

# Mutation@A Glance

## Quick guide

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# 1. Getting started

Access the web page via a modern web browser:

<http://mutation.nagahama-i-bio.ac.jp/>

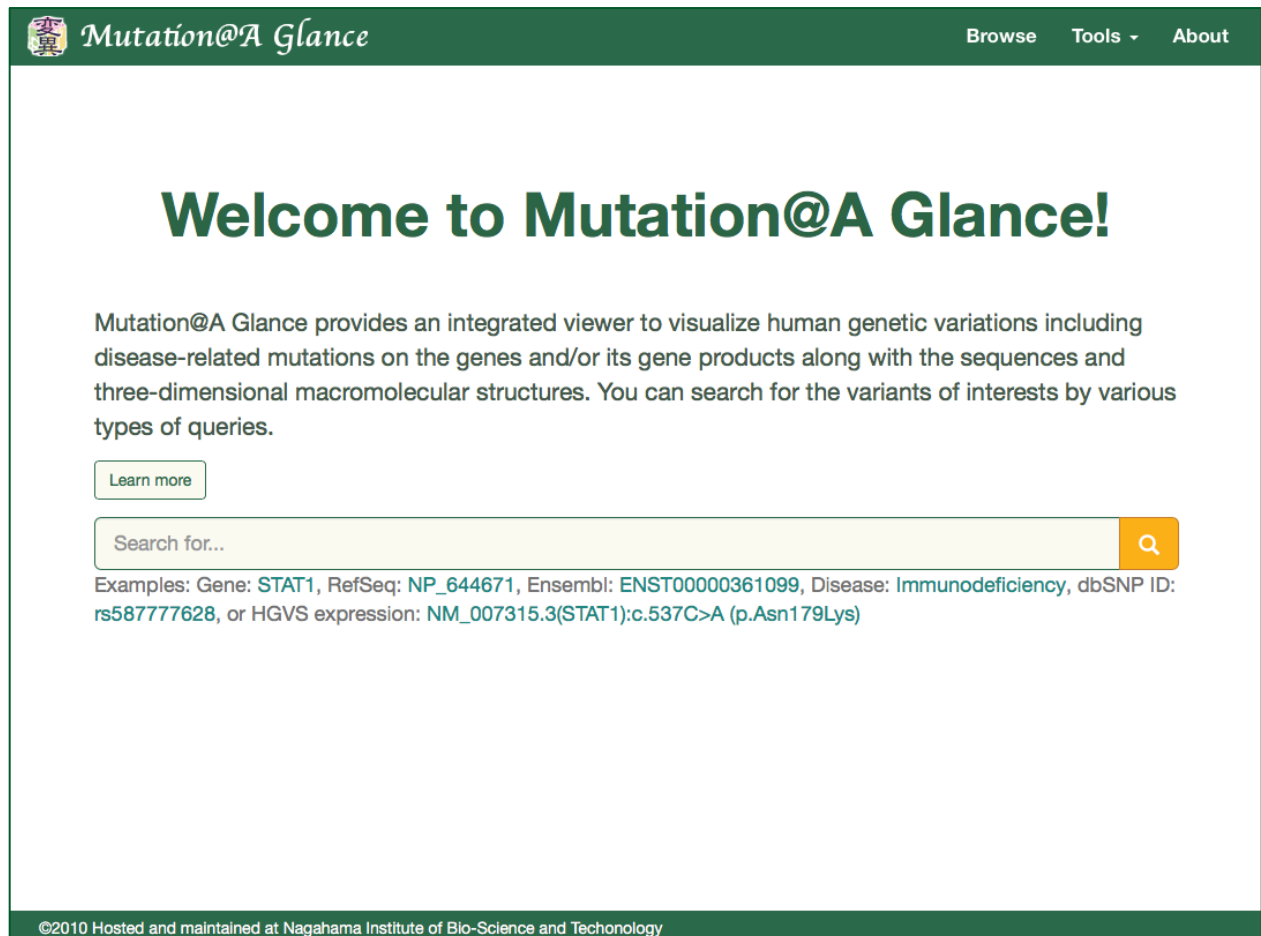


Fig.1 The home page of Mutation@A Glance.

