Infinium® DNA Analysis BeadChips

The Illumina DNA Analysis product line coupled with the Infinium Assay provide powerful tools to accelerate the discovery of disease-related genetic regions in whole-genome association and DNA copy number studies.

INTRODUCTION

The Illumina family of DNA Analysis BeadChips uses the powerful Infinium Assay to interrogate up to one million single nucleotide polymorphism (SNP) loci efficiently and accurately on a single BeadChip. The Infinium Assay uses a single-tube, PCR-free, whole-genome amplification method[1,2], and enables intelligent marker selection of nearly all known SNPs in the genome.

Tag SNPs are loci that can serve as proxies for many other SNPs. The use of tag SNPs greatly improves the power of association studies, as the same information and power from a larger number of SNPs can be gathered by genotyping only a subset of loci. BeadChips in the DNA Analysis product line greatly improve the power of whole-genome association applications by genotyping a subset of highly informative loci. Data from the International HapMap Project[3] were used to derive tag SNPs for all four HapMap populations: Caucasian [CEU], Han Chinese/Japanese [CHB+JPT], and Yoruba [YRI][4], using the linkage disequilibrium statistic, r^2.

In addition, the new Human1M and HumanCNV370-Duo BeadChips target other content categories such as reported and novel regions that show copy number variation (CNV) and non-synonymous SNPs. With over one million SNPs the Human1M offers dense, even spacing throughout the genome. See Table 1 for a full description of the content of each BeadChip in the Illumina DNA Analysis product line.

HIGHLIGHTS OF INFINIUM ASSAY BEADCHIPS

- **High-Quality Data:** Infinium Assay provides high reproducibility and call rates
- **Intelligent SNP Selection:** Genome-wide coverage of all populations using tag SNPs chosen from the International HapMap Project
- **Simple Workflow:** Single-tube sample preparation without PCR or ligation steps

FIGURE 1: INFINIUM BEADCHIPS

Infinium Assay BeadChips enable interrogation of ~317,000 to over one million SNPs and offer comprehensive coverage of CNV regions. Shown above, from left to right, are the HumanHap300-Duo, HumanHap550-Duo, and Human1M BeadChips.

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TABLE 1: ILLUMINA DNA ANALYSIS BEADCHIP FEATURES

	HUMANHAP300-DUOv2	HUMANCNV370-DUO	HUMANEXON510S-DUO	HUMANHAP550-DUOv3	HUMANHAP650Yv3	HUMAN1M
Number of Markers	318,237	370,404	511,354	561,466	660,918	1,072,820
Number of Samples	2	2	2	2	1	1
Genomic Coverage						
CEU (Mean/Median/r^2>0.8)	0.87/0.97/0.81	0.87/1.0/0.81	0.72/0.86/0.55	0.93/1.0/0.90	0.94/1.0/0.91	0.95/1.0/0.94
CHB+JPT	0.81/0.94/0.68	0.82/0.95/0.68	0.74/0.88/0.57	0.91/1.0/0.86	0.92/1.0/0.88	0.95/1.0/0.92
YRI	0.57/0.55/0.34	0.59/0.58/0.34	0.59/0.57/0.36	0.74/0.86/0.57	0.81/ 0.93/0.67	0.85/1.0/0.73
Minor Allele Frequency*						
CEU (Mean/Median)	0.26/0.25	0.25/0.25	0.16/0.12	0.23/0.23	0.22/0.21	0.20/.019
CHB+JPT	0.23/0.23	0.23/0.23	0.16/0.11	0.21/0.20	0.20/0.19	0.19/0.17
YRI	0.23/0.22	0.22/0.22	0.20/0.15	0.22/0.21	0.22/0.20	0.20/0.18
Spacing (kb)						
(Mean/Median)	9.25/5.5	7.9/5.0	5.7/3.2	5.3/2.9	4.5/2.4	2.7/1.7
Marker Categories						
Markers within 10kb of a known RefSeq Gene	143,317	164,485	312,925	252,793	292,543	565,718
Non-Synonymous SNPs**	6,663	7,181	16,182	7,107	7,350	23,288
MHC[†]/ADME[‡]/Indel SNPs	1,451/1,671/0	5,058/2,022/0	7,883/12,520/501	2,190/2,949/0	2,374/3,431/0	10,073/15,468/501
Sex Chromosome Content (X/Y/PAR loci)	9,035/0/2	12,556/1,412/361	26,277/2,273/671	13,820/10/15	16,472/10/15	40,097/2,283/686
Mitochondrial SNPs	na	na	na	163	163	163
CNV Coverage						
Number of DGV[§] Regions Represented	2,735	3,034	3,079	2,991	3,026	3,298
Number of Markers in DGV Regions	54,480	79,631	108,009	98,656	114,837	206,665
Average Markers per Region	19.9	26.2	35.1	33.0	38.0	62.6
Targets Novel CNV Regions (~9K)	No	Yes	Yes	No	No	Yes

