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 Cysteine into a Glycine at position 62.

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 is more hydrophobic than the mutant 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 is annotated in UniProt to be involved in a cysteine bridge, which is important for stability of the protein. Only cysteines can make these type of bonds, the mutation causes loss of this interaction and will have a severe effect on the 3D-structure of the protein.

Together with loss of the cysteine bond, the differences between the old and new residue can cause destabilization of the structure.

Structure

The mutation is located within a stretch of residues that is repeated in the protein, this repeat is named TNFR-Cys 1. The mutation into another residue might disturb this repeat and consequently any function this repeat might have.

The mutation introduces a glycine at this position. Glycines are very flexible and can disturb the required rigidity of the protein at this position.

Variants

This mutation matches a previously described variant, with the following description: Familial hibernian fever (FHF) [MIM:142680].

See the ExPASy site about this variant:

VAR_019303 (http://www.expasy.org/cgi-bin/variant_pages/get-sprot-variant.pl?VAR_019303)
The variant is annotated with severity: DISEASE

The mutation is located in a region with known splice variants, described as:

Familial hibernian fever (FHF) [MIM:142680] Familial hibernian fever (FHF) [MIM:142680]

Conservation

Only this residue type was found at this position. Mutation of a 100% conserved residue is usually damaging for the protein.

The mutant and wild-type residue are not very similar. Based on this conservation information this mutation is probably damaging to the protein.

Domains

Interpro Domain	Gene Ontology Term	Broad Gene Ontology Term
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. The mutated residue is in contact with residues in another domain. It is possible that the mutation disturbs these contacts.

Amino Acid Properties

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

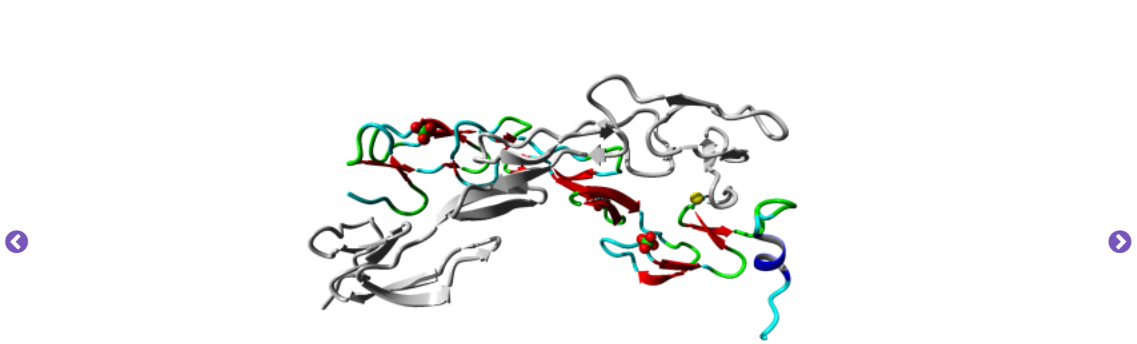
The mutant residue is smaller than the wild-type residue.

The mutation will cause an empty space in the core of the protein.

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

The mutation will cause loss of hydrophobic interactions in the core of the protein.

Images



Download (/hope/yasara/94214ee3-183d-441c-a1a1-c4a8e768cf26/16GLY_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)