## 1.1. Search for genes

Mutation@A Glance provides an integrated viewer to visualize human genetic variations including disease-related mutations on the genes and/or its gene products along with the sequences and three-dimensional macromolecular structures. You can search for the variants of interests by various types of queries.

[Learn more](#)

Search for...

Examples: Gene: [STAT1](#), RefSeq: [NP\\_644671](#), Ensembl: [ENST00000361099](#), Disease: [Immunodeficiency](#), dbSNP ID: [rs587777628](#), or HGVS expression: [NM\\_007315.3\(STAT1\):c.537C>A \(p.Asn179Lys\)](#)

Fig.2 The search form on the home page.

You can search for a gene of interest from the form shown above with various types of queries:

- Gene symbol,
- Gene/Protein names,
- Sequence accessions (RefSeq, Ensembl, UniProt),
- OMIM ID,
- Disease names, etc.

For instance, enter “STAT” in the text form and click the hand glass button.

## 1.2. Search result

Search result for "STAT1":

Genes 2 Diseases 3 ← Click

Gene ...	Location	Name	Type	Phenotypes
filter column	filter column...	filter column...	filter column...	filter column...
STAT1	Chr2:190,969,036-191,014,250	signal transducer and activator of transcripti...	protein-coding	OMIM
STAT2	Chr12:56,341,597-56,360,253	signal transducer and activator of transcripti...	protein-coding	OMIM

GO

Genes 2 Diseases 3 ← Click

OMIM ID	Title	Cytolocation	Gene(s) as...	Mode of Inheritances
#614892	Immunodeficiency 31A, mycobacteriosis, autosomal do...	2q32.2	STAT1	AD
#613796	Immunodeficiency 31B, mycobacterial and viral infectio...	2q32.2	STAT1	AR
#614162	Immunodeficiency 31C, autosomal dominant, 614162 (3)	2q32.2	STAT1	AD

GO

Fig.2 An example of the search result page.

When two or more genes or diseases are hit with the query term, each of them are listed separately. In the case, the result of search by "STAT1". Click either "Genes" or "Disease" tab to switch the view. Click "GO" button to jump the viewer for a given gene page.

# 1.3. Main view

The main view is shown when a given gene was selected. The view consists of two-layers, one for DNA and another for protein. If a protein-coding gene is selected, the protein layer is displayed first. At default, the genetic variants are mapped on 1) a schematic diagram of primary structure, 2) a multiple sequence alignment, 3) three dimension protein structures. The genetic variants are colored by its sources (ClinVar, COSMIC, or Polymorphisms (ExAC, 1000Genomes, 2KJPN). If pathogenic mutations associated with different OMIM accessions, they are colored differently.

