COMPREHENSIVE CHARACTERIZATION OF REPEAT EXPANSIONS WITH PURETARGET

PureTarget™

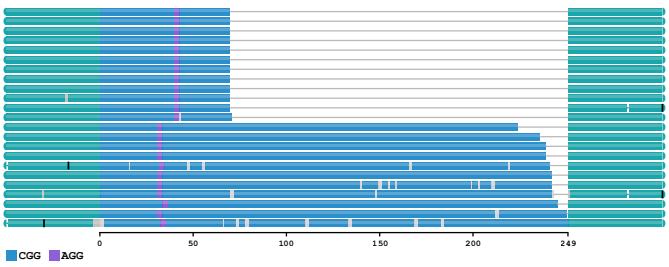
Shine a light on dark regions of the genome

Expansions of repetitive DNA sequences have been linked to over 50 monogenic disorders and cancers where the repeat length, sequence context and methylation can be factors in disease severity and/or age of onset. Once notoriously difficult to characterize, these regions can now be comprehensively genotyped at scale with the PacBio® PureTarget™ repeat expansion panel. Offering a gene panel for 20 of the most important repeat expansions for human health, PureTarget now grants a clear view of these once-dark regions of the genome.

What can PureTarget do?

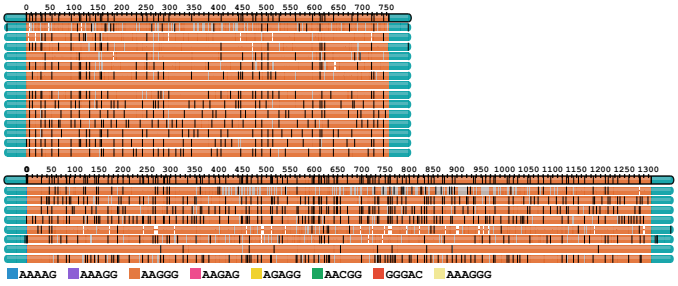
Powered by the *Tandem Repeat Genotyping Tool* (TRGT)[1] and deep coverage of long and accurate HiFi reads, the PureTarget panel provides [A] single-base resolution of repeats, [B] precise sizing of long repeats, [C] methylation profiles, and [D] deep coverage to characterize mosaicism.

Resolve repeat sequence



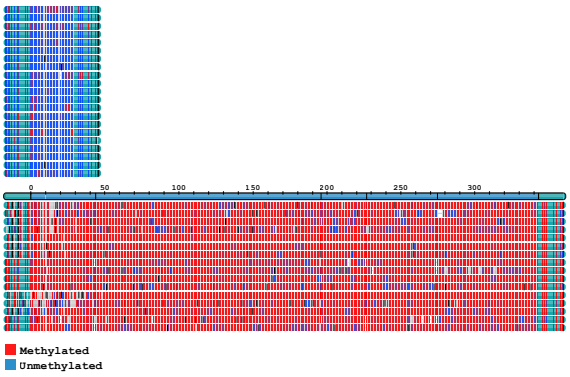
A. Single-base resolution of *FMR1* repeat sequence detects AGG interruptions in female carrier (NA06905). Consensus alleles are 23 and 79 repeats long, respectively.[2] Axis unit is base pairs.

Size long repeat expansions



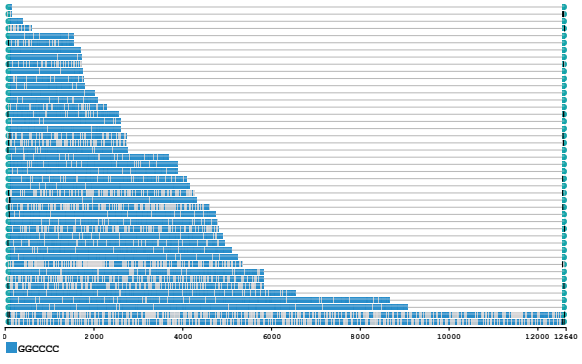
B. Double expansion of pathogenic AAGGG repeat in *RFC1* with long allele consensus length of 1300 repeats (~6.5 kb).[3] Axis unit is number of repeat motifs.

Detect methylation



C. Profile at *FMR1* shows consistent methylation of expanded allele in female carrier (NA07537). Axis unit is number of 3 bp repeat motifs.

