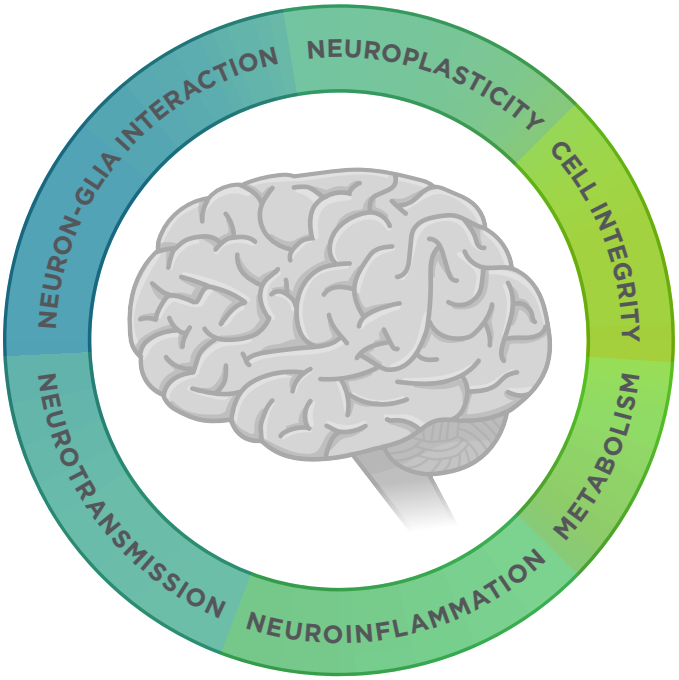
nCounter® Neuropathology Panel

Gene Expression Panel

For the study of neurodegenerative diseases

The nCounter Neuropathology panels are designed to encompass all aspects of neurodegeneration for use in basic and translational research. Each human or mouse panel provides an effective means to comprehensively evaluate neurodegeneration and research the pathogenesis of all types of neurodegenerative diseases.



Applications

- Gene expression profiling of neurodegenerative disease mechanisms for Alzheimer's disease, Parkinson's disease, Frontotemporal Dementia, Amyotrophic Lateral Sclerosis, and others
- Therapeutics research and signature generation
- Biomarker characterization

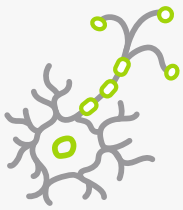
Product Highlights

- Comprehensive assessment of neurodegenerative pathways and processes
- Unique cell typing feature measures the abundance of five important cell types including neurons, astrocytes, microglia, oligodendrocytes and endothelial cells
- Customizable with Panel Plus option—add up to 55 genes of your choosing
- nCounter workflow is simple, user-friendly, and efficient with just 15 minutes total hands-on time

Feature	Specifications
Number of Targets	770 (Human), 770 (Mouse) including internal reference genes
Standard Input Material (No amplification required)	25 ng–300 ng
Sample Material - Low Input	As little as 1 ng with nCounter RNA Low Input Kit and Panel specific primer pools (sold seperately)
Sample Type(s)	FFPE-derived RNA, total RNA, fragmented RNA, PBMCs, whole blood/plasma, iPS cells, cerebrospinal fluid
Customizable	Add up to 55 unique genes with Panel Plus
Time to Results	Approximately 24 hours
Data Analysis	nSolver™ Analysis software and the ROSALIND® Platform

Neural Cell Types

Genes included in the Neuropathology Panels provide unique cell profiling data for measuring the abundance1 of five important cell types including neurons, astrocytes, microglia, oligodendrocytes and endothelial cells. The table below summarizes each cell type represented in the panel along with the gene content qualified through biostatistical approaches and selected literature in the field of neurodegenerative diseases.

