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### 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, Ecatrina 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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Characteristics of Immune Memory and Effector Activity to Cancer-Expressed MHC Class I Phosphopeptides Differ in Healthy Donors and Ovarian Cancer Patients


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.

CD8+ T-Cell Immune Surveillance against a Tumor Antigen Encoded by the Oncogenic Long Noncoding RNA PVT1

Yasuhiro Kikuchi, Serina Tokita, Tomomi Hirama, Vitaly Kochin, Munehide Nakatsugawa, Tomoyo Shinkawa, Yoshihiko Hirohashi, Tomohide Tsukahara, Pumitake Hata, Ichiro Takemasa, Noriyuki Sato, Takayuki Kanie, and Toshihiko Torigoe

The oncogenic IncRNA PVT1 gives rise to an immunogenic HLA I-restricted peptide in patients with colorectal cancer. The data demonstrate that T cells from patients can recognize peptides resulting from altertions in noncoding regions of the genome.

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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.

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