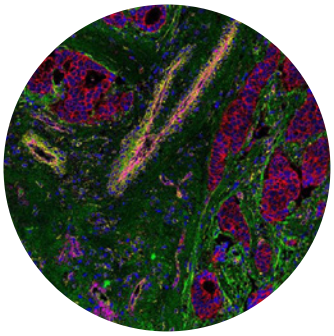
IMC TRENDING TOPICS

Trending Topics in Immuno-Oncology

Immuno-oncology is a burgeoning field with many promising approaches to improving a patient's outcome through immunotherapy. Imaging Mass Cytometry™ (IMC™) has been influential in understanding underlying mechanisms of immune response and in developing strategies for new treatments. Trending Topics in IMC covers the latest research, past publications and news involving IMC in exploring the tumor-immune landscape, biomarker discovery and methods associated with therapeutics development.

Tumor landscape

These notable examples of cancer research using Imaging Mass Cytometry demonstrate its use in gaining a better understanding of the tumor-immune landscape. High-multiplex imaging of complex single-cell phenotypes and their spatial context has enabled the architecture of cancer tissue to be characterized based on cellular composition and tissue organization.



The single-cell pathology landscape of breast cancer

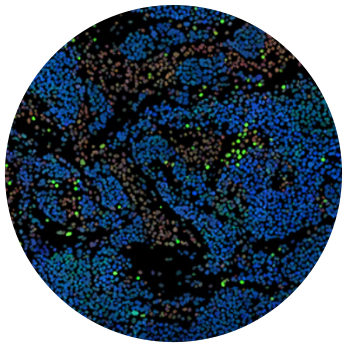
A team at the University of Zurich used IMC to simultaneously quantify 35 biomarkers, resulting in 720 high-dimensional pathology images of tumor tissue from 352 patients with breast cancer. The findings show multicellular features of the tumor microenvironment and novel subgroups of breast cancer associated with distinct clinical outcomes, with the potential to inform patient-specific diagnosis.

Jackson, H.W. et al. "The single-cell pathology landscape of breast cancer." *Nature* 578 (2020): 615–620.

The phenogenomic landscape of breast cancer

In a related study, IMC was used to investigate the relationship between genomic alterations, cell phenotype and the structure of tumor ecosystems. Researchers quantified the expression of 37 proteins with subcellular spatial resolution in 483 tumors, revealing distinct combinations of cell phenotypes and cell-cell interactions associated with genomic subtypes of breast cancer and how genomic alterations can impact phenotype.

Ali, H.R. et al. "Imaging Mass Cytometry and multiplatform genomics define the phenogenomic landscape of breast cancer." *Nature Cancer* 1 (2020): 163–175.



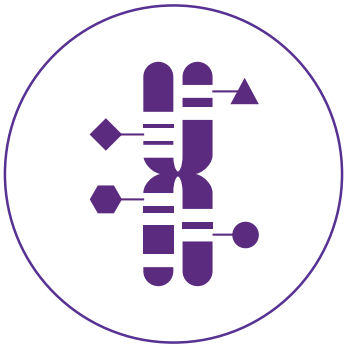
Features of response to immunotherapy in metastatic melanoma

In this study, a team used IMC in the co-detection of protein markers and RNA transcripts to analyze the chemokine landscape and immune infiltration in metastatic melanoma. Its analysis demonstrated the co-localization of chemokines with dysfunctional T cells expressing CXCL13, which was strongly associated with B cell recruitment and anti-tumor immunity. The data highlights RNA and protein co-detection as critical to deciphering specialized immune microenvironments in inflamed tumors based on chemokine expression.

Hoch, T. et al. "Multiplexed Imaging Mass Cytometry of chemokine milieus in metastatic melanoma characterizes features of response to immunotherapy." *bioRxiv* (2021): doi:10.1101/2021.07.29.454093.

Biomarker discovery

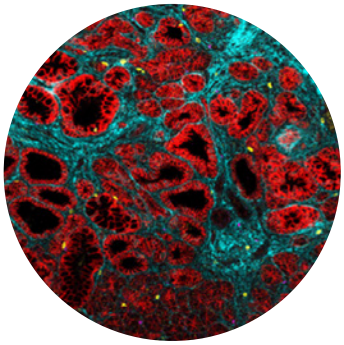
Imaging Mass Cytometry offers a novel approach to biomarker discovery, enabled by multiplex analysis of more than 40 markers simultaneously. For cancer and other diseases with high tumor heterogeneity and broad cellular signatures, the technology can help uncover new phenotypes and identify therapeutic targets that may be relevant to developing biomarkers and future treatment strategies.



Biomarker discovery in immunotherapy-treated melanoma patients

Biomarker discovery by IMC revealed significant association of 12 markers for progression-free survival and 7 markers for overall survival in patients with metastatic melanoma who received immunotherapy. A team from the Yale School of Medicine developed a newly designed analysis workflow using IMC and automated quantitative analysis software to find indicative factors of treatment response.

Martinez-Morilla, S. et al. "Biomarker discovery in immunotherapy-treated melanoma patients with Imaging Mass Cytometry." *Clinical Cancer Research* 27 (2021): 1,987–1,996.



