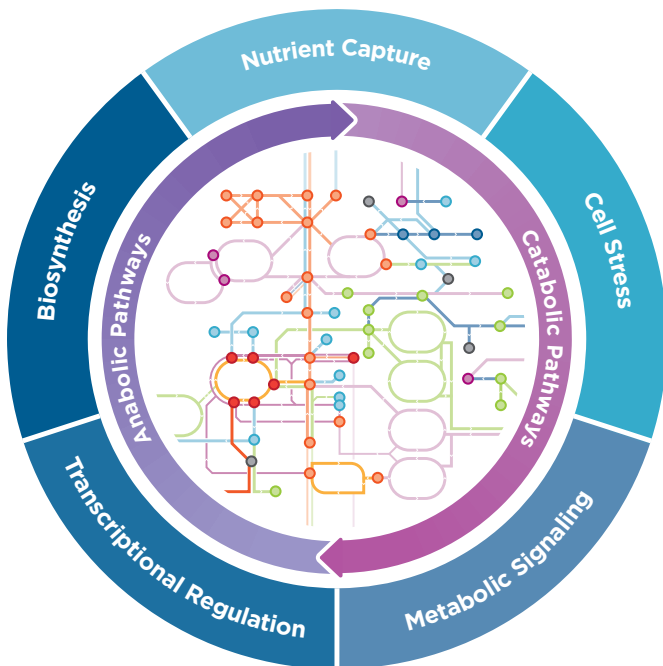


# nCounter® Metabolic Pathways Panel

## Gene Expression Panel

Cancer Metabolism • Immunometabolism • Metabolic Disease

Quantify the expression of hundreds of genes involved in core metabolic processes and signaling pathways in the context of cancer and immunity. The underlying molecular mechanisms behind alterations in metabolic pathways, signaling pathways, and cell stress can now be fully elucidated, giving researchers a complementary tool to traditional metabolite assays for profiling metabolic checkpoints and discovering potential therapeutic targets.



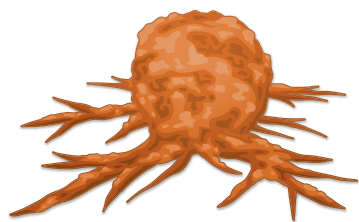
### Product Highlights

- Profile 768 genes across 34 annotated pathways involved in five important themes for metabolism research
  - Biosynthesis and Anabolic Pathways
  - Nutrient Capture and Catabolic Pathways
  - Cell Stress
  - Metabolic Signaling
  - Transcriptional Regulation
- Understand mechanisms of metabolic adaptation, metabolic switching and metabolic alterations.
- Study changes in mitochondrial respiration and glycolysis.
- Quantify the presence and relative abundance of 14 different immune cell types for immunometabolism studies.
- Advance efforts towards novel therapeutic targets

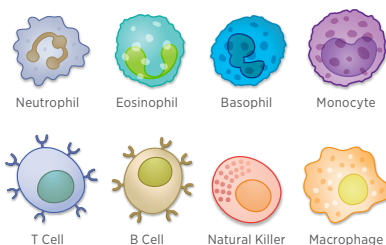
| Feature   | Specifications  |
|---|---|
| Number of Targets                                   | 768 (Human), 768 (Mouse), including internal reference genes  |
| Sample Input - Standard (No amplification required) | 25-300 ng   |
| Sample Input - Low Input                            | As little as 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 |
| Customization                                       | 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)  |

## Key Applications with the nCounter Metabolic Pathways Panel

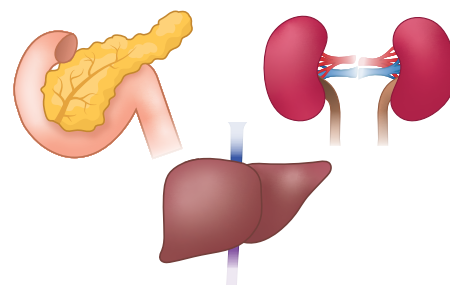
### Cancer Metabolism



### Immunometabolism



### Metabolic Disease



#### How does cancer impact normal metabolic function?

- Study key pathways involved in reprogrammed metabolism
- Identify metabolic changes that can be exploited for therapeutic development

