Twist Human Methylome Panel

Discovery in methylation profiling

KEY BENEFITS

Exceptional, Consistent Performance Design and workflow efficiency

- Optimized performance with an end to end workflow
- Increased library complexity
- Flexibility in adding spike-in content

Broader Coverage versus average microarray

- ~4x more coverage of all CpG sites
- More coverage of CpG island bases
- Based on updated reference databases

Advantage over average microarrays

- Higher calls at differentially methylated regions
- More upstream and downstream coverage of adjacent CpG sites

OVERVIEW

The Twist Human Methylome Panel targets 3.98M CpG sites through 123 Mb of genomic content to target biologically relevant methylation markers. Expansive content makes this panel an ideal choice for investigators to explore the methylation fraction in a diverse range of applications from cancer metastasis, human development, and functional genomics.

The panel is optimized and validated for use with the Twist methylation detection system for a complete end-to-end workflow with industry leading performance. High capture efficiency increases the sensitivity of detection across the footprint of the epigenome while decreasing sequencing costs. The panel is ideal for screening cohort samples and differentially methylated region discovery.

ADVANTAGES OF TARGETED METHYLATION

Design and Workflow Efficiency

The Twist Targeted Methylation System introduces a complete solution that produces highly complex and uniform sequencing reads for methylation analysis. The end-to-end protocol achieves this by combining an innovative, enzymatic conversion process, optimized target enrichment workflow, and highly developed panel design process.

Twist Bioscience partnered with New England Biolabs to offer NEBNext® EMseq (enzymatic methyl-sequencing) library prep as part of the Twist Targeted Methylation System. This innovative, enzymatic process accomplishes equivalent (or slightly better) methylation conversion versus bisulfite treatment without the degradation of chemical conversion, yielding a complex library for capture. The hybridization conditions, buffers, and enhancers are optimized and validated for peak performance. A simple workflow modification enables secondary panels (or spike-ins) to be added to the methylome, useful when investigating new applications or areas of epigenetic research.

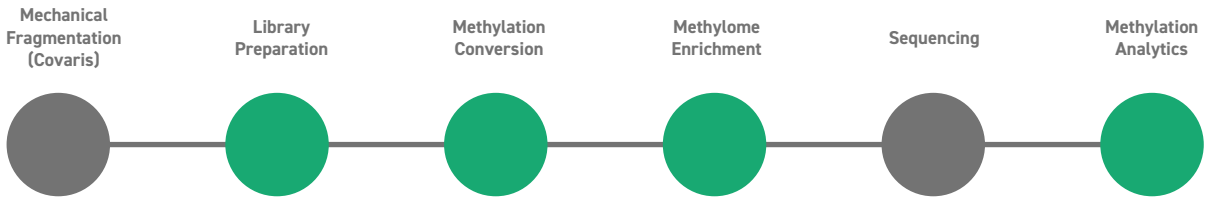

Figure 1: Twist Methylation Detection System workflow. Twist supplied reagents and utility displayed in green.

Broader Coverage versus Average Microarray

The Twist Human Methylome contains 3.98M CpG sites through the 123 Mb of genomic content target biologically relevant methylation markers (Figure 2). The panel is highly targeted to capture and detect the most current, annotated, and relevant CpG methylation regions in the genome. 84% (17,915,988) of the CpG islands in the genome are identified through enrichment with this panel. An additional 105,288,339 bases of subsequent shores, shelves, and open sea CpG's and base pairs are covered (Figure 3).

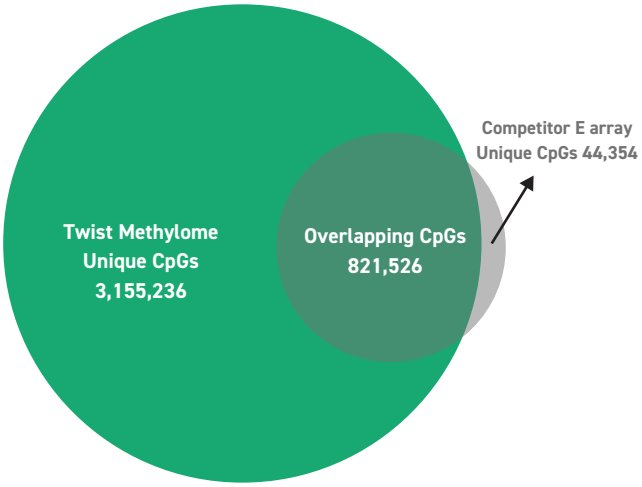

Figure 2: Venn diagram of the target space of CpG sites of the Twist Human Methylome vs Competitor E. 3.15M more unique CpG sites are included while giving a 94.9% overlap of content (source: internal data)

