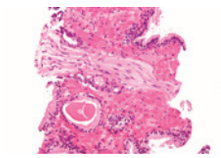
Cancer Immunology Research

What We're Reading

Article Recommendations from Our Deputy and Senior Editors

Effective combinatorial immunotherapy for castration-resistant prostate

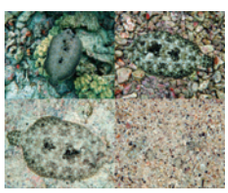


Prostate adenocarcinoma (by Nephron, Wikimedia Commons).

A chimeric mouse model with reliable formation of prostate tumors was used to test therapies for advanced prostate cancer. Checkpoint blockade alone was ineffective, but, by also targeting MDSCs (by inhibiting tyrosine kinases and the PI3K pathway), IL1 receptor antagonist was upregulated, suppressive Gr-MDSCs and the supporting cytokines were reduced, infiltration of $CD8^+$ T cells into tumors increased, and growth of tumors and metastases were inhibited.

Lu X, . . ., DePinho RA. **Nature** 2017 Mar 20; doi: 10.1038/nature21676.

Dendritic cells display subset and tissue-specific maturation dynamics over human life



DCs and peacock flounder have signatures responsive to their locales (by B. Inaglory, Wikimedia).

Organ donor tissue from 78 people of different ages was used to assess DC populations in mucosal tissues and lymph nodes during the human lifespan. cDC2s were the dominant cDCs in lymph nodes from an early age. DC subset composition varied by location, with DCs expressing tissue-specific signatures. cDC2s also appear to function as the primary guardians at mucosal surfaces.

Granot T, . . ., Farber DL. **Immunity** 2017;46:504–15.

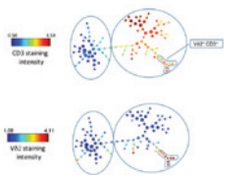
Class IIa HDAC inhibition reduces breast tumours and metastases through anti-tumour macrophages

Strengthening macrophage antitumor responses (from PublicDomainPictures.net).

Tumor-associated macrophages are often immunosuppressive. The class IIa HDAC inhibitor TMP195 was found to activate macrophages at the tumor site and normalize the vasculature without directly altering lymphocytes. Administering the drug reduced tumor burdens and decreased metastasis. When combined with checkpoint blockade, TMP195 induced a durable antitumor response in a mouse MMTV-PyMT breast cancer model.

Guerriero JL., . . ., Letai A. **Nature** 2016;543:428–32.

Human γδ T cells are quickly reconstituted after stem-cell transplantation and show adaptive clonal expansion in response to viral infection

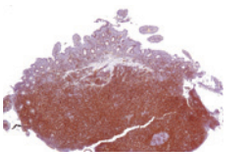


SPADE tree of V δ2 subsets (Lo Presti et al. Cancer Immunol Res 2017. DOI: 10.1158/2326-6066.CIR-16-0348).

Knowledge of the human γδ TCR repertoire during development or after infection is scant. Next-gen sequencing revealed that repertoires of rearranged genes encoding γδ TCRs in the peripheral blood of healthy adults were stable over time. Although γδ T cells were quickly reconstituted after hematopoietic stem cell transplantation, the TCR repertoires were profoundly altered. CMV infection resulted in clonal expansion of distinct γδ T cell responses, underscoring the clinical association between increased γδ T cells and improved long-term disease-free survival, and providing further evidence for adaptive anti-viral γδ T cell immunity.

Ravens S, . . ., Prinz I. **Nat Immunol** 2017 Apr; 18:393–401.

Antigen presentation profiling reveals recognition of lymphoma immunoglobulin neoantigens



Mantle cell lymphoma of the terminal ileum (by Nephron, Wikimedia Commons).

Analysis by liquid chromatography and tandem mass spectrometry of 17 human mantle cell lymphomas revealed that all presented neoepitopes were derived from the lymphoma's unique immunoglobulin. The neoantigenic peptides were exclusively derived from the Ig heavy and light chain variable regions, and presented by MHC class II. Circulating $CD4^+$ T cells specific for these neoantigens were isolated from patients and could kill autologous lymphoma cells. Peptides from other genes were not recovered from MHC, supporting a focus for immunotherapy on tumor-expressed immunoglobulins.

Khodadoust MS, . . ., Alizadeh AA. **Nature** 2017;543:723–7.

PD-1 dampens stimulation through CD28

PD-1 blocks signal flow from CD28 (from Siena College on Flickr)..

Two papers in *SCIENCE* looked at the interplay between PD-1 and CD28 signaling, in different systems. Kamphorst and colleagues found that blockade of PD-1 will not restore T cell responsiveness unless CD28 can signal. A biochemical analysis by Hui and colleagues surprisingly revealed that CD28 is more sensitive than the TCR to PD-1 and SHP-2 dephosphorylation. These studies suggest costimulatory pathways play key roles in regulating responses to anti-PD-L1/PD-1 therapy, and imply a distinct early memory population may be the target of rescue.

Kamphorst AO, . . ., Ahmed R. **Science** 2017 Mar 31;355:1423–7.
Hui E, . . ., Vale RD. **Science** 2017 Mar 31;355:1428–33.