

How Fulcrum Genomics Independently Validated a Dual Direct Ligation Library Prep for Improved Early-Cycle Accuracy

Fulcrum Genomics collaborated with Canal Biosciences to independently evaluate an end-repair-free library preparation chemistry that attaches adaptors via dual direct ligation to improve early-cycle sequencing accuracy ahead of the company's TrueLink™ product launch. By avoiding conventional end-repair/A-tailing (ER/AT), Canal's approach supports adaptor attachment to both single-stranded DNA and dsDNA fragments with native non-end-repaired termini.

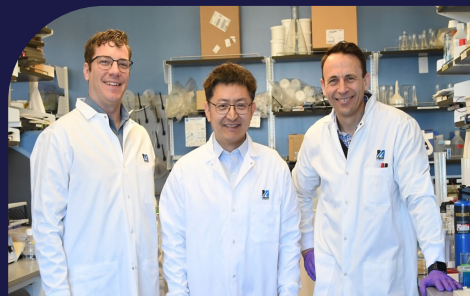
The Challenge

Short-read sequencing workflows can show elevated error rates at the starts of reads, where localized artifacts can reduce confidence in variant calls and lead teams to down-weight or trim early-cycle bases, especially in low-input settings. Canal Biosciences sought independent validation that dual direct ligation adaptor attachment, without ER/AT, could mitigate these errors while maintaining broad DNA compatibility.

The Results

- Confirmed ~4-fold reduction in early-cycle sequencing error within the first ~10-15 bases relative to standard ER/AT-based library prep
- Increased effective use of early-cycle bases that are frequently down-weighted or excluded in downstream analyses
- Equivalent or improved standard QC metrics, including chimera rate, mappability, and coverage uniformity
- Validated adapter attachment and recovery for both dsDNA and ssDNA templates, extending applicability to low-input and challenging samples
- Independent confirmation of data robustness

These results afforded the Canal team the evidence needed to communicate the performance benefits of TrueLink™ with confidence ahead of public presentation and commercialization efforts.



"From day one, Fulcrum Genomics operated like an extension of our team — iterating quickly with us as our protocols evolved and translating cycle-resolved error signatures into clear, actionable insights. Their independent evaluation strengthened our confidence in TrueLink™ performance and sharpened how we communicate the data to the sequencing community as we move toward launch."

Yu Zheng, Ph.D. Founder/co-CEO, Canal Biosciences Inc.

Fulcrum's Approach



Specialized Bioinformatics Team

Fulcrum staffed the engagement with expert level bioinformatics scientists Zach Norgaard and Yossi Farjoun, combining expertise in sequencing error modeling, statistical analysis, and pipeline development. They built a flexible, tested analysis framework that supported rapidly evolving laboratory protocols, enabled multiple processing strategies, and produced customized quality metrics and visualizations highlighting Canal's technical differentiators.



Use of well-characterized reference material

Sequencing data was generated from established reference genomes with known variant truth sets, enabling clear separation of true biological variation from library preparation and sequencing artifacts.



Fine-grained error profiling

Rather than reporting a single average error rate, Fulcrum decomposed error across multiple dimensions, including: sequencing cycle, strand, and reference base context.



Validation of single-stranded DNA compatibility

To assess Canal's ability to capture single-stranded DNA, Fulcrum supported targeted experiments using defined spike-in ssDNA material. Analysis confirmed that single-stranded fragments were successfully incorporated and detected without requiring major pipeline modifications.

Why Fulcrum Genomics

Canal engaged Fulcrum Genomics to help design and execute an analysis strategy that went beyond high-level quality metrics. Rather than focusing on aggregate error rates, which often mask localized failures, Fulcrum brought deep experience in dissecting sequencing errors at a fine-grained level.

This combination allowed Canal to evaluate its TrueLink™ rigorously without relying on ad hoc or unproven analysis methods. Fulcrum is committed to support Canal as the TrueLink™ platform expands to address additional limitations posed by current library prep methods.

Next Steps

If you saw something that made you think “we need that level of analysis”, we'd love to explore how the Fulcrum team can help.



Bioinformatics expertise trusted by scientists who demand accuracy, reproducibility, and speed.