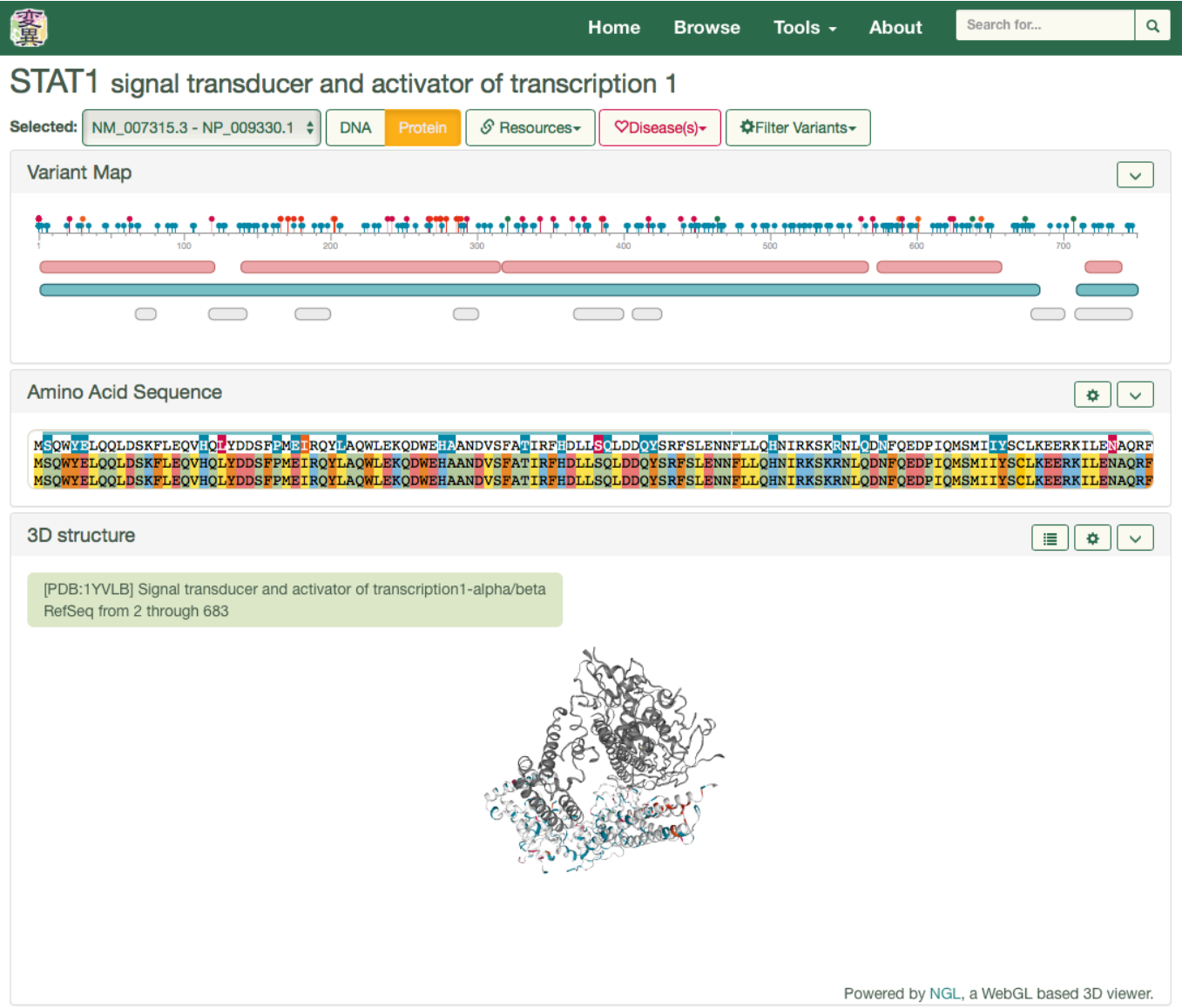


Fig.3 Main view for STAT1 gene at the protein layer.

## 1.3.1 Main page menus

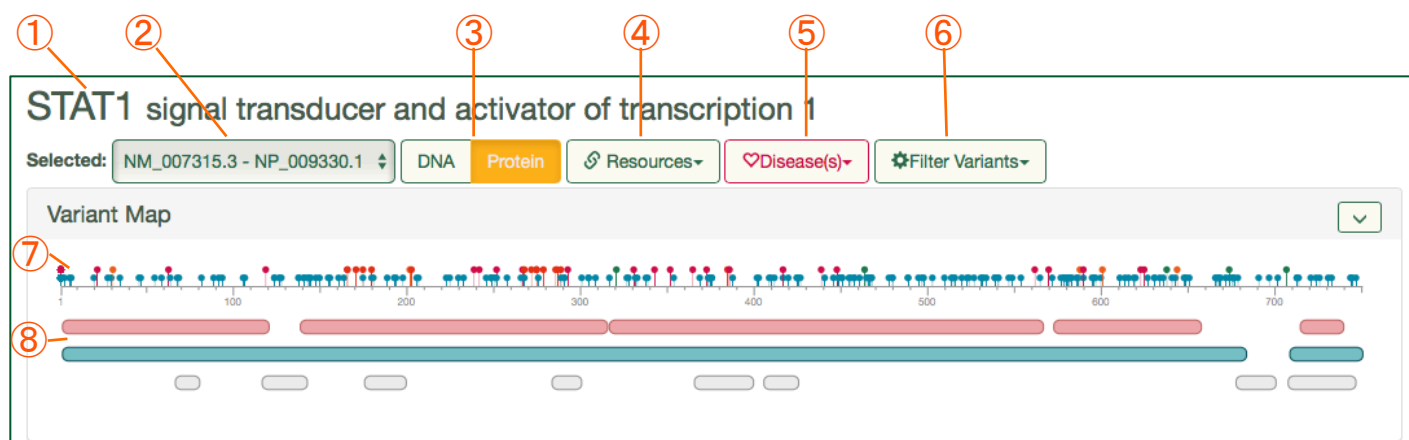


Fig.4 Main menu on the top of Main page for STAT1.

