

HIGHLIGHTS FROM THE LITERATURE

- 345** What We're Reading

MASTERS OF IMMUNOLOGY

- 346** About the Master
- 347** Human Tumor Antigens Yesterday, Today, and Tomorrow
Olivera 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
Daniel Y. Wang, Zeynep Eroglu, Alpaslan Ozgun, Paul D. Leger, Shilin Zhao, Fei Ye, Jason J. Luke, Richard W. Joseph, Rizwan Haq, Patrick A. Ott, F. Stephen Hodi, Jeffrey A. Sosman, Douglas B. Johnson, and Elizabeth I. Buchbinder
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.

RESEARCH ARTICLES

- 363** 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.

- 376** Identification of Glycopeptides as Posttranslationally Modified Neoantigens in Leukemia



Stacy A. Malaker, Sarah A. Penny, Lora G. Steadman, Paisley T. Myers, Justin C. Loke, Manoj Raghavan, Dina L. Bai, Jeffrey Shabanowitz, Donald F. Hunt, and Mark Cobbold

The identification of neoepitopes 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.

- 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, Yadira Ledesma-Soto, Carlos G. Pérez-Plasencia, 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 I. 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 $\gamma\delta$ T Cells Producing either IL17 or IFN γ Depending on the Tumor Stage

Elena Lo Presti, Francesca Toia, Sebastiano Oieni, Simona Buccheri, Alice Turdo, Laura Rosa Mangiapane, Giuseppina Campisi, Valentina Caputo, Matilde Todaro, Giorgio Stassi, Adriana Cordova, Francesco Moschella, Gaetana Rinaldi, Serena Meraviglia, and Francesco Dieli
Tumor-infiltrating lymphocytes contain $\gamma\delta$ T cells. In early-stage SCC tumors, $\gamma\delta$ T cells had antitumor properties, such as production of IFN γ . However, clinically advanced tumors contained many more $\gamma\delta$ T cells that produced IL-17 and promoted tumor growth.

- 408** Increased PD-1⁺ and TIM-3⁺ TILs during Cetuximab Therapy Inversely Correlate with Response in Head and Neck Cancer Patients

Hyun-Bae Jie, Raghvendra M. Srivastava, Athanassios 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.

Table of Contents

417 Liver Metastasis and Treatment Outcome with Anti-PD-1 Monoclonal Antibody in Patients with Melanoma and NSCLC

Paul C. Tumeh, Matthew D. Hellmann, Omid Hamid, Katy K. Tsai, Kimberly L. Loo, Matthew A. Gubens, Michael Rosenblum, Christina L. Harview, Janis M. Taube, Nathan Handley, Neharika Khurana, Adi Nosrati, Matthew F. Krummel, Andrew Tucker, Eduardo V. Sosa, Phillip J. Sanchez, Nooriel Banayan, Juan C. Osorio, Dan L. Nguyen-Kim, Jeremy Chang, I. Peter Shintaku, Peter D. Boasberg, Emma J. Taylor, Pamela N. Munster, Alain P. Algazi, Bartosz Chmielowski, Reinhard Dummer, Tristan R. Grogan, David Elashoff, Jimmy Hwang, Simone M. Goldinger, Edward B. Garon, Robert H. Pierce, and Adil Daud

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.

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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.

