

Comprehensive Coverage

Illumina DNA Analysis BeadChips provide optimized panels for surveying genetic variants^{1,4}. All genome-wide Infinium DNA Analysis products start with a broad set of tag SNPs and other valuable SNPs from the International HapMap Project and NCBI's dbSNP to provide high genomic coverage and uniformity across the genome. All genome-wide DNA Analysis products also include a set of additional CNV-targeted markers designed to increase coverage of regions underrepresented by tag SNPs.

In the Illumina portfolio, individual BeadChips offer slightly different content and numbers of markers to provide flexible options for using the optimal content panel in any study design (Table 1).

HumanCytoSNP-12 DNA Analysis BeadChip Content

The HumanCytoSNP-12 BeadChip represents the most efficiency-optimized DNA Analysis content selection strategy. It includes a complete panel of genome-wide tag SNPs and additional markers targeting all regions of known cytogenetic importance.

Illumina scientists employed 200,000 “best of the best” SNPs that have the highest tagging power. This content maintains the exceptional genome-wide SNP coverage that Illumina is known for (70% in CEU at $r^2 > 0.8$) because of the efficient marker design strategy². At the same time, a set of 220,000 markers provides extra utility for cytogenetic analysis. This includes dense coverage of ~250 genomic regions commonly studied in cytogenetics labs and targeted coverage in additional genes, subtelomeric regions, pericentromeric regions, and sex chromosomes⁵.

Furthermore, the HumanCytoSNP-12 takes advantage of the industry's first 12-sample whole-genome BeadChip and Illumina's high-density array technology to provide the highest throughput and most cost-effective BeadChip.

Human660W-Quad DNA Analysis BeadChip Content

The Human660W-Quad BeadChip offers comprehensive genomic coverage across many populations and the majority of known variation in regions of the genome based on HapMap data.

The Human660W-Quad BeadChip builds on the content of the highly successful HumanHap550 BeadChip. The broad, evenly spaced whole-genome marker set provides high genomic coverage for powerful GWAS. In addition, the Human660W-Quad BeadChip provides 87%, 85%, and 56% coverage of CEU, CHB+JPT, and YRI populations at $r^2 > 0.8$ (Figure 2).

For equally powerful CNV and cytogenetic analysis, this dense backbone content is combined with an additional ~100,000 markers that target observed common CNVs.

The entire panel of 657,000 markers provides exceptional genomic coverage and identification of known and novel structural variants, combined with an efficient multi-sample format.

Human1M-Duo DNA Analysis BeadChip Content

With nearly 1.2 million markers per sample, the Human1M-Duo provides a powerful combination of quality, coverage, and throughput. The comprehensive set of markers on the Human1M-Duo BeadChip provides access to dense genome-wide tag SNP coverage as well as additional content targeted to high-value genomic regions of interest. Other probes are located in SNP deserts to fill in gaps.

The uniform genome-wide coverage results in a median spacing between markers of 1.5 kb (mean = 2.4 kb) and few large gaps for high-resolution CNV identification and cytogenetics analysis. Ensuring no regions are skipped, the 90th percentile largest gap between SNPs on the Human1M-Duo BeadChip is 6 kb. The result of this comprehensive design strategy is 95%, 93%, and 76% coverage of CEU, CHB+JPT, and YRI populations at $r^2 > 0.8$.

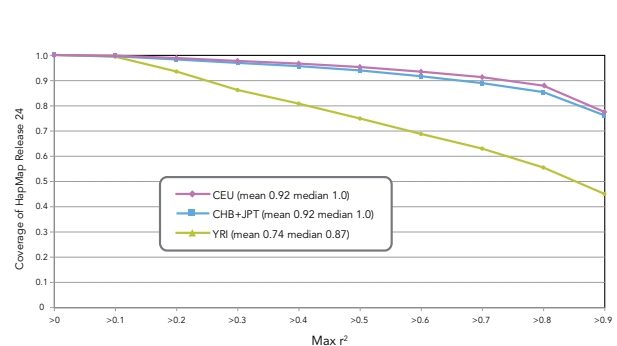
In addition to the broad coverage crucial for successful whole-genome association studies, the Human1M-Duo BeadChip targets other high-value content. Gene-centric markers selected in and around genes target both synonymous and non-synonymous SNPs to increase genic coverage. In addition, more than 10,000 markers are included for the major histocompatibility complex (MHC) region, which contains a high density of genes often associated with autoimmune and infectious diseases.