*Based on HapMap release 22 data
**Based on RefSeq and Ensembl databases
[†]MHC region as defined by de Bakker and colleagues[5]
[‡]Markers within 10kb of a known ADME related gene
[§]Toronto Database of Genomic Variants (http://projects.tcag.ca/variation) containing 3,644 CNV regions as of March 2007

TABLE 2: DNA ANALYSIS BEADCHIP PERFORMANCE

BEADCHIP	AVERAGE CALL RATE		REPRODUCIBILITY		MENDELIAN INCONSISTENCIES		HAPMAP CONCORDANCE	COPY NUMBER DATA	
	Percent	Product Specification	Percent	Product Specification	Percent	Product Specification	Percent	SD BAF†	SD Log R Ratio‡
HumanHap300-Duo v2	99.79%	> 99%	99.99%	> 99.9%	0.04%	< 0.1%	99.79%	0.04	0.20
HumanCNV370-Duo	99.64%	> 99%*	99.99%	> 99.9%	0.03%	< 0.1%	99.87%	0.04	0.20
HumanExon510S-Duo	99.32%	> 99%	99.99%	> 99.9%	0.05%	< 0.1%	99.55%	0.04	0.21
HumanHap550-Duo	99.57%	> 99%	99.99%	> 99.9%	0.06%	< 0.1%	99.81%	0.04	0.21
HumanHap650Y v3	99.54%	> 99%	99.97%	> 99.9%	0.04%	< 0.1%	99.74%	0.04	0.20
Human1M	99.66%	> 99%	99.99%	>99.9%	0.05%	< 0.1%	99.66%	0.04	0.20

Performance results for the HumanHap300-Duo, HumanExon510S-Duo, HumanHap550-Duo BeadChips are based on 120 samples, 8 replicates, and 28 trios. Results for the HumanHap650Y are based on 159 samples, 11 replicates, and 28 trios. Results for the HumanCNV370-Duo and Human1M BeadChips are based on 123 samples, 8 replicates, 28 trios, and 125 samples, 7 replicates, 28 trios, respectively.
*The presence of CNVs may impact the final call rate.
†Standard deviation B allele frequency (heterozygotes only)
‡Standard deviation Log R ratio

COMPREHENSIVE GENOMIC COVERAGE

Genomic coverage for all Illumina DNA Analysis BeadChips has been calculated using more than two million common SNPs (minor allele frequency of ≥ 0.5%) in the HapMap data set as a reference. Using these data to estimate genomic coverage, each product provides comprehensive coverage across many populations *(Table 1)*. It has been shown that HapMap population tag SNPs are broadly transferable for association studies using samples from many independent populations[6]. In addition, these panels were designed to have broad coverage of all areas of the genome to provide a high density of markers in both reported and novel CNV regions.

HIGH-QUALITY DATA

Whole-genome disease association studies are successful due in part to high call rates and accurately called genotypes. All SNP assays on Illumina DNA Analysis BeadChips are subjected to rigorous functional testing to ensure strong performance in the Illumina Infinium Assay. For whole-genome genotyping, the Infinium product line averages call rates of > 99% and reproducibility ≥ 99.9%. The Infinium product line also provides copy number metrics with high signal-to-noise ratios and low overall noise levels (*Table 2*).