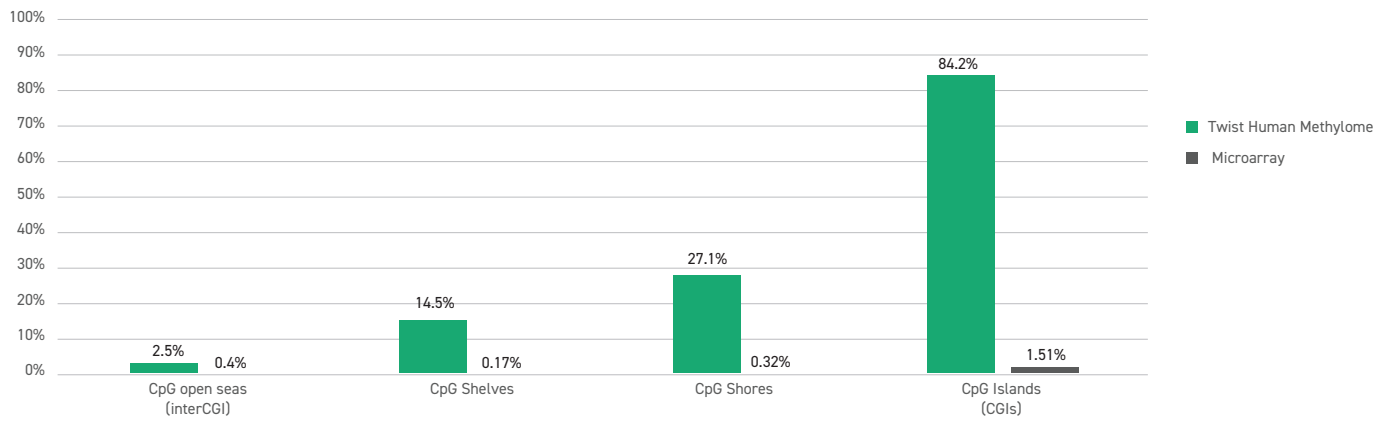

Figure 3: CpG site coverage relative to the whole genome of the Twist Human Methylome vs Competitor E. Hybrid-capture panels greatly expand the end users investigation territory through single base resolution across the entire sequencing read (source: internal data).

Advantage Over Average Microarrays

A microarray provides a convenient and low cost workflow. However, static content design can hinder discovery of new epigenetic targets of interest. Current arrays on the market also have limited coverage of the methylome across the epigenome leaving a large proportion of Methylated CpG sites left unmeasured. The Twist Human Methylome targeted enrichment approach addresses these limitations with hybrid-capture panels that enable expanded content and single base resolution across the entire sequence read provided by NGS platforms.

Microarrays have inherent limitations on extreme ends of methylation detection attributed to high background noise at the low end and signal saturation at the high end. Because of the higher dynamic range provided by NGS, the Twist Human Methylome Panel can provide a more accurate calling of differentially methylated regions (DMRs) especially at both the low and high ends of the methylation fraction (figure 4).

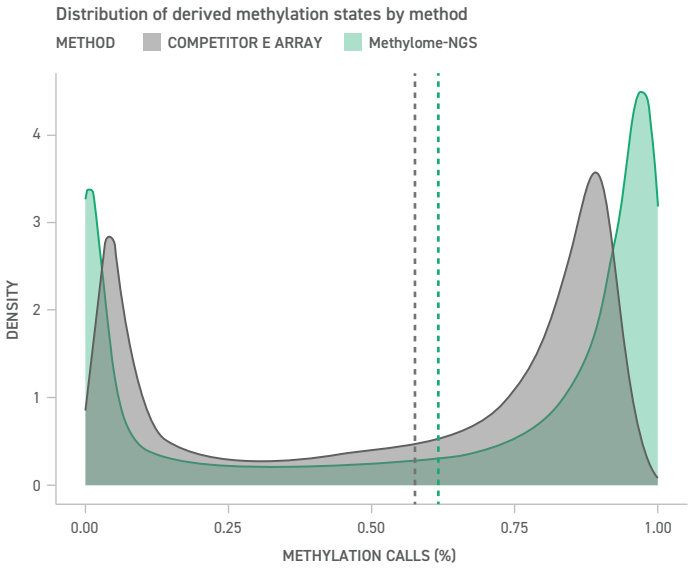

Figure 4: Distribution of derived methylation states by method. NGS data is more sensitive at the extreme ends of the methylation fraction creating a higher dynamic range of signal calling (source: internal data)

