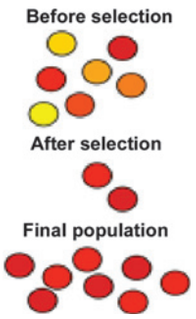
Cancer Immunology Research

A Sampling of Highlights from the Literature

Article Recommendations from our Deputy and Senior Editors

Evolutionary pressure against MHC Class II binding cancer mutations



Tumor cells select for weak MHCII binding (by Wykis via Wikimedia Commons)

Antitumor responses to neoantigens has largely focused on $CD8^+$ T cells. However, $CD4^+$ T-cell responses also contribute, and how this impacts the tumor mutational landscape has not been well documented. Marty and colleagues show that mutations with weak MHCII binding are strongly selected during tumor progression. Using TCGA datasets representing more than 5,000 tumor samples, a score linking MHCII genotype to presentation of specific mutations was generated and shown to reflect the mutated epitopes that are presented to immune cells. The analysis reveals not only that peptides binding poorly to MHCII are selected, but also that the ability to bind to MHCII has more influence on the selective pressure put on tumors than MHCI binding. These results highlight how $CD4^+$ T cells may be playing a key role in shaping antitumor immunity.

Marty R, . . ., Carter H. **Cell** 2018 Sep 20. doi: 10.1016/j.cell.2018.08.048.

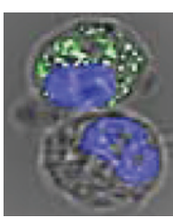
A homing system targets therapeutic T cells to brain cancer

ALCAM-specific homing allows T cells to better infiltrate (by RRZEicons via Wikimedia Commons)

T-cell infiltration into brain tumors remains a challenge. Samaha and colleagues demonstrate that tumor endothelium, as a mechanism of immune evasion, downregulates specific adhesion molecules commonly upregulated by inflammation and needed by immune cells for extravasation. However, the endothelium also upregulates the adhesion molecule, ALCAM, and this was used to develop a high-avidity ALCAM-specific homing system that allows circulating T cells to better adhere to cancer tissues, resulting in improved cytotoxic T-cell infiltration and potent antitumor responses.

Samaha H, . . ., Ahmed N. **Nature** 2018 Sep 5;561:331–7.

LC3-associated phagocytosis in myeloid cells promotes tumor immune tolerance

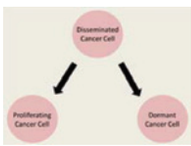


Autophagy in macrophages (green indicates LC3; by Kam23lesh via Wikimedia Commons)

The role of autophagy proteins in tumors and the tumor microenvironment have not yet been fully elucidated. Cunha and colleagues show myeloid cell LC3-associated phagocytosis (LAP), which functions in engulfment of dying cells, contributes to immune suppression in the tumor microenvironment. Targeting LAP, which recruits components of the autophagy machinery, specifically in myeloid cells inhibits tumor progression. Tumor-associated macrophages deficient for LAP lose suppressive functions and gain a pro-inflammatory M1 phenotype, promoting T-cell antitumor activity. These data highlight that autophagy proteins can play a role in the suppression of antitumor responses in the tumor microenvironment.

Cunha LD,. . ., Green DR. **Cell** 2018 Sep 20. doi: 10.1016/j.cell.2018.08.061.

Neutrophil extracellular traps produced during inflammation awaken dormant cancer cells in mice

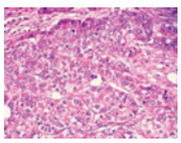


Disseminated cancer cells can enter into dormancy or proliferate causing recurrence (by AliMicJones via Wikimedia).

Recurrence of many cancers occurs from activation of dormant tumor cells. The mechanisms behind awakening disseminated cancer from dormancy to cause metastasis are not fully known. Albrengues and colleagues show that chronic inflammatory conditions produce neutrophil extracellular traps (NETs) that result in remodeling laminin and integrin signaling that awakens dormant single disseminated cancer cells and metastases in both breast and prostate cancer models. By inhibiting NET formation, or by degrading the DNA scaffold in NETs, dormant cancer cells do not reactivate and metastasis is prevented. This highlights how targeting NETs could aid in the prevention of cancer recurrence in patients.

Albrengues J, . . ., Egeblad M. **Science** 2018 Sep 28;361:eaao4227.

A structured tumor-immune microenvironment in triple negative breast cancer revealed by multiplexed ion beam imaging

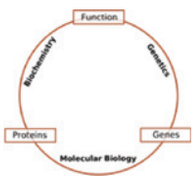


Triple negative breast carcinoma (by Sarahkayb via Wikimedia Commons)

Interactions occurring in the tumor microenvironment are complex. Using a multiplexed ion beam imaging system that detects 36 proteins with roles in cell phenotype, function, and regulation, Keren and colleagues analyzed the composition of the tumor microenvironment (TME) in triple-negative breast cancer samples. Coupling the imaging to machine learning allowed determination of the cellular composition, cell localization and spatial relationships to other cell types, and functionality across 41 patients. Immune composition could be classified as compartmentalized or mixed, with compartmentalization at the tumor border having a better prognoses. This analysis not only revealed a structured TME but also allows for characterizing the complex and dynamic interactions taking place in the TME, providing a deeper understanding of how tumor composition can affect prognosis.

Keren L, . . ., Angelo M. **Cell** 2018 Sep 6;174:1373–87.e19.

Genetic mechanisms of target antigen loss in CAR19 therapy of acute lymphoblastic leukemia



Gene expression affects what protein is expressed, as well as its function (by OldakQuill via Wikimedia Commons)

CD19-negative acute lymphoblastic leukemia (ALL) relapse can occur with CAR T-cell therapy. Orlando and colleagues demonstrate that CAR-resistant tumor cells usually possess CD19 mutations that lead to a truncated protein leading to CD19 loss on the surface of ALL cells, rather than epitope loss as previously reported. This finding suggests concurrently targeting additional molecules such as CD22 should improve CD19 CAR T cell treatment.

Orlando EJ, . . ., Winckler W. **Nat Med** 2018 Oct 1. DOI: 10.1038/s41591-018-0146-z.