INTEGRATED SNP AND CNV ANALYSIS

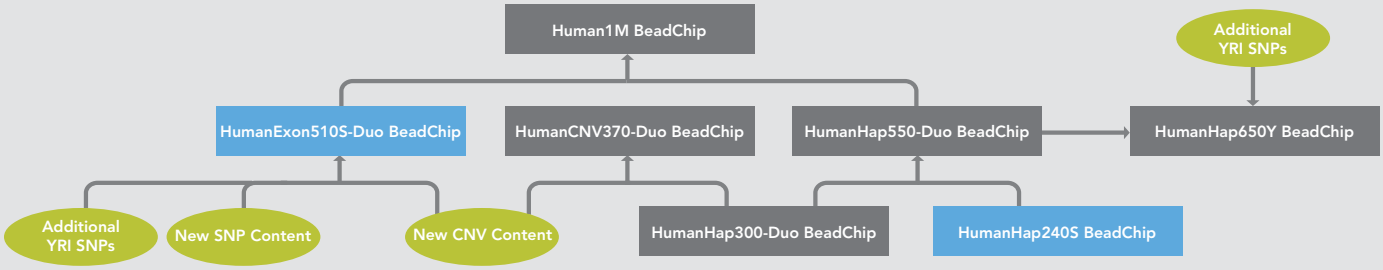
Illumina's BeadStudio analysis software package offers integrated copy number tools and a Genome Viewer. BeadStudio also offers an open plug-in interface that accepts other downstream analysis tools created in collaboration between Illumina and various partners. BeadStudio plug-ins are available for download from illumina•Connect[5].

Importantly, all of the SNPs and probes on Infinium DNA Analysis BeadChips are created using the same design strategy for unified genome-wide SNP and copy number measurements. Consequently, all markers can be analyzed together with BeadStudio software without changes to the normalization algorithm. Because of this continuity across all BeadChips, Illumina allows for completely integrated genotyping and copy number analysis.

SUMMARY

The high-quality data and low per-sample cost of Infinium Assay BeadChips are part of the powerful Illumina Whole-Genome Genotyping solution. The combination of proprietary assay technologies developed by Illumina and flexible content deployment delivers the most comprehensive solution for genotyping now available. In addition, optional automation and the Laboratory Information Management System (LIMS) lower costs by eliminating errors associated with manual processing. Illumina genotyping products (standard or custom content) can be assessed via Illumina FastTrack Genotyping Services, the Illumina Customer Sample Evaluation (CSE) Program, or your own Illumina BeadStation. Illumina solutions provide industry-leading levels of accuracy, flexibility, and affordability.

FIGURE 2: INFINIUM DNA ANALYSIS BEADCHIP PRODUCT LINE OVERVIEW



The HumanHap240S and HumanExon510S-Duo BeadChips serve as supplemental products to the HumanHap300-Duo and HumanHap550-Duo BeadChips, respectively.

TABLE 3: INFINIUM DNA ANALYSIS BEADCHIP CONTENT COMPOSITION AND COMPATIBILITY

PANEL OR BEADPOOL	NUMBER OF SNPS & MARKERS	HUMAN1M	HUMANCNV370-DUO	HUMAN650Y	HUMANHAP550-DUO	HUMANEXON510S-DUO
HumanHap240S	243,229 SNPs	•		•	•	
HumanHap300-Duo	318,237 SNPs	•	•	•	•	
New CNV Content	52,167 Markers	•	•			•
Additional YRI SNPs	99,452 SNPs	•		•		•
New SNP Content	359,735 Markers	•				•

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(3) Altshuler D, Brooks LD, Chakravarti A, Collins FS, Daly MJ, et al. International HapMap Consortium. (2005) A haplotype map of the human genome. Nature 437: 1299-1320.
(4) Carlson CS, Eberle MA, Rieder MJ, Qian Y, Kruglyak L, et al. (2004) Selecting a maximally informative set of single-nucleotide polymorphisms for association analyses using linkage disequilibrium. Am J Hum Genet 74: 106-120.
(5) illumina •Connect http://www.illumina.com/pages.ilmn?ID=67

ADDITIONAL INFORMATION

To learn more about Illumina's custom Infinium DNA Analysis Solutions and intelligent tag SNP selection, please visit www.illumina.com or contact us at the address below.

Illumina, Inc.
Customer Solutions
9885 Towne Centre Drive
San Diego, CA 92121-1975
1.800.809.4566 (toll free)
1.858.202.4566 (outside the U.S.)
techsupport@illumina.com
www.illumina.com

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