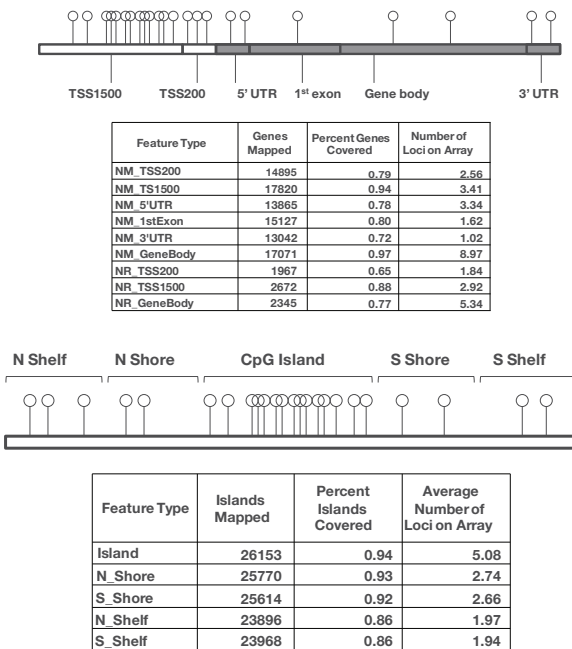




**Figure 2: HumanMethylation450 BeadChip Provides Coverage Throughout Gene Regions**



The HumanMethylation450 BeadChip offers broad coverage across gene regions, as well as CpG islands/CPG island regions, shelves, and shores for the most comprehensive view of methylation state.

derived from limited DNA sources. HumanMethylation450 BeadChip kits contain all required reagents for performing methylation analyses (except for the bisulfite conversion kit, which is available separately).

### Data Integration

Of all the genes represented on the HumanMethylation450 BeadChip, more than 20,000 are also present on the HumanHT-12 v4 Expression BeadChip<sup>2</sup>, permitting combined analysis of global methylation status and gene expression levels. In addition, investigators may integrate methylation data with genotyping data from GWAS studies to better understand the interplay between genotype and methylation state in driving phenotypes of interest.

### High-Quality Data

The HumanMethylation450 BeadChip applies both Infinium I and II assay chemistry technologies (Figure 3) to enhance the depth of coverage for methylation analysis. The addition of the Infinium II design allows use of degenerate oligonucleotide probes for a single bead type, enabling each of up to three underlying CpG sites to be either methylated or unmethylated with no impact on the result for the queried site.

Illumina scientists rigorously test every product to ensure strong and reproducible performance, enabling researchers to achieve industry-leading data quality.

### Precision and Accuracy

Reproducibility has been determined based on the correlation of results generated from technical replicates. The HumanMethylation450 BeadChip showed strong correlation between replicates ( $r^2 > 0.98$ ), as well as with the HumanMethylation27 BeadChip and whole-genome bisulfite sequencing (Figure 4).

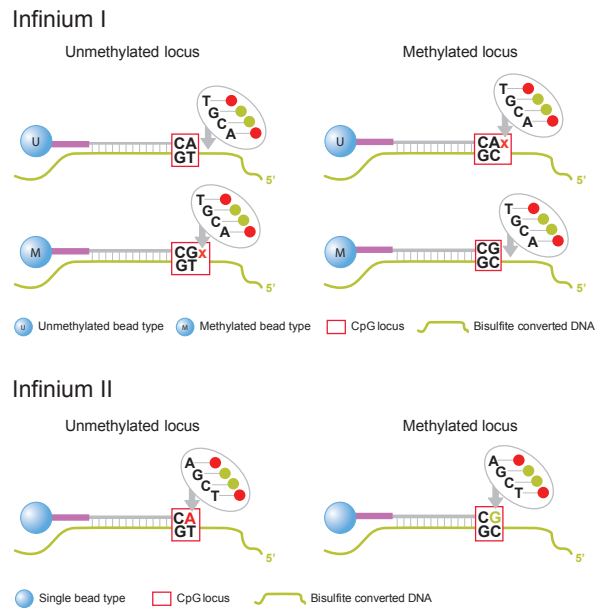
### Sensitivity

By comparing the results of replicate experiments (duplicates of eight biological samples), Illumina scientists have shown that the HumanMethylation450 BeadChip reliably detects a delta-beta value of 0.2 with a lower than 1% false positive rate.

### Internal Quality Controls

Infinium HD-based assays possess several sample-dependent and sample-independent controls so researchers have confidence in producing the highest quality data. The HumanMethylation450 BeadChip includes 600 negative controls, which are particularly important in methylation analysis assays since sequence complexity is decreased after bisulfite conversion. The GenomeStudio<sup>®</sup> Methylation Module Software has an integrated Controls Dashboard where the performance of all controls can be easily monitored.

**Figure 3: Broader Coverage Using Infinium I and II Assay Designs**



The HumanMethylation450 BeadChip employs both Infinium I and Infinium II assays, enhancing its breadth of coverage. Infinium I assay design employs two bead types per CpG locus, one each for the methylated and unmethylated states. The Infinium II design uses one bead type, with the methylated state determined at the single base extension step after hybridization.



