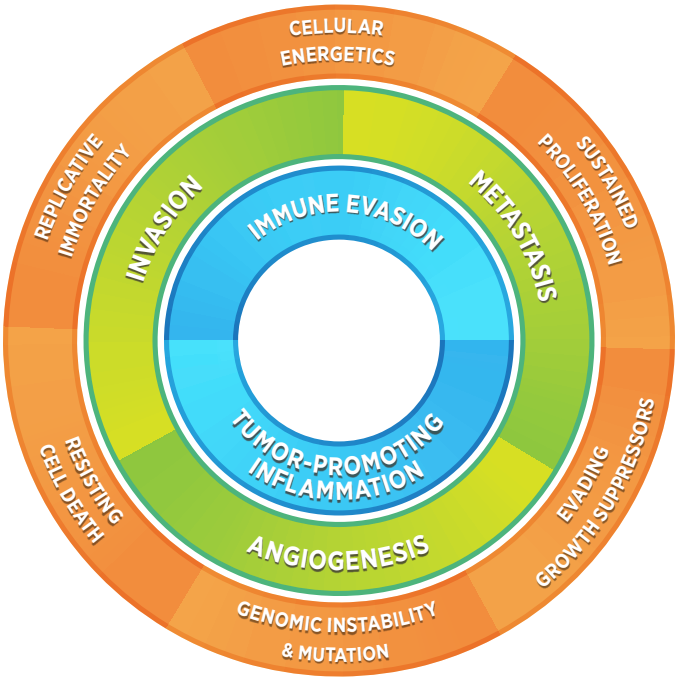
nCounter® Tumor Signaling 360 Panel

Gene Expression Panel

Targeted Therapeutics • Tumor Signaling • Immune Response

Covering hundreds of genes involved in tumorigenesis, metastasis, and inflammation, the nCounter Tumor Signaling 360 Panel offers a holistic view of the biology of the tumor, microenvironment, and immune response with an emphasis on dysfunctional cell signaling in cancer. Identify targets for novel therapies and understand the mechanism of action for current ones with a comprehensive look at 40+ pathways involved in tumor biology, immune evasion, and remodeling of the microenvironment.



Product Highlights

- Profile 780 genes across 40+ annotated pathways involved in tumor signaling
- Assess altered signaling pathways
- Identify targets for novel therapeutics
- Understand the mechanism of action of targeted therapies
- Measure the anti-tumor immune response
- Quantify the relative abundance of immune cell types

Feature	Specifications
Number of Targets	780 (Human), 780 (Mouse), including internal reference genes
Sample Input - Standard (No amplification required)	25-300 ng
Panel Standard	Synthetic oligonucleotide pool corresponding to all panel gene targets used for normalization
Sample Input - Low Input	As little as 1 ng with nCounter Low Input Kit (sold separately)
Sample Type(s)	Cultured cells/cell lysates, sorted cells, FFPE-derived RNA, total RNA, fragmented RNA, PBMCs, and whole blood/plasma
Customizable	Add up to 55 unique genes with Panel-Plus and up to 10 custom protein targets
Time to Results	Approximately 24 hours
Data Analysis	nSolver™ Analysis Software (RUO)

Core Themes and Annotations

The nCounter 360 series of cancer gene expression panels have been developed to comprehensively profile the tumor, immune response, and microenvironment. As therapeutics that target tumor signaling evolve, a greater understanding of tumor signaling is required as well as a better understanding of the interactions of tumor cells with the tissue milieu. The Tumor Signaling 360 Panel is intended to play this exact role, enabling deeper profiling of the tumor that is complete, yet focused on signaling pathways of interest for targeted therapeutic development.

Tumor Signaling					
Cellular Energetics (Hs/Mm)	**Sustained Proliferation (Hs/Mm)**	**Evading Growth Suppressors (Hs/Mm)**	**Enabling Replicative Immortality (Hs/Mm)**	**Genomic Instability & Mutation (Hs/Mm)**	**Resisting Cell Death (Hs/Mm)**
105/104 Genes	223/221 Genes	79/79 Genes	48/48 Genes	111/111 Genes	23/23 Genes
Autophagy	Androgen Signaling	Cell Cycle	Immortality & Stemness	DNA Damage & Repair	Apoptosis
Glucose Metabolism	EGFR Signaling	Senescence	Epigenetic & Transcriptional Regulation	TNF Superfamily	
Glutamine Metabolism	ERBB2 Signaling		p53 Signaling		
Lipid Metabolism	Estrogen Signaling				
mTOR Signaling	FGFR Signaling				
Nrf2 & Oxidative Stress	Hedgehog				
	MAPK Signaling				
	MET Signaling				
	Myc				
	Notch Signaling				
	PI3K-Akt Signaling				
	TGF-beta Signaling				
	Wnt Signaling				

