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Variant: NM_000155.4(GALT):c.626A>G (p.Tyr209Cys)

Version: 1.0

CA312567

25231 (ClinVar)

Gene: GALT (HGNC:2592)
Condition: galactosemia (MONDO:0018116)
Inheritance Mode: Autosomal recessive inheritance
UUID: a3010b82-ff9a-4c73-9fdc-edde809792db
Approved on: 2026/6/23
Published on: 2026/6/23

HGVS expressions

NM_000155.4(GALT):c.626A>G (p.Tyr209Cys)
NM_000155.4:c.626A>G
NC_000009.12:g.34648395A>G
CM000671.2:g.34648395A>G
NC_000009.11:g.34648392A>G
CM000671.1:g.34648392A>G
NC_000009.10:g.34638392A>G
NG_009029.1:g.6758A>G
NG_028966.1:g.1211A>G
NG_009029.2:g.6807A>G
ENST00000691183.1:c.*214A>G
ENST00000378842.8:c.626A>G
ENST00000378842.7:c.626A>G
ENST00000450095.6:c.299A>G
ENST00000472111.5:n.882A>G
ENST00000473506.6:c.*214A>G
ENST00000473529.5:n.785A>G
ENST00000487381.5:n.1011A>G
ENST00000489643.6:n.401A>G
ENST00000554085.5:c.*370A>G
ENST00000554550.5:c.*246A>G
ENST00000554638.5:n.1098A>G
ENST00000555020.5:n.782A>G
ENST00000555086.5:n.630A>G
ENST00000555214.5:n.447A>G
ENST00000556244.1:c.613A>G
ENST00000556278.1:c.371A>G
ENST00000556494.5:n.747A>G
ENST00000557706.5:n.1188A>G
NM_000155.3:c.626A>G
NM_001258332.1:c.299A>G
NM_001258332.2:c.299A>G

Pathogenic

Met criteria codes 5

PM3_Very Strong | PP3 | PP4 | PM2_Supporting | PS3_Supporting

Evidence Links 0

Expert Panel

Galactosemia VCEP

Criteria Specification Information

- **Criteria Specification:** *ClinGen Galactosemia Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GALT Version 1.0.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Galactosemia VCEP

The c.626A>G variant in GALT is a missense variant predicted to cause substitution of tyrosine by cysteine at amino acid 209 (p.Tyr209Cys). The filtering allele frequency (the upper threshold of the 95% CI of 4/91092) of the c.626A>G variant in GALT is 0.00001425 for South Asian chromosomes by gnomAD v4.1.0, which is lower than the ClinGen Galactosemia threshold (≤ 0.0005) for PM2_Supporting, and therefore meets this criterion (PM2_Supporting). The computational predictor REVEL gives a SCORE of 0.825, which is equal to or above the threshold of 0.7, evidence that correlates with impact to GALT function (PP3). This variant has been detected in at least 9 individuals with galactosemia. All of those individuals were compound heterozygous for the variant and a pathogenic variant (PM3_Very Strong; PMID: 10399107, 11397328, 22693313, 10535394, Internal lab contributors). At least one patient with this variant displayed no detectable Galac-1-Phos Uridyltransferase activity, which is highly specific for galactosemia (PP4; Internal lab contributors). GALT activity in a null-background yeast expression system for the human enzyme showed 13.6 ± 1.3% of WT activity, indicating that this variant impacts protein function (PS3_Supporting; PMID: 22743281). In summary, this variant meets the criteria to be classified as pathogenic for galactosemia based on the ACMG/AMP criteria applied, as specified by the ClinGen Galactosemia VCEP: PM3_Very Strong, PM2_Supporting, PS3_Supporting, PP3, PP4 (GALT specifications v1.0).

Met criteria codes

PM3_Very Strong	✔	This variant has been detected in at least 9 individuals with galactosemia. All of those individuals were compound heterozygous for the variant and a pathogenic variant (PM3_Very_Strong; PMID: 10399107, 11397328, 22693313, 10535394, Internal lab contributors).
PP3	✔	The computational predictor REVEL gives a SCORE of 0.825, which is equal to or above the threshold of 0.7, evidence that correlates with impact to GALT function (PP3).
PP4	✔	At least one patient with this variant displayed no detectable Galac-1-Phos Uridyltransferase activity, which is highly specific for galactosemia (PP4; Internal lab contributors).
PM2_Supporting	✔	The filtering allele frequency (the upper threshold of the 95% CI of 4/91092) of the c.626A>G variant in GALT is 0.00001425 for South Asian chromosomes by gnomAD v4.1.0, which is lower than the ClinGen Galactosemia threshold (≤ 0.0005) for PM2_Supporting, and therefore meets this criterion (PM2_Supporting).
PS3_Supporting	✔	GALT activity in a null-background yeast expression system for the human enzyme showed 13.6 ± 1.3% of WT activity, indicating that this variant impacts protein function (PS3_Supporting; PMID:22743281).

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000155.4(GALT):c.626A>G (p.Tyr2…	Pathogenic	Galactosemia	2026-06-23	1.0	ClinGen Galactosemia Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GALT Version 1.0.0	GALT

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