WATCHMAKER DNA LIBRARY PREP KIT WITH TAPS+

WATCHMAKER GENOMICS

THE POWER OF POSITIVE

Direct 5mC sequencing for multimodal insights

TAPS+ is a positive-readout methylation sequencing chemistry that converts methylated C's (5mC's) to T's while preserving unmethylated C's. Unlike traditional methyl-seq approaches, it maintains full base complexity (ATCG) without damaging DNA, enabling high-quality performance with low-input and degraded samples. This unified approach delivers 5mC, SNV/indel, and CNV detection from a single library for multimodal analysis across discovery, translational, and population studies to support field innovations in applications such as early disease detection and monitoring.

HIGHLIGHTS

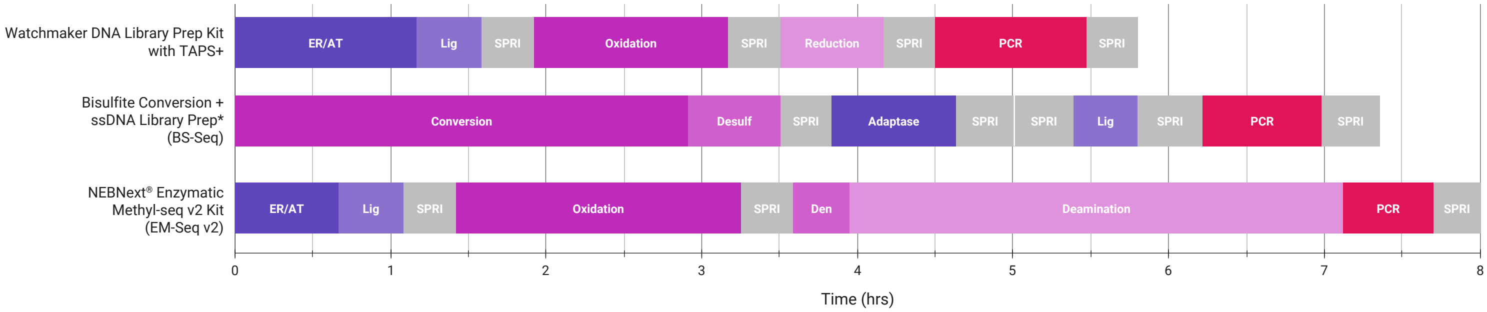
- **Direct 5mC readout** enables simultaneous detection of genetic variants (SNV/Indels and CNVs) and epigenetic modifications from the same library
- **Greater than 98% 5mC conversion** — including both hypo- and hyper-methylated regions — delivers high true positive and low false positive rates
- Non-damaging workflow delivers robust performance with **degraded FFPE and low-input samples (down to 1 ng), including cfDNA**
- Streamlined, **automation-friendly** workflow generates libraries in 6 hours — no columns required
- Higher sequence diversity **boosts mappability**, reduces multi-mapping/low-complexity dropouts, and **lifts CpG coverage** at a given read depth
- **Reduces computational analysis time by 30% or more**, saving hours and associated costs on a 30X genome

APPLICATIONS

- Whole-genome or targeted methyl sequencing
- Simultaneous detection of methylation and genomic variants
- Differential methylation analysis
- Allele-specific methylation analysis
- Tumor profiling, including FFPE
- Liquid biopsy (cfDNA/ctDNA) studies
- Fragmentomics
- Epigenotyping
- Epigenome-wide association studies (EWAS)
- Biomarker discovery

SINGLE-DAY, AUTOMATION-FRIENDLY LIBRARY PREP

A streamlined workflow with shortened reaction times and minimal bead cleanups generates sequencing-ready libraries in under six hours. Generous reagent overages and minimum transfer volumes enable high-throughput processing on liquid handling platforms.



*Bisulfite Conversion = EZ DNA Methylation-Gold Kit (Zymo Research) and ssDNA Library Prep = xGen Methyl-Seq Library Prep Kits (IDT)

FIGURE 1. Reduce turnaround time with an automatable workflow. The Watchmaker DNA Library Prep Kit with TAPS+ delivers libraries in under 6 hours with a workflow that smoothly translates to automated liquid handlers for high-throughput processing. The method does not require speciality consumables (like conversion columns often used in bisulfite workflows).

