Cancer Immunology Research

What We're Reading

Article Recommendations from Our Deputy and Senior Editors

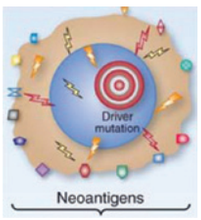
Identification of essential genes for cancer immunotherapy

APLNR model (from PDB structure 5VBL)

A two-cell genome-wide CRISPR deletion screen of melanoma was established that detected genes whose loss made tumors resistant to T cells. Loss of the G protein–coupled receptor APLNR, which interacts with JAK1 and modulates responsiveness to IFNγ, was found to make tumor cells more resistant to T-cell antitumor responses.

Patel SJ, . . ., Restifo NP. **Nature** 2017 Aug 31; 548:537–42.

Mismatch repair deficiency predicts response of solid tumors to PD-1 blockade

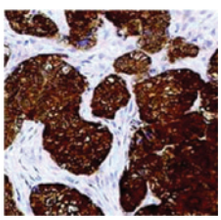


Mismatch repair is a neoantigen generator (from Xiao & Freeman, Cancer Discovery 2015)

Patients with mismatch-repair deficiencies in 24 different tumor types were assessed for responses to anti–PD-1 treatment. Tumors across multiple cancer types were sensitive to blockade therapy: 53% of patients experienced regression, with 21% complete responses. Tumor-specific T cells and clonotypes increased during these responses, affirming this deficiency as a biomarker predicting responsiveness independent of tumor type.

Le DT, . . ., Diaz LA Jr. **Science** 2017 Jul 28; 357:409–13.

Heterogeneous tumor-immune microenvironments among differentially growing metastases in an ovarian cancer patient

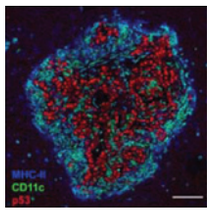


Ovarian cancer (from Konecny et al. Clin Cancer Res 2011)

Multiple tumor sites in a patient with high-grade serous ovarian cancer were sampled during debulking surgery after a treatment-free period. Progressing tumors excluded immune cells, whereas regressing and stable tumors were infiltrated with local, oligoclonally expanded T cells. Thus, multiple tumor immune microenvironments can coexist within the same patient, perhaps explaining the often heterogenous responses of metastatic lesions.

Jiménez-Sánchez, A, . . ., Miller ML. **Cell** 2017 Aug 24; 170: 927–38.

An immunosuppressive dendritic cell subset accumulates at secondary sites and promotes metastasis in pancreatic cancer



DCs in micrometastatic liver (from Fig. 1)

A particular type of dendritic cell (DC) ($CD11b^{+}CD11c^{+}MHC\text{-}II^{+}CD24^{+}$-$CD64^{low}F4/80^{low}$) was found early in sites of metastatic pancreatic cancer that supported the development of Tregs and the suppression of $CD8^{+}$ T cells, which encouraged metastatic growth. These DCs expressed MGL2 and PD-L2, through which this subset could be targeted or blocked to reduce Treg formation and promote activation of $CD8^{+}$ T cells, respectively.

Kenkel JA, . . ., Engleman EG. **Cancer Res** 2017 Aug; 77:4158–70.

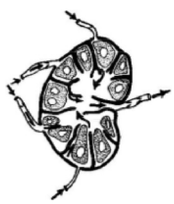
Tumor immunoevasion by the conversion of effector NK cells into type 1 innate lymphoid cells

Evading detection in Italy (by Mentnafunangavin via Wikimedia Commons)

Exposure to TGFβ *in vitro* or *in vivo* can convert natural killer (NK) cells into ILC1s and intILC1s, which, unlike NK cells, were unable to control local tumor growth and metastasis. The ILC1s produce more TNF and less IFNγ than NK cells, which interferes with antitumor activity and is responsible, in part, for the reduced innate immunosurveillance mediated by TGFβ.

Gao Y, . . ., Smyth MJ. **Nat Immunol** 2017 Sep; 18:1004–15.

Dendritic cell and antigen dispersal landscapes regulate T cell immunity



Lymph node flow (from Sunshineconnelly via Wikimedias Commons)

Lymph-node antigen concentration is greatest near sinuses and lesser in the paracortex. DC2s, located in the antigen-rich regions, present antigen to $CD4^{+}$ T cells, whereas DC1s, located in antigen-scarcer paracortical regions, present antigen to $CD8^{+}$ T cells. Thus, the localization of the distinct DC subsets and nature of antigen dispersal makes CD8 responses more sensitive than CD4 responses to even modest reductions in antigen.

Gerner MY, . . ., Germain RN. **J Exp Med** 2017 Aug 28. doi: 10.1084/jem.20170335.

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Cancer Immunol Res 2017;5:831.