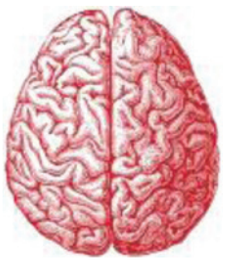
What We're Reading

Article Recommendations from Our Deputy and Senior Editors

Regression of glioblastoma after chimeric antigen receptor T-cell therapy



Progress in brain treatments (from A. Ajifo on Flickr)

CAR T cells have had great success against hematological cancers but thus far limited activity with solid tumors. In this case study, CAR T cells targeting IL13Rα2 on glioma cells administered both intracranially and intraventricularly reduced metastatic glioma to undetectable levels for an extended period of time.

Brown CE, . . ., Badie B., **NEJM** 2016 Dec 29; 375:2561–9.

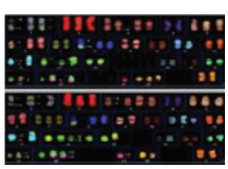
Systemic immunity is required for effective cancer immunotherapy

Global coordination (Shipping routes from D. Alves on Flickr)

As antitumor immune responses are deciphered, data have amassed that describe in great detail what transpires in the tumor itself. However, using a systems-wide assessment, it was found that tumor eradication depends upon an organism-wide coordinated immune response.

Spitzer MH, . . ., Engleman EG. **Cell** 2017 Jan 19; doi: 10.1016/j.cell.2016.12.022.

Tumor aneuploidy correlates with markers of immune evasion and with reduced response to immunotherapy



Tumor karyotype from Goodison et al. BMC Genomics. 2003;4:39.

The relationship between a tumor's state of aneuploidy and the immune response it elicits or evades is not well understood. Focal, localized aneuploidy was closely associated with tumor cell proliferation, whereas whole arm/chromosome changes produced dosage effects leading to reduced T-cell infiltration. High aneuploidy correlated with poor response to anti–CTLA-4 treatment, and the combination of aneuploidy score and mutational load was a better predictor of survival than either biomarker alone.

Davoli T, . . ., Elledge SJ. **Science** 2017 Jan 20; 355: doi:10.1126/science.aaf8399.

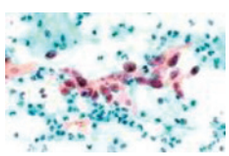
The EGR2 targets LAG-3 and 4-1BB describe and regulate dysfunctional antigen-specific CD8$^+$ T cells in the tumor microenvironment

Finding the dysfunctional (from PikiWiki Israel on Wikipedia Commons)

Although CD8$^+$ T cells are often within or near tumors, they can quickly become dysfunctional. This can include expression of EGR2, which drives 4-1BB and LAG-3 expression. These two proteins were found to mark dysfunctional intratumoral T cells that had skewed functional phenotypes. Treatment with a mAb that stimulates 4-1BB plus one that blocks LAG-3 synergistically restored strong antitumor activity and TIL function.

Williams JB, . . ., Gajewski TF. **J Exp Med** 2017 Jan 23; 10.1084/jem.20160485.

Integrated genomic and molecular characterization of cervical cancer

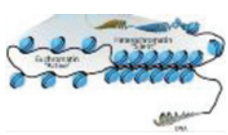


Cervical cancer (from the NCI on Wikimedia Commons)

Cervical cancer is the leading cause of death from gynecological cancers. An extensive genomic, RNA, epigenetic, histologic, protein, and clinical analysis of 228 primary cervical cancers revealed not only distinct mutations and molecular pathways associated with different HPV and histologic/molecular types, but also identified associated potential therapeutic targets.

The Cancer Genome Atlas Research Network. **Nature** 2017 Jan 23; doi:10.1038/nature21386.

SATB1 expression governs epigenetic repression of PD-1 in tumor-reactive T cells



Closing chromatin (from K. Sha and LA. Boyer on Wikipedia)

PD-1 expression is tightly controlled in T cells. SATB1, a chromatin organizer, prevented premature PD-1 expression and exhaustion by recruiting a deacetylase, NuRD, to regulatory regions of the *Pdcd1* gene to reduce transcription. TGFβ was found to inhibit both production of SATB1 and the binding of SATB1 to the *Pdcd1* promoter, encouraging PD-1 expression and exhaustion. Thus, dysregulation of SATB1 can diminish antitumor immunity.

Stephen TL, . . ., Conejo-Garcia JR. **Immunity** 2017 Jan 17; 46: 51–64.