WHAT WE’RE READING

1  What We’re Reading

MASTERS OF IMMUNOLOGY

2  About the Master

3  Myeloid-Derived Suppressor Cells
   Dmitry I. Gabrilovich

PRIORITY BRIEF

9  Efficacy of PD-1 Blockade Is Potentiated by
   Metformin-Induced Reduction of Tumor Hypoxia
   Nicole E. Scharping, Ashley V. Menk, Ryan D. Whetstone,
   Xue Zeng, and Greg M. Delgoffe
   Low oxygen levels in tumors can act as a barrier to effective
   antitumor immunity. Mitigation of tumor hypoxia using a
   commonly prescribed type II diabetes drug, metformin, resulted in
   significant synergy with PD-1 blockade immunotherapy.

RESEARCH ARTICLES

17  Angiopoietin-2 as a Biomarker and Target for
    Immune Checkpoint Therapy
    Xinqi Wu, Anita Giobbie-Hurder, Xiaoyun Liao,
    Courtney Connelly, Erin M. Connolly, Jingjing Li,
    Michael P. Manos, Donald Lawrence, David McDermott,
    Mariano Severgini, Jun Zhou, Evisa Gjini, Ana Lako,
    Mikel Lipschitz, Christine J. Pak, Sara Abdelrahman,
    Scott Rodig, and F. Stephen Hodi
    Outcomes for metastatic melanoma patients treated with
    checkpoint blockade were poor when circulating Ang-2 was high.
    Ang-2 promoted recruitment of tumor macrophages and
    upregulated PD-L1, making it a predictive and/or prognostic
    biomarker and potential target to combine with checkpoint
    blockade.

29  Rational Selection of Syngeneic Preclinical Tumor
    Models for Immunotherapeutic Drug Discovery
    Suzanne I.S. Mosely, John E. Prime, Richard C.A. Sainson,
    Jens-Oliver Koopmann, Dennis Y.Q. Wang,
    Danielle M. Greenawalt, Miika J. Ahdesmaki,
    Rebecca Leyland, Stefanie Mullins, Luciano Parelli,
    Danielle Marcus, Judith Anderton, Amanda Watkins,
    Jane Coates Ulrichsen, Philip Brotzmann, Brandon W. Higgs,
    Matthew McCourt, Hazel Jones, James A. Harper,
    Michelle Morrow, Viia Valge-Archer, Ross Stewart,
    Simon J. Dovedi, and Robert W. Wilkinson
    Murine syngeneic tumor models are used to study responses to
    antitumor immunotherapies. To rationalize model selection, the
    underlying genetic and immunologic biology of the models was
    analyzed, allowing parallels to be drawn between models and
    human disease phenotypes.

42  Bortezomib Relieves Immune Tolerance in
    Nasopharyngeal Carcinoma via STAT1
    Suppression and Indoleamine 2,3-Dioxygenase
    Downregulation
    Guan-Min Jiang, Hong-Sheng Wang, Jun Du, Wei-Feng Ma,
    Hui Wang, Yu Qiu, Qiu-Gui Zhang, Wei Xu, Hui-Fang Liu,
    and Jian-Ping Liang
    The proteasome inhibitor bortezomib can synergize with other
    chemotherapies to kill nasopharyngeal carcinoma cells.
    Bortezomib released the immune suppression imposed by IFNγ-
    induced IDO (indoleamine 2,3-dioxygenase) through
    inhibition of NF-kB translocation, IRF-1 production, and STAT1
    signaling.

52  Human Dendritic Cells Mitigate NK-Cell
    Dysfunction Mediated by Nonselective JAK1/2
    Blockade
    Shane A. Curran, Justin A. Shyer, Erin T. St. Angelo,
    Lillian R. Talbot, Sneh Sharma, David J. Chung,
    Glenn Heller, Katharine C. Hsu, Brian C. Betts, and
    James W. Young
    Broad JAK inhibitors can improve graft-versus-host disease caused
    by stem cell transplants, but they reduce NK-cell numbers and
    activity. Selective inhibitors of JAK2, in concert with moDCs or
    Langerhans cells, preserve STAT5 signaling and NK-cell
    proliferation and function.

61  IL4 from T Follicular Helper Cells Downregulates
    Antitumor Immunity
    Hidekazu Shirota, Dennis M. Klinman, Shuku-ei Ito,
    Hiroyasu Ito, Masato Kubo, and Chikashi Ishioka
    The source and role of IL4 in tumors is not clear. T follicular helper
    cells in the tumor-draining lymph nodes produced most of the IL4,
    which profoundly influenced the tumor microenvironment,
    enhancing M2 macrophage polarization and suppressing
    antitumor immunity.
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<td>Takumi Kumai, Sujin Lee, Hyun-Il Cho, Hussain Sultan, Hiroya Kobayashi, Yasuaki Harabuchi, and Esteban Celis</td>
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<td>84</td>
<td>Somatic Mutations and Neoepitope Homology in Melanomas Treated with CTLA-4 Blockade</td>
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**ABOUT THE COVER**

Syngeneic mouse models are used extensively to acquire a better understanding of tumor-immune system interactions and the effects of immunotherapeutic interventions. Because selection of the most suitable mouse model for a particular study is not always straightforward, Mosely et al. compared the tumor microenvironment of a number of syngeneic tumor model systems in immunocompetent mice for genomic signatures and immunophenotype. An example of the tumor microenvironment, the CT26 tumor model shown on the far right, illustrates the presence of CD3+ T cells infiltrating the tumor. Visualized with immunohistochemistry, the T cells are identified with an antibody to CD3 and detected with the Alexa-568 fluorochrome (pale yellow). The DNA in cell nuclei is labeled blue with DAPI. Read more in the article by Mosely et al. in this issue of *Cancer Immunology Research*, starting on page 29. Images provided by Arthur Lewis and Lee Brown, Translational Sciences Pathology, MedImmune. Artwork by Lewis Long.