Application brief

SUPERIOR SENSITIVITY FOR ctDNA DETECTION ON THE ONSO SYSTEM

Unlock the accuracy needed for liquid biopsy with the Onso™ system

Liquid biopsy, a noninvasive assay for circulating tumor DNA (ctDNA) in blood, holds the promise to revolutionize research on cancer detection and monitoring. Current sequencing by synthesis (SBS) approaches to liquid biopsy are constrained by their accuracy, which affects the limit of detection of rare variants. However, the introduction of the Onso system, powered by the extraordinary accuracy of sequencing by binding (SBB™) chemistry, now enables the sensitivity necessary to detect low-frequency variants in liquid biopsy applications.

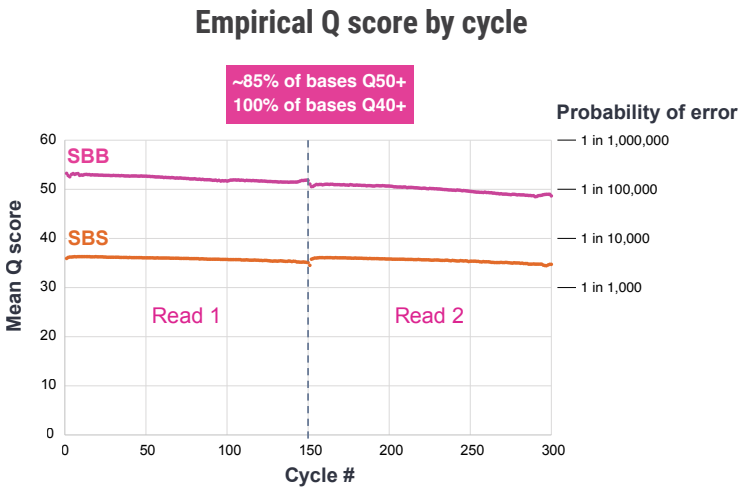

Figure 1. SBB consistently achieves Q40+ quality scores, and the quality reaches Q50+ for much of the read, compared to the lower Q scores of SBS.

Distinguish the variant from the noise

Since higher Q scores mean a higher signal-to-noise ratio, the Q40+ accuracy of the Onso system enables confident variant detection with fewer confounding errors.

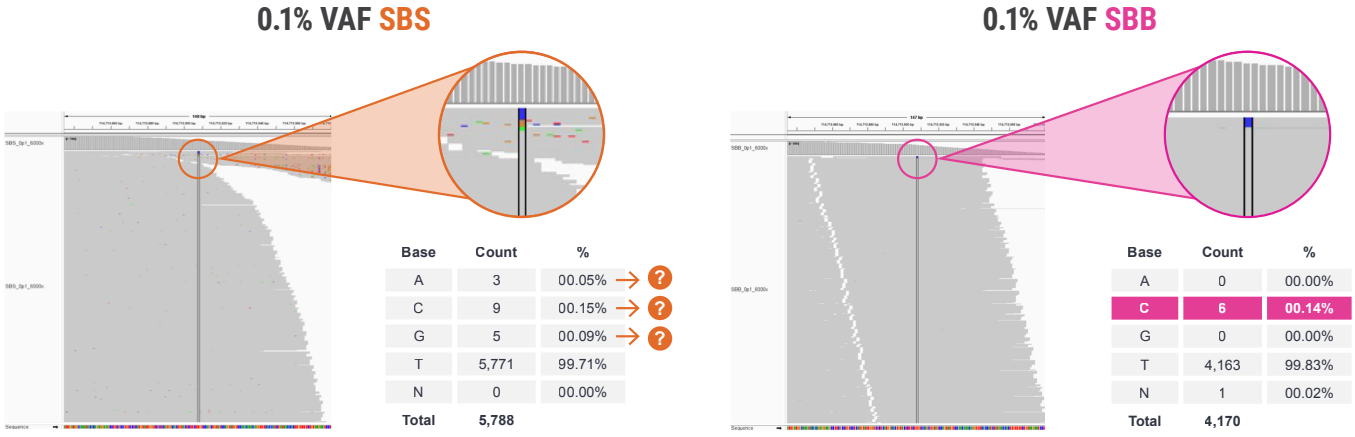

Figure 2. IGV output of SBS and SBB sequencing of example *NRAS* Q61R variant from the SeraCare ctDNA complete mutation mix at 6,000x coverage.

