

WHAT WE'RE READING

- 629** Literature Round-Up: Impactful Published Papers

CANCER IMMUNOLOGY MINIATURE

- 630** Sarcoid-Like Granulomatosis of the Lung Related to Immune-Checkpoint Inhibitors: Distinct Clinical and Imaging Features of a Unique Immune-Related Adverse Event
Mizuki Nishino, Lynette M. Sholl, Mark M. Awad, Hiroto Hatabu, Philippe Armand, and F. Stephen Hodi
Development of sarcoid-like granulomatosis of the lung after immune-checkpoint inhibition was observed in four patients with different tumor types. This manifestation had distinct clinical, imaging, and histological features, which characterized it as an immune-related adverse event.


PRIORITY BRIEF

- 636** NetH2pan: A Computational Tool to Guide MHC Peptide Prediction on Murine Tumors
Christa I. DeVette, Massimo Andreatta, Wilfried Bardet, Steven J. Cate, Vanessa I. Jurtz, Kenneth W. Jackson, Alana L. Welm, Morten Nielsen, and William H. Hildebrand
An improved peptide prediction tool for murine MHC class I presentation, NetH2pan, was created and cross-validated on MMTV-PyMT tumors. Its predictive powers were more accurate than other tools, enabling epitope discovery in the FVB and other mouse strains.

RESEARCH ARTICLES

- 645** IL17A Regulates Tumor Latency and Metastasis in Lung Adeno and Squamous SQ.2b and AD.1 Cancer
Ran You, Francesco J. DeMayo, Jian Liu, Sung-Nam Cho, Bryan M. Burt, Chad J. Creighton, Roberto F. Casal, Donald R. Lazarus, Wen Lu, Hui-Ying Tung, Xiaoyi Yuan, Andrea Hill-McAlester, Myunghoo Kim, Sarah Perusich, Loraine Cornwell, Daniel Rosen, Li-zhen Song, Silke Paust, Gretchen Diehl, David Corry, and Farrah Kheradmand
The pro-inflammatory cytokine IL17A has antitumor effects in certain subtypes of non-small cell lung cancer. Mice whose tumors were infiltrated with IL17A-expressing T cells were associated with increased lung cancer latency and had fewer metastasis.

- 658** Disruption of IFN-I Signaling Promotes HER2/Neu Tumor Progression and Breast Cancer Stem Cells
Luciano Castiello, Paola Sestili, Giovanna Schiavoni, Rosanna Dattilo, Domenica M. Monque, Fiorella Ciaffoni, Manuela Iezzi, Alessia Lamolinara, Antonella Sistigu, Federica Moschella, Anna Maria Pacca, Daniele Macchia, Maria Ferrantini, Ann Zeuner, Mauro Biffoni, Enrico Proietti, Filippo Belardelli, and Eleonora Aricò
Type I interferon (IFN-I) inhibits tumor growth and activates antitumor responses. HER2-driven tumors in mice lacking IFN-I receptor were more aggressive, more vascularized, and were enriched in stem cells, suggesting that IFN-I exerts key control over tumor progression.

- 671** Targeting Tissue Factor for Immunotherapy of Triple-Negative Breast Cancer Using a Second-Generation ICON
 Zhiwei Hu, Rulong Shen, Amanda Campbell, Elizabeth McMichael, Lianbo Yu, Bhuvanewari Ramaswamy, Cheryl A. London, Tian Xu, and William E. Carson III
Expression of tissue factor (TF) on the cancer cells and tumor neovasculature of triple-negative breast cancer provides a target for immunotherapy. An improved TF-targeting second-generation immunoconjugate (called L-ICON1) was tested for immunotherapy of this malignancy in preclinical mouse models.

- 685** IL21 Therapy Combined with PD-1 and Tim-3 Blockade Provides Enhanced NK Cell Antitumor Activity against MHC Class I-Deficient Tumors
 Hyungseok Seo, Byung-Seok Kim, Eun-Ah Bae, Byung Soh Min, Yoon Dae Han, Sang Joon Shin, and Chang-Yuil Kang
Combination rIL21 and anti-PD-1/anti-Tim-3 additively enhanced NK cell responses in mice bearing MHC class I-deficient tumors. This combination facilitated NK effector functions in cancer patients, highlighting its therapeutic potential for patients with MHC class I-deficient tumors.



- 696** Secretory IgM Exacerbates Tumor Progression by Inducing Accumulations of MDSCs in Mice
 Chih-Hang Anthony Tang, Shiun Chang, Ayumi Hashimoto, Yi-Ju Chen, Chang Won Kang, Anthony R. Mato, Juan R. Del Valle, Dmitry I. Gabrilovich, and Chih-Chi Andrew Hu
In a mouse model of chronic lymphocytic leukemia, production of secretory IgM led to more MDSCs, fewer T cells, and shorter survival times for the mice. Thus, secretory IgM may aggravate the progression of this cancer.

