**Supp. Table S1**. Classifying the *FBN1* c.2678-15C>A variant as pathogenic

| Type of evidence | Criteria | Evidence of pathogenicity | Evidence code |
|---|---|---|---|
| Population data | Absent in population databases | moderate | PM2 |
| Predictive data | Predicted null variant in a gene where LOF is a known mechanism of disease | very strong | PVS1 |
| Predictive data | Computational evidence support a deleterios effect on the gene product | supporting | PP3 |
| Functional data | *In vitro* functional studies supportive of a damaging effect on the gene product | strong | PS3 |
| Other data | Patient's phenotype is highly specific for a disease with a single genetic etiology | supporting | PP4 |

LOF - loss of function; PM - pathogenic moderate; PVS - pathogenic very strong; PP - pathogenic supporting; PS - pathogenic strong. A variant is considered pathogenic if the following criteria are met: 1 PVS1 + ≥1 Strong (PS1–PS4) or 1 PVS1 + 1 Moderate (PM1–PM6) and 1 supporting (PP1–PP5) or 1 PVS1 + ≥2 Supporting (PP1–PP5), according to Richards et al., 2015 [20].

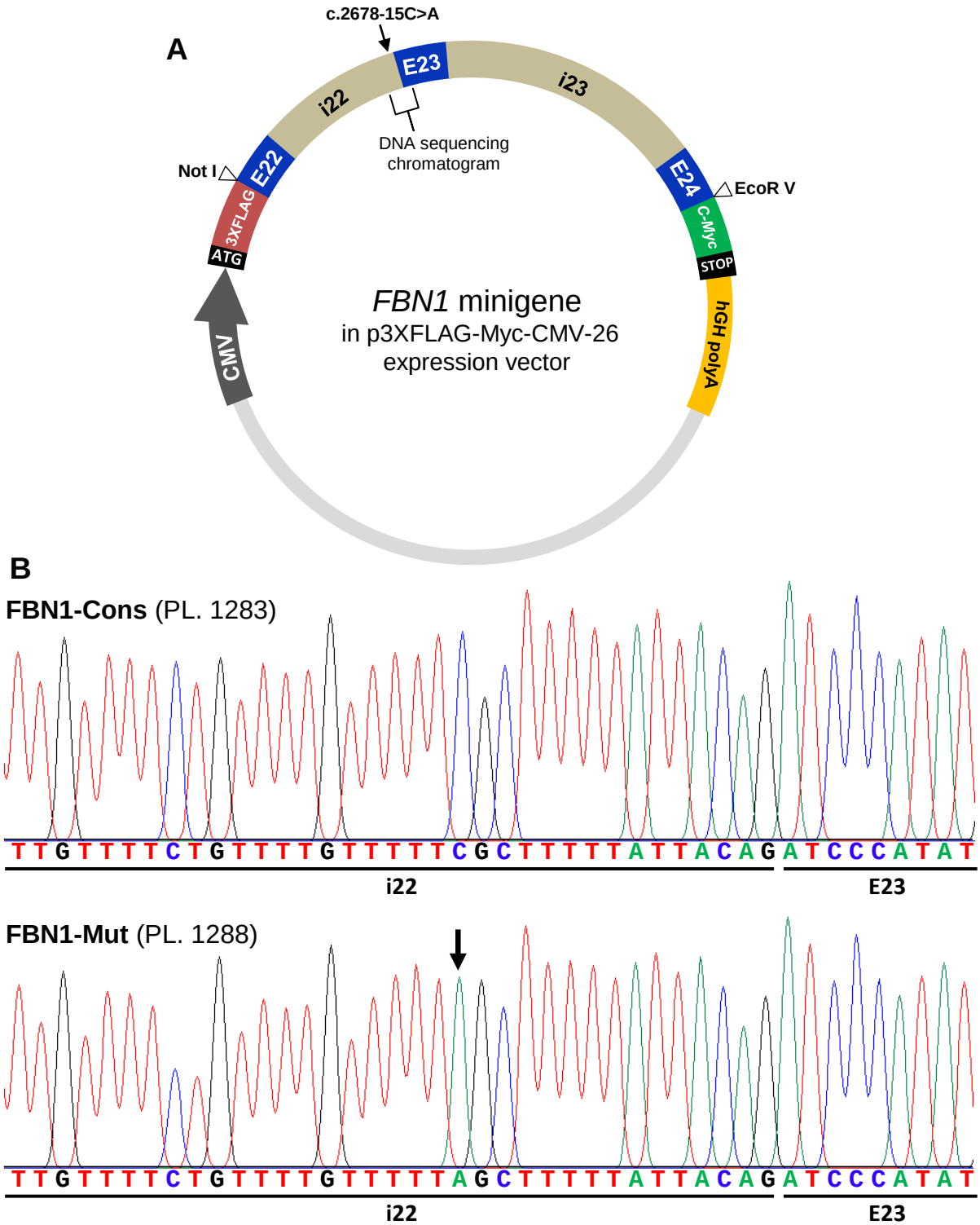
A
c.2678-15C>A
E23
i22
i23
DNA sequencing
chromatogram
Not I
E22
3XFLAG
ATG
E24
EcoR V
C-Myc
STOP
hGH polyA
CMV
FBN1 minigene
in p3XFLAG-Myc-CMV-26
expression vector
B
FBN1-Cons (PL. 1283)
T T G T T T T C T G T T T T G T T T T T C G C T T T T T A T T A C A G A T C C C A T A T
i22
E23
FBN1-Mut (PL. 1288)
T T G T T T T C T G T T T T G T T T T T A G C T T T T T A T T A C A G A T C C C A T A T
i22
E23

