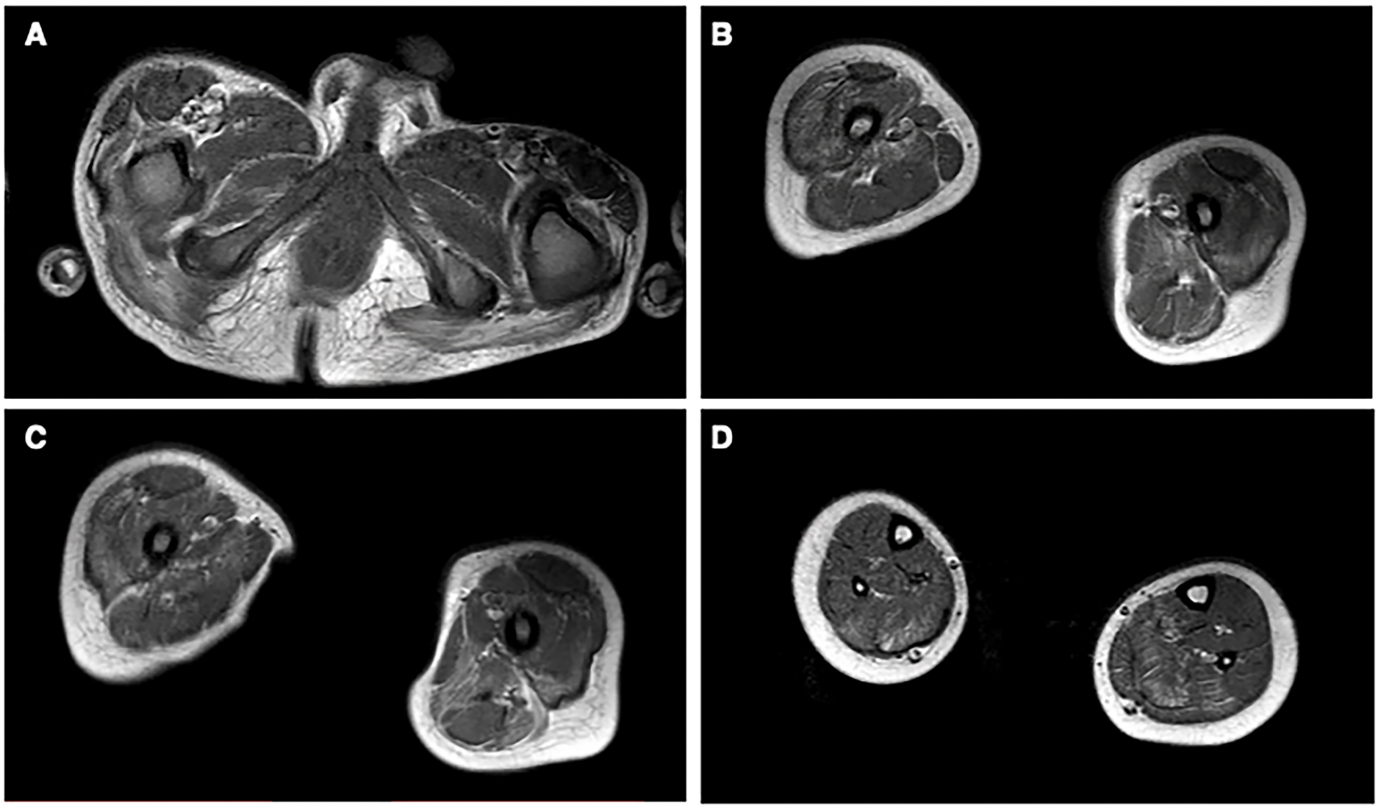
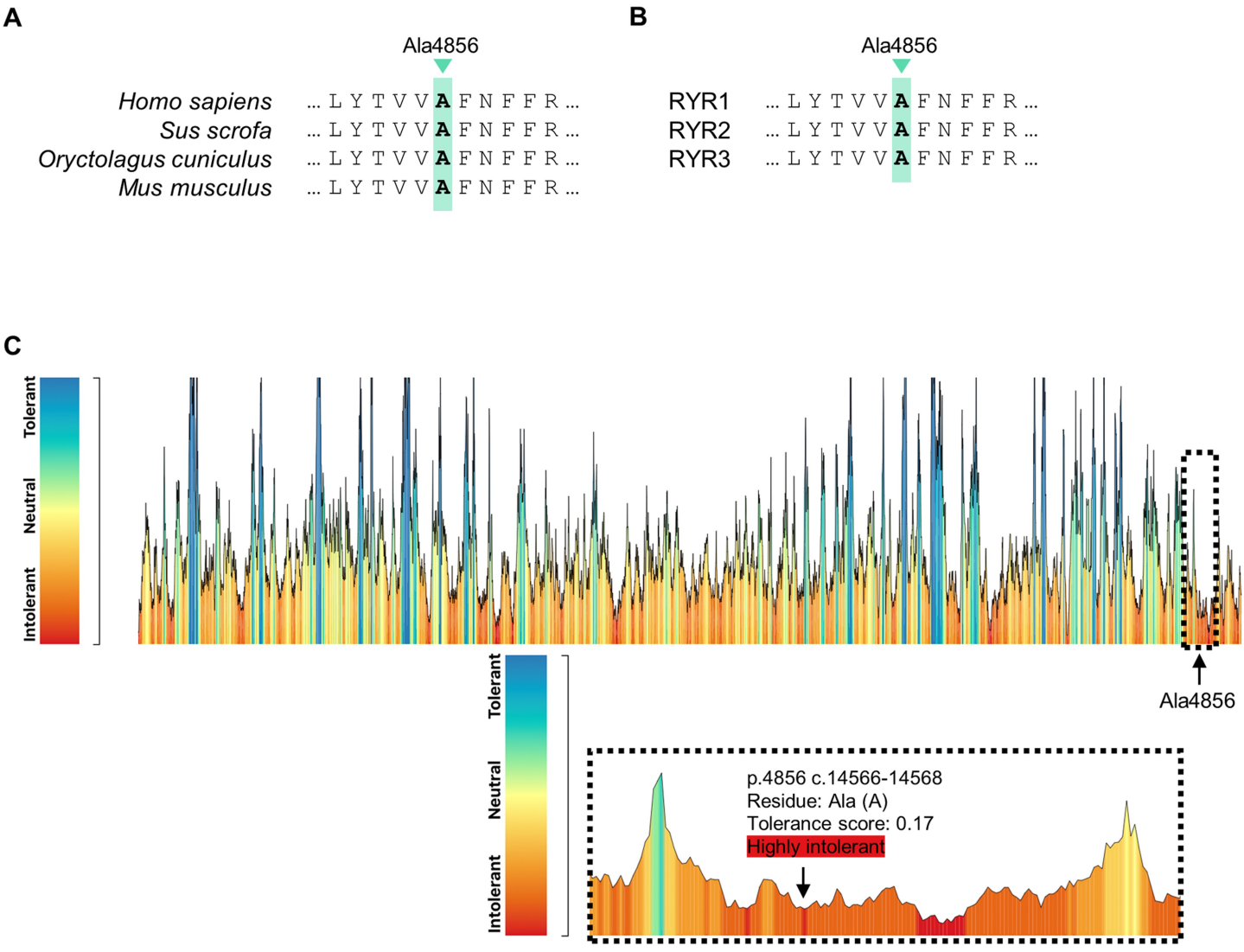
Supplementary figure 1. T1-weighted MRI sequences of the affected child.