#### How does the immune response change as a result of alterations in metabolism?

- Profile immune cell types
- Link pathway activity to immune phenotype

#### How is metabolism altered in disease?

- Understanding disease pathogenesis
- Identify potential therapeutic targets

## Gene Coverage across Core Themes of Metabolism

| Theme                                   | Description  | Pathways  | Number of Human Genes | Number of Mouse Genes |
|---|--|---|-----------------------|-----------------------|
| Biosynthesis and Anabolic Pathways      | The processes involved in the production of complex macromolecules by enzyme-catalyzed biosynthetic pathways. The products of these pathways are required for nearly all cellular functions, including proliferation.                                  | Amino Acid Synthesis, Arginine Metabolism, Cell Cycle, Fatty Acid Synthesis, Glutamine Metabolism, Glycolysis, IDH1/2 Activity, Mitochondrial Respiration, Nucleotide Synthesis, Pentose Phosphate Pathway, Tryptophan/Kynurenine Metabolism, Vitamin and Cofactor Metabolism | 354                   | 348                   |
| Cell Stress                             | Cells are impacted by the availability of nutrients and presence of toxic compounds. Adaptive responses to the stress are required for tumorigenesis, metastasis, and immune responses.  | DNA Damage Repair, Hypoxia, KEAP1/NRF2 Pathway, Reactive Oxygen Response  | 82                    | 82                    |
| Nutrient Capture and Catabolic Pathways | The processes involved in the breakdown of macromolecules, scavenging of cellular materials, or import of nutrients in order to stimulate ATP production or fuel anabolic pathways.  | Amino Acid Transporters, Autophagy, Endocytosis, Fatty Acid Oxidation, Glucose Transport, Lysosomal Degradation, Nucleotide Salvage   | 161                   | 159                   |
| Metabolic Signaling                     | The pathways that are commonly disrupted in cancer cells or altered in immune cells that impact metabolic function. In the context of cancer, mutations allow these regulated signaling pathways to allow for metabolic change enabling tumorigenesis. | AMPK, mTOR, MAPK, Myc, NF-kB, p53 Pathway, PI3K, TCR and Costimulatory Signaling, TLR Signaling   | 237                   | 235                   |
| Transcriptional Regulation              | Processes involved in the alteration of epigenetic and transcriptional activity of the cell that enables sustained metabolic reprogramming. This reprogramming allows for tumorigenesis and underlies stable changes in immune cell phenotype.         | Epigenetic Regulation, Transcriptional Regulation   | 77                    | 69                    |

## Metabolic Pathways Panel Functional Annotations

Functional annotations for different pathways and processes were assigned to the genes in the Metabolic Pathways Panel. The pathways and processes that are included in this panel provide a comprehensive view of cell metabolism.

| Annotation              | Number of Human Genes | Number of Mouse Genes |
|-------------------------|-----------------------|-----------------------|
| AMPK                    | 48                    | 48                    |
| Amino Acid Synthesis    | 93                    | 89                    |
| Amino Acid Transporters | 9                     | 9                     |
| Arginine Metabolism     | 16                    | 16                    |
| Autophagy               | 54                    | 54                    |
| Cell Cycle              | 65                    | 65                    |
| DNA Damage Repair       | 31                    | 31                    |
| Endocytosis             | 39                    | 41                    |
| Epigenetic Regulation   | 26                    | 26                    |
| Fatty Acid Oxidation    | 24                    | 21                    |
| Fatty Acid Synthesis    | 11                    | 11                    |
| Glucose Transport       | 6                     | 5                     |
| Glutamine Metabolism    | 31                    | 30                    |
| Glycolysis              | 40                    | 37                    |
| Hypoxia                 | 15                    | 15                    |
| IDH1/2 Activity         | 15                    | 15                    |
| KEAP1/NRF2 Pathway      | 5                     | 5                     |
| Lysosomal Degradation   | 16                    | 16                    |
| mTOR                    | 57                    | 57                    |