**Fig. S1**

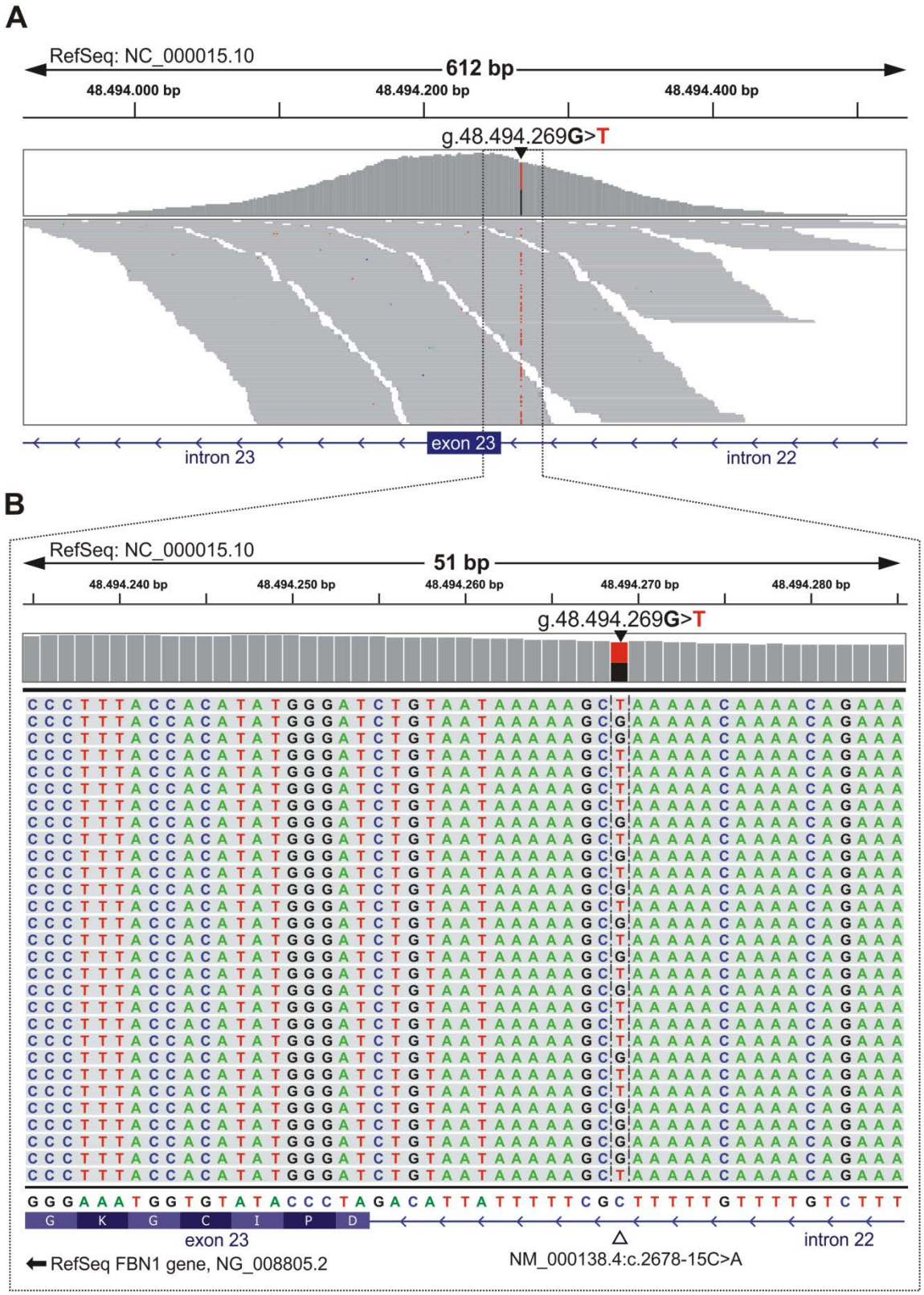
A
RefSeq: NC_000015.10
612 bp
48.494.000 bp
48.494.200 bp
48.494.400 bp
g.48.494.269G>T
exon 23
intron 23
intron 22
B
RefSeq: NC_000015.10
51 bp
48.494.240 bp
48.494.250 bp
48.494.260 bp
48.494.270 bp
48.494.280 bp
g.48.494.269G>T
G G G A A A T G G T G T A T A C C C T A G A C A T T A T T T T T C G C T T T T T G T T T T G T C T T T
G K G C I P D
exon 23
intron 22
RefSeq FBN1 gene, NG_008805.2
NM_000138.4:c.2678-15C>A