POSITIVE METHYLATION READOUT PRESERVES SEQUENCE COMPLEXITY

TAPS+ provides a positive methylation readout that maintains native sequence diversity, overcoming the loss of complexity inherent to traditional methyl-seq methods. By preserving the genome's four-base composition and distinguishing 5mC as a fifth base, TAPS+ improves alignment quality, reduces computation time, and enables genomic variant detection.

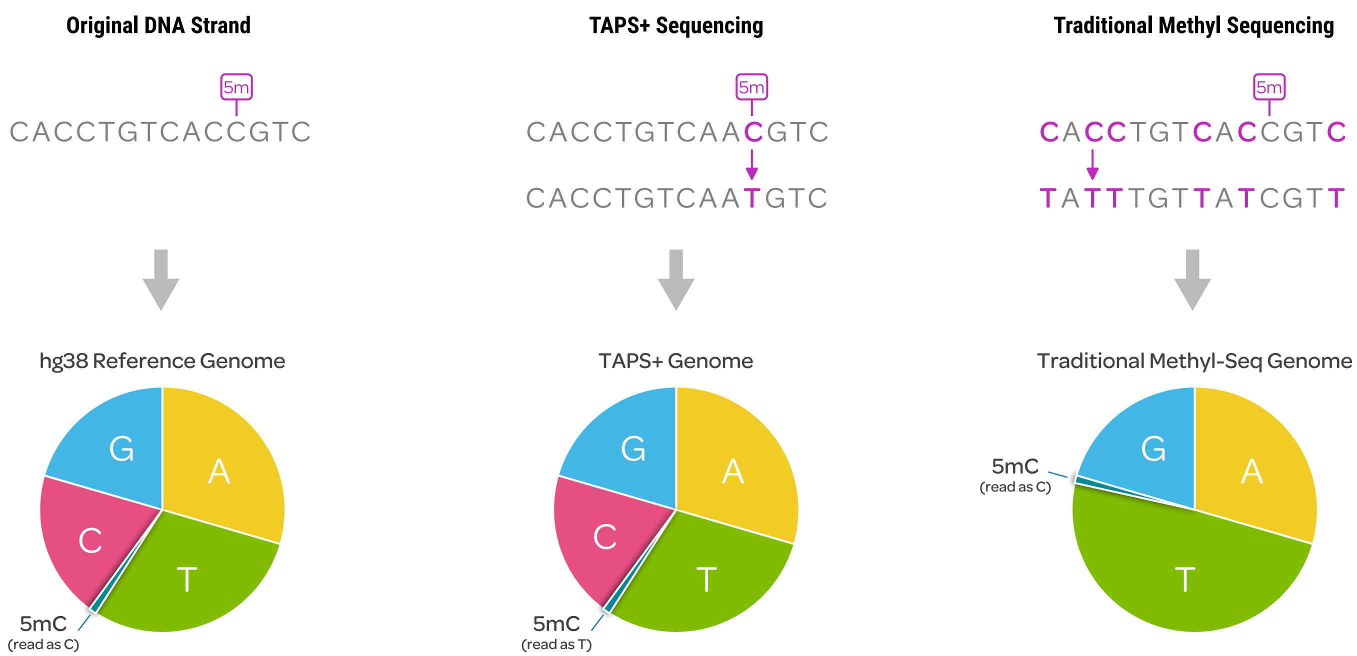


FIGURE 2. Sequence a five-base genome. Only ~1 – 2% of bases in the human genome are cytosines in CpG context, which is where most methylation occurs. TAPS+ converts just those methylated CpG cytosines, leaving the remaining ~20% of cytosines unchanged. The result is a library that preserves native four-base complexity, more closely matches the human genome, and also delivers 5mC detection (the fifth base).

UNLOCK MULTIMODAL INSIGHTS FROM A SINGLE LIBRARY

TAPS+ combines high-efficiency 5mC conversion with minimal false positives to deliver accurate methylation profiling. By preserving base complexity, it also enables sensitive and precise genomic variant detection as demonstrated by SNV F1 scores and CNV profiles closely matching those of whole-genome sequencing controls.