Performance

The Twist Human Methylome Panel is designed and wet lab optimized to provide accurate, sensitive and high performance hybrid-capture efficiency. Internal data generated and analyzed using Picard Metrics shows the Twist Human Methylome Panel achieves a depth of coverage of 90% of bases at 30x coverage with high probe specificities of 95% on-target rates. The panel also achieved a fold 80 of 1.54 providing high uniformity across the target region by decreasing the delta between the peaks and valleys of the base call pile ups. Library complexity was inversely represented by a <4% duplication rate at a high sequencing depth of 150x raw coverage. The overall panel capture efficiency metrics obtained here provides a high level of confidence in detection across the methylation fraction with minimized sequencing cost.

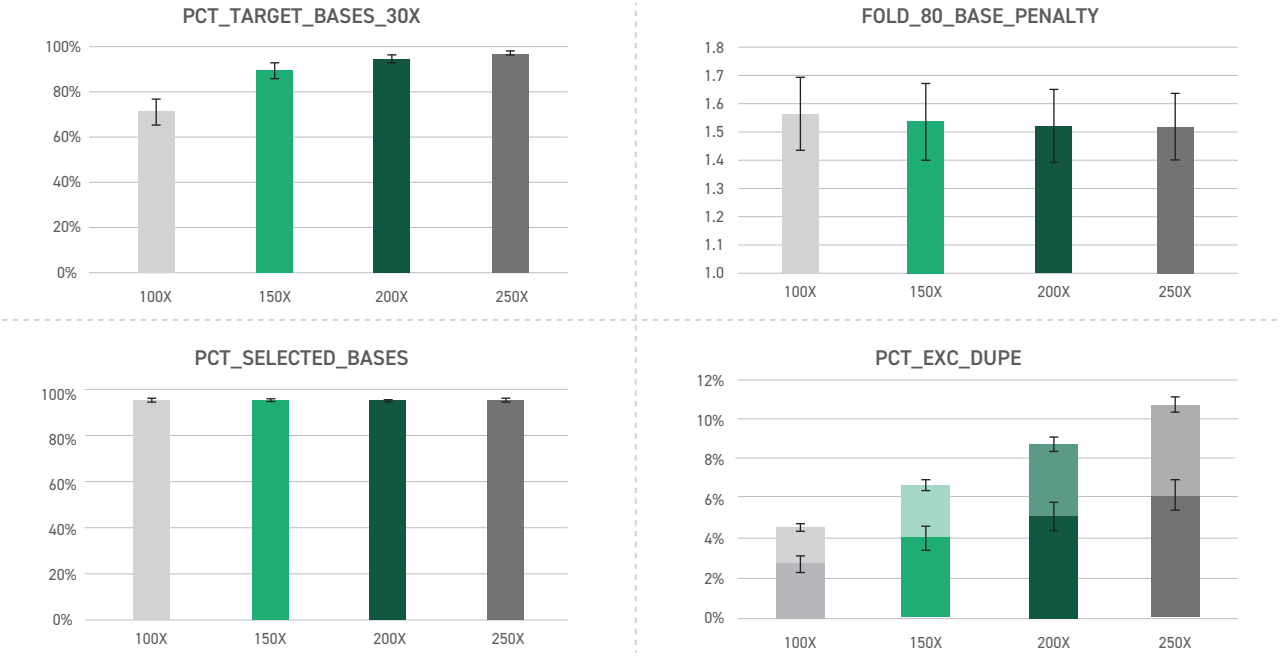

Figure 5: Key Picard performance metrics for hybridization capture efficiency. Sequencing data was downsampled to 100x–250x RAW coverage on a NovaSeq instrument. Raw coverage from 100–250x. At 150x raw coverage; Upper Left: Percent of the target bases covered at 30x - depth of coverage at 30x is 90%; Bottom Left: Percent Selected Bases - Specificity is 95% on-target; Upper Right: Uniformity is 1.54 Fold 80; Bottom Right: Duplication rate is 3.9% with optical duplicates removed.

LEARN MORE

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PRODUCT SKUS

105517: Twist Human Methylome Panel, 2 Reactions

105520: Twist Human Methylome Panel, 12 Reactions

105521: Twist Human Methylome Panel, 96 Reactions

Twist Custom Panels can be ordered separately. Please contact your sales representative for more information.