

# Literature Round-Up: Impactful Published Papers

Article Recommendations from Our Deputy and Senior Editors

## Antibody-mediated inhibition of MICA and MICB shedding promotes NK cell-driven tumor immunity

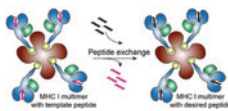


Foiling cleavage (by Marie-Lan Nguyen via Wikimedia Commons)

Tumors can avoid immune elimination by NK cells by shedding MICA and MICB, ligands for the activating receptor NKG2D. An antibody that blocks cleavage of these ligands prevents shedding, enhances NKG2D-mediated killing of the tumor cells, and reduces tumor growth in models of lung and melanoma metastasis. The prevalence of MICA and MICB expression on human tumors indicates that such antibodies could have broad therapeutic potential in combination with other approaches.

de Andrade LF, . . . , Wucherpennig KW. *Science* 2018 Mar 30; 359:1537–42.

## A flexible MHC class I multimer loading system for large-scale detection of antigen-specific T cells

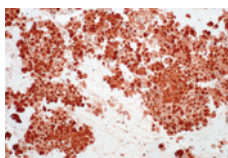


Multimer peptide exchange (from Fig. 2 of Luimstra et al.)

Personalized approaches to antitumor immunity rely upon identification of the tumor epitopes recognized by T cells and quantitation of specific antitumor responses. A simplified, temperature-based method was devised to produce the peptide-MHC multimers needed to identify antigen-specific T cells. Conditional peptides that bind to multimers at 4°C are replaced at higher temperatures by the peptides of interest. Antigen-specific T cells can be detected and immune responses monitored.

Luimstra JJ, . . . , Ovaa H. *J Exp Med* 2018 Apr 17. DOI: 10.1084/jem.20180156.

## T cell-induced CSF1 promotes melanoma resistance to PD1 blockade



Malignant melanoma (by Ed Uthman via Flickr)

Human CD8<sup>+</sup> T cells induce colony-stimulating factor-1 (CSF1) expression by melanoma cells. This attracts immunosuppressive macrophages into the tumor. Treatment of mice with transplanted Braf<sup>V600E</sup>-driven melanoma tumors with blocking antibodies to both PD-1 and the CSF1 receptor synergistically inhibits tumor growth and increases the survival of tumor-bearing mice.

Neubert NJ, . . . , Speiser DE. *Sci Transl Med* 2018 Apr 11;10:eaa3311.

## Cancer-germline antigen expression discriminates clinical outcome to CTLA-4 blockade

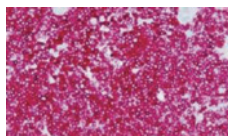


Discriminating with autophagy (from Amaravadi et al. *Clin Cancer Res* 2011)

Some resistance of melanoma to CTLA-4, but not PD-1, blockade is now linked to expression of the proteins encoded by the MAGE-A supercluster of genes. The MAGE-A proteins interfere with autophagy, a process important to the generation of antitumor responses. Patients whose melanoma expresses these proteins are resistant to anti-CTLA-4, but no association was seen in two cohorts of patients treated with anti-PD-1. This key insight suggests combining autophagy induction with CTLA-4 blockade for patients whose melanomas express the supercluster.

Shukla SA, . . . , Wu CJ. *Cell* 2018 Apr 19;173:624–33.

## Determinants of response and resistance to CD19 chimeric antigen receptor (CAR) T-cell therapy of chronic lymphocytic leukemia

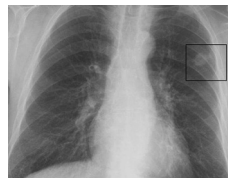


CLL in bone marrow (from Skarzynski et al. *Clin Cancer Res* 2016)

Only a quarter of chronic lymphocytic leukemia patients respond to CAR T-cell therapy. Complete responders experience expansion and persistence of their CAR T cells, even after 5 years, which are properties found to be intrinsic to the initial transferred T cells. Transcriptome analysis found that the T cells infused into responders are more highly enriched in early memory differentiation genes, and the presence of CD45RO<sup>+</sup>CD27<sup>+</sup>CD8<sup>+</sup> T cells in peripheral blood prior to CAR transduction is a predictor of response to CAR T-cell therapy.

Fraietta JA, . . . , Melenhorst JJ. *Nat Med* 2018 Apr 30;24:563–71.

## Neoadjuvant PD-1 blockade in resectable lung cancer



Lung tumor (by Lange123 via Wikimedia Commons)

A pilot study that treated 20 early-stage lung cancer patients with anti-PD-1 prior to removal of their lung tumors showed that this treatment was safe. Tumor pathology showed responses in 45% of those treated, and responders were more likely to have tumors with greater numbers of mutated sequences. TCR analysis revealed increased expansion of clones specific for tumor neoepitopes.

Forde PM, . . . , Pardoll DM. *N Engl J Med* 2018 Apr 16. DOI: 10.1056/NEJMoa1716078.

# Cancer Immunology Research

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*Cancer Immunol Res* 2018;6:629.

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