Infinium® Neuro Consortium Array

A high-density array for fine mapping and interrogation of the underlying genetic markers associated with neurodegenerative diseases.

Overview

The Infinium Neuro Consortium Array (Figure 1) is a next-generation genotyping array designed for deep replication of genome-wide association studies (GWAS) and fine mapping of genetic variants in neurodegenerative diseases. It allows for efficient, high-throughput characterization of genetic variants associated with common neurodegenerative diseases, including variants recently identified by whole-genome sequencing (WGS) and whole-exome sequencing (WES) (Tables 1–4).

The Infinium Neuro Consortium Array uses the Infinium 24-sample high-throughput screening (HTS) format, enabling maximum throughput productivity, and genotyping accuracy. When combined with the iScan® or HiScan® Systems, the Infinium Neuro Consortium Array provides exceptional coverage of common, intermediate, and rare single nucleotide polymorphisms (SNPs) for optimized genotyping (Tables 5–8). The Infinium Neuro Consortium Array enables insights into the relationship of gene variants and neurodegenerative diseases.

The Infinium Neuro Consortium Array is compatible with the Infinium FFPE QC Kit and the Infinium HD FFPE DNA Restore Kit, enabling genotyping of formalin-fixed, paraffin-embedded (FFPE) samples. The Infinium Neuro Consortium Array includes convenient kit packaging, containing reagents and BeadChips for amplifying, fragmenting, hybridizing, labeling, and detecting genetic variants using the streamlined Infinium PCR-free protocol.

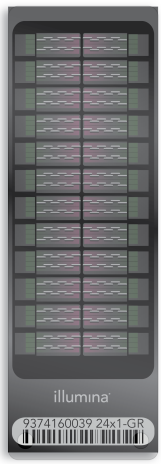

Figure 1: Infinium Neuro Consortium Array—A comprehensive microarray providing excellent coverage of relevant, consortium-selected markers associated with common neurodegenerative disorders.

Neurological Content

Content for the Infinium Neuro Consortium Array includes many known markers associated with neurodegenerative disorders from:

- Infinium Core-24 BeadChip backbone
- Content from the NeuroX Custom Array[1]
- Known neurodegenerative disease genes for coding/splice variants reported in the Exome Aggregation Consortium (ExAC)[2]
- Tagging single nucleotide polymorphisms (SNPs) to capture all common variation in ExAC genes
- Additional novel content based on ongoing whole-exome sequencing and whole-genome sequencing studies
- Full list of all GWAS hits in the National Human Genome Research Institute (NHGRI) database[3]

Flexible Content

The Infinium Neuro Consortium Array supports additional research requirements by featuring modular neurological content that is portable as add-on targeted content to some other Illumina genome-wide backbone arrays. Also, the Infinium Neuro Consortium Array has the added capacity to include up to 120,000 additional custom bead types.

Table 1: Product Information

Feature	Description	
Species	Human	
Total Number of Markers	486,670	
Number of Samples per BeadChip	24	
DNA Input Requirement	200 ng	
Assay Chemistry	Infinium HTS	
Instrument Support	iScan or HiScan System	
Sample Throughput[a]	~ 3456 samples/week	
Scan Time per Sample	iScan System 2.5 min	HiScan System 2.5 min

a. Estimate assumes 2 iScan Systems, 1 AutoLoader 2.x, 3 Tecan robots, and a 5-day work week.

Table 2: Diseases Included on the Infinium Neuro Consortium Array

Marker Categories	No. of Markers
Alzheimer's Disease	48,153
Amyotrophic Lateral Sclerosis (ALS)	1114
Frontotemporal Dementia (FTD)	29,148
Multiple System Atrophy (MSA)	1090
Parkinson's Disease	92,488
Progressive Supranuclear Palsy (PSP) / Corticobasal Degeneration (CBD)	6836

Table 3: Marker Information

Marker Categories			No. of Markers
Exonic Markers[a]			119,238
Intronic Markers[a]			203,677
Nonsense Markers[b]			7301
Missense Markers[b]			75,969
Synonymous Markers[b]			8375
Mitochondrial Markers[c]			160
Indels[c]			16,386
Sex Chromosomes[c]	X 9835	Y 1899	PAR/Homologous 106

a. RefSeq - NCBI Reference Sequence Database. www.ncbi.nlm.nih.gov/refseq. Accessed September 2016.
b. Compared against the University of California, Santa Cruz (UCSC) Genome Browser. genome.ucsc.edu. Accessed July 2016.
c. NCBI Genome Reference Consortium.Version GRCh37, released February 27, 2009. www.ncbi.nlm.nih.gov/grc/human. Accessed July 2016.

Abbreviations: PAR, pseudoautosomal region.

Table 4: High-Value Content

Content	Number of Markers	Research Application/Note
ADME Core and Extended Genes3	8137	Drug metabolism and excretion
ADME Core and Extended Genes +/- 10 kb	9163	Drug metabolism and excretion (plus regulatory regions)
APOE[5]	128	Cardiovascular disease, Alzheimer's disease, immunoregulation, and cognition
Blood Phenotype Genes[6]	336	Blood phenotypes
COSMIC[7] Genes	284,042	Somatic mutations in cancer
GO[8] CVS Genes	77,471	Cardiovascular conditions
Database of Genomic Variants[9]	380,532	Genomic structural variation
eQTLs[10]	2591	Genomic loci regulating mRNA expression levels
Fingerprint SNPs[11]	148	Human identification
HLA Genes[5]	344	Disease defense, transplant rejection, and autoimmune disorders
Extended MHC*[12]	2708	Disease defense, transplant rejection, and autoimmune disorders
KIR Genes[5]	8	Autoimmune disorders and disease defense
Neanderthal SNPs[13]	537	Neanderthal ancestry and human population migration
NHGRI GWAS Catalog[14]	3947	Markers from published genome-wide association studies
RefSeq[15] 3' UTRs	17,185	3' untranslated regions of known genes
RefSeq 5' UTRs	8426	5' untranslated regions of known genes
RefSeq All UTRs	24,482	All untranslated regions of known genes
RefSeq	307,426	All known genes
RefSeq +/- 10 kb	336,501	All known genes plus regulatory regions
RefSeq Promoters	10,289	2 kb upstream of all known genes to include promoter regions
RefSeq Splice Regions	6299	Variants at splice sites in all known genes

*Extended MHC is a ~ 8 Mb region.