Sequencing errors in SBS sequencing make it almost impossible to distinguish the variant from the noise (left), whereas sequencing on the Onso system makes the true variant clear (right). Explore the dataset yourself.[1]

PacBio

Why SBB sequencing?

Increased sensitivity for rare variant detection with the same sequencing depth

OR

Four-fold reduction in sequencing required to achieve equivalent or better performance

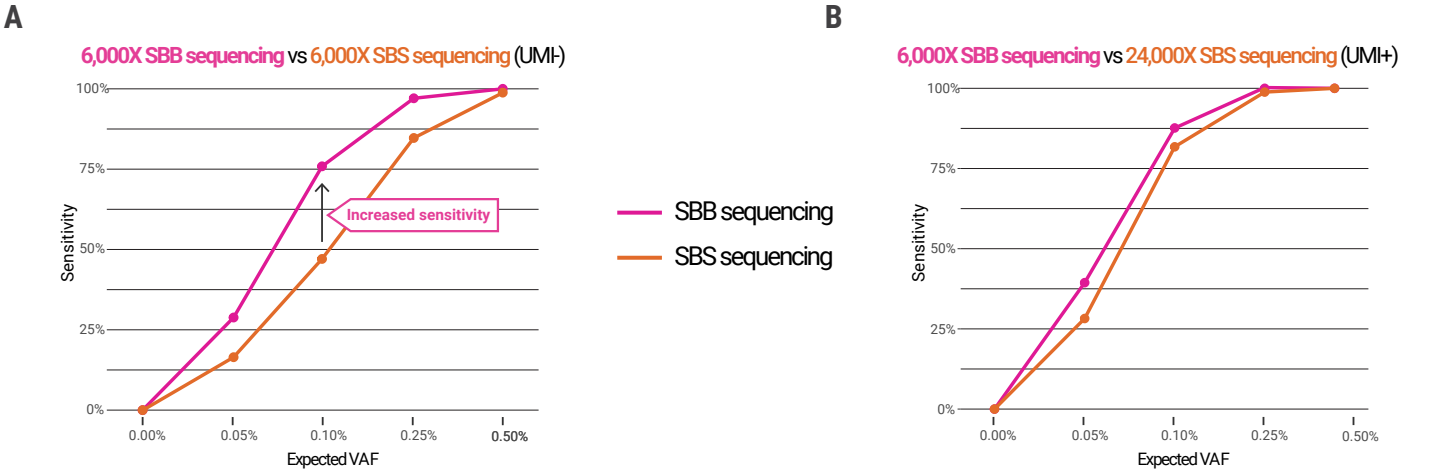

Figure 3. Variant detection performance was tested for SBB and SBS sequencing using the SeraCare complete ctDNA mutation mix with 17 known variants in 10 genes across five variant allele frequencies (VAF): 0% (WT), 0.05%, 0.1%, 0.25%, and 0.5%. (A) 6,000X SBB UMI- vs 6,000X SBS UMI-, (B) 6,000X SBB UMI+ vs 24,000X SBS UMI+.

In a comparison using the SeraCare ctDNA reference standard, the Onso system vastly outperforms traditional SBS sequencing with nearly **twice the sensitivity for rare variant detection** at equivalent sequencing depth (figure 3A). SBB sequencing also achieves equivalent or **better sensitivity with 4-fold less sequencing** (figure 3B). Adding UMI-based deduplication increases the Onso system's performance even further (SBB sequencing in figure 3A vs 3B).

Library prep/conversion

- Onso native library prep **OR**
- Conversion kit to make existing P5/P7 libraries Onso-compatible

Sequencing on the Onso system

- ≥90% of reads at Q40+
- Low duplication rate
- Minimal index hopping
- Improved performance in homopolymer and other repetitive regions

Analysis

- On-board demultiplexing of indexed libraries
- Industry-standard FASTQ output
- Compatible with existing short-read analysis pipelines

Learn more about the Onso sequencing platform: **pacb.com/onso**

ADDITIONAL RESOURCES

1. pacb.com/seracare-dataset
2. pacb.com/wp-content/uploads/Onso-specification-sheet.pdf
3. pacb.com/wp-content/uploads/SBB-Product-note.pdf

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