Immune Response		Tumor Microenvironment	
Immune Evasion (Hs/Mm)	**Tumor-Promoting Inflammation (Hs/Mm)**	**Activating Invasion and Metastasis (Hs/Mm)**	**Angiogenesis (Hs/Mm)**
122/124 Genes	178/171 Genes	146/146 Genes	67/67 Genes
Antigen Presentation	Chemokine Signaling	Cell Adhesion & Motility	HIF1 Signaling
B cell Function	Inflammation	ECM Remodeling & Metastasis	PDGF Signaling
Cytotoxicity	Interferon Response	EMT	VEGF Signaling
Myeloid Immune Evasion	JAK-STAT Signaling	Hippo Signaling	
T cell Co-stimulation	NF-kB Signaling		
T cell Exhaustion			
TCR Signaling			
Tumor Antigen			

To view the annotated gene lists for the Tumor Signaling 360 Panel, visit nanostring.com/TS360

nSolver™ Analysis Software

NanoString offers advanced software tools that address the continuous demands of data analysis and the need to get simple answers to specific biological questions easily. Genes included in the Tumor Signaling 360 Panel are organized and linked to various advanced analysis modules to allow for efficient analysis of cell signaling pathways.

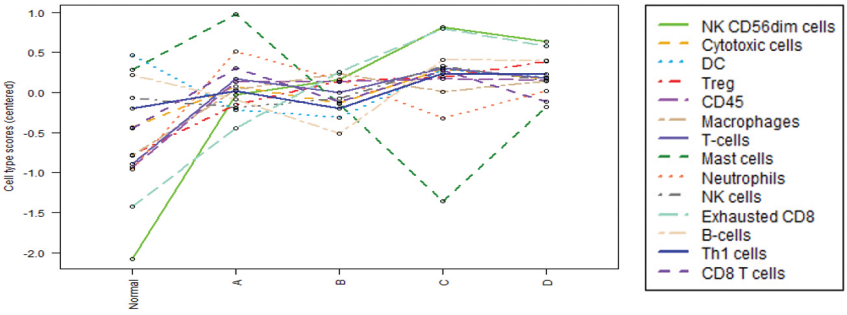
Advanced Analysis Modules available for Tumor Signaling 360:

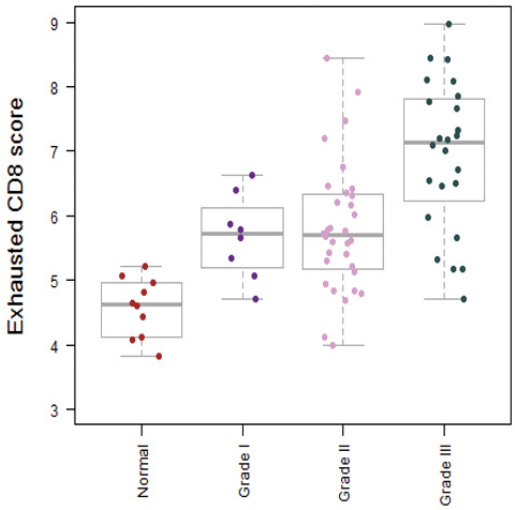
- Normalization
- Quality Control
- Individual Pathway Analysis
- Cell Profiling
- Differential Expression
- Gene Set Analysis
- Built-in compatibility for Panel-Plus and Protein analysis

Immune Cell Profiling Feature

Genes included in the Tumor Signaling 360 Panel provide unique cell profiling data to measure the relative abundance of 14 different human immune cell types. The table below summarizes each cell type represented by gene content in the panel, as qualified through biostatistical approaches and selected literature in the field of immunology.

Cell Type	Associated Human Genes
B Cells	BLK, CD19, FAM30A, FCRL2, MS4A1, PNOC, SPIB, TCL1A, TNFRSF17
CD45	PTPRC
CD8	CD8A, CD8B
Cytotoxic Cells	CTSW, GNLY, GZMA, GZMB, GZMH, KLRB1, KLRD1, KLRK1, NKG7, PRF1
Dendritic Cells	CCL13, CD209, HSD11B1
Exhausted CD8	CD244, EOMES, LAG3, PTGER4
Macrophages	CD163, CD68, CD84, MS4A4A
Mast Cells	CPA3, HDC, MS4A2, TPSAB1/B2
Neutrophils	CEACAM3, CSF3R, FCAR, FCGR3A/B, FPR1, S100A12, SIGLEC5
NK Cells	NCR1, XCL1/2
NK CD56dim Cells	IL21R, KIR2DL3, KIR3DL1, KIR3DL2
T Cells	CD3D, CD3E, CD3G, CD6, SH2D1A, TRAT1
Th1 Cells	TBX21
Treg	FOXP3





Tumor Inflammation Signature

Included within the Tumor Signaling 360 panel is the Tumor Inflammation Signature (TIS). This 18-gene signature measures activity known to be associated with response to PD-1/PD-L1 inhibitors.