No.	Feature
1	Gene symbol, name
2	Sequence selection menu
3	Switch of DNA <-> Protein layers
4	Links to external resources for a given gene
5	List of diseases from OMIM with which the gene associated.
6	Filter menus for variant selection
7	Variant positions colored by the sources (described in the next section)
8	Protein features (Pfam domain, 3D structure known region, intrinsically disordered region, transmembrane helices, etc.)

## 1.3.2. Focusing on a specific variant

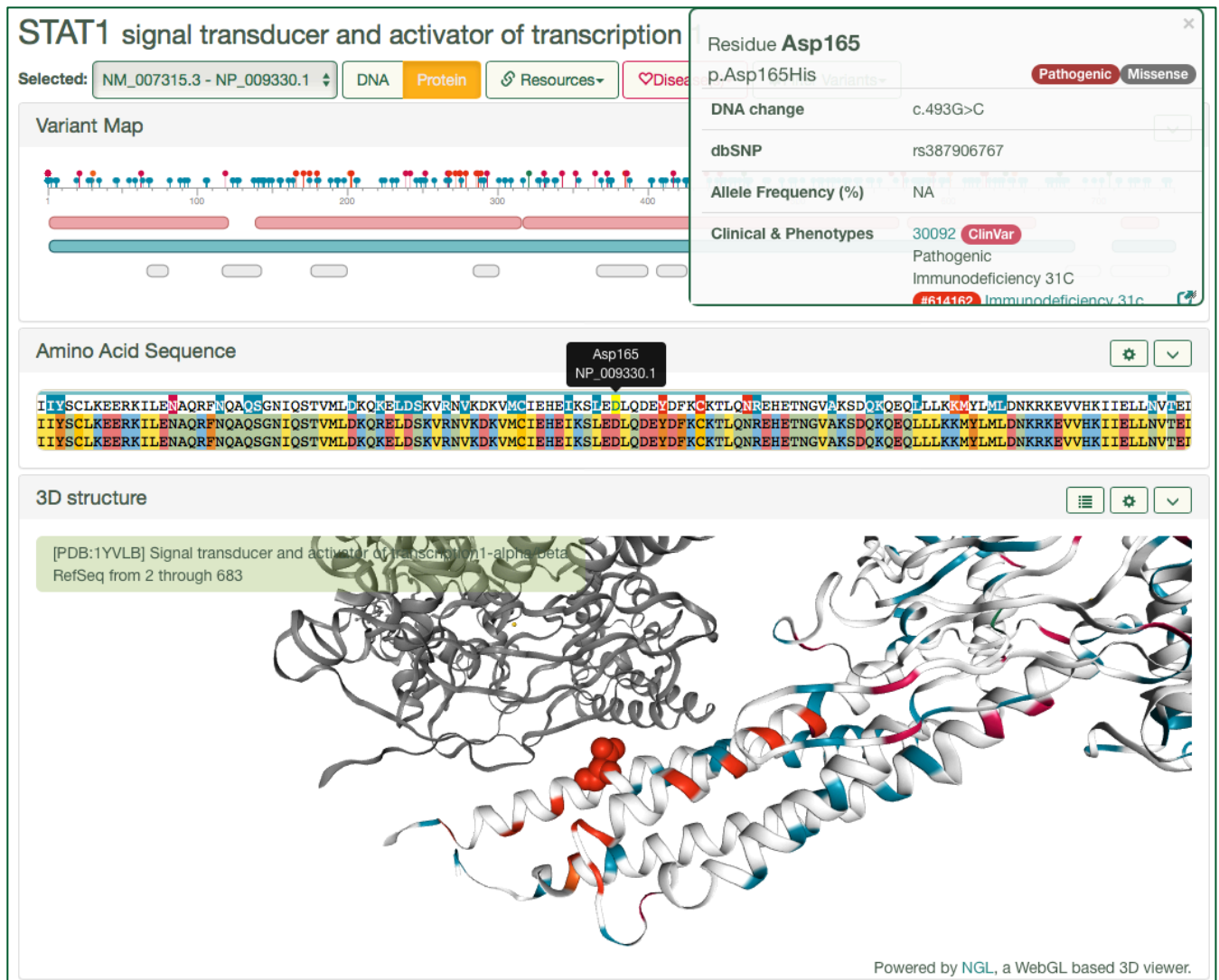


Fig.6 Focusing a specific variant (the case of Asp165)

Clicking a particular residues on on of the three view components (Variant Map, Amino Acid Sequence or 3D structure), the