Sentrix® HumanHap300 Genotyping BeadChip

Illumina's Sentrix HumanHap300 Genotyping BeadChip delivers high-quality data and enables whole-genome genotyping of over 317,000 tagSNP markers derived from the International HapMap Project.

INTRODUCTION

Illumina's Sentrix HumanHap300 Genotyping BeadChip (*Figure 1*) uses the powerful Infinium™ II Assay to interrogate over 317,000 single nucleotide polymorphism (SNP) loci efficiently and accurately on a single BeadChip. The Infinium II Assay uses a single-tube, whole-genome amplification method that does not require PCR[1,2] and enables intelligent SNP selection utilizing tagSNPs.

TagSNPs are loci that can serve as proxies for many other SNPs. The use of tagSNPs greatly improves the power of association studies, as the same information and power from a larger number of SNPs can be gathered from genotyping only a subset of loci. TagSNPs on the HumanHap300 BeadChip were selected from the recently completed Phase I International HapMap Project[3] (www.hapmap.org). The Phase I HapMap dataset contains over 1 million common SNPs, with a minor allele frequency (MAF) ≥ 0.05 in each population studied (Caucasian [CEU], Han Chinese/Japanese [CHB+JPT], and Yoruba [YRI])[4]. To capture this variation, Illumina scientists used an algorithm for the linkage disequilibrium (LD) statistic 'r^2' to select tagSNPs[5]. A threshold of $r^2 = 0.8$ was used for SNPs within 10kb of genes or evolutionarily conserved regions, and $r^2 = 0.7$ for all other regions.

In addition, approximately 7,300 non-synonymous SNPs (nsSNPs) and a higher density of tagSNPs in the Major Histocompatibility Complex (MHC) region were selected. Because tagSNP content has been employed on the HumanHap300 Beadchip, scientists can achieve more statistical power and genomic coverage, using fewer SNPs and statistical tests, compared to other strategies using larger numbers of randomly chosen SNPs[4,5].

HIGHLIGHTS OF THE SENTRIX® HUMANHAP300 BEADCHIP

- High-Quality Data
  Infinium™ II assay provides high reproducibility and call rates
- Intelligent SNP Selection
  genome-wide coverage using > 317,000 tag SNPs chosen from the International HapMap Project
- Simple Workflow
  PCR-less protocol using a single BeadChip for each sample

TAG SNP CONTENT PROVIDES COMPREHENSIVE GENOMIC COVERAGE

The HumanHap300 BeadChip displays high genomic coverage as measured by Phase I+II HapMap genotype data (*Figure 2*). Eighty percent of all Phase I+II loci (MAF ≥ 0.05) are covered by at least one SNP on the HumanHap300 BeadChip content (for the CEU population). SNP assays on the HumanHap300 BeadChip incorporate the majority of variation in regions of the genome exhibiting higher LD based on the Phase I+II HapMap data[6].

Although assays on the Human Hap300 BeadChip were chosen using tagSNPs, SNPs are evenly spaced across the genome to ensure comprehensive coverage. On average, there is 1 SNP every 9 kb across the genome (median spacing = 5kb). The average 90th percentile gap on the HumanHap300 BeadChip is 19kb.

FIGURE 1: SENTRIX® HUMANHAP300 GENOTYPING BEADCHIP

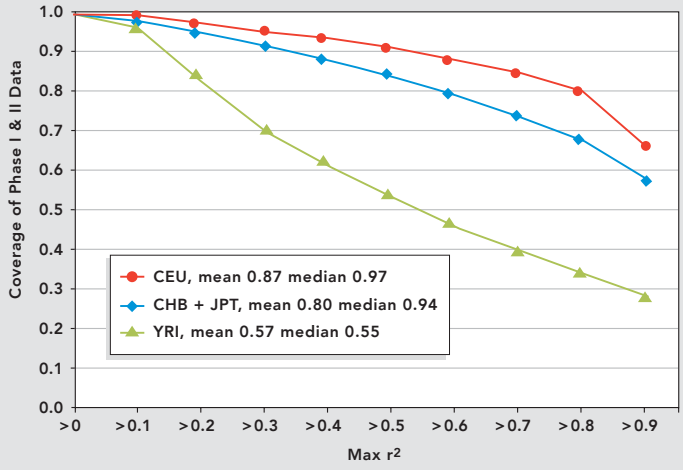
The Sentrix HumanHap300 Genotyping BeadChip, based on tagSNPs, interrogates > 317,000 SNPs while boosting genotyping study statistical power.

HIGH-QUALITY DATA

The > 317,000 SNP assays on the HumanHap300 BeadChip were subjected to rigorous functional testing to ensure strong performance using Illumina's Infinium II Assay. Whole-genome association studies are successful, in part, due to high call rates. Since complex disease traits often have relatively small gene effects, potential associations may be missed if the assayed SNP, in LD with the disease SNP, has a low call rate. Data acquired from the HumanHap300 BeadChip show strong concordance with the International HapMap Project (99.79% for > 300,000 loci, *Table 1*), which demonstrates high concordance with other genotyping platforms.

MAFs for loci in three ethnic groups were determined using the HumanHap300 BeadChip (*Figure 3*). The mean MAFs were 0.26, 0.23 and 0.23 for the CEU, CHB/JPT and YRI populations, respectively[6]. The loci assessed using the HumanHap300 BeadChip with the Infinium II Assay have MAFs within the range to accurately assess disease associations.

