig. 7F. Artwork by Lewis Long.