detail information of the residue is displayed in the small window. At the same time, the residue on sequence or 3D structure is highlighted and centered smoothly (Fig.6).



### 1.3.3. Filter variant menus

Click

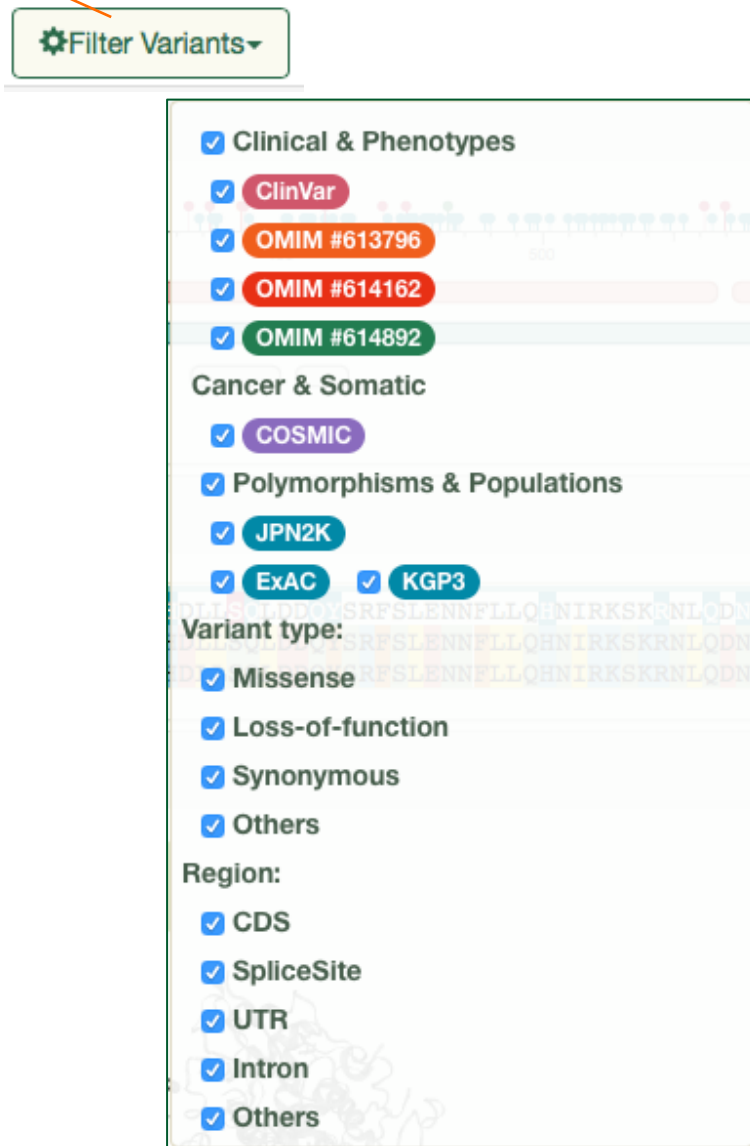


Fig.5 Filter menu

Clicking “Filter Variants” button on the main menu, the window shown above is displayed for variant selection. The variant on the schematic diagram, sequences, or 3D structures are colored by the ones indicated in the window. If you check-off the checkbox, the variants are disappeared from the view page. You also filter the variants by combination of the checkboxes, e.g. selection only in ClinVar and Missense variants.

