## WHAT WE’RE READING

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A Sampling of Highlights from the Literature

## OBITUARY

1244  
Martin A. "Mac" Cheever, MD: In Memoriam (1944–2021)  
Olivera J. Finn, Nina Bhardwaj, Steven P. Fling, and Judith C. Kaiser

## COMMENTARY

1245  
Supporting the Next Generation of Scientists to Lead Cancer Immunology Research  

## REVIEW

1252  
Engineered T-cell Receptor T Cells for Cancer Immunotherapy  
Uri Greenbaum, Ecaterina I. Dumbrava, Amadeo B. Biter, Cara L. Haymaker, and David S. Hong

## PRIORITY BRIEF

1262  
Spatial UMAP and Image Cytometry for Topographic Immuno-oncology Biomarker Discovery  
Nicolas A. Giraldo, Sneha Berry, Etienne Becht, Deniz Ates, Kara M. Schenk, Elizabeth L. Engle, Benjamin Green, Peter Nguyen, Abha Soni, Julie E. Stein, Farah Succaria, Aleksandra Ogurtsova, Haiying Xu, Raphael Gottardo, Robert A. Anders, Evan J. Lipson, Ludmila Danilova, Alexander S. Baras, and Janis M. Taube  
The authors developed and validated a multiplex immunofluorescence data-analysis pipeline and spatial UMAP algorithm. These user-friendly tools enable the quantification and visualization of spatial arrangements of immune populations in the tumor microenvironment and associated immuno-oncology topographic biomarker development.

## RESEARCH ARTICLES

1270  
Simultaneous Engagement of Tumor and Stroma Targeting Antibodies by Engineered NK-92 Cells Expressing CD64 Controls Prostate Cancer Growth  
Hallie M. Hintz, Kristin M. Snyder, Jianming Wu, Robert Hullsiek, James D. Dahlvang, Geoffrey T. Hart, Bruce Walcheck, and Aaron M. LeBeau  
The data in this study suggest targeting the tumor stroma and malignant cells with engineered natural killer cells and therapeutic antibodies could overcome immunotherapy resistance in prostate cancer and result in a next-generation targeted therapy approach.
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**Jer-Yuan Hsu**
Martina Molgora, Marco Colonna, Daniel D. Kaplan, and Raj Haldankar


In this study, the fibronectin–ILT3 interaction is shown to represent a “stromal checkpoint” through which the extracellular matrix actively suppresses tumor-associated myeloid cells. Therapeutics targeting this interaction can potentially reprogram suppressive myeloid cells, increasing antitumor immune responses.

In this study, healthy donors are shown to have preexisting memory and active responses to a broad array of cancer-expressed MHC class I-restricted phosphopeptides, whereas cancer patient responses are limited, suggesting a way to enhance cancer immunotherapy.

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Multiplex immunofluorescence (mIF) is a powerful technology that enables visualization of the spatial relationships between cells in the tumor microenvironment (TME). Using tumor tissue from 93 patients with metastatic melanoma, Giraldo et al. developed and validated a mIF data-analysis pipeline and spatial uniform manifold approximation and projection (UMAP) algorithm to cluster and visualize the data. This approach revealed that PD-L1 and PD-1 expression intensity was spatially encoded in the TME. For example, PD-L1 expression intensity was highest on CD163\(^+\) cells in neighborhoods with a high density of CD8\(^+\) cells. The differences in spatial clustering correlated with distinct clinical outcomes, highlighting the potential for using this approach to identify prognostic and predictive immuno-oncology biomarkers. Read more in this issue on page 1262. Original image from Fig. 1B. Artwork by Lewis Long.