

# Uniprot activity

- Search for your protein: human glycyl-tRNA
  - Choose only reviewed, human proteins
  - What does “reviewed” mean?
  - Download the list of proteins (Uniprot IDs). This time pay attention: Make sure you focus on your protein of interest.

BLAST

Align

Download

Add to basket

Columns

1 to 25 of 41

Show

25

Entry	Entry name		Protein names	Gene names	Organism	Length
5 result(s) selected. <a href="#">(Clear Selection)</a>						
<input checked="" type="checkbox"/> P41250	GARS_HUMAN		<b>Glycine--tRNA ligase</b>	<b>GARS</b>	Homo sapiens (Human)	739
<input checked="" type="checkbox"/> P15692	VEGFA_HUMAN		<b>Vascular endothelial growth factor ...</b>	<b>VEGFA</b> VEGF	Homo sapiens (Human)	232
<input checked="" type="checkbox"/> Q8TEA8	DTD1_HUMAN		<b>D-aminoacyl-tRNA deacylase 1</b>	<b>DTD1</b> C20orf88, DUEB, HARS2	Homo sapiens (Human)	209
<input checked="" type="checkbox"/> O14786	NRP1_HUMAN		<b>Neuropilin-1</b>	<b>NRP1</b> NRP, VEGF165R	Homo sapiens (Human)	923
<input checked="" type="checkbox"/> Q96FN9	DTD2_HUMAN		<b>D-aminoacyl-tRNA deacylase 2</b>	<b>DTD2</b> C14orf126	Homo sapiens (Human)	168

- For the top entry (your protein of interest),
  - What is the UniProt ID?
    - P41250
  - note active site, binding site or other functionally important residues


## Sites

Feature key	Position(s)	Description	Actions	Graphical view	Length
Binding site <sup>i</sup>	299	Glycine  Combined sources  1 Publication  2 Publications			1
Binding site <sup>i</sup>	350	Glycine  Combined sources  1 Publication  2 Publications			1
Binding site <sup>i</sup>	583	ATP  Combined sources  1 Publication			1

## ▪ Note natural variants (Feature viewer)


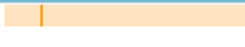

















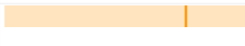


### Involvement in disease<sup>i</sup>

#### Charcot-Marie-Tooth disease 2D (CMT2D) 9 Publications

The disease is caused by mutations affecting the gene represented in this entry. Contrary to the wild-type protein, CMT2D variants Gly-125 and Arg-294 strongly interact with NRP1. This interaction may compete out VEGFA binding and inhibits VEGFA-NRP1 signaling which is essential for motor neuron survival, as suggested by experiments done in a mouse model.  1 Publication

**Disease description:** A dominant axonal form of Charcot-Marie-Tooth disease, a disorder of the peripheral nervous system, characterized by progressive weakness and atrophy, initially of the peroneal muscles and later of the distal muscles of the arms. Charcot-Marie-Tooth disease is classified in two main groups on the basis of electrophysiologic properties and histopathology: primary peripheral demyelinating neuropathies (designated CMT1 when they are dominantly inherited) and primary peripheral axonal neuropathies (CMT2). Neuropathies of the CMT2 group are characterized by signs of axonal degeneration in the absence of obvious myelin alterations, normal or slightly reduced nerve conduction velocities, and progressive distal muscle weakness and atrophy.