FIGURE 2: HUMANHAP300 GENOMIC COVERAGE BY POPULATION



The HumanHap300 Genotyping Beadchip content covers the majority of HapMap Phase I+II common variation.

TABLE 1: HUMANHAP300 GENOTYPING BEADCHIP DATA QUALITY ON 127 DNA SAMPLES (15 REPLICATES, 25 TRIOS)

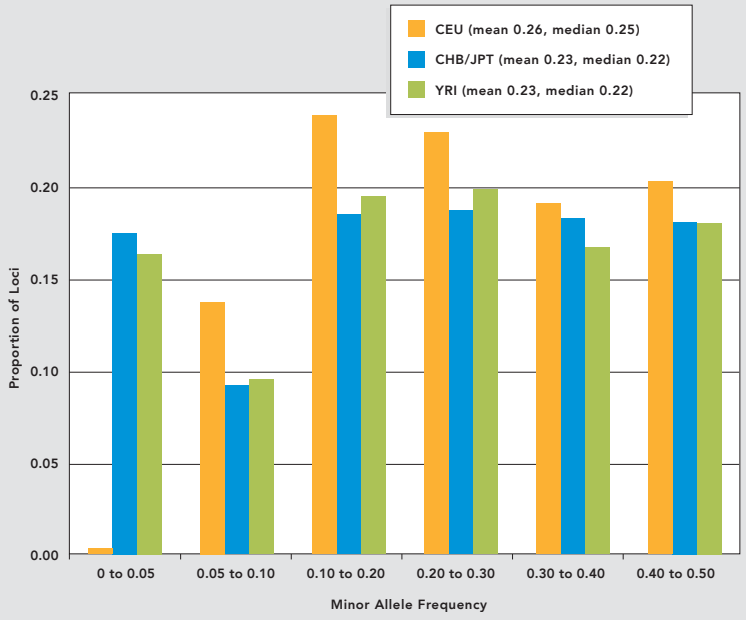
Parameter	Counts	Percent	Product Specification
Call Rate	40,295,386 / 40,322,881	99.93%	> 99.0%*
Reproducibility	4,760,834 / 4,760,893	> 99.99%	> 99.9%
Mendelian Inconsistencies	2,610 / 7919883	0.03%	< 0.1%
HapMap Concordance*	33,776,528 / 33,847,060	99.79%	

*Average

ILLUMINA SOLUTIONS FOR GENOTYPING

The high-quality data and low per-sample cost of the HumanHap300 BeadChip are part of the powerful Illumina Whole-Genome Genotyping Solution. The combination of Illumina's proprietary assay technologies 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. Whether using standard or custom content, Illumina genotyping products can be accessed via Illumina Fast Track Genotyping Services, the Illumina Customer Sample Evaluation (CSE) Program or one's own Illumina BeadStation. Illumina solutions provide industry-leading levels of accuracy, flexibility and affordability.

FIGURE 3: DISTRIBUTION OF MINOR ALLELE FREQUENCY BY POPULATION



A histogram of MAFs from unrelated individuals in three populations is shown.

ORDERING INFORMATION

CATALOG NO.	PRODUCT	DESCRIPTION
WG-30-301	Sentrix HumanHap300 Whole-Genome Genotyping Kit (for 8 Samples)	Each Sentrix HumanHap300 Genotyping BeadChip can process one sample and genotype > 317,000 loci. Each package contains eight BeadChips and reagents for processing eight samples.
WG-30-302	Sentrix HumanHap300 Whole-Genome Genotyping Kit (for 24 samples)	Each Sentrix HumanHap300 Genotyping BeadChip can process one sample and genotype > 317,000 loci. Each package contains twenty-four BeadChips and reagents for processing twenty-four samples.

REFERENCES

(1) Gunderson, K. L., Steemers, F.J., Lee, G., Mendoza, L.G., Chee, M.S. (2005). A genome-wide scalable SNP genotyping assay using microarray technology. Nat. Genetics 37, 549-554.

(2) Steemers, F. J., Weihua Chang, W., Lee, G., Barker, D.L., Shen, R., Gunderson, K.L. (2006). Whole-genome genotyping with the single-base extension assay. Nat. Methods 3 (1), 31-33.

(3) The International HapMap Consortium. (2003). The International HapMap Project. Nature 426, 789-796.

(4) Hinds, D. A., Stuve, L. L., Nilsen, G. B., Halperin, E., Eskin, E., Ballinger, D. G. Frazer, K. A. Cox, D. R. (2005). Whole-genome patterns of common DNA variation in three human populations. Science 307, 1072-1079.

(5) Carlson, C.S., Eberle, M.A. Rieder, M.J., Qian, Y., Kruglyak, L., Mickerson, D.A. (2004). Selecting a maximally informative set of single-nucleotide polymorphisms for association analyses using linkage disequilibrium. Am. J. Hum. Genet. 74, 106-120.

(6) Ilumina Technical Bulletin. Whole-Genome Genotyping with the Sentrix® HumanHap300 Genotyping BeadChip and the Infinium™ II Assay. www.illumina.com/technology/publications.

ADDITIONAL INFORMATION

Visit our website or contact us at the address below to learn more about the Sentrix HumanHap300 Genotyping BeadChip.

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

FOR RESEARCH USE ONLY

Pub. No. 370-2006-007 06Mar06

illumina®
making sense out of life