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Variant: NM_000152.5(GAA):c.755dup (p.Pro253fs)

Version: 1.0

CA658824779

553981 (ClinVar)

Gene: GAA (HGNC:2548)
Condition: glycogen storage disease II (MONDO:0009290)
Inheritance Mode: Autosomal recessive inheritance
UUID: 7a5678af-163d-421d-b3f4-15705f3aa88f
Approved on: 2020/7/20
Published on: 2020/11/11

HGVS expressions

NM_000152.5(GAA):c.755dup (p.Pro253fs)
NM_000152.5:c.755dup
NC_000017.11:g.80107619dup
CM000679.2:g.80107619dup
NC_000017.10:g.78081418dup
CM000679.1:g.78081418dup
NC_000017.9:g.75696013dup
NG_009822.1:g.11064dup
ENST00000570803.6:c.755dup
ENST00000572080.2:c.755dup
ENST00000577106.6:c.755dup
ENST00000302262.8:c.755dup
ENST00000302262.7:c.755dup
ENST00000390015.7:c.755dup
ENST00000570803.5:c.755dup
NM_000152.3:c.755dup
NM_001079803.1:c.755dup
NM_001079804.1:c.755dup
NM_000152.4:c.755dup
NM_001079803.2:c.755dup
NM_001079804.2:c.755dup
NM_001079803.3:c.755dup
NM_001079804.3:c.755dup

Pathogenic

Met criteria codes 3
PP4 PM2 PVS1

Not Met criteria codes 1
PM3

Evidence Links 1

Expert Panel
Lysosomal Diseases VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Lysosomal Diseases VCEP

This variant, c.755dup (p.Pro253AlafsTer77), is a frameshift variant that is predicted to result in a premature termination codon, nonsense mediated decay, and lack of gene product, meeting PVS1. This variant is not in gnomAD v2.1.1, meeting PM2. One patient has been reported who meets the ClinGen LSD VCEP's specifications for PP4 and who is compound heterozygous for the variant and c.569G>A (p.Arg190His) (PMID 29124014). The phase is unknown. This is intrans data will be used in the assessment of p.Arg190His and is therefore not included here in order to avoid a circular argument. There is a ClinVar entry for this variant (Variation ID: 553981, one star review status) with one submitter classifying the variant as likely pathogenic. In summary, this variant meets the criteria to be classified as pathogenic for Pompe disease. GAA-specific ACMG/AMP criteria applied, as specified by the ClinGen LSD VCEP: PVS1, PM2, PP4.

Met criteria codes

PP4	✔	One patient meeting the ClinGen LSD VCEP's specifications for PP4 has been reported (PMID 29124014). This patient has <10% normal GAA activity in leukocytes.
PM2	✔	This variant is not in gnomAD v2.1.1.
PVS1	✔	This is a frameshift variant which is predicted to result in a premature termination codon, nonsense mediated decay, and lack of gene product. Therefore, PVS1 can be applied.

Not Met criteria codes

PM3	✖	One patient meeting the ClinGen LSD VCEP's specifications for PP4 has been reported (PMID 29124014). This patient is compound heterozygous for the variant and c.569G>A (p.Arg190His). The phase is unknown. This is intrans data will be used in the assessment of p.Arg190His and is therefore not included here in order to avoid a circular argument.

PubMed:29124014

Curation History

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