

What We're Reading

Article Recommendations from Our Deputy and Senior Editors

Neoantigen landscape dynamics during human melanoma-T-cell interactions

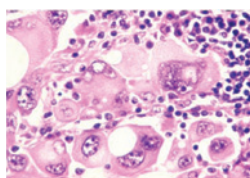


Image source: https://commons.wikimedia.org/wiki/File:Melanoma_%287%29.jpg

Tumors and their infiltrating T-cell populations reciprocally pressure each other—tumors to avoid recognition, and T cells to spot neoantigens. Longitudinal examination allowed tracking of the dynamic emergence–response relationship between neopeptide expression and T-cell reactivity.

Verdegaal EM, de Miranda NF, Visser M, Harryvan T, van Buuren MM, Andersen RS, et al. *Nature* 2016;536:91–5.

Targeting focal adhesion kinase renders pancreatic cancers responsive to checkpoint immunotherapy



Image source: <https://en.wikipedia.org/wiki/PTK2>

For the immune system to successfully eradicate tumors, T cells must first penetrate them. Jiang and colleagues found that FAK induces fibrosis. Inhibiting FAK allowed immune cells to infiltrate, greatly increasing the effectiveness of various immuno- and chemotherapies.

Jiang H, Hegde S, Knolhoff BL, Zhu Y, Herndon JM, Meyer MA, et al. *Nat Med* 2016;22:851–60.

Systemic RNA delivery to dendritic cells exploits antiviral defence for cancer immunotherapy

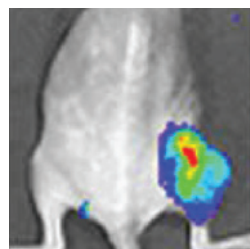


Image source: <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0041647>

Multiple approaches to tumor vaccines are in clinical trials. Kranz and colleagues devised an RNA nanoparticle that, regardless of the antigen, is taken up by DCs. The ensuing innate and adaptive immune responses successfully rejected tumors in an IFN α -dependent process.

Kranz LM, Diken M, Haas H, Kreiter S, Loquai C, Reuter KC, et al. *Nature* 2016;16:534:396–401.

Identification of shared TCR sequences from T cells in human breast cancer using emulsion RT-PCR

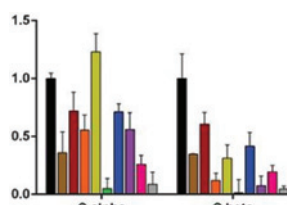


Image source: Munson et al., PNAS

Knowledge of the T-cell receptors used in antitumor responses could enhance immunotherapy. Munson and colleagues developed an enhanced single-cell emulsion RT-PCR assay that identifies TCR pairs, giving insight into antitumor TCR repertoires and potentially identifying tumor antigens.

Munson DJ, Egelston CA, Chiotti KE, Parra ZE, Bruno TC, Moore BL, et al. *Proc Natl Acad Sci U S A* 2016;113:8272–7.

Mutations associated with acquired resistance to PD-1 blockade in melanoma

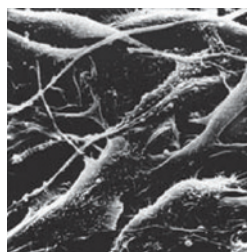


Image source: <https://visualsonline.cancer.gov/details.cfm?imageid=1760>

Immune-based cancer therapies are promising, but not always permanent, with potential outgrowth of tumor cells insensitive to the treatment. Genetic analysis of resistance to a checkpoint blockade revealed mutations that led to loss of IFN γ expression or HLA surface expression.

Zaretsky JM, Garcia-Diaz A, Shin DS, Escuin-Ordinas H, Hugo W, Hu-Lieskovan S, et al. *N Engl J Med* 2016 Jul 13; doi: 10.1056/NEJMoa1604958.

Inhibition of T cell receptor signaling by cholesterol sulfate, a naturally occurring derivative of membrane cholesterol

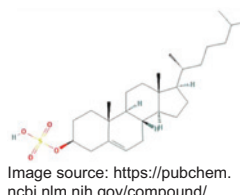


Image source: https://pubchem.ncbi.nlm.nih.gov/compound/Cholesterol_sulfate

Successful cancer immunotherapies require a firm understanding of the environmental signals affecting T-cell activation and regulation. Wang and colleagues found a ubiquitous cholesterol derivative that physiologically functions to inhibit TCR activation by disrupting the TCR-CD3 nanoclusters necessary for T-cell activation.

Wang F, Beck-García K, Zorzín C, Schamel WW, Davis MM. *Nat Immunol* 2016;17:844–50.