Cancer Immunology Research

A Sampling of Highlights from the Literature

Article Recommendations from Our Deputy and Senior Editors

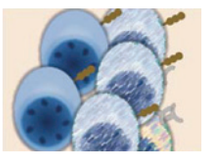
Neutrophils driving unconventional T cells mediate resistance against murine sarcomas and selected human tumors

Cellular teamwork builds resistance to carcinogenic disaster (by A. Wieser Wilson)

Tumor-associated neutrophils (TANs) have generally been linked to tumor progression. However, carcinogen-induced sarcomas develop earlier and grow faster in G-CSFR$^{-/-}$ mice than in wildtype. TANs promote type-1 tumor–associated macrophages to produce IL12, which activates IFNγ production from unconventional, CD4^{-}CD8^{-} αβ T cells soon after carcinogen injection, interfering with tumor progression. Patients with undifferentiated sarcomas dense with TANs exhibit type 1 immunity and have better outcomes, suggesting neutrophils and innate immunity are key to antitumor responses in some tumor types.

Ponzetta A, . . ., Jaillon S. **Cell** 2019 Jul 25;178:346–60.

Plasma cell polarization to the immunoglobulin G phenotype in hepatocellular carcinomas involves epigenetic alterations and promotes hepatoma progression in mice



Polyclonal plasma cells (from A. Lesokhin et al., Cancer Immunol Res 2019)

IgG-expressing plasma cells accumulate in hepatocellular carcinomas (HCC) and in a web of interactions support tumorigenesis. This result requires CD4^{+} T cells, tumor-associated macrophages (TAMs), and B cells stimulated by CXCR3 from TAMs producing CXCL10, which induces them to become IgG-producing plasma cells. The IgG interacts with TAM Fcγ receptors, promoting production of IL6, IL10, and CCL20. Plasma cells interfered with T-cell effector functions in HCC, and depleting B cells prevented plasma cell accumulation and led to infiltration of functional effector T cells.

Wei Y, . . ., Kuang DM. **Gastroenterology** 2019 May 1;156:1890–904.

Membrane cholesterol efflux drives tumor-associated macrophage reprogramming and tumor progression

Dropping off efflux to reprogram (from U.S. EPA in the National Archives)

Tumor-associated macrophages (TAMs) can accumulate and polarize to support tumor growth. In a mouse model of metastatic ovarian cancer, circulating monocyte-derived TAMs become the dominant macrophage population in the tumors. The tumor secretes hyaluronic acid, which promotes membrane-cholesterol efflux and depletion of lipid rafts from macrophages. This results in macrophage reprogramming to a pro-tumor phenotype, with expression of IL4-induced genes and inhibition of IFNγ-induced gene expression. Genetic deletion of ABC transporters, which mediate cholesterol efflux, reverts the tumor-promoting functions of TAMs and reduces tumor progression, suggesting a novel therapeutic strategy.

Goossens P, . . ., Lawrence T. **Cell Metab** 2019 Jun 4;29:1376–89.

Intratumoral activation of the necroptotic pathway components RIPK1 and RIPK3 potentiates antitumor immunity

Oil spills choke wildlife, necroptotic cells initiate strangling of tumors (by J. Messina, EPA)

RIPK1 and RIPK3 are components of the oligomeric "necrosome" that initiates necroptosis, an immunogenic form of programmed cell death. Injection into tumors of necroptotic cells controls tumor outgrowth, prolongs animal survival, and induces abscopal effects. This effect requires BATF3^{+} conventional dendritic cells, CD8^{+} T cells, and NF-κB activation in necroptotic cells. An AAV-based activated RIPK3 virus synergizes with PD-1 pathway blockade to promote durable tumor rejection. Analysis of patient melanoma samples reveals a survival advantage if patient tumors have high expression of RIPK3.

Snyder AG, . . ., Oberst A. **Sci Immunol** 2019 Jun 21;4:eaaw2004.

Symbiotic macrophage-glioma cell interactions reveal synthetic lethality in *PTEN*-null glioma

Another symbiotic dependence (by S. Baron via Flickr from Wikimedia Commons)

Patients with glioblastoma (GBM) have limited responses to interventions and have a median survival of a year. A subset of glioblastomas lack or have inactivating mutations of the tumor suppressor PTEN, which correlates with overproduction of macrophage chemoattractants like LOX and more infiltration with tumor-associated macrophages (TAMs). Without PTEN's regulation of the YAP1 pathway, LOX is upregulated, macrophage β_1 integrins internalize LOX, and resulting TAM recruitment promotes tumor growth. LOX inhibitors increase survival in mouse orthotopic GBM models through decreased TAM recruitment, suggesting a potential glioma therapy.

Chen P, . . ., DePinho RA. **Cancer Cell** 2019 Jun 10;35:868–84.E6.

Single-cell transcriptomics of human and mouse lung cancers reveals conserved myeloid populations across individuals and species

Comparing landscapes with complex and diverse subsets (from L. Miller)

The landscape of myeloid cell subsets in human lung cancer is exceedingly diverse, and differs phenotypically from myeloid cells in murine lung cancer models. Analyzing single-cell transcriptome profiles of tumor-associated and circulating myeloid cells in patient and mouse lung tumors reveals near identity between the species in monocyte, neutrophil, and dendritic cell subsets, although interspecies tumoral macrophages greatly differ. Distinct myeloid subsets are associated with prognosis. The similarities in subsets between mouse and man should facilitate studies to therapeutically target distinct populations.

Zilionis R, . . ., Klein AM. **Immunity** 2019 May 21;50:1317–34.