

Variant: NM_001083962.2(TCF4):c.1741G>T (p.Val581Phe)

Version: 1.0

CA272702 [↗](#)

160079 (ClinVar) [↗](#)

Gene: TCF4 ([HGNC:6925](#))

Condition: Pitt-Hopkins syndrome ([MONDO:0012589](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 79c2b5b6-3037-44fa-ae71-0b48cd373e7a

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HGVS expressions

NM_001083962.2:c.1741G>T

NM_001083962.2(TCF4):c.1741G>T (p.Val581Phe)

NC_000018.10:g.55228985C>A

CM000680.2:g.55228985C>A

NC_000018.9:g.52896216C>A

CM000680.1:g.52896216C>A

NC_000018.8:g.51047214C>A

NG_011716.1:g.364645G>T

NG_011716.2:g.412009G>T

ENST00000354452.8:c.1741G>T

ENST00000635822.2:c.1621G>T

ENST00000635990.2:n.1421G>T

ENST00000636400.2:c.1669G>T

ENST00000636751.2:c.*1449G>T

ENST00000636822.2:c.1351G>T

ENST00000637115.2:c.*1619G>T

ENST00000637169.2:c.1093G>T

ENST00000637239.2:n.1796G>T

ENST00000637250.2:n.1435G>T

ENST00000637923.2:c.1339G>T

ENST00000638154.3:c.1768G>T

ENST00000643689.1:c.1351G>T

ENST00000674764.1:c.*1352G>T

ENST00000675707.1:c.1351G>T

ENST00000354452.7:c.1741G>T

ENST00000356073.8:c.1729G>T

ENST00000398339.5:c.2047G>T

ENST00000457482.7:c.1261G>T

ENST00000537578.5:c.1669G>T

ENST00000537856.7:c.1339G>T

ENST00000540999.5:c.1657G>T

ENST00000543082.5:c.1603G>T

ENST00000544241.6:c.1528G>T

ENST00000561831.7:c.1249G>T

ENST00000561992.5:c.1339G>T

ENST00000562680.5:n.5264G>T

ENST00000564228.5:c.1516G>T

ENST00000564403.6:c.1759G>T
ENST00000564999.5:c.1729G>T
ENST00000565018.6:c.1477G>T
ENST00000566279.5:c.1561G>T
ENST00000566286.5:c.1720G>T
ENST00000567880.5:c.1549G>T
ENST00000568673.5:c.1669G>T
ENST00000568740.5:c.1654G>T
ENST00000570177.6:c.1339G>T
ENST00000570287.6:c.1249G>T
ENST00000616053.4:c.1477G>T
ENST00000626466.1:n.764G>T
ENST00000626584.2:c.1081G>T
ENST00000629387.2:c.1741G>T
NM_001083962.1:c.1741G>T
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NM_001243227.1:c.1669G>T
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NM_001243230.1:c.1720G>T
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NM_001243236.1:c.1249G>T
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NM_003199.2:c.1729G>T
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NM_001243233.2:c.1339G>T
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NM_001369577.1:c.1666G>T
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NM_001369580.1:c.1666G>T
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NM_001369582.1:c.1657G>T
NM_001369583.1:c.1657G>T
NM_001369584.1:c.1654G>T
NM_001369585.1:c.1654G>T
NM_001369586.1:c.1672G>T
NM_003199.3:c.1729G>T
NM_001243230.2:c.1720G>T

Likely Pathogenic

Met criteria codes 5

- PS4_Supporting
- PP3
- PM2_Supporting
- PM1
- PM6

Evidence Links 0

Expert Panel

Rett and Angelman-like Disorders VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Rett and Angelman-like Disorders VCEP

The p.Val581Phe variant in TCF4 is located in the basic Helix-Loop-Helix domain (bHLH) (PMID 17436254, 22045651) (PM1). This variant is absent from gnomAD (PM2_supporting). The p.Val581Phe variant in TCF4 occurs in the de novo state (biological parentage unconfirmed) in an individual with delays, hypotonia, not walking, dysmorphic features (University of Chicago internal database) (PM6). Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own (PP3). The p.Val581Phe variant in TCF4 has been observed in at least 2 individuals with neurodevelopmental phenotype (University of Chicago internal database, Invitae internal database) (PS4_supporting). In summary, the p.Val581Phe variant in TCF4 is classified as likely pathogenic for Pitt-Hopkins syndrome based on the ACMG/AMP criteria (PM1, PM2_supporting, PM6, PP3, PS4_supporting).

Met criteria codes			
PS4_Supporting			The p.Val581Phe variant in TCF4 has been observed in at least 2 individuals with neurodevelopmental phenotype (University of Chicago internal database, Invitae internal database).
PP3			Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own.
PM2_Supporting			The p.Val581Phe variant in TCF4 is absent from gnomAD.
PM1			This variant is located in the basic Helix-Loop-Helix domain (bHLH) (PMID 17436254, 22045651).
PM6			The p.Val581Phe variant in TCF4 occurs in the de novo state (biological parentage unconfirmed) in an individual with delays, hypotonia, not walking, dysmorphic features (University of Chicago internal database).

Curation History 	
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