In this case, there are mutations associated with three diseases in OMIM (#613796, #614162, #614892) indicated by different colors, and filtered other variants to display only these mutations.

#613796

Immunodeficiency 31b [AR]

#614162

Immunodeficiency 31c [AD]

#614892

Immunodeficiency 31a [AD]

Fig.6 Disease list

☒ Clinical & Phenotypes

☐ ClinVar

☒ OMIM #613796

☒ OMIM #614162

☒ OMIM #614892

Cancer & Somatic

☐ COSMIC

Polymorphisms & Populations

☐ JPN2K

☐ ExAC

☐ KGP3

Variant type:

☒ Missense

☐ Loss-of-function

☐ Synonymous

☐ Others

Fig.7 Variant selection

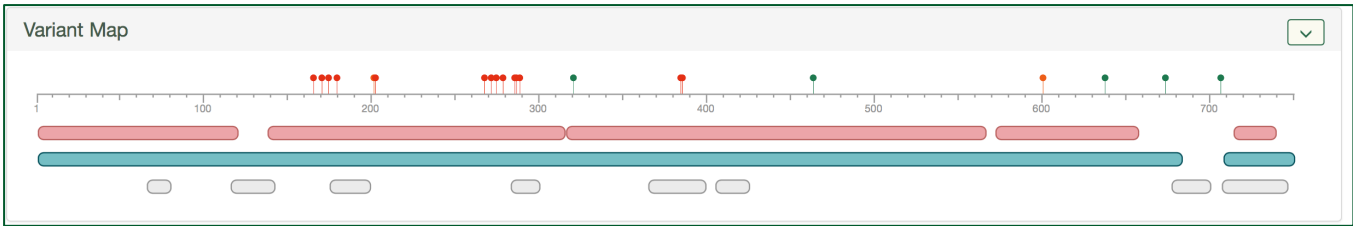


Fig.8 Variants only selected are displayed.

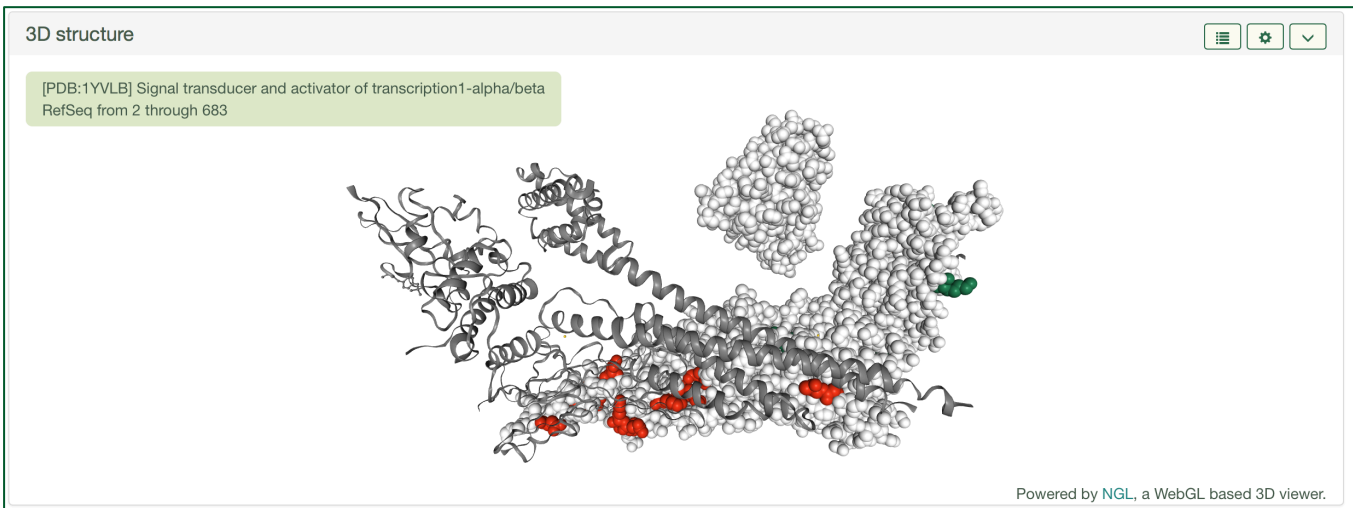


Fig.9 Variants colored red associated with MIM #614162 are spatially located in the interface of the dimer interface.

