神經基因體學研究新助力

PureTarget™ Repeat Expansion Panel

PureTarget™

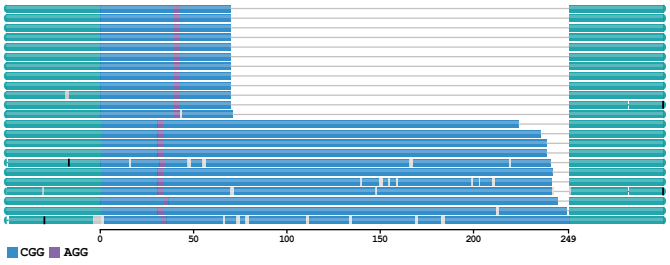
照亮暗處，找出隱藏的神經系統疾病基因體變異

已有研究指出，近 50 多種單基因遺傳疾病和癌症與 **DNA 重複序列擴增 (repeat expansion)** 有關，這些重複序列的長度、片段內容和甲基化程度可能影響疾病的嚴重程度和發病年齡。過去，這些基因體區域一直難以研究，但現在科學家們可以透過 PacBio 全新推出的【**PureTarget™ Repeat Expansion Panel**】全面地分析這些區域。

PureTarget 讓重複擴增區域不再深奧難解

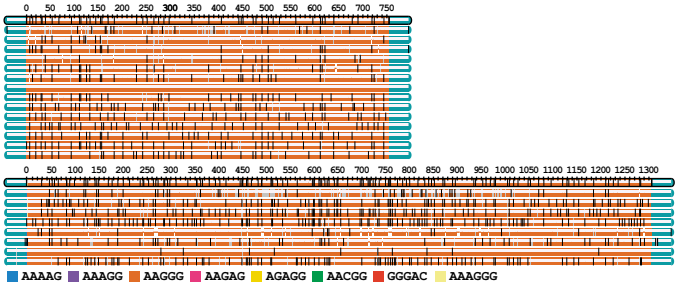
PureTarget 為人類神經系統疾病最相關的 20 個重複擴增區域提供了一個 gene panel，搭配長且精準的 HiFi reads 及後端 TRGT 重複序列基因型分析工具[1]，科學家們將能以前所未有的清晰度觀察這些曾經難以捉摸的基因體區域，包含：(**圖 A**) 逐個 base 解讀重複序列區域、(**圖 B**) 計數重複擴增區域內的片段重複次數、(**圖 C**) 檢測重複序列的 DNA 甲基化狀態、(**圖 D**) 找出等位基因的鑲嵌型變化。

(A). Resolve repeat sequence



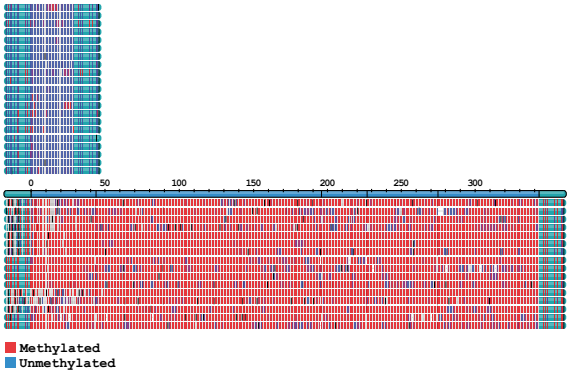
Single-base resolution of *FMR1* repeat sequence detects AGG interruptions in female carrier (NA06905). Consensus alleles are 23 and 79 repeats long, respectively.[2] Axis unit is base pairs.

(B). Size long repeat expansions



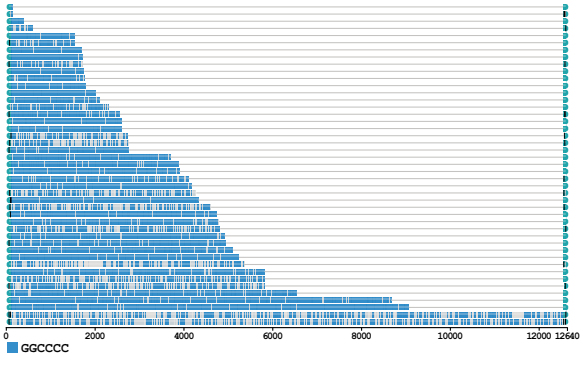
Double expansion of pathogenic AAGGG repeat in *RFC1* with long allele consensus length of 1300 repeats (~6.5 kb).[3] Axis unit is number of repeat motifs.

(C). Detect methylation



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

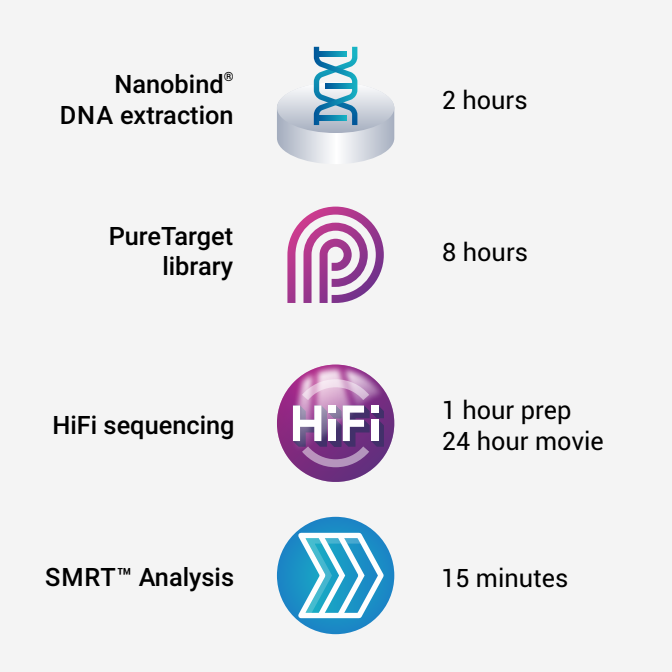
(D). Profile mosaicism



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.

簡易高效

PureTarget 具有簡單易上手的工作流程，搭配 Revio™ 定序系統，能在三個工作天內完成 48 個樣本、20 個重複序列基因的標靶定序與分析。



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.

標靶基因與相關疾病對照表

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

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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