ClinVar Submission Wizard submission: SUB14653120

SUB14653120

> **clinvar: Processing**
> SCV005184308

Review & Submit

Info

Submission name	SUB14653120
Data from a named study	no
Release status	hold until published
Accessions requested	yes

Organization(s)

Organization(s)	
From a single organization or multiple organizations?	single
On behalf of another organization?	no

Variant

Classification	germline
Type	single
Method of description	hgvs
Assembly	hg19
Accession and version of reference sequence	NM_007375.4
Description of the sequence change	c.800A>G
Gene	TARDBP: TAR DNA binding protein
Variation identifiers	dbSNP:rs80356718

Conditions

Type of condition being submitted	diagnostic

Type of database identifier for this condition	Database identifier for this condition or your preferred name
OMIM	612069 (Amyotrophic lateral sclerosis type 10)

Classification

Type of classification	germline
Classification	Likely pathogenic
Mode of inheritance	Autosomal dominant inheritance
Date last evaluated	2024-08-10
Comment on Classification	TARDBP c.800A>G (NM_007375.4) sequence change replaces Asparagine to Serine at codon 267 of TAR DNA-binding protein 43 (p.Asn267Ser). TARDBP c.800A>G has been reported in in ClinVar in at least 5 cases with Amyotrophic lateral sclerosis. The variant is present at low allele frequencies population databases. Missense variant in a gene with low rate of benign missense mutations and for which missense mutation is a common mechanism of a disease (PP2) and 38 pathogenic or likely pathogenic reported variants were found in a 531bp region surrounding this variant in exon 6 within the region 11082180-11082711 without any missense benign variants (PM1). In summary, the currently available evidence indicates that the variant is Likely pathogenic.

Assertion criteria

Assertion criteria	ACMG Guidelines 2015

Observations

Aggregate observations

Indvidual observations

ALS_affected female

Experimental observations

ClinVar Submission Wizard submission: SUB14653154

SUB14653154

> **clinvar: Processing**
> SCV005184319

Review & Submit

Info

Submission name	SUB14653154
Data from a named study	no
Release status	hold until published
Accessions requested	yes

Organization(s)

Organization(s)	
From a single organization or multiple organizations?	single
On behalf of another organization?	no

Variant

Classification	germline
Type	single
Method of description	hgvs
Assembly	hg19
Accession and version of reference sequence	NM_013254.4
Description of the sequence change	c.1760+1G>A
Gene	TBK1: TANK binding kinase 1

Conditions

Type of condition being submitted	diagnostic

Type of database identifier for this condition	Database identifier for this condition or your preferred name
OMIM	616439 (Frontotemporal dementia and/or amyotrophic lateral sclerosis 4)

Classification

Type of classification	germline
Classification	Likely pathogenic
Mode of inheritance	Autosomal dominant inheritance
Date last evaluated	2024-08-10
Comment on Classification	TBK1 c.1760+1G>A (NM_013254.4) sequence change affects a donor splice site of exon16. Algorithms developed to predict the effect of sequence changes on RNA splicing suggest that this variant may disrupt the consensus splice site. Null variant in a gene where loss of function is a known mechanism of disease and 55 pathogenic null variants were reported in ClinVar for this gene, of which 1 variants in this exon16 (PVS1). The variant is present in extremely low frequency in gnomAD population databases (PM2). In summary, the currently available evidence indicates that the variant is likely pathogenic.

Assertion criteria

Assertion criteria	ACMG Guidelines 2015

Observations

Aggregate observations

Indvidual observations

ALS_affected female

Experimental observations

ClinVar Submission Wizard submission: SUB14653157

SUB14653157

> **clinvar: Processing**
> SCV005184320

Review & Submit

Info

Submission name	SUB14653157
Data from a named study	no
Release status	hold until published
Accessions requested	yes

Organization(s)

Organization(s)	
From a single organization or multiple organizations?	single
On behalf of another organization?	no

Variant

Classification	germline
Type	single
Method of description	hgvs
Assembly	hg19
Accession and version of reference sequence	NM_014845.6
Description of the sequence change	c.295G>T
Gene	FIG4: FIG4 phosphoinositide 5-phosphatase
Variation identifiers	dbSNP:rs756709973

Conditions

Type of condition being submitted	diagnostic

Type of database identifier for this condition	Database identifier for this condition or your preferred name
OMIM	612577 (Amyotrophic lateral sclerosis type 11)

Classification

Type of classification	germline
Classification	Uncertain significance
Mode of inheritance	Autosomal dominant inheritance
Date last evaluated	2024-08-10
Comment on Classification	FIG4 c.295G>T (NM_014845.6) sequence change replaces Valine to Phenylalanine at codon 99 of FIG4 (FIG4 Phosphoinositide 5-Phosphatase) protein (p.Val99Phe). The variant is present in extremely low frequency in gnomAD population databases (PM2). However vailable data are incomplete and not able to determine the clinical significance of the variant at this time. In summary, the currently available evidence indicates that the variant is of an uncertain significance.

Assertion criteria

Assertion criteria	ACMG Guidelines 2015

Observations

Aggregate observations

Indvidual observations

ALS_affected male

Experimental observations

ClinVar Submission Wizard submission: SUB14653179

SUB14653179

> **clinvar: Processing**
> SCV005184321

Review & Submit

Info

Submission name	SUB14653179
Data from a named study	no
Release status	hold until published
Accessions requested	yes

Organization(s)

Organization(s)	
From a single organization or multiple organizations?	single
On behalf of another organization?	no

Variant

Classification	germline
Type	single
Method of description	hgvs
Assembly	hg19
Accession and version of reference sequence	NM_018446.4
Description of the sequence change	c.713C>G
Gene	GLT8D1: glycosyltransferase 8 domain containing 1

Conditions

Type of condition being submitted	diagnostic

ClinVar Submission Wizard submission: SUB14653195

SUB14653195

> **clinvar: Processing**
> SCV005184322

Review & Submit

Info

Submission name	SUB14653195
Data from a named study	no
Release status	hold until published
Accessions requested	yes

Organization(s)

Organization(s)	
From a single organization or multiple organizations?	single
On behalf of another organization?	no

Variant

Classification	germline
Type	single
Method of description	hgvs
Assembly	hg19
Accession and version of reference sequence	NM_001003800.2
Description of the sequence change	c.1180C>A
Gene	BICD2: BICD cargo adaptor 2
Variation identifiers	dbSNP:rs775633720

Conditions

Type of condition being submitted	diagnostic

Type of database identifier for this condition	Database identifier for this condition or your preferred name
Orphanet	ORPHA803 (Amyotrophic lateral sclerosis)

Classification

Type of classification	germline
Classification	Uncertain significance
Mode of inheritance	Autosomal dominant inheritance
Date last evaluated	2024-08-10
Comment on Classification	BICD2 c.1180C>A (NM_001003800.2) sequence change replaces Leucine to Methionine at codon 394 of BICD Cargo Adaptor 2 protein (p.Leu394Met). The variant is present in extremely low frequency in gnomAD population databases (PM2). In silico, prediction analysis showed that this variant is damaging, however, available data are incomplete and are not able to determine the clinical significance of the variant at this time. In summary, the currently available evidence indicates that the variant is of an uncertain significance.

Assertion criteria

Assertion criteria	ACMG Guidelines 2015

Observations

Aggregate observations

Indvidual observations

ALS_affected female

Experimental observations