Cell Type	Cell Description	Associated Human Genes	Associated Mouse Genes
 Neurons	Neuronal cell death and loss of function is a key driver of neurodegeneration.	DLX1, DLX2, GRM2, ISLR2, SLC17A6, TBR1	Dlx1, Dlx2, Grm2, Islr2, Slc17a6, Tbr1
 Astrocytes	Astrocytes represent the most numerous and diverse glial cells in the brain, responsible for a wide variety of homeostatic functions including modulation of synaptic function, network regulation, energy metabolism, neurotransmitter synthesis, among others. The loss of normal homeostatic functions and gain of toxic functions is implicated in the onset and progression of neurodegeneration.	ALDH1L1, EGFR, ENTPD2, GDPD2, ITGA7, KIAA1161, NWD1, SOX9	Aldh1l1, Egfr, Entpd2, Gdpd2, Itga7, AI464131, Nwd1, Sox9
 Microglia	Microglia represent a CNS resident myeloid cell population ontologically distinct from peripheral macrophages/monocytes. Microglia act to maintain brain homeostasis, contribute to neuroplasticity, and serve as a first line of innate immune defense in the brain. Their activation may serve as an early indicator of pathology, while chronic microglia activation or dysfunction may contribute to disease pathogenesis.	GPR84, IRF8, LRRC25, NCF1, TLR2, TNF, AIF1, TMEM119, ITGAM, CX3CR1, P2RY12, SPI1	Gpr84, Irf8, Lrrc25, Ncf1, Tlr2, Aif1, Tmem119, Itgam, Cx3cr1, P2ry12, Spi1
 Oligodendrocytes	Oligodendrocytes are highly specialized glial cells that synthesize myelin to ensheath axons of the central nervous system. Injury to or loss of oligodendrocyte function puts neuronal network function and survival at risk. Oligodendrocyte injury and death and axonal demyelination are hallmarks of some devastating neurological diseases.	BCAS1, ERBB3, FA2H, GAL3ST1, GJB1, GSN, MYRF, NINJ2, PLLP, PLXNB3, PRKCQ, SOX10, UGT8	Bcas1, Erbb3, Fa2h, Gal3st1, Gjb1, Gsn, Myrf, Ninj2, Pllp, Plxnb3, Prkcq, Sox10, Ugt8a
 Endothelial Cells	Endothelial cells form the blood-brain barrier and play a critical role in protecting the central nervous system from dangerous pathogens. Endothelial cells are equipped with a defense system against oxidative stress and their dysfunction can release inflammatory and neurotoxic agents in the CNS.	CLDN5, EMCN, ESAM, FLT1, ICAM2, LSR, MYCT1, NOSTRIN, TIE1	Cldn5, Emcn, Esam, Flt1, Icam2, Lsr, Myct1, Nostrin, Tie1

Neuropathology Panel Functional Annotations

Functional annotations for 23 fundamental pathways and processes were assigned across all genes in the Neuropathology Panels allowing for a practical view of important aspects of the onset and progression of neurodegenerative disease.

Fundemental Themes of Neurodegeneration	Description	Annotation	Human Genes	Mouse Genes
Neurotransmission	Neurotransmission is the core function of the nervous system, and is critically impaired in neurodegenerative disorders.	Transmitter Release	165	164
		Vesicular Trafficking	156	155
		Transmitter Response/Reuptake	148	147
		Transmitter Synthesis and Storage	59	59
Neuron-Glia Interaction	Glia protect neurons and maintain homeostasis within the CNS, making their function crucial to brain health and the prevention of neurodegenerative disorders.	Myelination	47	47
		Secretion of Trophic Factors	48	48
Neuroplasticity, Development, and Aging	The ability of the nervous system to form new connections during development and throughout life in response to environmental changes or injury. The brain's ability to repair itself declines with age and loss of plasticity is characteristic of neurodegenerative disorders.	Growth Factors	150	149
		Angiogenesis	78	82
		Chromatin Modification	62	62
		Apoptosis	61	59
Compartmentalization and Structural Integrity	Neurodegenerative diseases are characterized by a relentlessly progressive loss of the functional and structural integrity of the nervous system.	Neuronal Cytoskeleton	17	17
		Axon and Dendrite Structure	160	159
		Inter-Neuron Connectivity	166	166
		Tissue Integrity	45	44
Neuroinflammation	Inflammation within the central nervous system which may be initiated by neuronal death, aberrant protein aggregation, infection, traumatic brain injury, toxic metabolites or autoimmunity.	Activated Microglia	92	97
		Matrix Remodeling	5	7
		Pro-Inflammatory Cytokines	52	50
Metabolism	Impaired metabolic pathways, including RNA transcription/splicing, protein translation/degradation, carbohydrate metabolism, lipid metabolism, autophagy, and oxidative stress are hallmarks and causative agents in neurodegenerative disorders.	Unfolded Protein Response	48	47
		Oxidative Stress	91	91
		Transcription and mRNA Splicing	47	46
		Autophagy	33	33
		Carbohydrate Metabolism	44	44
		Lipid Metabolism	41	41

To view the complete gene lists for either the Human or Mouse Neuropathology Panels, visit: nanostring.com/neuroscience/neuropathology/

Proven Performance for Neurobiology Research

Neuroscientists have been using the nCounter technology for many years with thousands of publications from leading institutes worldwide. The technology has proven performance creating publication quality results across many neurological diseases and disorders. Visit our website for examples of how the nCounter is used for mechanistic studies, biomarker ID and many other areas.

For a complete view of nCounter publications, visit: **www.nanostring.com/scientific-content/publications**

Examples include:

- Neuroinflammation caused by microglia in Alzheimer's disease in mouse
- Gene expression of astrocytes and their role in disease progression of ALS patients
- Understanding oxidative stress and inflammation in Parkinson's disease striatum
- PDE10 inhibition as treatment for Huntington's disease in mouse
- Analysis of microbial communities in MS patients using frozen and FFPE samples

About the nCounter® System

The nCounter Pro Analysis System utilizes a novel digital color-coded barcode technology that is based on direct multiplexed measurement of gene expression and offers high levels of precision and sensitivity. For more information visit **http://www.nanostring.com** or contact your local specialist.

nSolver™ Analysis Software

NanoString offers advanced software tools that address the continuous demands of data analysis and help answer the specific biological questions encompassed in our most popular panels.