Supplementary figure 1. T1-weighted MRI sequences of pelvic girdle (A), thighs (B, C), and calfs (D) of the affected child at 3 years old revealed T1 signal hyperintensity suggestive of a fatty replacement in the gluteus maximus, the anterior compartments of both thighs, predominantly on the right side, the posterior compartments of both thighs, predominantly on the left side, and the posterior compartments of both legs. No signs of muscular edema were identified. Note the relative sparing of the rectus femoris muscle as related to the vastus lateralis muscle in B and C.

Supplementary figure 2. *In-silico* evaluation of the RYR1 genetic variant found in the affected child and mother.



Supplementary figure 2. (A) Alignment of human, pig, rabbit and mouse RYR1 sequences. The alignment shows the highly conserved residue (Ala4856) in a conserved region. (B) Alignment of RYR1, RYR2 and RYR3 from human. (C) Tolerance landscape of RYR1 according to MetaDome. The lower panel shows a detail of the generally intolerant region with the tolerance score and its interpretation for the reported variant.

Supplementary table 1. Pathogenic effect evaluation of *RYR1* genetic variant.

Gene (Ref. sequence)	Nucleotide (amino acid) change	gnomAD frequency	Segregation	Variant classification (ACMG) (Last accessed Oct 2023)	*In-silico* pathogenicity predictors			
					CADD	Mutation taster	FATHMM-MKL	PROVEAN
RYR1 (NM_000540.3)	c.14566G>A (p.Ala4856Thr)	NR	Heterozygosis	LP	29.0 (Damaging)	0.99 (Disease causing)	0.99 (Damaging)	-3.46 (Damaging)

Supplementary table 1. Allele frequency in total population (gnomAD). Classification based on the ACMG guidelines, using Franklin. *In-silico* pathogenicity predictors: CADD (≥ 20 indicating that the variant is predicted to be among the 1% of the most deleterious substitutions in the human genome), Mutation taster and FATHMM-MKL (with scores ranging from 0 to 1, being 1 the most damaging) and PROVEAN (with scores ≤− 2.5 being deleterious). NR, not reported; LP, likely pathogenic.