Cancer Immunology Research

# Literature Round-Up: Impactful Published Papers

*Article Recommendations from Our Deputy and Senior Editors*

## Bystander CD8$^+$ T cells are abundant and phenotypically distinct in human tumor infiltrates

*Identifying those with greatest specific values (from Elembis via Wikimedia Commons)*

Patient responses to immunotherapy can vary due to the heterogeneity of TIL populations. CD8$^+$ T cells infiltrating human lung and colon tumors show specificity for not only tumor antigens but also antigens unrelated to cancer. These "bystander" CD8$^+$ T cells have varied phenotypes, but all lack CD39 expression, a marker of chronic antigen stimulation. Thus, CD39 could offer a shortcut to identifying cancer-specific and -nonspecific T-cell populations.

Simoni Y, . . ., Newell EW. **Nature** 2018 May 16. DOI: 10.1038/s41586–018-0130-2.

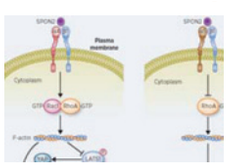
## Epigenomic-guided mass cytometry profiling reveals disease-specific features of exhausted CD8 T cells

*Different subsets of the exhausted (from Australian Paralympic Committee via Wikimedia Commons)*

Exhausted T cells develop upon chronic exposure to antigen and interfere with productive immune responses. Through the use of multidimensional CyTOF, epigenomics, and transcriptomics, subsets of exhausted T cells were identified from chronic LCMV infection, through which the functionally relevant exhausted T-cell subsets in HIV and cancercould be identified. Monitoring the changes in these subsets in patients may aid in the evaluation of disease progression and response to therapies.

Bengsch B, . . ., Wherry EJ. **Immunity** 2018 May 15;48:1029–1045.e5.

## SPON2 promotes M1-like macrophage recruitment and inhibits hepatocellular carcinoma metastasis by distinct integrin–Rho GTPase-Hippo pathways

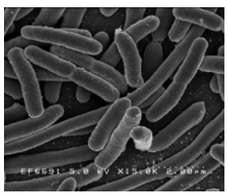


*Two cells, two pathways, two functions affected (from Graphical Abstract of Zhang et al.)*

The extracellular matrix protein SPON2 binds to certain 1 integrins, which can initiate immune responses, recruit inflammatory cells, and prime T cells. Using different integrin signaling pathways through different integrins, SPON2 recruits M1-like macrophages into the tumor microenvironment of hepatocellular carcinomas while simultaneously inhibiting metastasis. Thus, SPON2 plays a critical role in regulating the pathogenesis of this cancer.

Zhang Y-L, . . ., Zhang Z-G. **Cancer Res** 2018 May 1;78:2305–17.

## Gut microbiome–mediated bile acid metabolism regulates liver cancer via NKT cells

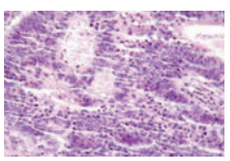


*Gut commensals (by Rocky Mountain Laboratories, NIAID-NIH via Wikimedia Commons)*

The liver is exposed to gut commensal bacterial metabolites that can affect antitumor immunity. Altering the gut microbiome affects bile acid metabolism, which causes the accumulation of NKT cells, attracted into the liver through increased CXCL16 production. These NKT cells produce IFN and can control tumor growth in multipletumor models. Mechanisms relying on interplay between hosts and their symbionts can affect health outcomes and have implications for anticancer therapeutic approaches.

Ma C, . . ., Greten TF. **Science** 2018 May 25;360:eaan5931.

## International validation of the consensus Immunoscore for the classification of colon cancer: a prognostic and accuracy study

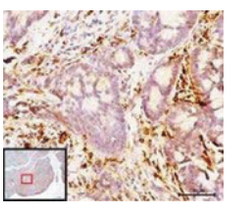


*T cells infiltrating colorectal cancer (by Nephron via Wikimedia Commons)*

The Immunoscore is a quantification of the total T cells and CD8$^+$ T cells within the tumor and at the invasive margin. This measure was used to evaluate a large cohort of colon cancer patients, and it accurately and reproducibly predicts patients' risk of recurrence, highlighting its prognostic value. Hence, the Immunoscore offers an improved parameter in the classification of colon cancer that allows for better stratification of patients.

Pagés F, . . ., Galon J. **Lancet** 2018 May 26;391:2128–39.

## Macrophages and monocytes responsible for cytokine-release syndrome induced by CAR T cells



*Tumor-associated macrophages (from Lan et al. Molec Cancer Therapeutics 2018)*

Cytokine-release syndrome is a life-threatening adverse event that hampers the use of CAR T-cell therapy. Two papers in *Nature Medicine* develop new mouse and humanized-mouse models that replicate this severe side effect and show that it ismediated through macrophage production of IL1 and IL6. Blocking IL1 and IL6 lessens this syndrome, with each cytokine having different major effects.

Giavridis T, . . ., Sadelain M. **Nat Med** 2018 May 28. doi:10.1038/s41591-018-0041-7.

Norelli M, . . ., Bondanza A. **Nat Med** 2018 May 28. doi:10.1038/s41591-018-0036-4.