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# *Variant: NM_000155.4(GALT):c.413C>T (p.Thr138Met)*

Version: 1.0

*CA259387*

*25174 (ClinVar)*

**Gene**: GALT (HGNC:2592)
**Condition**: galactosemia (MONDO:0018116)
**Inheritance Mode**: Autosomal recessive inheritance
**UUID:** ad2ab86e-b4d4-4a3c-b918-3a02ba25940b
**Approved on**: 2026/6/23
**Published on**: 2026/6/23

## *HGVS expressions*

**NM_000155.4:c.413C>T**
**NM_000155.4(GALT):c.413C>T (p.Thr138Met)**
NC_000009.12:g.34647867C>T
CM000671.2:g.34647867C>T
NC_000009.11:g.34647864C>T
CM000671.1:g.34647864C>T
NC_000009.10:g.34637864C>T
NG_009029.1:g.6230C>T
NG_028966.1:g.683C>T
NG_009029.2:g.6279C>T
ENST00000691183.1:c.*1C>T
ENST00000378842.8:c.413C>T
ENST00000378842.7:c.413C>T
ENST00000450095.6:c.86C>T
ENST00000465543.6:n.752C>T
ENST00000472111.5:n.669C>T
ENST00000473506.6:c.*1C>T
ENST00000473529.5:n.549C>T
ENST00000485531.1:n.854C>T
ENST00000487381.5:n.798C>T
ENST00000489643.6:n.283-248C>T
ENST00000554085.5:c.*157C>T
ENST00000554139.5:n.592C>T
ENST00000554550.5:c.*33C>T
ENST00000554638.5:n.885C>T
ENST00000554897.5:c.*33C>T
ENST00000554944.5:n.609C>T
ENST00000555020.5:n.569C>T
ENST00000555086.5:n.417C>T
ENST00000555214.5:n.262-181C>T
ENST00000556244.1:c.400C>T
ENST00000556278.1:c.253-248C>T
ENST00000556494.5:n.534C>T
ENST00000557541.5:n.557C>T
ENST00000557706.5:n.975C>T
NM_000155.3:c.413C>T
NM_001258332.1:c.86C>T

NM_001258332.2:c.86C>T

**Pathogenic**

**Met criteria codes** 6

PM3_Very Strong | PP1 | PP3 | PM2_Supporting | PS3_Supporting | PP4_Moderate

**Not Met criteria codes** 3

BA1 | PM1 | BS1

Evidence Links 1

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.413C>T variant in GALT is a missense variant predicted to cause substitution of Threonine by Methionine at amino acid 138 (p.Thr138Met). This variant has been detected in at least 14 individuals reported to have galactosemia. At least 11 probands with this variant had reported GALT activity <10% of wild type, which is highly specific for galactosemia (PP4_moderate; PMIDs: 8741038, 29350350, 8741038, 10960497, 11397328, 17876724, 30172461, Internal Lab Contributor). Of those individuals, at least 10 were assumed to be compound heterozygous for the variant and a pathogenic or likely pathogenic variant (p.Q188R, p.K285N, p.Ser135Leu, PMIDs: 30172461, 29350350, 17876724, 11397328, 10960497, 8741038, internal lab contributors, phase unknown, PM3 points=5; PM3_very strong). The variant has been reported to segregate with galactosemia in 2 affected family members from 1 family (PP1; PMID 29350350). GALT activity level assay in yeast showed a residual activity of 6.90+/-1.12% of WT indicating that this variant impacts protein function (PS3_Supporting; PMID 23690308). The filtering allele frequency of the c.413C>T (p.Thr138Met) variant in GALT is 0.000005530 for Admixed American 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 0.971, which is equal to or above the threshold of 0.7, evidence that correlates with impact to GALT function (PP3). 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, PP4_moderate, PM2_supporting, PP1, PP3, PS3_supporting (GALT specifications v1.0.0).**

**Met criteria codes**

| | | |
|---|---|---|
| **PM3_Very Strong** | ✔ | This variant has been detected in at least 14 individuals with galactosemia. Of those individuals also meeting criteria for PP4 (GALT RBC enzyme<10%), 10 were assumed to be compound heterozygous for the variant and a pathogenic or likely pathogenic variant and included in the analysis for PM3 (PMID 30172461, PMID 29350350, PMID 17876724, PMID 11397328, PMID 10960497, PMID 8741038, internal lab contributors). (PM3_VERY STRONG). |
| **PP1** | ✔ | The variant has been reported to segregate with galactosemia in 1 affected family member from 1 family (PP1; PMID 29350350). |
| **PP3** | ✔ | The computational predictor REVEL gives a SCORE of 0.971, which is equal to or above the threshold of 0.7, evidence that correlates with impact to GALT function (PP3). |
| **PM2_Supporting** | ✔ | The filtering allele frequency of the c.413C>T (p.Thr138Met) variant in GALT is 0.000005530 for Admixed American 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 level assay in yeast showed a residual activity of 6.90+/-1.12% of WT indicating that this variant impacts protein function (PMID 23690308)(PS3_Supporting).

supplemental table 1: GALT activity levels detected in null-background yeast expressing each hGALT allele, T138M residual GALT activity 6.90+/-1.12% of WT PubMed:23690308

**PP4_Moderate** ✔

At least 11 probands with this variant displayed GALT activity <10% of wild type, which is highly specific for galactosemia (PP4_moderate) PMID 8741038, PMID 29350350, Internal Lab Contributor, PMID 8741038, PMID 10960497, PMID 11397328, PMID 17876724, PMID 30172461).

**Not Met criteria codes**

**BA1** ✖

No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

**PM1** ✖

No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

**BS1** ✖

No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

## 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.413C>T (p.Thr1… | 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 |

Showing 1 to 1 of 1 rows

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