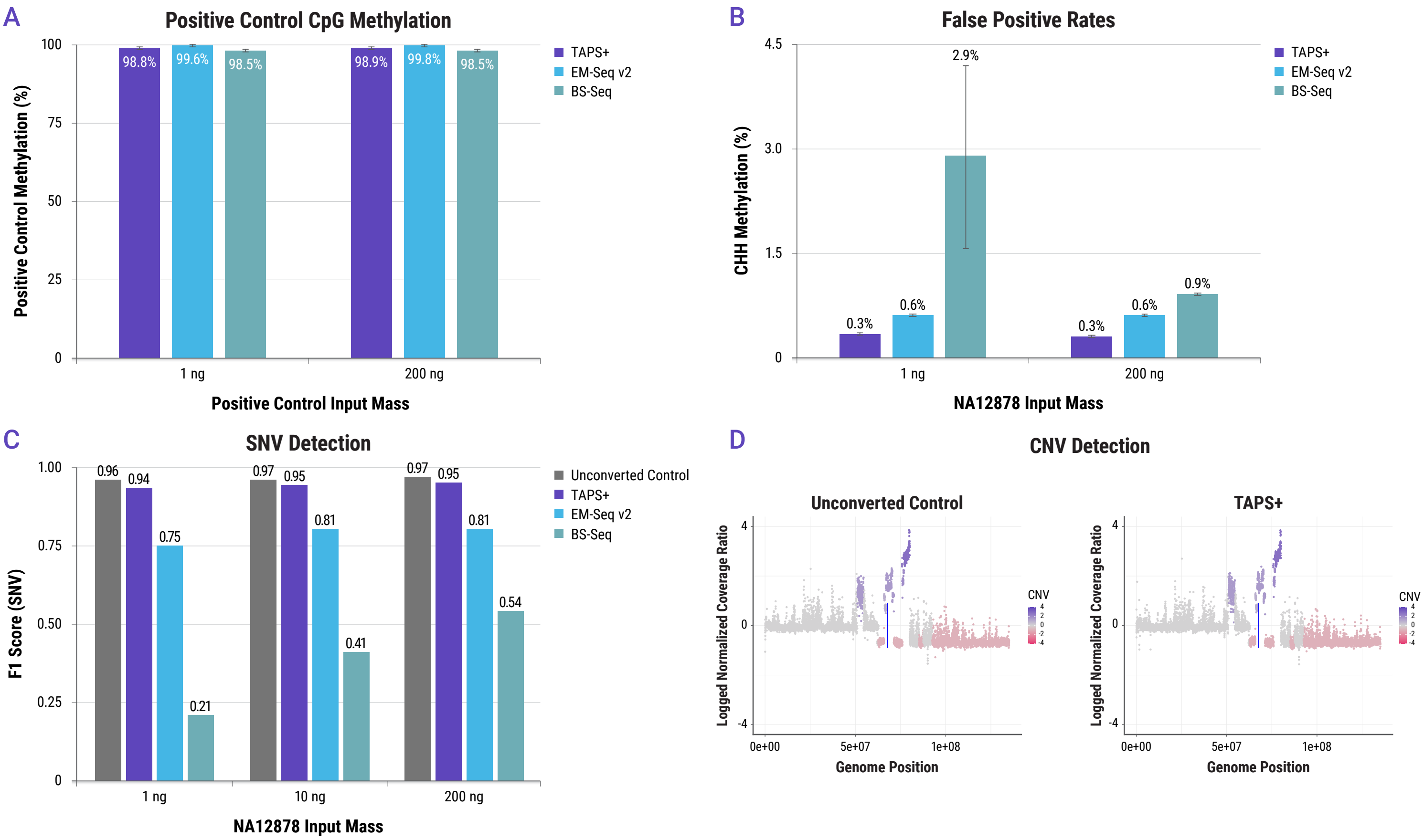


FIGURE 3. Simultaneous methylation profiling and genomic variant detection. Libraries were prepared in duplicate using the workflows outlined in Figure 1, along with an unconverted control (Watchmaker DNA Library Prep Kit). **(A)** Positive control CpG methylation rates, measured using fully methylated Lambda DNA. **(B)** False positive rates as assessed by measured CHH methylation in NA12878. **(C)** F1 scores for SNV detection. Libraries were subsampled to equivalent reads. TAPS+ Variant Caller was used for unconverted control and TAPS+ libraries, and BS-SNPer was used for EM-Seq v2 and BS-Seq libraries. **(D)** CNV analysis on TAPS+ and unconverted control libraries prepared from 35 ng breast tumor total nucleic acid.

