Method

The 3D-structure of your protein of interest is known. Information from this 3D-structure will be obtained using WHAT IF Web services, the UniProt database and the Reprof software.

The structural information was obtained from the analysis of PDB:

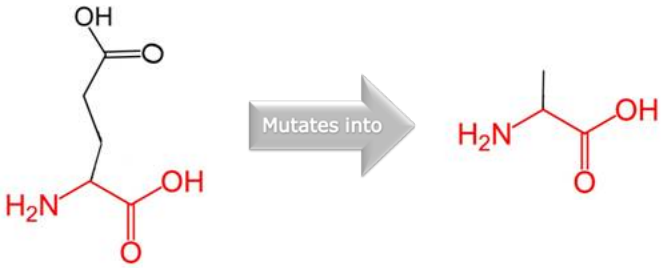
1EXT (http://www.rcsb.org/pdb/explore/explore.do?structureId=1EXT)
Annotations about this protein were obtained from UniProt entry

p19438 (http://www.uniprot.org/uniprot/p19438)
See the method page for more information.

Amino Acids

You are interested in the mutation of a Glutamic Acid into a Alanine at position 138.

The figure below shows the schematic structures of the original (left) and the mutant (right) amino acid. The backbone, which is the same for each amino acid, is colored red. The side chain, unique for each amino acid, is colored black.



Each amino acid has its own specific size, charge, and hydrophobicity-value. The original wild-type residue and newly introduced mutant residue often differ in these properties.

The mutant residue is smaller than the wild-type residue.

The wild-type residue charge was NEGATIVE, the mutant residue charge is NEUTRAL.

The mutant residue is more hydrophobic than the wild-type residue.

The report will evaluate the effect of the mutation on the following features: Contacts made by the mutated residue, structural domains in which the residue is located, modifications on this residue and known variants for this residue. A feature will only be shown when information is available. A short conclusion based on just the amino acid properties is shown always. In case a 3D-structure/model is available you will also find images and animations in the report.

Contacts

The wild-type residue forms a salt bridge with:

- Proline at position 368
- Leucine at position 390

The difference in charge will disturb the ionic interaction made by the original, wild-type residue.

Structure

The mutation is located within a stretch of residues that is repeated in the protein, this repeat is named TNFR-Cys 3. The mutation into another residue might disturb this repeat and consequently any function this repeat might have.

Conservation

The wild-type residue occurs often at this position in the sequence, but other residues have also been observed here.

Your mutant residue is among the other residue types that have been observed at this position in homologous sequences. This means that this mutation can occur at this position and is probably not damaging to the protein.

Domains

Interpro Domain	Gene Ontology Term	Broad Gene Ontology Term

Hope Version 1.1.1

Interpro Domain	Gene Ontology Term	Broad Gene Ontology Term
Tumour Necrosis Factor Receptor 1A IPR020419 (http://www.ebi.ac.uk/interpro/entry/IPR020419)	Tumor Necrosis Factor-Activated Receptor Activity GO:0005031 (http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0005031)	Molecular Transducer Activity GO:0060089 (http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0060089) Molecular_Function GO:0003674 (http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0003674)
Tnfr/Ngfr Cysteine-Rich Region IPR001368 (http://www.ebi.ac.uk/interpro/entry/IPR001368)	Protein Binding GO:0005515 (http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0005515)	Binding GO:0005488 (http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0005488) Molecular_Function GO:0003674 (http://www.ebi.ac.uk/QuickGO/GTerm?id=GO:0003674)
Tumor Necrosis Factor Receptor 1A, N-Terminal IPR033993 (http://www.ebi.ac.uk/interpro/entry/IPR033993)	None	None

The mutated residue is located in a domain that is important for binding of other molecules and in contact with residues in a domain that is also important for binding. The mutation might disturb the interaction between these two domains and as such affect the function of the protein.

The mutated residue is located in a domain that is important for binding of other molecules and in contact with residues in a domain that is important for the activity of the protein. The mutation might affect this interaction and thereby disturb signal transfer from binding domain to the activity domain.

The mutated residue is located in a domain that is important for binding of other molecules. The mutated residue is in contact with residues in another domain. It is possible that the mutation disturbs these contacts.

Amino Acid Properties

There is a difference in charge between the wild-type and mutant amino acid.

The charge of the wild-type residue is lost by this mutation. This can cause loss of interactions with other molecules.

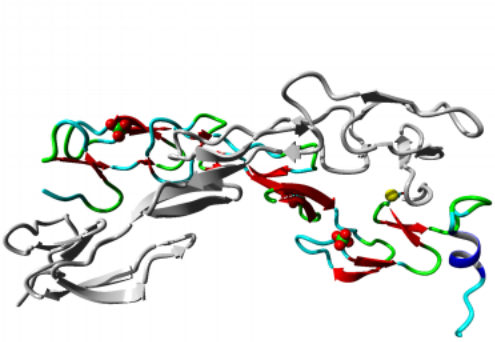
The wild-type and mutant amino acids differ in size.

The mutant residue is smaller than the wild-type residue.

This will cause a possible loss of external interactions.

The hydrophobicity of the wild-type and mutant residue differs.

Images



Download (/hope/yasara/5ecdbfa0-57b7-4570-b5d0-0def9401cf33/25ALA_overview.png/)

Overview of the protein in ribbon-presentation. The protein is coloured by element; α-helix=blue, β-strand = red, turn=green, 3/10 helix=yellow and random coil=cyan. Other molecules in the complex are coloured grey when present.

Citation

Please use the following citation when referencing the results in your report:

Protein structure analysis of mutations causing inheritable diseases. An e-Science approach with life scientist friendly interfaces.

BMC Bioinformatics. 2010 Nov 8;11(1):548. DOI: 10.1186/1471-2105-11-548. (http://dx.doi.org/10.1186/1471-2105-11-548) PubMed: 21059217. (http://www.ncbi.nlm.nih.gov/pubmed/21059217)