Abbreviations: ADME, absorption, distribution, metabolism, and excretion; APOE, apolipoprotein E; COSMIC, catalog of somatic mutations in cancer; GO CVS, gene ontology annotation of the cardiovascular system; eQTL, expression quantitative trait loci; HLA, human leukocyte antigen; KIR, killer cell immunoglobin-like receptor; MHC, major histocompatibility complex; NHGRI, national human genome research institute; GWAS, genome-wide association study; UTR, untranslated region; RefSeq, reference sequence.

Table 5: Imputation Accuracy (Aggregate r^2) from 1000G[a]

Population[b]	Imputation Accuracy			
	MAF ≥ 5%	MAF ≥ 1%	MAF 1–5%	MAF 0.5–1%
AFR	0.90	0.83	0.76	0.62
AMR	0.94	0.89	0.80	0.71
EAS	0.92	0.85	0.66	0.41
EUR	0.94	0.89	0.77	0.58
SAS	0.93	0.86	0.71	0.47

a. Compared against Phase 3, version 5 of the 1000 Genomes Project (1000G). www.1000genomes.org. Accessed July 2016.
b. www.1000genomes.org/category/frequently-asked-questions/population. Accessed July 2016.

Abbreviations: MAF, minor allele frequency; AFR, African; AMR, Ad-mixed American; EAS, East Asian; EUR, European; SAS, South Asian.

Table 6: Number of Markers Imputed at $r^2 \geq 0.80$ from 1000G[a]

Population[b]	No. of Markers Imputed at $r^2 \geq 0.80$ (% of Total Markers)			
	MAF ≥ 5%	MAF ≥ 1%	MAF 1–5%	MAF 0.5–1%
AFR	8.5 M (73%)	14.7 M (64%)	6.2 M (53%)	2.8 M (79%)
AMR	6.2 M (87%)	10.5 M (84%)	4.3 M (80%)	0.1 M (82%)
EAS	5.6 M (84%)	7.8 M (77%)	2.2 M (60%)	0.3 M (70%)
EUR	6.1 M (87%)	8.9 M (81%)	2.9 M (69%)	0.4 M (84%)
SAS	6.2 M (84%)	9.2 M (77%)	3.0 M (64%)	0.4 M (75%)

a. Compared against Phase 3, version 5 of the 1000 Genomes Project (1000G). www.1000genomes.org. Accessed July 2016.
b. www.1000genomes.org/category/frequently-asked-questions/population. Accessed July 2016.

Abbreviations: AFR, African; AMR, Ad-mixed American; EAS, East Asian; EUR, European; SAS, South Asian.

Table 7: LD $r^2 \geq 0.80$ from 1000G[a]

Population[b]	LD Coverage ($r^2 \geq 0.80$)			
	MAF ≥ 5%	MAF ≥ 1%	MAF 1–5%	MAF 0.5–1%
AFR	0.28	0.17	0.03	0.01
AMR	0.56	0.39	0.11	0.03
EAS	0.67	0.54	0.19	0.07
EUR	0.62	0.49	0.17	0.06
SAS	0.58	0.44	0.13	0.05

a. Compared against Phase 3, version 5 of the 1000 Genomes Project (1000G). www.1000genomes.org. Accessed July 2016
b. www.1000genomes.org/category/frequently-asked-questions/population. Accessed July 2016.

Abbreviations: LD, linkage disequilibrium; AFR, African; AMR, Ad-mixed American; EAS, East Asian; EUR, European; SAS, South Asian.

Table 8: LD Mean r^2 from 1000G[a]

Population[b]	LD Coverage (Mean r^2)			
	MAF ≥ 5%	MAF ≥ 1%	MAF 1–5%	MAF 0.5–1%
AFR	0.46	0.29	0.06	0.03
AMR	0.71	0.53	0.22	0.07
EAS	0.77	0.64	0.27	0.10
EUR	0.74	0.60	0.26	0.12
SAS	0.72	0.56	0.21	0.07

a. Compared against Phase 3, version 5 of the 1000 Genomes Project (1000G). www.1000genomes.org. Accessed July 2016
b. www.1000genomes.org/category/frequently-asked-questions/population. Accessed July 2016.

Abbreviations: AFR, African; AMR, Ad-mixed American; EAS, East Asian; EUR, European; SAS, South Asian.

Ordering Information

To place an order, contact consortiamanager@illumina.com, a genotyping specialist, or a sales representative:
North America: 800.809.4566
Europe, Middle East, Africa: +44.1799.53400
Other regions: www.illumina.com/company/contact-us.html

Learn More

To learn more about the Infinium Neuro Consortium Array and other Illumina consortia genotyping products and services, visit www.illumina.com/applications/genotyping/consortia.html.

References

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This data sheet contains preliminary information specific to the Consortium version of the Infinium Neuro Array and is subject to change.

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