If two or more structures are available, you can switch the structure to map the variants by clicking the list button shown on the title bar of the 3D structure. If the click the button, a modal window is displayed (Fig. 11)



Fig.10 The title bar of 3D structure.

Available Structures for STAT1

Monomer structure(s)

Region	PDB	Exper...	Resol...	Molecule name	Seq.I...	3D
	1YVL[B]	X-RAY	3.0	Signal transducer and activator of transcriptio...	95.7	<button>View</button>
	2KA6[B]	NMR	NA	Signal transducer and activator of transcriptio...	97.6	<button>View</button>

Biological complex structure(s)

Region	PDB	Exper...	Resol...	Molecule name	Seq.I...	3D
	1YVL[B]	X-RAY	3.0	Signal transducer and activator of transcriptio...	95.7	<button>View</button>
	4E68[A]	X-RAY	2.6	Signal transducer and activator of transcription 3	54.1	<button>View</button>
	1BG1[A]	X-RAY	2.3	Protein (transcription factor stat3b)	54.1	<button>View</button>
	1BF5[A]	X-RAY	2.9	Signal transducer and activator of transcriptio...	94.8	<button>View</button>
	3CWG[B]	X-RAY	3.0	Signal transducer and activator of transcription3	54.2	<button>View</button>
	3WWT[A]	X-RAY	2.0	Signal transducer and activator of transcriptio...	100.0	<button>View</button>
	4ZIA[D]	X-RAY	2.7	Signal transducer and activator of transcription 3	54.2	<button>View</button>
	1BGF[A]	X-RAY	1.4	Stat-4	53.4	<button>View</button>
	2KA6[B]	NMR	NA	Signal transducer and activator of transcriptio...	97.6	<button>View</button>

Close

Fig.11 The list of structures available

If one of the “View” button without highlighted is clicked, another structure data is loaded. In this case, 1BF5A was selected. Interestingly, the mutations associated with MIM #614892 are located in spatially different region, namely DNA binding site or another interface for dimerization. For more details, refer to our recent paper (Hijikata et al., Sci. Rep., 2017).

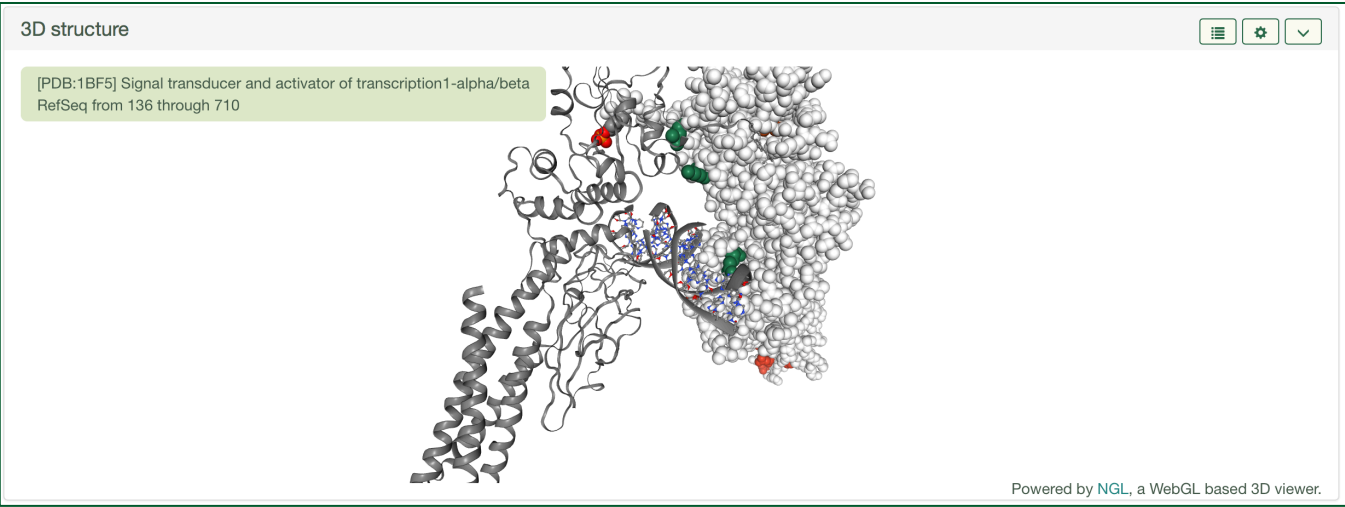


Fig.12 Variants located in another structures.

