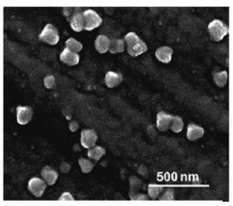
Cancer Immunology Research

What We're Reading

Article Recommendations from Our Deputy and Senior Editors

Exosome RNA unshielding couples stromal activation to pattern recognition receptor signaling in cancer



Exosomes (from Cancer Res 2016; 76: 1770-80).

Exosomes are small extracellular vesicles that pass cellular contents from cell to cell and can contain protein-shielded RNA enriched in noncoding sequences. In the tumor microenvironment, cancer cells responsive to interferon-stimulated genes (ISGs) promoted the incorporation of unshielded RNA into exosomes released by stroma. When taken up by cancer cells, the RNA bound the pattern-recognition receptor RIG-I, activated STAT1, and induced ISGs. This unshielding and transfer illustrates a commonality between tumor– and viral–host interactions.

Nabet BY, . . ., Minn AJ. **Cell** 2017 July 13; 170: 352–66.

IgG Fc domains that bind C1q but not effector Fcγ receptors delineate the importance of complement-mediated effector functions

Model of C1 (from ProcNatlAcadSci USA 2017; 114: 986-91).

Therapeutic antibodies activate complement- and Fc receptor–mediated phagocytosis and cytotoxic mechanisms, both of which could be important for their antitumor effects. A mutant form of IgG was devised whose Fc region bound complement but not Fc receptors and could kill tumor cells just as well as Abs utilizing FcRs. These antibodies avoid adverse reactions specific to FcR activation, and provide additional options for specific immunotherapies.

Lee C-H, . . ., Georgiou G. **Nat Immunol** 2017 August; 18: 889–898.

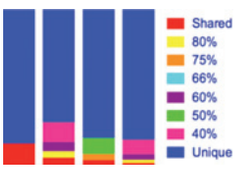
IFNγ-dependent tissue-immune homeostasis is coopted in the tumor microenvironment

Staying steady - and inconspicuous (from Pixabay).

Phagocytes from different developmental stages and tissues were found to run the same homeostatic program, which is initiated by IFN-γ. The coordinately regulated suite of genes was also expressed in cells found in metastatic cutaneous melanomas, with SOCS being key to limiting tumor surveillance. Thus, a native macrophage program is usurped in the tumor microenvironment and promotes immune evasion.

Nirschl CJ, . . ., Anandasabapathy N. Cell 2017 June 29; 170: 127–41.

TCR repertoire intratumor heterogeneity in localized lung adenocarcinomas: An association with predicted neoantigen heterogeneity and postsurgical recurrence



Heterogeneous TCR profiles (from Fig. 3).

Neoantigenic differences between lung tumor nodules have been associated with resistance to checkpoint blockade. Reuben et al. found, through TCR profiling of individual nodules, that most T-cell specificities were restricted to single nodules, though a few clones were shared. Internodule TCR heterogeneity correlated with risk of relapse, suggesting it has clinical significance. Manipulating T-cell access while targeting neoantigens with wide intratumoral distribution may be key to better antitumor therapies.

Reuben A, . . ., Zhang J. **Cancer Discov** 2017 July 21; doi: 10.1158/2159-8290.CD-17-0256.

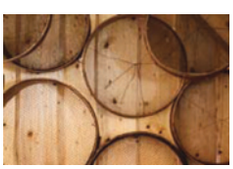
Mismatch-repair deficiency predicts response of solid tumors to PD-1 blockade

Pre-mismatch repair (from Elizabeth Augusta via Wikimedia Commons).

Eighty-six patients subjected to at least one previous therapy were enrolled in a prospective study to determine the efficacy of anti–PD-1 treatment in DNA repair–defective cancers across multiple tumor types. Overall survival after 3 years was 64% in these patients, regardless of tumor origin, supporting the use of checkpoint blockade as a standard of care for the more than 60,000 refractory patients with MMR-deficient tumors diagnosed annually in the United States.

Le DT, . . ., Diaz LA Jr. **Science** 2017 June 8; doi: 10.1126/science.aan6733.

In vivo CRISPR screening identifies *Ptpn2* as a cancer immunotherapy target



Other screens (from Pixabay).

CRISPR-mutated melanoma cells were screened *in vivo* in mice treated with GVAX + anti–PD-1 therapy, revealing proteins that increased either resistance or sensitivity to immunotherapy. IFNγ pathway deletions predictably enabled immunotherapy resistance. In contrast, loss of the phosphatase PTPN2 increased antigen presentation, recognition, and activation of $CD8^+$ T cells. This synergy with immunotherapy suggests genetic screens can identify new immunotherapy targets.

Manguso RT, . . ., Haining WN. **Nature** 2017 July 19; doi: 10.1038/nature23270.

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Cancer Immunol Res 2017;5:717.