Related information in OMIM

Feature key	Position(s)	Description	Actions	Graphical view	Length
Natural variant <sup>i</sup> (VAR_073187)	111	A → V in CMT2D; shows a reduction in aminoacylation activity.  2 Publications Corresponds to variant dbSNP:rs370531212 <a href="#">Ensembl</a> .			1
Natural variant <sup>i</sup> (VAR_018718)	125	E → G in CMT2D; phenotype overlapping with DSMA-V; complements the defect of the wild-type gene in yeast; contrary to the wild-type protein, strongly binds to NRP1 and competes with VEGFA for NRP1-binding; displays slightly elevated aminoacylation activity over wild-type.  5 Publications Corresponds to variant dbSNP:rs137852645 <a href="#">Ensembl</a> , <a href="#">ClinVar</a> .			1
Natural variant <sup>i</sup> (VAR_073188)	200	D → N in CMT2D and HMN5A; shows a large reduction in aminoacylation activity.  2 Publications			1
Natural variant <sup>i</sup> (VAR_074016)	200	D → Y in CMT2D.  1 Publication			1
Natural variant <sup>i</sup> (VAR_073189)	265	S → F in CMT2D and HMN5A; shows a large reduction in aminoacylation activity; demonstrates a change in the subcellular location pattern; does not associate with granules.  2 Publications Corresponds to variant dbSNP:rs1554337974 <a href="#">Ensembl</a> , <a href="#">ClinVar</a> .			1
Natural variant <sup>i</sup> (VAR_074017)	292	M → R in CMT2D.  1 Publication			1
Natural variant <sup>i</sup> (VAR_018720)	294	G → R in CMT2D; shows a large reduction in aminoacylation activity; does not impair transcription or translation or protein stability; contrary to the wild-type protein, strongly interacts with NRP1.  4 Publications Corresponds to variant dbSNP:rs137852643 <a href="#">Ensembl</a> , <a href="#">ClinVar</a> .			1
Natural variant <sup>i</sup> (VAR_073190)	298	P → L in CMT2D; shows a large reduction in aminoacylation activity; demonstrates a change in subcellular location pattern; does not associate with granules.  2 Publications Corresponds to variant dbSNP:rs137852648 <a href="#">Ensembl</a> , <a href="#">ClinVar</a> .			1
Natural variant <sup>i</sup> (VAR_073191)	334	I → F in CMT2D; shows a large reduction in aminoacylation activity; demonstrates a change in subcellular location pattern; does not associate with granules; unknown pathological significance.  3 Publications Corresponds to variant dbSNP:rs1554338260 <a href="#">Ensembl</a> , <a href="#">ClinVar</a> .			1
Natural variant <sup>i</sup> (VAR_073193)	554	D → N in CMT2D; demonstrates no change in subcellular location pattern.  1 Publication Corresponds to variant dbSNP:rs137852647 <a href="#">Ensembl</a> , <a href="#">ClinVar</a> .			1
Natural variant <sup>i</sup> (VAR_073195)	652	G → A in CMT2D; shows a large reduction in aminoacylation activity; demonstrates a change in subcellular location pattern; does not associate with granules.  2 Publications			1

## ▪ Are these natural variants close to the active site in **sequence**?

- Yes! Some examples.....
- The original function of our protein is the transfer of glycine to the cognate tRNA. At position 299 is the Glycine binding site. Change from Proline to Leucine at **position 298 as well as position 294 (Glycine → Arginine)** apparently leads to a large reduction of the aminoacylation activity (which is the intermediate formed during the “glycine transfer”). This might be due to the fact that the protein structure changes so that the glycine may not be accessible anymore.

- Same for the second glycine binding site (position 350). The variant (I → F) at position 334 also reduces aminoacylation activity
- At position 583 is the ATP binding site. (glycine transfer is ATP dependent). The variant where G → A at position 652 also leads to a reduction of the aminoacylation activity. But in this case it is not that the transfer of glycine is inhibited/reduced (e.g. due to inaccessibility) but the site where ATP binds.
- Find out more about your protein. What is its biological function? What does it do?
  - Catalyzes the ATP-dependent ligation of glycine to the 3'-end of its cognate tRNA, via the formation of an aminoacyl-adenylate intermediate (Gly-AMP) (PubMed:[17544401](#), PubMed:[28675565](#), PubMed:[24898252](#)).
- GO terms give you information about molecular function, cellular component, biological process. You can read more about them here: <http://geneontology.org/>
- •Report the GO terms for your protein.

#### GO - Molecular function:

- [ATP binding](#) : GO:0005524
- [bis\(5'-nucleosyl\)-tetrphosphatase \(asymmetrical\) activity](#): GO:0004081
- [glycine-tRNA ligase activity](#): GO:0004820
- [identical protein binding](#) GO:0042802
- [protein dimerization activity](#) GO:0046983
- [transferase activity](#) : GO:0016740

#### GO - Biological process:

- [diadenosine tetrphosphate biosynthetic process](#) GO: 0046983
- [glycyl-tRNA aminoacylation](#) GO: 0006426
- [mitochondrial glycyl-tRNA aminoacylation](#) GO: 0070150
- [tRNA aminoacylation for protein translation](#) GO: 0006418