## 1.4 View at the DNA level

Variants without protein-coding region, namely UTR, splice sites or 5' or 3' flanking region can be viewed at the DNA level.

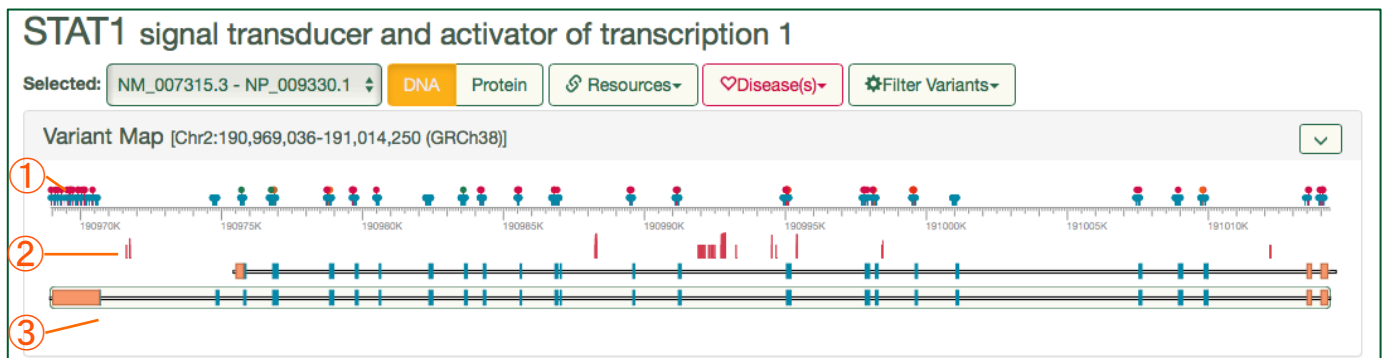


Fig.7. Main view at the DNA level

No.	Feature
1	Variant positions colored by the sources (described in the next section), same as view at protein level.
2	Low mappability score region calculated by GEM mappability program ( <a href="http://algorithms.cnag.cat/wiki/The_GEM_library">http://algorithms.cnag.cat/wiki/The_GEM_library</a> ).
3	Transcripts mapped on the genomic locus.

## 2. Search for variants

### 2.1. Search by accessions, etc.

The variants can be specified by:

- Variant IDs (dbSNP rsID, COSMIC accessions)  
e.g. rs774611299, COSM6240
- HGVS expression  
e.g. NM\_005228.3(EGFR):c.2369C>T (p.Thr790Met),  
NM\_005228.3:c.2369C>T
- Variant with colon delimited format  
e.g. chr7:55181378:C:T

All of the expressions above are acceptable from the search form on the homepage.

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Fig.8 The search form on the home page.

 [Home](#) [Browse](#) [Tools](#) [About](#) Search for... 

Fig.9 The search form in the navigation bar.

## 2.2. Search by sequences.

DNA sequences containing genetic variants can be detected by aligning with the reference genome. A multi-FASTA format is acceptable.

HomeBrowseTools ▾AboutSearch for...

# Mutation Finder

This functions to find mutations from input DNA sequences by aligning to the DNA sequence of a given gene.

Please specify a gene symbol and a sequence file with multi-FASTA format.

Gene symbol


FASTA file

Choose

Submit

## 2.3. Search by VCF file.

Batch job for mapping is available with a VCF file. Currently a limitation of the number of variants (up to 500 variants).

HomeBrowseTools ▾AboutSearch for...

# Variant Mapper

This tool enables to map variants on the genomic or protein coordinate including macromolecular structures. Please upload a VCF file to map.

NOTE: Currently **500** variants at maximum can be uploaded for limitation of the computation resources.

VCF file

Choose

Submit