| Annotation                       | Number of Human Genes | Number of Mouse Genes |
|----------------------------------|-----------------------|-----------------------|
| MAPK                             | 52                    | 52                    |
| Mitochondrial Respiration        | 73                    | 72                    |
| Myc                              | 20                    | 20                    |
| NF-kB                            | 27                    | 27                    |
| Nucleotide Salvage               | 23                    | 23                    |
| Nucleotide Synthesis             | 48                    | 48                    |
| p53 Pathway                      | 38                    | 38                    |
| PI3K                             | 82                    | 82                    |
| Pentose Phosphate Pathway        | 19                    | 19                    |
| Reactive Oxygen Response         | 37                    | 37                    |
| TCR and Costimulatory Signaling  | 54                    | 54                    |
| TLR Signaling                    | 33                    | 31                    |
| Transcriptional Regulation       | 59                    | 51                    |
| Tryptophan/Kynurenine Metabolism | 32                    | 32                    |
| Vitamin and Cofactor Metabolism  | 28                    | 28                    |
| Internal Reference               | 20                    | 20                    |

## Immune Cell Profiling Feature

Genes included in the Human Metabolic Pathways Panel provide unique cell profiling data to measure the relative abundance of 14 different human immune cell types<sup>1</sup>. 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         | 9                      |
| CD45            | 1                      |
| CD8 T cells     | 2                      |
| Cytotoxic Cells | 10                     |
| Dendritic Cells | 3                      |
| Exhausted CD8   | 4                      |
| Macrophages     | 4                      |

| Cell Type        | Associated Human Genes |
|------------------|------------------------|
| Mast cells       | 4                      |
| Neutrophils      | 6                      |
| NK CD56dim cells | 3                      |
| NK Cells         | 2                      |
| T cells          | 6                      |
| Th1 Cells        | 1                      |
| Treg             | 1                      |

## Selected Panel References

1. DanaHER, P et al. Gene Expression Markers of Tumor Infiltrating Leukocytes. *J Immunother Cancer*. 2017;21(5):18.
2. Peng, X et al. Molecular Characterization and Clinical Relevance of Metabolic Expression Subtypes in Human Cancers. *Cell Reports*. 2018;23(1):255-69.
3. DeBerardinis RJ, Chandel, NS. Fundamentals of Cancer Metabolism. *Science Advances*. 2016;2(5).
4. O'Neill LA et al. A Guide to Immunometabolism for Immunologists. *Nature Reviews Immunology*. 2016;16(9):553-65.
5. Stine, ZE et al. MYC, Metabolism, and Cancer. *Cancer Discovery*. 2015;10:1024-39.
6. Renner, K et al. Metabolic Hallmarks of Tumor and Immune Cells in the Tumor Microenvironment. *Frontiers in Immunology*. 2017;8:248.
7. Andrejva, G and Rathmell, JC. Similarities and Distinctions of Cancer and Immune Metabolism in Inflammation and Tumors. *Cell Metabolism*. 2017;26(1):49-70.

## 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 Metabolic Pathways panel are organized and linked to various advanced analysis modules to allow for efficient analysis of the 34 pathways involved in cellular metabolism.

## Advanced Analysis Modules available for Metabolic Pathways:

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

To view the annotated gene lists for the Metabolic Pathways Panel, visit:

<https://www.nanostring.com/metabolic-pathways>

## 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 Metabolic Pathways Panel                           | Includes 768 genes; 20 internal reference genes for data normalization                                 | 12 Reactions  | XT-CSO-HMP1-12  |
| nCounter Mouse Metabolic Pathways Panel                           | Includes 768 genes; 20 internal reference genes for data normalization                                 | 12 Reactions  | XT-CSO-MMP1-12  |
| 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 |

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