ROSALIND

ROSALIND is a cloud-based platform that enables scientists to analyze and interpret differential gene expression data without the need for bioinformatics or programming skills. ROSALIND makes analysis of nCounter data easy, with guided modules for:

- Normalization
- Quality Control
- Individual Pathway Analysis
- Differential Expression
- Gene Set Analysis

Smart Content in every Panel

nCounter Gene Expression panels are developed in collaboration with leading experts in the field. Each panel is curated to include the most current and relevant genes along with the following features:

- Functionally annotated gene lists with sortable gene to function pathway mapping
- Panel draws top genes with known genetic associations to several neurodegenerative diseases
- Individual probe accession numbers, aliases and target sequence information
- Gene expression analysis for optimal performance on nCounter Analysis System for research use

Selected Panel References

1. Glaab, E. et al., Comparative pathway and network analysis of brain transcriptome changes during adult aging and in Parkinson's disease. Neurobiology of Disease 74, 1-13 (2015)
2. Loring J.F. et al., A Gene Expression Profile of Alzheimer's Disease. DNA and Cell Biology 20, 683-695 (2001)
3. Kudo, LC. et al., Integrative gene-tissue microarray-based approach for identification of human disease biomarkers: application to amyotrophic lateral sclerosis. Human Molecular Genetics 19, 3233-3253 (2010)
4. Holtman, IR. Induction of a common microglia gene expression signature by aging and neurodegenerative conditions: a co-expression meta-analysis. Acta Neuropathologica Communications 3, 0001-0018 (2015)
5. Ferrari, R. et al., Frontotemporal dementia: insights into the biological underpinnings of disease through gene co-expression network analysis. Molecular Neurodegeneration 11, 21 (2016)
6. Mariani, E. et al., Meta-Analysis of Parkinson's Disease Transcriptome Data Using TRAM Software: Whole Substantia Nigra Tissue and Single Dopamine Neuron Differential Gene Expression. PloS One 11, e0161567 (2016)
7. Rosen, E. et al., Genomic Analyses Identify Pathways Dysregulated by Progranulin Deficiency, Implicating Wnt Signaling. Neuron 71, 1030-1042 (2011)
8. Chiu, I. et al., A neurodegeneration-specific gene-expression signature of acutely isolated microglia from an amyotrophic lateral sclerosis mouse model. Cell Reports 4, 385-401 (2013)
9. Hickman S. et al., The microglial sensome revealed by direct RNA sequencing. Nature Neuroscience 16, 1896-1905 (2013)
10. Zhang, C. et al., Integrated Systems Approach Identifies Genetic Nodes and Networks in Late-Onset Alzheimer's Disease. Cell 153, 707-720 (2013)
11. Twine, N. et al., Whole transcriptome sequencing reveals gene expression and splicing differences in brain regions affected by Alzheimer's disease. PloS One 6, e16266 (2011)
12. Lee C. et al., Gene-expression profile of the ageing brain in mice. Nature Genetics 25, 294-297 (2000)
13. Jiang, CH. et al., The effects of aging on gene expression in the hypothalamus and cortex of mice. Proceedings of the National Academy of Sciences of the United States of America 98, 1930-4 (2001)

Ordering Information

Gene Expression Panel CodeSets arrive ready-to-use and generally ship within 24-hours following purchase.

Product	Product Description	Quantity	Catalog Number
nCounter Human Neuropathology Panel	Includes 770 genes, including 10 internal reference genes for data normalization	12 Reactions	XT-CSO-HNROP1-12
nCounter Mouse Neuropathology Panel	Includes 770 genes, including 10 internal reference genes for data normalization	12 Reactions	XT-CSO-MNROP1-12
nCounter Analysis System Master Kit Reagents and Cartridges	Reagents, cartridges, and consumables necessary for sample processing on the nCounter Analysis System	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
Low Input RNA Reagent Kit	48rxn kit for profiling from low sample input amounts	48 Reactions	LOW-RNA-48
Human Neuropathology Primer Pools	MTE primer pools for Low Input RNA profiling (770 genes) 760 neuropathology related human genes + 10 internal reference controls. Master Kit, RNA Low Input Kit, and Panel CodeSet Required	12 Reactions	PP-HNROP1-12
Mouse Neuropathology Primer Pools	MTE primer pools for Low Input RNA profiling (770 genes) 760 neuropathology related human genes + 10 internal reference controls. Master Kit, RNA Low Input Kit, and Panel CodeSet Required	12 Reactions	PP-MNROP1-12

For more information, please visit nanostring.com

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