Fig. S2

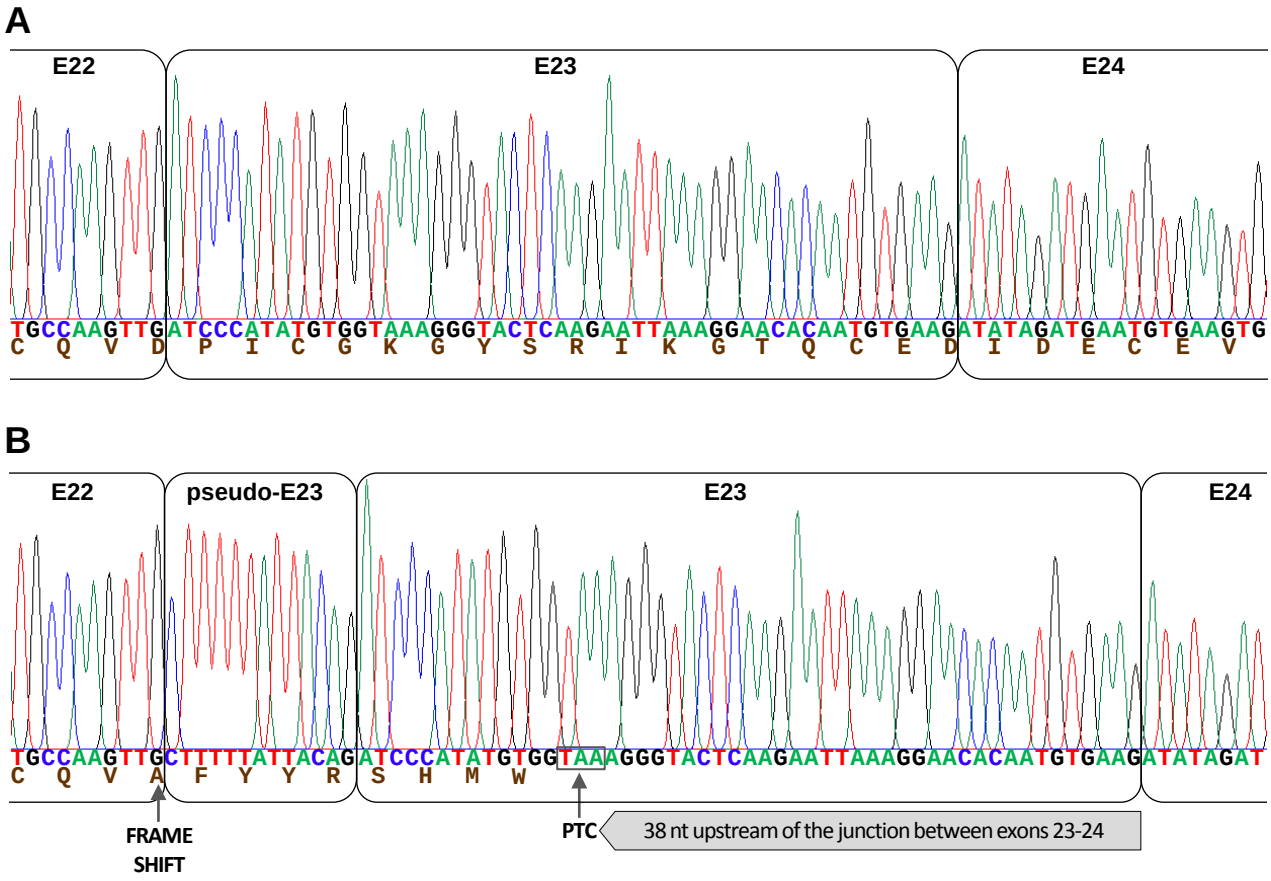
A
E22
E23
E24
TGCCAAGTTGATCCCATATGTGGTAAAGGGTACTCAAGAATTAAAGGAACACAATGTGAAGATATAGATGAATGTGAAGTG
C Q V D P I C G K G Y S R I K G T Q C E D I D E C E V
B
E22
pseudo-E23
E23
E24
TGCCAAGTTGCTTTTTATTACAGATCCCATATGTGGTAAAGGGTACTCAAGAATTAAAGGAACACAATGTGAAGATATAGAT
C Q V A F Y Y R S H M W
FRAME SHIFT
PTC
38 nt upstream of the junction between exons 23-24

**Fig. S3**