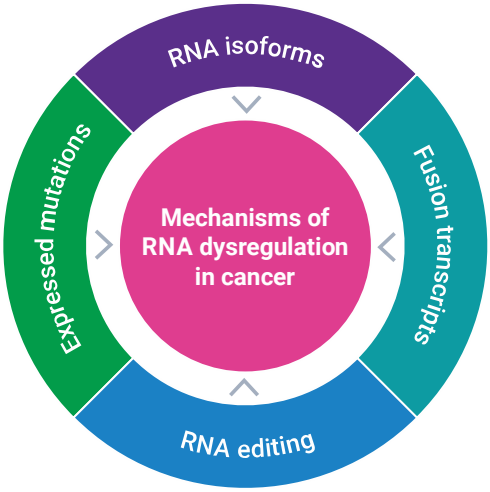
A MORE COMPLETE CANCER TRANSCRIPTOME WITH THE ISO-SEQ METHOD – **SINGLE-CELL AND BULK RNA SEQUENCING**

Highly accurate long-read RNA sequencing reveals novel mechanisms of RNA dysregulation in cancer

The potential for RNA alterations to serve as key signatures for tumor progression and targets for cancer therapy have recently emerged, underlining the importance of accurate and comprehensive RNA sequencing technology. The PacBio® Iso-Seq® method spans the length of full transcripts, enabling you to generate a more complete cancer transcriptome.

The option to sequence in **bulk** (using the Iso-Seq method) and **single-cell** (using the MAS-Seq method) empowers you to discover novel insights into the mechanisms of RNA dysregulation in cancer at any resolution.



Adapted from Pan, Y., et al. (2021)[1]

The Iso-Seq method offers robust detection of isoforms, fusions, and expressed mutations

RNA variant type	Use cases	Iso-Seq advantage	Other short reads	Other long reads	PacBio long reads
RNA isoforms	Discover RNA isoforms as source of cancer biomarkers and drug targets	**Read length:** >2.5X isoform discovery power compared to short reads.[2] **Accuracy:** Superior accuracy offers more robust isoform discovery power than other long-read technologies.[3]	○	◑	●
RNA fusions	Identify known, novel, and complex RNA fusions	**Read length:** More robust fusion discovery power than short-read approaches.[4,5] **Accuracy:** Highly accurate sequencing allows for robust detection of fusion isoforms.[5]	◑	◑	●
Expressed mutations	Detect expressed mutations in RNA for genotyping and neoantigen discovery	**Read length:** Long reads provide phasing information of expressed mutations.[6] **Accuracy:** Highly accurate mutation detection compared to other long-read technologies.[6,7]	◑	○	●

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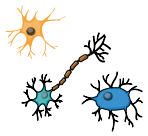
The Iso-Seq method offers an end-to-end approach for cancer transcriptomics

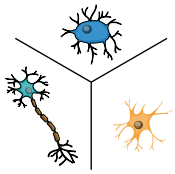


Bulk

Library prep
Iso-Seq protocol

SMRT® sequencing
PacBio long-read systems

Data analysis
SMRT® Link



Single cell

Single-cell cDNA generation
10x Chromium Single Cell Gene Expression technology

MAS-Seq library preparation
MAS-Seq for 10x Single Cell 3' kit

SMRT sequencing
PacBio long-read systems

Data analysis
SMRT Link

The Iso-Seq advantage

Biological insight

Long-read RNA sequencing enables detection of the true biology of the cancer transcriptome, including improved isoform and fusion detection.

Exceptional versatility

With the Iso-Seq method, you can sequence at the single-cell level, or entire transcriptomes, achieving remarkable insight at any resolution.

Accuracy matters

PacBio provides the most accurate long-read RNA sequencing platform for reliable sequencing of full-length transcripts at the RNA level.

A single solution

The Iso-Seq method provides a complete view of molecular heterogeneity in cancer cells at the RNA level. No other single technology can offer detection of RNA isoforms, fusions, and expressed mutations.

KEY REFERENCES

1. Pan, Y., et al. (2021) **RNA dysregulation: an expanding source of cancer immunotherapy targets.** *Trends in Pharmacological Sciences*, 42(4), 268-282. PMID: 33711255
2. Viega, D.F.T., et al. (2022) **A comprehensive long-read isoform analysis platform and sequencing resource for breast cancer.** *Science Advances*, 8(3), eabg6711. PMID: 35044822
3. Mikheenko, A., et al. (2022) **Sequencing of individual barcoded cDNAs using Pacific Biosciences and Oxford Nanopore Technologies reveals platform-specific error patterns.** *Genome Research*, 32(4), 726-737. PMID: 35301264
4. Nattestad, M., et al. (2018) **Complex rearrangements and oncogene amplifications revealed by long-read DNA and RNA sequencing of a breast cancer cell line.** *Genome Research*, 28(8), 1126-1135. PMID: 29954844
5. Miller, A. et al. (2022) **Pacific Biosciences Fusion and Long Isoform Pipeline for Cancer Transcriptome-Based Resolution of Isoform Complexity.** *The Journal of Molecular Diagnostics*, 2022 Dec;24(12):1292-1306. PMID: 36191838
6. Cavelier, L. et al. (2015) **Clonal distribution of BCR-ABL1 mutations and splice isoforms by single-molecule long-read RNA sequencing.** *BMC Cancer*, 15:45. PMID: 25880391
7. Olson, N. et al. (2022) **PrecisionFDA Truth Challenge V2: Calling variants from short and long reads in difficult-to-map regions.** *Cell Genomics*, 2, 100129. PMID: 35720974

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