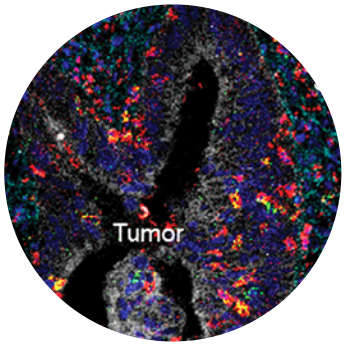
Pancreatic tumor growth and gemcitabine resistance in mice

A study led by the Georgetown Lombardi Comprehensive Cancer Center found a way to disrupt interactions among cancer-associated fibroblasts, the immune system and cancer cells, ultimately reducing pancreatic tumor growth and increasing tumor response to therapy. The study highlights the application of IMC in both protein and RNA detection, a capability that is extremely valuable for investigators studying the biological processes in single cells and within precious tissue samples.

Peran, I. et al. "Cadherin 11 promotes immunosuppression and extracellular matrix deposition to support growth of pancreatic tumors and resistance to gemcitabine in mice." *Gastroenterology* 160 (2021): 1,359–1,371.E13.

PD-1 pathway

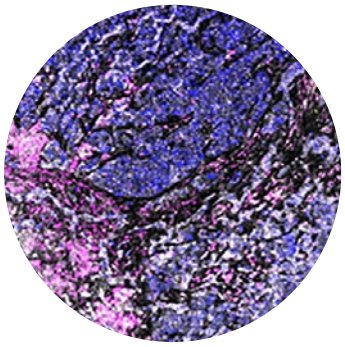
Programmed death receptor 1 (PD-1) is an immune checkpoint inhibitor that can be overexpressed in cancer and lead to T cell exhaustion and reduced anti-tumor response. PD-1 blockades can help restore immune function by activation of cytotoxic T cells. Imaging Mass Cytometry has been instrumental in identifying immune escape mechanisms and developing strategies to increase the effectiveness of checkpoint blockade therapies.



PD-1 blockade therapy for early-stage biliary tract cancer

Scientists at the National Cancer Center in Japan used IMC to examine the immune status of the tumor microenvironment (TME) in biliary tract cancer (BTC). Their findings show that tumor-infiltrating PD-1+CD8+ T cells were localized adjacent to tumor cells versus in the stroma of the TME. The team observed higher PD-1 expression by tumor-infiltrating CD8+ T cells in smaller tumors, indicating a sensitivity to PD-1 blockade, while large tumors became resistant. This data marks the potential application of PD-1 blockade therapy for early-stage BTC.

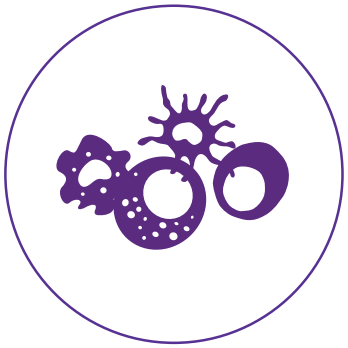
Umemoto, K. et al. "The potential application of PD-1 blockade therapy for early-stage biliary tract cancer." *International Immunology* 32 (2020): 273–281.



Tumor-infiltrating mast cells and resistance to anti-PD-1 therapy

Using a humanized-mouse melanoma model treated with anti-PD-1 therapy, tumor RNA-seq, IMC and immunohistology staining show high expression of chemokines, as well as recruitment of FOXP3+ Treg and mast cells, associated with resistance to anti-PD-1 treatment. Wistar Institute researchers discovered that combining anti-PD-1 with sunitinib or imatinib results in the depletion of mast cells and complete regression of tumors, implicating mast cell depletion in improving the efficacy of anti-PD-1 therapy.

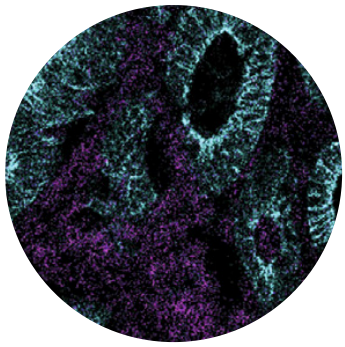
Somasundaram, R. et al. "Tumor-infiltrating mast cells are associated with resistance to anti-PD-1 therapy." *Nature Communications* 12 (2021): 346.



Tumor growth and immunotherapy resistance with T cell subset

A group at Yale University discovered a potential biomarker associated with resistance to cancer immunotherapy in patients with non-small cell lung cancer. Using single-cell mass cytometry and tissue imaging technologies, they identified a highly proliferative dysfunctional tumor-infiltrating lymphocyte subset that is expanded in lung cancer tissues in a PD-1/B7-H1-dependent manner. These findings could help develop more effective strategies to overcome immunotherapy resistance.

Sanmamed, M. et al. "A burned-out CD8+ T-cell subset expands in the tumor microenvironment and curbs cancer immunotherapy." *Cancer Discovery* 11 (2021): 1,700–1,715.



Immunogenomics of colorectal cancer response to checkpoint blockade

In an effort to better understand the variable response of colorectal cancer to immune checkpoint blockade, researchers at the Francis Crick Institute determined that tumor mutational burden is insufficient to predict response in colorectal cancer. Through whole exome and RNA sequencing of tumor cells, high-dimensional IMC, in situ detection of PDL-1 interactions, multiplexed immunofluorescence and computational spatial analysis of the TME, the team discovered additional predictors to be clonal immunogenic mutations, clonally expanded T cells, low Wnt activation, active immune escape and high CD8 T cell and antigen-presenting macrophage infiltration.

Bortolomeazzi, M. et al. "Immunogenomics of colorectal cancer response to checkpoint blockade: analysis of the KEYNOTE 177 trial and validation cohorts." *Gastroenterology* 161 (2021): 1,179–1,193.

Click here to view presentations by Michele Bortolomeazzi and other researchers on their use of IMC.

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FLDM-00910 Rev 02