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Variant: NM_001083962.2(TCF4):c.1086G>A (p.Trp362Ter)

Version: 2.0

CA266818

93540 (ClinVar)

Gene: TCF4 (HGNC:6925)
Condition: Pitt-Hopkins syndrome (MONDO:0012589)
Inheritance Mode: Autosomal dominant inheritance
UUID: 0318c444-bec7-4c3c-b7be-61b4e0c8ba2a
Approved on: 2026/4/23
Published on: 2026/6/19

HGVS expressions

NM_001083962.2(TCF4):c.1086G>A (p.Trp362Ter)
NM_001083962.2:c.1086G>A
NC_000018.10:g.55257375C>T
CM000680.2:g.55257375C>T
NC_000018.9:g.52924606C>T
CM000680.1:g.52924606C>T
NC_000018.8:g.51075604C>T
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NG_011716.2:g.383619G>A
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ENST00000630720.3:c.603G>A
ENST00000635822.2:c.1086G>A
ENST00000635990.2:n.766G>A
ENST00000636400.2:c.1014G>A
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ENST00000636822.2:c.696G>A
ENST00000637115.2:c.*976G>A
ENST00000637169.2:c.438G>A
ENST00000637239.2:n.1153G>A
ENST00000637250.2:n.780G>A
ENST00000637923.2:c.684G>A
ENST00000638154.3:c.1113G>A
ENST00000643689.1:c.696G>A
ENST00000674764.1:c.*697G>A
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ENST00000398339.5:c.1392G>A
ENST00000457482.7:c.606G>A
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ENST00000537856.7:c.696G>A
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ENST00000543082.5:c.960G>A
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ENST00000561992.5:c.696G>A
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ENST00000566279.5:c.906G>A
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NM_001369585.1:c.1011G>A
NM_001369586.1:c.1017G>A
NM_003199.3:c.1086G>A
NM_001243230.2:c.1077G>A

Likely Pathogenic

Met criteria codes 2

PM2_Supporting PVS1

Not Met criteria codes 1

PP4

Evidence Links 0

Expert Panel

Rett and Angelman-like Disorders VCEP

Criteria Specification Information

Criteria Specification: *ClinGen Rett and Angelman-like Disorders Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for TCF4 Version 5.0.0*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Rett and Angelman-like Disorders VCEP

The p.Trp362Ter variant in TCF4 is predicted to cause a premature stop codon that leads to a truncated or absent protein in a TCF4 where loss-of-function is an established mechanism. There is significant evidence that loss of this region of the TCF4 is pathogenic (PVS1). The p.Trp362Ter variant in TCF4 is absent from gnomAD (PM2_Supporting). In summary, the p.Trp362Ter variant in TCF4 is classified as likely pathogenic for Pitt-Hopkins syndrome based on the ACMG/AMP criteria (PVS1, PM2_supporting). (TCF4 Specifications v5.0.0; curation approved on 4/23/2026).

Met criteria codes

PM2_Supporting	✔	The p.Trp362Ter variant in TCF4 is absent from gnomAD.
PVS1	✔	The p.Trp362Ter variant in TCF4 is predicted to cause a premature stop codon that leads to a truncated or absent protein in a TCF4 where loss-of-function is an established mechanism. There is significant evidence that loss of this region of the TCF4 is pathogenic.

Not Met criteria codes

PP4	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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