

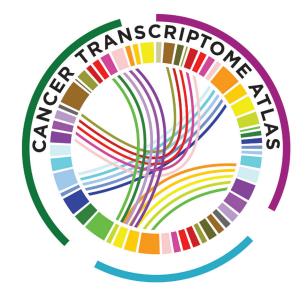
GeoMx® Cancer Transcriptome Atlas

The GeoMx Cancer Transcriptome Atlas (CTA) is designed for comprehensive profiling of the tumor, tumor microenvironment, and tumor immune status. Profile over 1,800 RNA targets simultaneously with spatial resolution in any region of interest from a single tissue section using the GeoMx Digital Spatial Profiler (DSP).



Product Highlights

- Comprehensive RNA content designed for cancer biology research
 - Includes coverage of the global immune response, microenvironment immune activity, tumor reactivity, Tumor Inflammation Signature (TIS)¹, and PAM50
 - Over 50 pathways to explore all aspects of cancer and tumor biology
- Compatible with RNAscope® and antibody visualization markers
- Supplement with up to 30 additional targets of interest
- For use with Illumina next-generation sequencer (NGS) readout and compatible with DSP Data Center Software



GeoMx® Cancer Transcriptome Atlas Design

Designed to profile over 1,800 RNA targets simultaneously with spatial resolution. The Cancer Transcriptome Atlas (CTA) contains targets for broad cell profiling and includes necessary controls for all GeoMx DSP experiments. The CTA covers 55 pathways critical to immune response, tumor biology, and the microenvironment. GeoMx RNA assays contain *in situ* hybridization (ISH) probes conjugated to unique DNA indexing-oligonucleotides via a UV-photocleavable linker. After selecting regions of interest (ROIs) on GeoMx DSP, the DNA oligonucleotides are UV cleaved and then sequenced on an Illumina sequencer. DNA oligonucleotide sequences contain ROI indices mapping them back to their tissue location, an RNA target identification sequence matching them to their ISH probes, and a unique molecular identifier (UMI) to deduplicate reads. Sequenced oligonucleotides are processed then imported back into the GeoMx platform for integration with the slide images and ROI selections for spatially-resolved RNA expression.

Curated Content for Cancer Biology

The GeoMx CTA is designed to profile all aspects of the tumor and tumor microenvironment biology.

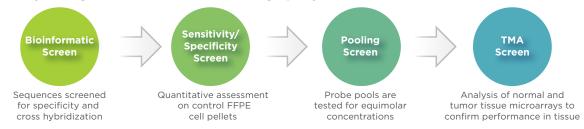
- Profile the global immune response.
- · Assess microenvironment immune activity.
- Quantify tumor reactivity to the immune response and therapeutic treatments.
- Measure clinically-derived gene sets including the 18-gene Tumor Inflammation Signature (TIS) known to be associated with response
 to PD-1/PD-L1 inhibitor pathway blockade, and the 50-gene Prediction Analysis of Microarray 50 signature (PAM50) known to be
 associated with breast cancer metastasis.

Annotation	# Genes	Annotation	# Genes	Annotation	# Genes	Annotation	# Genes
Angiogenesis	51	CT Antigens	31	Insulin Signaling	64	Notch Signaling	78
Antigen Presentation	104	Costimulatory Signaling	48	Interferon Signaling	89	Nucleic Acid Sensing	80
Apoptosis	62	Cytosolic DNA-sensing	30	Interleukin Signaling	205	PDGF Signaling	34
Autophagy	14	Cytotoxicity	108	JAK-STAT Signaling	115	PI3K-Akt	226
BCR Signaling	79	Death Receptor Signaling	118	Lymphocyte Regulation	89	Proteotoxic Stress	11
C-type Lectin Activation	64	DNA Damage Repair	155	Lymphocyte Trafficking	43	Regulation of Cell Motility	90
cAMP Signaling	68	ECM Organization	126	MAPK Signaling	220	TCR signaling	52
Carbon Metabolism	48	EMT	81	Matrix Remodeling and Metastasis	115	TGF-beta Signaling	65
Cell Adhesion	207	Epigenetic Regulation	58	Metabolism	174	TLR Signaling	90
Cell Adhesion Signaling	117	Fc Receptor Signaling	63	mTOR Signaling	35	Transcriptional Misregulation	118
Cell Cycle	139	FoxO Signaling	82	Myeloid Activity	174	Type I Interferon Signaling	48
Chemokine Signaling	119	Hedgehog Signaling	49	Neutrophil Activation	120	Type II Interferon Signaling	49
Circadian Clock	19	Hippo Signaling	71	NF-kB Signaling	105	Wnt Signaling	128
Complement System	43	Hypoxia	73	NK Cell Activation	108		

Accompanying Morphology Marker Kits are available for tissue visualization and ROI selection.

Validated Assays Ready for Use

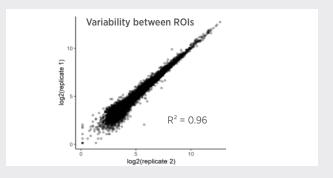
All GeoMx RNA Assays undergo extensive validation to ensure high quality GeoMx DSP data.



Spatial RNA Profiling with High Reproducibility

RNA detection shows high reproducibility between regions of interest selected from 6 cell lines within a cell pellet array (FIGURE 1).





 $\textbf{FIGURE 1:} \ \ \text{High reproducibility between two 300} \ \ \mu \text{m ROIs selected in 6 different cell lines. An example cell pellet is pictured on the left with ROIs selected.}$

A Targeted Approach for High Sensitivity

The GeoMx CTA detects high, medium, and low expressing genes with broad coverage of the genes in The Cancer Genome Atlas (TCGA)².