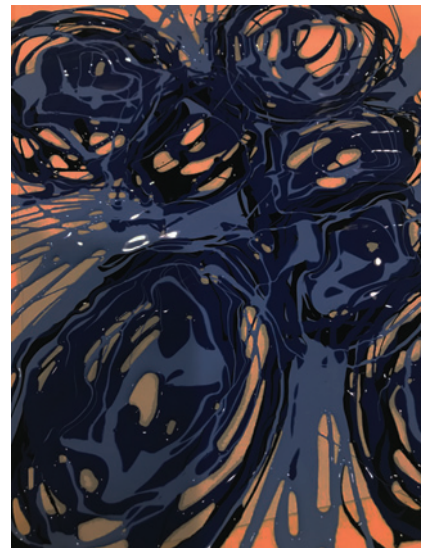
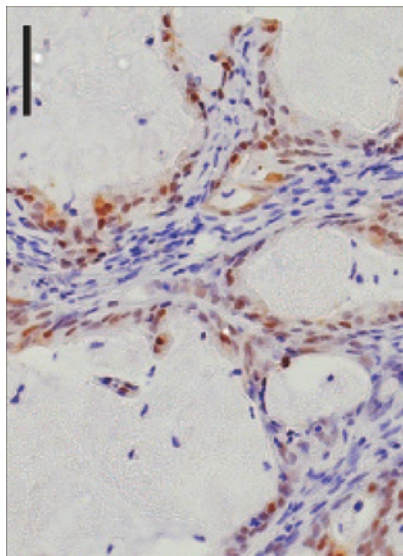
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- 711** **TK Inhibitor Pazopanib Primes DCs by Downregulation of the β -Catenin Pathway**
Ilaria Grazia Zizzari, Chiara Napoletano, Andrea Botticelli, Salvatore Caponnetto, Fabio Calabrò, Alain Gelibter, Aurelia Rughetti, Ilary Ruscito, Hassan Rahimi, Ernesto Rossi, Giovanni Schinzari, Paolo Marchetti, and Marianna Nuti
Pazopanib, a kinase inhibitor that targets angiogenesis, primed dendritic cells from patients with metastatic renal cell carcinoma and healthy donors. The resultant immune response indicates that this could be exploited to improve outcomes for patients undergoing combination immunotherapy.
- 723** **PPAR γ Contributes to Immunity Induced by Cancer Cell Vaccines That Secrete GM-CSF**
Girija Goyal, Karrie Wong, Christopher J. Nirschl, Nicholas Souders, Donna Neuberger, Niroshana Anandasabapathy, and Glenn Dranoff
PPAR γ deficiency in myeloid cells reduced the efficacy of GVAX cancer vaccines, altered DC gene expression and function, and decreased the ratio of vaccine-induced CD8⁺ T cells to Tregs. Correspondingly, PPAR γ agonists improved the efficacy of cancer immunotherapy.
- 733** **Introduction of Genetically Modified CD3 ζ Improves Proliferation and Persistence of Antigen-Specific CTLs**
Kotaro Miyao, Seitaro Terakura, Shingo Okuno, Jakrawadee Julamanee, Keisuke Watanabe, Hiroshi Hamana, Hiroyuki Kishi, Reona Sakemura, Daisuke Koyama, Tatsunori Goto, Tetsuya Nishida, Makoto Murata, and Hitoshi Kiyoi
It may be safer to improve adoptive T-cell therapy through increased signaling rather than increased antigen affinity of the TCRs. Modifying intracellular signaling enhanced the proliferation and persistence of CTLs while improving antitumor efficacy.
- 745** **Allelic Polymorphisms of KIRs and HLA Predict Favorable Responses to Tyrosine Kinase Inhibitors in CML**
Hiroshi Ureshino, Takero Shindo, Hiroto Kojima, Yasushi Kusunoki, Yuki Miyazaki, Hidenori Tanaka, Hiroh Saji, Atsushi Kawaguchi, and Shinya Kimura
In CML patients treated with tyrosine kinase inhibitors, KIR alleles were associated with patient outcome. The combination of alleles at KIR3DL1 and HLA-B loci were found to predict the therapeutic effects of tyrosine kinase inhibitor therapy.

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ABOUT THE COVER

Little is known of the role of IL17A or Th17 cells in solid tumors. Non-small cell lung cancer (NSCLC) is a solid tumor driven by multiple oncogenic mutations. Mice with deletions in their airway cells of the *Pten* and *Smad4* genes, independent of *Kras* mutations, recapitulate NSCLC in humans, including histologic features and metastatic propensities of two subtypes of NSCLC. You et al. found that if these mice also lacked the cytokine IL17A, tumors developed more rapidly and were more metastatic. Comparison of the antitumor responses in mice with and without *Il17a* showed that the successful antitumor responses were mediated by T cells expressing IL17A. Read more starting on page 645 of this issue. Original image from Fig. 4. Artwork by Lewis Long.



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