The BeadChip also features ~60,000 CNV-targeted markers, developed in collaboration with deCODE Genetics, for regions likely to contain undiscovered CNV. Novel CNV-specific probes and the dense uniform genome-wide SNP coverage support unbiased discovery and analysis of copy number polymorphisms.

HumanOmni1-Quad DNA Analysis BeadChip Content

The HumanOmni1-Quad BeadChip provides an unparalleled, extensive view of the genome, in a highthroughput, cost-effective format. A complete optimization of the BeadChip design increases the available complexity, allowing nearly five million markers to be assayed across four different samples in parallel, while reducing the amount of required DNA to 200 ng. Each BeadChip features over one million

Figure 2: Human660W-Quad Genomic Coverage



The Human660W-Quad BeadChip content covers the majority of common variation in three distinct populations. Graphs are estimated, based on the HapMap release 24 data set of > 2.3 million common SNPs.

ATGATAACGTAACACACTTCTGTTAACCTTAAGATTACTTGATCCACTGATTCAACGTACCCTAACGAAACGTATCAATTGAGACTAAATATTAACGTACCATTAAAGAGCTACCGTCTCTGTTAACCTTAAGATTACTTGATCCACTGATTCAACGT
 AACGTACCCTAACGAAACGTATCATTAAAGATTACTTGATCCACTGATTCAACGTACCCTAACGAAACGTATCAATTGAGACTAAATATTAACGTACCATTAAAGAGCTACCGTCTCTGTTAACCTTAAGATTACTTGATCCACTGATTCAACGT
 ACGAAAGAAATGATAACAGTAACACACTTCTGTTAACCTTAAGATTACTTGATCCACTGATTCAACGTACCCTAACGAAACGTATCAATTGAGACTAAATATTAACGTACCATTAAAGAGCTACCGTCTCTGTTAACCTTAAGATTACTTGATCCACTGATTCAACGT
 GATAACAGTAACACACTTCTGTTAACCTTAAGATTACTTGATCCACTGATTCAACGTACCCTAACGAAACGTATCAATTGAGACTAAATATTAACGTACCATTAAAGAGCTACCGTCTCTGTTAACCTTAAGATTACTTGATCCACTGATTCAACGT
 TACTTGATCCACTGATTCAACGTACCATTAAAGAGCTGTTAACCTTAAGATTACTTGATCCACTGATTCAACGTACCCTAACGAAACGTATCAATTGAGACTAAATATTAACGTACCATTAAAGAGCTACCGTCTCTGTTAACCTTAAGATTACTTGATCCACTGATTCAACGT
 TACTTGATCCACTGATTCAACGTACCATTAAAGAGCTGTTAACCTTAAGATTACTTGATCCACTGATTCAACGTACCCTAACGAAACGTATCAATTGAGACTAAATATTAACGTACCATTAAAGAGCTACCGTCTCTGTTAACCTTAAGATTACTTGATCCACTGATTCAACGT

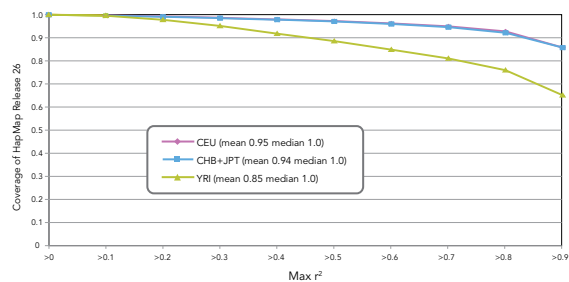
available assays per sample, containing carefully selected content that delivers dense coverage of the human genome and targets regions known to play a role in human disease. This comprehensive collection of genomic markers offers the best combination of power, price and throughput available for genome-wide association studies.

With recently released data from all three HapMap phases, intelligent tag SNP selection has been optimized to maintain comprehensive genomic coverage, while reducing SNP redundancy. This has enabled the inclusion of additional content carefully chosen to target high-value regions of the genome, such as the MHC region and new coding variants identified by the 1000 Genomes Project. The redesigned SNP selection strategy has maintained high genomic coverage rates of 93%, 92%, and 76% at $r^2 > 0.8$ for the CEU, CHB+JPT, and YRI populations, respectively (Figure 3). High density markers with a median spacing of 1.5 kb and the fewest number of large gaps for any BeadChip ensure the highest level of resolution for CNV identification in the industry.