SENSITIVE METHYLATION AND FRAGMENTOMICS ANALYSIS FROM cfDNA

Methylation signatures in liquid biopsy assays enable sensitive cancer detection, classification, and residual disease monitoring.[1,2] TAPS+ preserves cfDNA fragments, delivering high-resolution methylation and fragmentomic profiles with high CpG coverage.

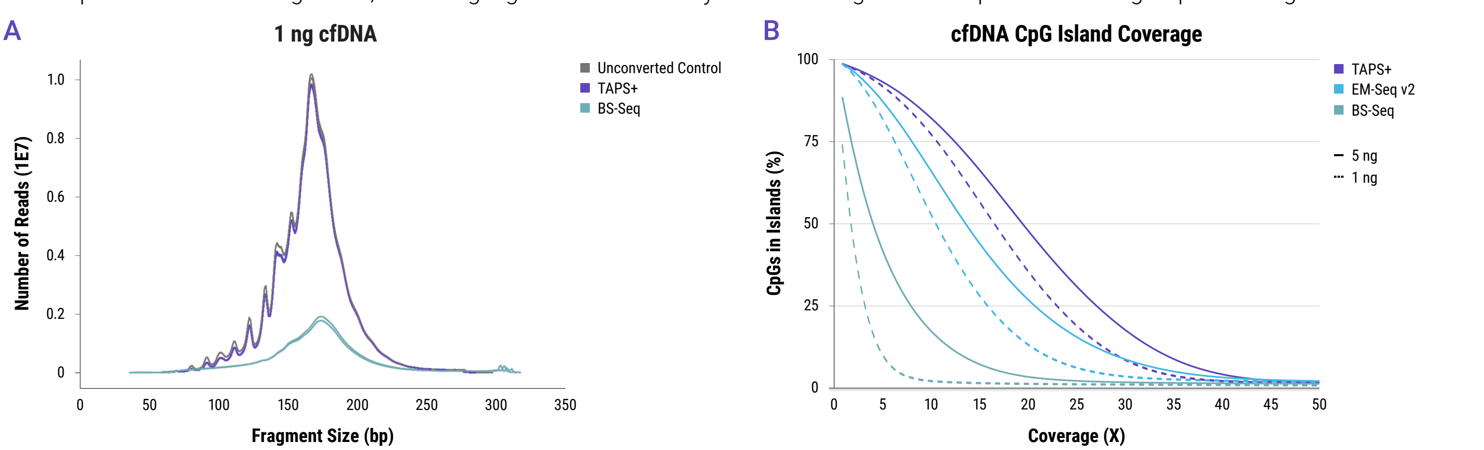


FIGURE 4. Non-damaging workflow preserves cfDNA fragments and delivers high CpG coverage. Libraries were prepared in duplicate using the workflows outlined in Figure 1, along with an unconverted control (Watchmaker DNA Library Prep Kit). **(A)** Read distribution by insert length, and **(B)** cumulative coverage of CpGs in CpG islands.

IMPROVE DATA QUALITY AND COVERAGE FROM FFPE SAMPLES

TAPS+ preserves DNA integrity from challenging FFPE specimens, enabling simultaneous methylation and variant analysis from a single library. The gentle chemistry improves CpG coverage and reduces false positives and sequence artifacts — enhancing accuracy for tumor-informed and archival studies and expanding the utility of degraded clinically relevant samples.

