Application brief

TRANSFORM YOUR NEUROSCIENCE RESEARCH WITH HIFI SEQUENCING

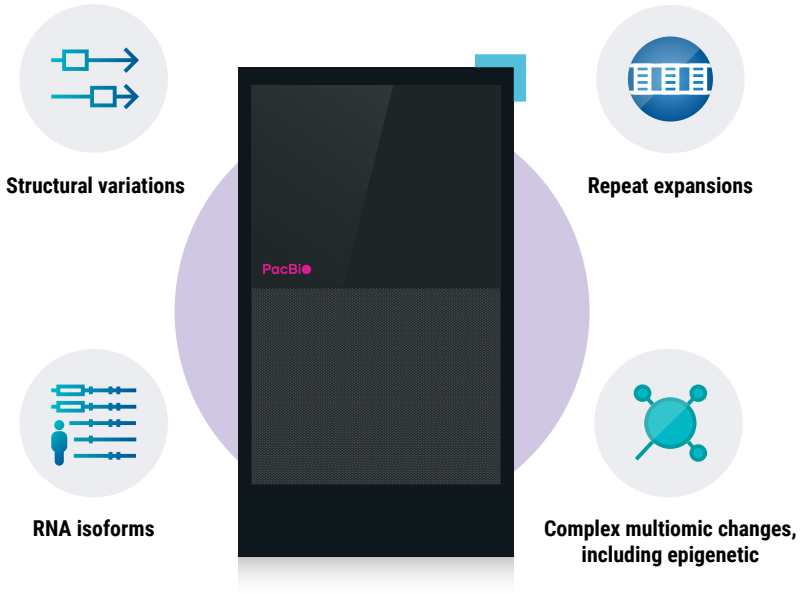
Unravel the complexity of your neuroscience research by unlocking more comprehensive and accurate data

Resolving the genomic complexity of the human nervous system presents significant challenges, requiring highly robust sequencing methods. From research into genetic variants associated with neurological disease to the characterization of neuronal cell types, PacBio® HiFi sequencing enables visibility into genetic information that would otherwise be missed.

Short-read sequencing can often have blind spots for important information like structural variants (SVs), repeat expansions, and RNA isoforms. This knowledge cannot be overlooked when investigating the determinants of health and disease.

HiFi sequencing overcomes these limitations to help you take your research to the next level.

Eliminate blind spots to access:



The benefits of HiFi sequencing

Long reads

Long read lengths of up to 25 kb to span complete genes or regions of interest

High accuracy

High accuracy of 99.9% (Q30) to provide Sanger-quality, base-level resolution

More comprehensively assess variants

Detect base-level modifications to structural rearrangements

Uniform coverage

Detect variants in repetitive and extreme GC-regions in an unbiased manner

PacBio

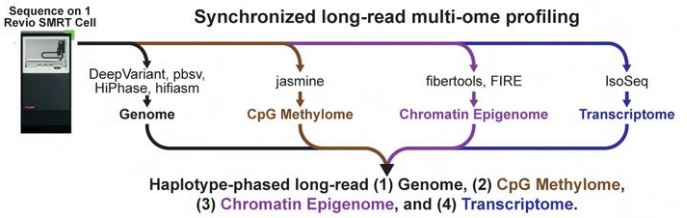
Identify disease-associated variants

Many neurological diseases have an underlying genetic component like structural variation such as repeat expansions, which pose serious limitations for short-read sequencing. A recent study reported that in a sample of >1000 patients, 13% of newly resolved disease cases without clear diagnosis were achieved by incorporating SVs in the analysis.[1]

	PacBio HiFi	SBS sequencing	Nanopore sequencing
Read length	15–20 kb	2×150 bp	10–100 kb
Read accuracy	99.95% (Q33)	99.92% (Q31)	99.26% (Q21)
Variant calling—SNVs	✓	✓	✓
Variant calling—indels	✓	✓	✗
Variant calling—SVs	✓	✗	✓
Phasing	✓	✗	✓