Profile mosaicism

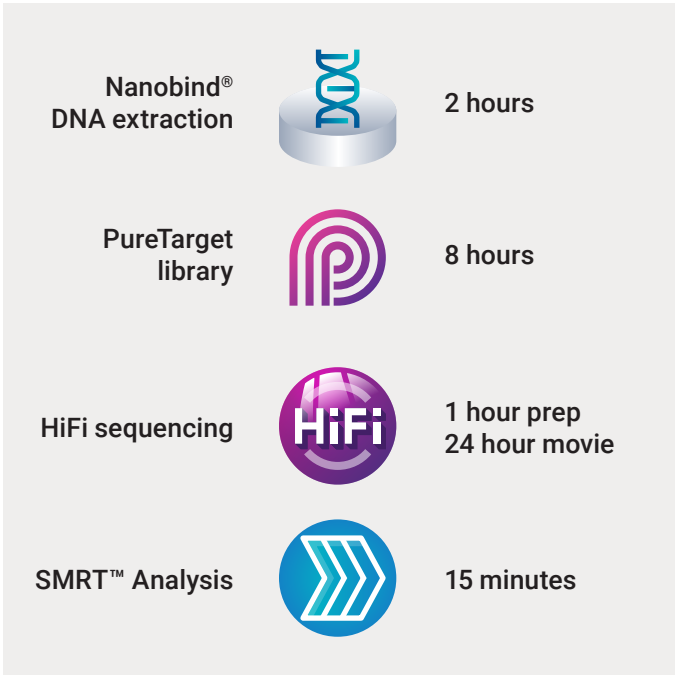


D. Waterfall plot shows deep coverage and distribution of repeat lengths within a sample with *C9orf72* expansion. Sample was prepared with 2 µg of DNA and sequenced in 16-plex on Sequel® IIe. A total of 458 reads span the *C9ORF72* repeat, 66 of which span the long allele. Axis unit is base pairs.

PacBio

Stay on target

PureTarget offers an easy and scalable workflow to capture repeat expansions and brings you from sample to answer in three days. Compatible with the Revio™ and Sequel II systems, PureTarget libraries can be multiplexed with up to 48 samples, generating deep coverage across the 20-gene target panel.



Spec	Metric
DNA input[1]	2 µg/sample
DNA quality[2]	GQN at 30 kb >5
Mean target coverage[3]	>200-fold
Minimum target coverage	50-fold
Sample multiplexing[4]	48 —Revio system 24 —Sequel II systems
Library size[5]	4–5 kb
Methylation[6]	Detected

1. 1–4 µg supported
2. 50% of mass of DNA molecules longer than 30 kb as measured on Femto Pulse (Agilent). Official product support for Nanobind-extracted DNA from human blood and cell line.
3. Mean and minimum target coverage is for 2 µg of input DNA from supported samples types (Nanobind-extracted human blood and cell line) for unexpanded alleles.
4. Kit supports smaller batches in multiples of 8 samples.
5. Inserts with expanded alleles will be longer.
6. Methylation probabilities for CpG sites encoded in BAM.

Disease	Targets
Spinocerebellar ataxia	*ATN1, ATXN1, ATXN2, ATXN3, ATXN7, ATXN8, ATXN10, CACNA1A, PPP2R2B, TBP*
Friedrich's ataxia	*FXN*
CANVAS disease	*RFC1*
Fragile-X disease (FXS)	*FMR1*
Huntington's disease	*HTT*
Myotonic dystrophy	*DMPK, CNBP*
Amyotrophic lateral sclerosis (ALS), frontotemporal dementia (FTD)	*C9orf72*
Fuchs endothelial corneal dystrophy	*TCF4*
Spinal bulbar muscular atrophy / Kennedy's disease	*AR*
Oculopharyngeal muscular dystrophy	*PABPN1*

KEY REFERENCES

1. Dolzhenko E, English A, Dashnow H, et al., (2024). Characterization and visualization of tandem repeats at genome scale. *Nature Biotechnology*, 1–9.
2. https://downloads.pacbcloud.com/public/dataset/PureTargetRE/Coriell/
3. https://downloads.pacbcloud.com/public/dataset/PureTargetRE/RFC1/ (sample NG24)

Learn more: pacb.com/target

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