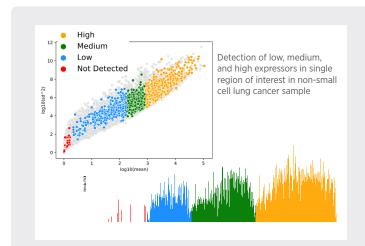


FIGURE 2: Coverage of the CTA compared to the TCGA with equally-sized bins of low, medium, and high expressors based on TCGA expression level data (left). Average TCGA expression levels below 1 FPKM are categorized as not detected.

Reveal Tissue Heterogeneity

Segmentation analysis of a region of interest (ROI) from a non-small cell lung cancer (NSCLC) sample demonstrates distinct RNA expression profiles in the tumor and tumor microenvironment segments, which would be lost if profiling the ROI as a whole (**FIGURE 3**).

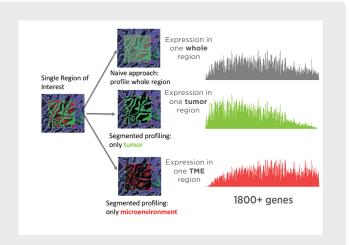


FIGURE 3: ROIs were selected with mixed tumor and tumor microenvironment (immune) segments in NSCLC tissue. ROIs were segmented based on PanCK and SYTO 13 (nuclear) morphology stain. RNA expression demonstrates distinct profiles in the tumor as compared to the microenvironment segments.

Comprehensive Coverage for Cancer Biology

Designed for cancer biology research, the Cancer Transcriptome Atlas provides complete coverage of tumor biology, the microenvironment, and the immune response, without sequencing unnecessary targets.





FIGURE 4: Cancer Transcriptome Atlas Pathways Analysis (left) compared to the Whole Transcriptome Pathways Analysis (right) illustrates the comprehensive coverage of the Cancer Transcriptome Atlas, which encompasses all areas of biology including signal transduction, metabolism, and the immune system³. Increasing the number of RNA targets from the 1,800+ CTA targets to the whole transcriptome yields only a minimal increase in coverage of cancer biology.



GeoMx® Data Center

Unique GeoMx software uniquely combines whole tissue visualization at single cell resolution with advanced ROI selection to enable comprehensive spatial profiling of tissue sections. The fully integrated workflow tracks image data to corresponding profiling data, allowing users to easily go from data collection to data analysis and to interact with either dataset in real time. The data analysis module assesses the quality of the raw data and provides a number of options to normalize data sets. Moreover, a variety of data visualization formats are enabled to export publication-quality figures. Visualization plots include: heatmap, cluster, bar graph, box plot, scatter plot, line/trend plot, strip plot, volcano plot, and PCA.

To view the RNA probe list visit: nanostring.com/geomxassays

Ordering Information

GeoMx Cancer Transcriptome Atlas								
Product	Product Description	Quantity	Catalog Number					
GeoMx Cancer Transcriptome Atlas Human RNA for Illumina Systems	RNA panel including over 1,800 targets plus controls for human immune response, tumor biology, and microenvironment. Includes RNA probes for Illumina NGS readout.	4 slides	GMX-RNA-NGS-CTA-4					
GeoMx Morphology Kits								
Product	Product Description	Quantity	Catalog Number					
GeoMx Solid Tumor TME Morphology Kit Human RNA Compatible	Morphology kit for visualization of human solid tumors and the tumor microenvironment. For use with RNA assays. Includes fluorescent antibodies against Pan-CK, CD45, and a nuclear stain.	12 slides	GMX-RNA-MORPH-HST-12					
GeoMx Melanoma TME Morphology Kit Human RNA Compatible	Morphology kit for visualization of human melanoma and the tumor microenvironment. For use with RNA assays. Includes fluorescent antibodies against S100B/Pmel17, CD45, and a nuclear stain.	12 slides	GMX-RNA-MORPH-HMEL-12					
Additional Assay Reagents								
Product	Product Description	Quantity	Catalog Number					
GeoMx Seq Code Pack Compatible with Illumina Systems	NGS readout reagents for GeoMx DSP RNA and protein analysis. Includes two Seq Code primer plates (choice of A&B, C&D, E&F, or G&H) and two universal enzyme master mixes.	192 AOI	GMX-NGS-SEQ-[XX]					
GeoMx RNA Slide Prep Kit for FFPE	Sample prep reagents for GeoMx DSP RNA analysis. Includes Buffer W, Buffer S, and Buffer R.	12 slides	GMX-PREP-RNA-FFPE-12					
GeoMx DSP Collection Plate	Barcoded collection plates for use on the GeoMx DSP. Required for AOI tracking. Kit includes 12 plates covering 1,152 AOI.	1 Pack	GMX-DSP-COLL-PLT					
GeoMx DSP Instrument Buffer Kit	Buffer kit for the GeoMx DSP. Includes Buffer S and Buffer H. Sufficient for ~48 samples with ~18 AOI each. Volume requirements may vary based on experimental design.	1 Kit	GMX-DSP-BUFF-KIT					

References

- Ayers, Mark, et al. IFN-γ-related mRNA profile predicts clinical response to PD-1 blockade. Journal of Clinical Investigation. 127.8 (2017).
- National Cancer Institute: The Cancer Genome Atlas Program. cancer.gov/tcga
- Pathway Analysis figures from Reactome, Copyright 2020 Reactome, License CC BY 4.0. Image cropped from original.

See more at nanostring.com/GeoMxPubs

For more information, please visit nanostring.com/GeoMxDSP

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