Synchronize multiomic data from one platform

Given the brain's cell type diversity and variability throughout development and disease states, it can be challenging to fully understand changes in the brain with only one data type. HiFi sequencing on the Revio™ system allows you to obtain DNA sequence, RNA isoform expression, 5mC methylation, and chromatin accessibility information in a single run. This approach has been successful in identifying gene disruption in a disease sample that could have otherwise gone unresolved.[2]



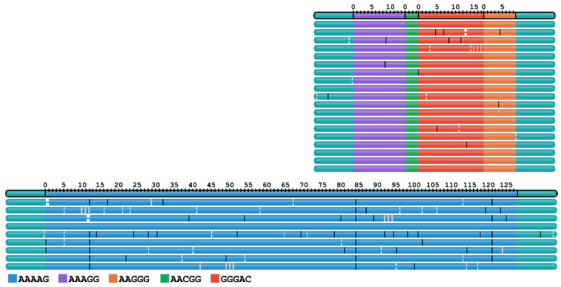
Approach to obtain synchronized multiomic data from a single Revio run

Amplification-free sequencing for difficult-to-diagnose neurological repeat expansion diseases

Over 40 inherited neurological diseases are caused by repeat expansions. The onset and severity of disease can be associated with the length of the repeat, making it an important criterion for diagnosis and prognosis. Other sequencing methods and PCR rely on amplification and are therefore imprecise when used to:

- Correctly size expanded alleles
- Characterize repeats at single-base resolution

The PacBio PureTarget™ repeat expansion panel enables an amplification-free targeted sequencing approach to investigate these repeat expansions accurately.



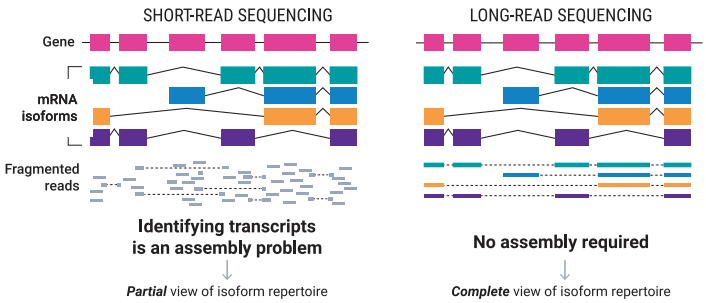
Expanded *RFC1* repeat at single base resolution[3]

Differentiate and characterize neural cell types at the RNA isoform level

The human brain has over 3300 different cell types, which are characterized by differential gene expression and splicing, leading to cell-type specific isoform expression. Isoform expression is an important consideration for brain health because it can change with aging and disease states.[3]

PacBio RNA isoform sequencing with Kinnex™ kits enables a multitude of applications:

- Discover novel transcripts and variants
- Identify alternatively expressed genes and transcripts
- Identify alternative splicing patterns
- Characterize cellular heterogeneity



Learn more about HiFi sequencing for Neuroscience research: pacb.com/research-focus/human/neuroscience/

KEY REFERENCES

1. Cohen ASA, Farrow EG, Abdelmoity AT, et al (2022) Genomic answers for children: Dynamic analyses of >1000 pediatric rare disease genomes. *Genet Med* 24:1336–1348. https://doi.org/10.1016/j.gim.2022.02.007
2. Vollger MR, Korlach J, Eldred KC, Swanson E, Underwood JG, Cheng Y-HH, et al. Synchronized long-read genome, methylome, epigenome, and transcriptome for resolving a Mendelian condition. *bioRxiv*. 2023;2023.09.26.559521.
3. Dolzhenko E, English A, Dashnow H, Brandine GDS, Mokveld T, Rowell WJ, et al. Resolving the unsolved: Comprehensive assessment of tandem repeats at scale. *bioRxiv*. 2023;2023.05.12.540470.

102-326-623 REV01 06SEP2024