- Measures 4 axes of biology to characterize a peripherally suppressed immune response
  - Antigen Presenting Cells
  - T Cell/NK Presence
  - IFNγ Biology
  - T Cell Exhaustion
- Tissue-of-origin agnostic (Pan-cancer)
- Potential surrogate for PD-L1 and mutational load in a research setting

Ordering Information

Gene Expression Panels arrive ready-to-use and generally ship within 24 hours following purchase

Product	Product Description	Quantity	Catalog Number
nCounter Human Tumor Signaling 360 Panel + Panel Standard	Includes 780 genes; 20 internal reference genes for data normalization The Tumor Signaling 360 panel includes a Panel Standard containing a pool of synthetic DNA oligonucleotides that correspond to the target sequence of each of the 780 unique probe targets in the panel. This allows for normalization for possible user, instrument, and lot-to-lot variation.	12 Reactions	XT-CSO-H-TS360-12
nCounter Mouse Tumor Signaling 360 Panel + Panel Standard	Includes 780 genes; 20 internal reference genes for data normalization The Tumor Signaling 360 panel includes a Panel Standard containing a pool of synthetic DNA oligonucleotides that correspond to the target sequence of each of the 780 unique probe targets in the panel. This allows for normalization for possible user, instrument, and lot-to-lot variation.	12 Reactions	XT-CSO-M-TS360-12
nCounter Master Kit (Max or FLEX Systems) Reagents and Cartridges	Reagents, cartridges, and consumables necessary for sample processing on nCounter MAX and FLEX Systems	12 Reactions	NAA-AKIT-012
nCounter SPRINT Cartridge 1 Cartridge, 12 lanes	Sample Cartridge for nCounter SPRINT System	12 Reactions	SPRINT-CAR-1.0
nCounter SPRINT Reagent Pack	nCounter SPRINT Reagent Pack containing Reagents A, B, C, and Hybridization Buffer	192 Reactions	SPRINT-REAG-KIT

Selected Publications

1. Bieging KT and Attardi LD. Deconstructing p53 Transcriptional Networks in Tumor Suppression. Trends Cell Biol. 2012; 22 (2), 97-106.
2. Bild, AH et al. Oncogenic Pathway Signatures in Human Cancers as a Guide to Targeted Therapies. Nature. 2006;439 (7074), 353-7.
3. Chiaradonna, F. Ras-dependent Carbon Metabolism and Transformation in Mouse Fibroblasts. Oncogene. 2006;25 (39), 5391-404.
4. Cordenonsi, M et al. The Hippo Transducer TAZ Confers Cancer Stem Cell-Related Traits on Breast Cancer Cells. Cell. 2011;147(4):759-72.
5. Hanahan D and Weinberg, RA. Hallmarks of cancer: the next generation. Cell. 2011;144(5):646-74.
6. Danaher, P et al. Gene Expression Markers of Tumor Infiltrating Leukocytes. J Immunother Cancer. 2017;21(5):18.
7. Jia, P and Zhao Z. Characterization of Tumor-Suppressor Gene Inactivation Events in 33 Cancer Types. Cell Reports. 2019;26, 496–506.
8. Malta, TM et al. Machine Learning Identifies Stemness Features Associated With Oncogenic Dedifferentiation. Cell. 2018;173(2): 338-354.e15.
9. Sanchez-Vega F et al. Oncogenic Signaling Pathways in The Cancer Genome Atlas. Cell. 2018; 173 (2), 321-337.e10.
10. Semenza, GL Hypoxia-inducible Factor 1: Oxygen Homeostasis and Disease Pathophysiology. Trends Mol Med. 2001;7(8):345-50.
11. Singh, A et al. RNAi-mediated Silencing of Nuclear Factor erythroid-2-related Factor 2 Gene Expression in Non-Small Cell Lung Cancer Inhibits Tumor Growth and Increases Efficacy of Chemotherapy. Cancer Res. 2008; 68 (19), 7975-84.
12. Sun, J et al. A systematic analysis of FDA-approved anticancer drugs. BMC Systems Biology. 2017, 11(Suppl 5):87.
13. Sweet-Cordero A et al. An Oncogenic KRAS2 Expression Signature Identified by Cross-Species Gene-Expression Analysis. Nat Genet. 2005; 37 (1), 48-55.
14. Way, GP et al. Machine Learning Detects Pan-cancer Ras Pathway Activation in The Cancer Genome Atlas. Cell Rep. 2018;23(1): 172-180.e3.

For more information, please visit nanostring.com

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