Cancer Immunology Research

What We're Reading

Article Recommendations from Our Deputy and Senior Editors

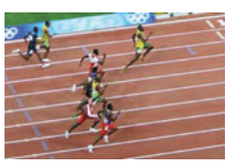
Inactivation of DNA repair triggers neoantigen generation and impairs tumour growth

Lack of mismatch repair (from Fayeena via Pinterest)

Mismatch repair–deficient solid tumors developed more mutations and neoantigens. Cells from such tumor proliferated normally, but in immunocompetent mice, tumor growth was impaired by a dynamic T-cell response. Mismatch repair–capable tumors could be converted to mismatch repair–defective tumors, which provided the immune system with a continuously renewed supply of neoantigens, a principle that could potentially be harnessed therapeutically with drugs targeting DNA repair pathways.

Germano G, . . ., Bardelli A. **Nature** 2017 Dec 7;552:116–120.

Antibody tumor targeting is enhanced by CD27 agonists through myeloid recruitment

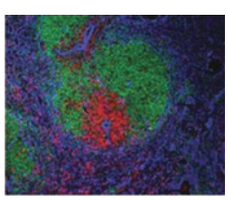


Best of the bunch (by PhotoBobil via WikiMedia)

Can the effectiveness of Ab-dependent killing of tumor cells be improved? Anti-CD20 binds to B-cell lymphomas and was systematically paired with mAbs to GITR, PD-L1, PD-1, CLTA-1, 4-1BB, OX40, TIGIT, or CD27 in B lymphoma-bearing mice. Anti-CD27 plus anti-CD20 had a dramatically greater effect on survival by an indirect effect: stimulated T and NK cells produced IFNγ and myeloid attractants. This led to myeloid infiltration, which enhanced both anti-CD20–dependent phagocytosis by macrophages and tumor destruction.

Turaj AH, . . ., Lim SH. **Cancer Cell** 2017 Dec 11;32:777–791.e6.

Spatial reconstruction of immune niches by combining photoactivatable reporters and scRNA-seq

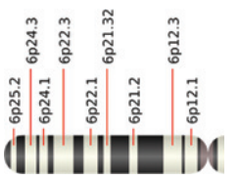


Lymph node niches (from Sangaletti et al., Cancer Discovery 2014;4:110)

Single-cell RNA-seq can provide signatures of cells present in a tissue, and histochemistry provides localization. However, knowing both has been a Schrödinger's cat dilemma. NICHE-seq addresses this by using two-photon laser-scanning microscopy, and transgenic mice that ubiquitously express photoactivatable GFP. Precise activation of a niche *in situ* before tissue dissociation allows scRNA-seq of the labeled cells. Infection and tumor development induced dynamic changes that could provide insights into differences in the tissue structures of responsive and resistant tumors.

Medaglia C, . . ., Amit I. **Science** 2017 Dec 22;358:1622–6.

Patient HLA class I genotype influences cancer response to checkpoint blockade immunotherapy

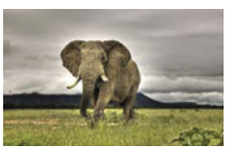


Chromosome 6p21 encodes HLA (by Mysid, based on NIH's Genetics Home Reference via Wikimedia Commons)

Immunotherapies often depend on efficient binding of neoepitopes to HLA class I and presentation to antitumor CTLs. Comparison of more than 1,500 genotypes in two independent treatment cohorts revealed that heterozygosity at all HLA loci and expression of certain HLA supertypes correlated with increased survival, whereas patients with some homozygous loci or HLA molecules containing elements that interfere with neoantigen recognition had poorer outcomes.

Chowell D, . . ., Chan TA. **Science** 2017 Dec 7. DOI: 10.1126/science.aao4572.

Origin of long-lived memory T cells



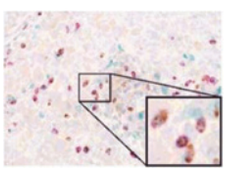
Long-lived memory mammal (from Miquitos via Flickr)

Memory T cells are quiescent yet primed to react upon antigenic re-exposure. Yellow fever virus induces long-lived human memory T cells, and Akondy et al. found that these cells proliferate during priming and retain chromatin structures resembling effector T cells, suggesting they derive from effector cells. Youngblood et al. used LCMV-specific murine T cells to study epigenetic changes to chromatin of long-term memory $CD8^+$ T cells and found a similar differentiation history. Some effector methylation patterns had reversed to naïve-associated patterns, but the demethylated state of some key effector genes were retained, allowing a swift reactivation upon rechallenge.

Akondy RS, . . ., Ahmed R. **Nature** 2017 Dec 21;552:362–7.

Youngblood B, . . ., Ahmed R. **Nature** 2017 Dec 21;552:404–9.

Antigen identification for orphan T-cell receptors expressed on tumor-infiltrating lymphocytes



Intratumor T cells (from Lo et al., CCR 2017;23:925)

Although identifying T cells that are specific for tumors has become easier, it is still difficult to determine a particular TCR's specificity. With the use of a yeast display library of random peptides that can bind to a particular HLA-A, peptides recognized by four intratumoral T cells were isolated, and their parent proteins identified using prediction algorithms and validated with synthetic peptides. Such tools could enable identification of immunogenic epitopes recognized by antitumor T cells.

Gee MH, . . ., Garcia KC. **Cell** 2018 Jan 25;172:1–15.