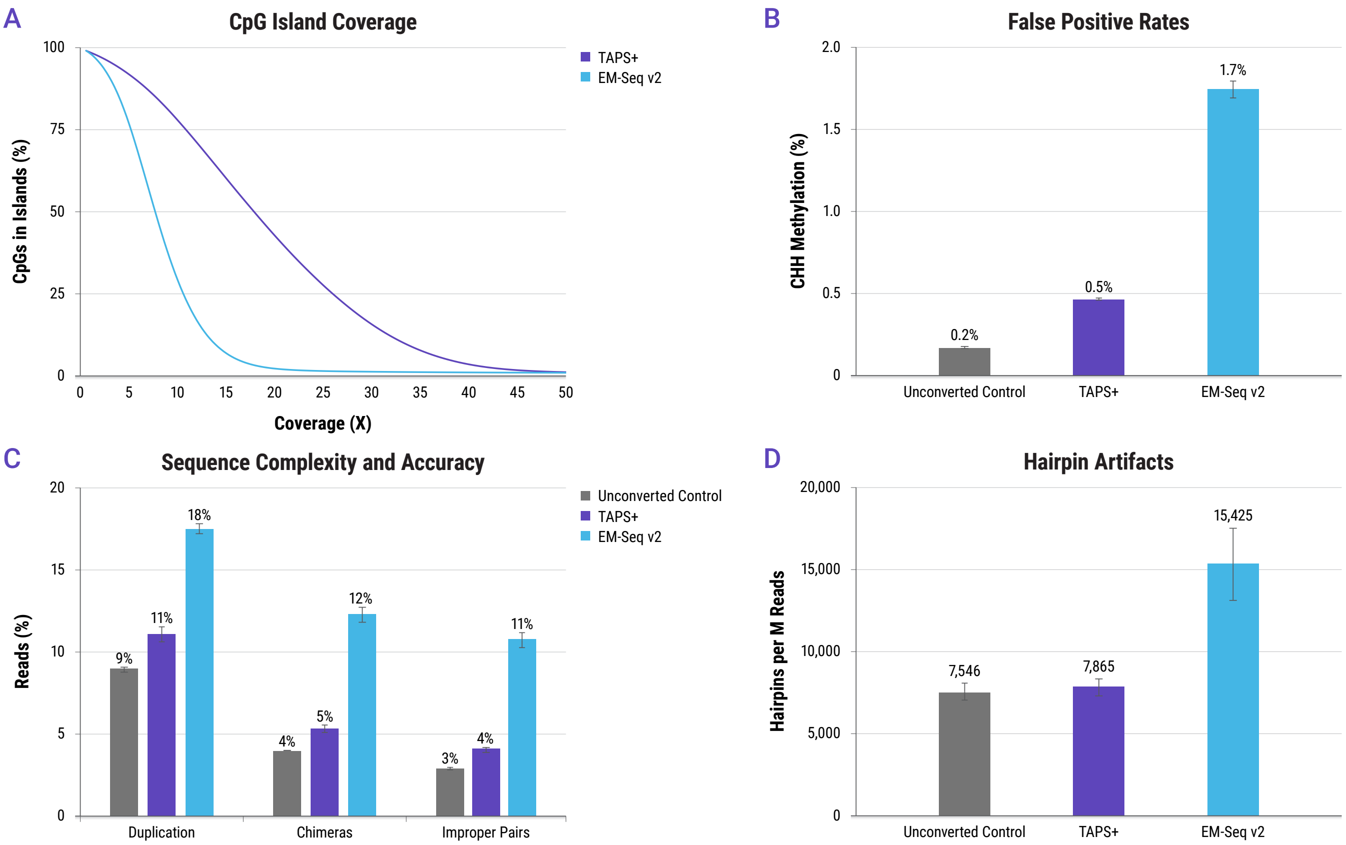


FIGURE 5. Increase confidence in methylation and genomic variant calls with FFPE. Libraries were prepared in duplicate from 10 ng of FFPE-derived DNA. **(A)** Cumulative coverage of CpGs in CpG islands. **(B)** False positive rates as assessed by measured CHH methylation. **(C)** Percent duplication, chimeric reads, and improper pairs as measured by Picard. **(D)** Hairpin sequence artifacts per million reads.

1. Vavoulis, D.V., Cutts, A., Thota, N. et al. Multimodal cell-free DNA whole-genome TAPS is sensitive and reveals specific cancer signals. *Nat Commun* 16, 430 (2025)
2. Paulina Siejka-Zielińska et al. Cell-free DNA TAPS provides multimodal information for early cancer detection. *Sci. Adv.* 7,eabh0534(2021).

PRODUCT	24 RXN	96 RXN
Watchmaker DNA Library Prep Kit with TAPS+ *Includes reagents for DNA library prep, TAPS+ conversion, and amplification*	7BK0003-024	7BK0003-096

Contact sales@watchmakergenomics.com or visit watchmakergenomics.com/taps to learn more.