The HumanOmni1-Quad is the only BeadChip to include cutting-edge content derived from the 1000 Genomes Project. This large international effort is dramatically increasing the information we have about genetic variation across human populations⁶. Already, the project has uncovered millions of rare and novel SNPs that will drive the next generation of microarrays. For the HumanOmni1-Quad, SNPs selected from the 1000 Genomes Project focus on regions already identified in GWAS to be associated with human disease. This content includes ~18,000 SNPs targeting four 1Mb regions known to be associated to three or more human diseases; over 50,000 SNPs predicted to be non-synonymous; 62,000 SNPs covering an additional 100 intervals surrounding published peak markers from the NHGRI GWAS database; and the remaining 950 top single-marker associated SNPs from the GWAS database.

With high-throughput processing, comprehensive genomic coverage and the ability to capture a vast amount of genetic variation, the HumanOmni1-Quad BeadChip lets you make more meaningful discoveries and take the fastest path to publication.

Figure 3: HumanOmni1-Quad Genomic Coverage



The HumanOmni1-Quad BeadChip content covers the majority of HapMap common variation in three distinct populations. Graphs are based on the HapMap release 26 data set of > 2.3 million common SNPs.

Sensitive Structural Variant Detection

Dense Uniform Markers

An important goal during the design of Infinium HD content panels was the uniform distribution of SNP markers to create the best panels for detecting structural variation, including loss of heterozygosity. With the fewest large gaps across the whole genome, the HumanOmni1-Quad BeadChip is an ideal tool for CNV researchers to use for discovery and high-resolution breakpoint mapping (Figure 4).

Intelligent Targeted Content

Of course, some regions of the genome are naturally underrepresented by tag SNPs. Illumina scientists have leveraged the flexible Infinium Assay design to generate marker sets that provide the industry's best CNV detection panels.

The HumanCytoSNP-12 BeadChip is optimized to efficiently detect cytogenetic abnormalities that are the most relevant to human disease. Its content panel targets common regions shown to be important for cytogenetic analysis⁵ and a dense backbone of coverage across the remainder of the genome.

The Human660W-Quad contains a set of ~100,000 markers that are highly informative for analyzing common CNV regions. These markers were identified in a high-density screen for CNVs that occur in two or more HapMap samples, which was conducted in collaboration with The Centre for Applied Genomics at the Hospital for Sick Children in Toronto, the Wellcome Trust Sanger Institute in the United Kingdom, and Harvard Medical School/Brigham and Women's Hospital in Boston.

The Human1M-Duo features content developed in collaboration with deCODE Genetics to blanket the "unSNPable genome" with additional non-polymorphic markers⁷. This includes difficult-to-analyze regions like megasatellites and segmental duplications, which are targeted with both SNPs and non-polymorphic probes. Many of these regions have been validated with other approaches, such as TaqMan and Southern blotting, to confirm variance in copy number in several representative populations.

The HumanOmni1-Quad includes extensive high-value content focused on disease-associated regions: cSNPs, eSNPs, indels, SNPs in mRNA splice sites, miRNA binding sites, introns, promoter regions, ADME genes, disease-associated SNPs, mitochondrial DNA, AIMS, ABO blood typing SNPs, PAR, Y-chromosome, MHC region, and HLA complex. The BeadChip also provides high CNV coverage (Figure 4), featuring 5,000+ rare CNV regions in addition to all the common CNV content available on the Human660W-Quad.

CNV-targeted probes share the same rational design strategy with all SNPs. All markers on Infinium HD BeadChips have high feature redundancy, yielding low overall noise, and all markers are used for reliable and sensitive detection of changes in copy number. The consistent marker design allows all markers to be analyzed together using GenomeStudio[®] Software. Completely integrated genotyping and copy number studies maximize analytical efficiency⁸⁻¹⁰.

The resulting rationally designed content on Infinium HD BeadChips supports the industry's most powerful SNP genotyping and CNV identification^{3,1}.

