

## CARGO: Cancer And Related Genes Online

### I. Introduction

A central aim of cancer research has been to identify the mutated genes that are causally implicated in oncogenesis. In 2004, Futreal *et al.* (*Nat Rev Cancer.*; 4(3):177-8) and Bamford *et al.* (*Br J Cancer.*; 91(2):355-8.) introduced a 'census' of cancer genes that indicates that somatic mutations in more than 1% of genes contribute to human cancer.

More recently, Sjöblom *et al.* (see *Science.* 2006; 314(5797):268-74) reported the analysis of large-scale genetic variability data generate lists of Candidate Cancer Genes associated with different types of cancer (breast and colon carcinomas). In this work, the authors described Candidate Cancer Genes as those genes most likely to have been subjected to mutational selection during tumorogenesis. Candidate Cancer Genes list reported includes genes previously observed to be mutationally altered in human cancers, but also, genes in which no previous mutations in human cancers had been discovered but had been linked to cancer through functional studies and genes with no previous strong connection to neoplasia.

CARGO has been constructed in order to provide complete information regarding Candidate Cancer Genes (and other cancer-related genes) using user-friendly interface for control and visualization of information.

### II. Terms of Use

CARGO is a free service from the academic domain - free to use for anyone. CARGO is free of charge, thus its continuity will depend on the community it was created for.

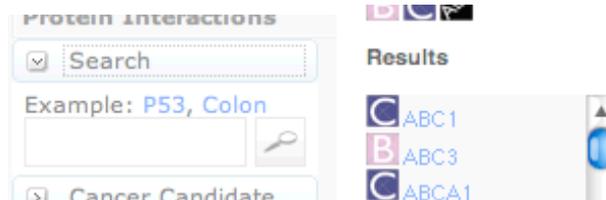
### III. Requirements

**CARGO works best in Mozilla Firefox 2.0.** If you use Explorer or previous versions of Firefox expect some glitches (view here the [known issues](#)). At this point, it does not support Safari or other Browsers such as Opera. We are working on extending support for other browsers. Some bioWidgets have additional requirements, check here the [full list](#).

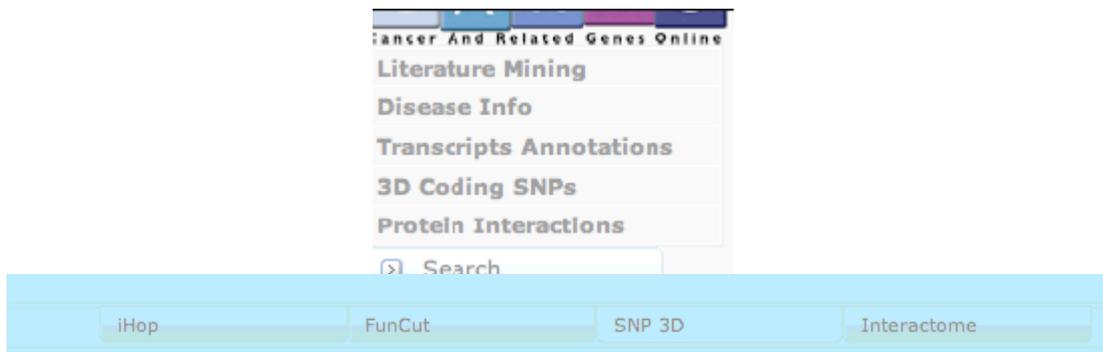
#### IV. Quick Start

CARGO displays biological information for human genes. To start using Cargo, follow these steps:

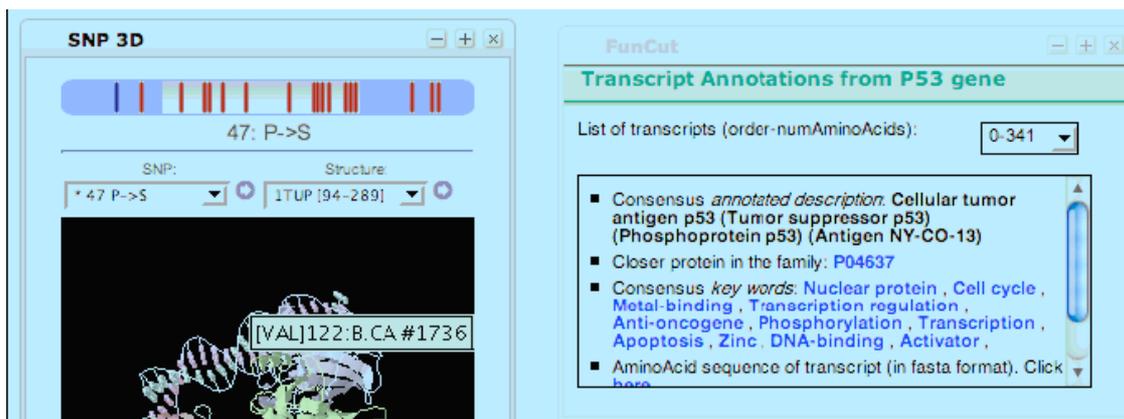
1. Search for a term (like "colon") or gene name ("p53") to obtain a list of genes or use one of our previously compiled gene lists.



2. Activate a few widgets, by clicking on their names on the top left or in the tabs on top of the Main board.



3. Click on one of the genes from the list and watch the information in the widgets refresh accordingly. That's it!



[Enter CARGO here](#)

## V. What can I get using CARGO?

CARGO reports complete information about experimentally described Candidate Cancer Genes obtained in large-scale genetic variability experiments among different types of tumours allowing gene/protein or disease queries (e.g. BRCA2, PCA, colon carcinoma, breast...). Moreover, CARGO permits to obtain accurate and detailed information concerning a particular gene/protein of your interest avoiding slow and tedious work searching in different databases and servers. The final goal of this tool is helping to answer biological questions integrating available public information (customizable according to the user needs) from different sources. Thus, this server presents all the user-required information all at once in a fast, flexible and intuitive way. Here, you can select *a priori* the type of information in which you are interested for your gene/protein (structural, literature mining, SNPs, interactions, etc) and display it interactively using bioWidgets.

## VI. What are the bioWidgets?

bioWidgets are the functional elements of CARGO. Control and visualization elements, which can be individually selected by users and which organize themselves to form a web control panel via the user interface (See Figure 3). In other words, CARGO is able to load the whole information concerning a particular gene showing only those fields (bioWidgets) in which you are interested.

Currently, 5 bioWidgets are implemented in CARGO:

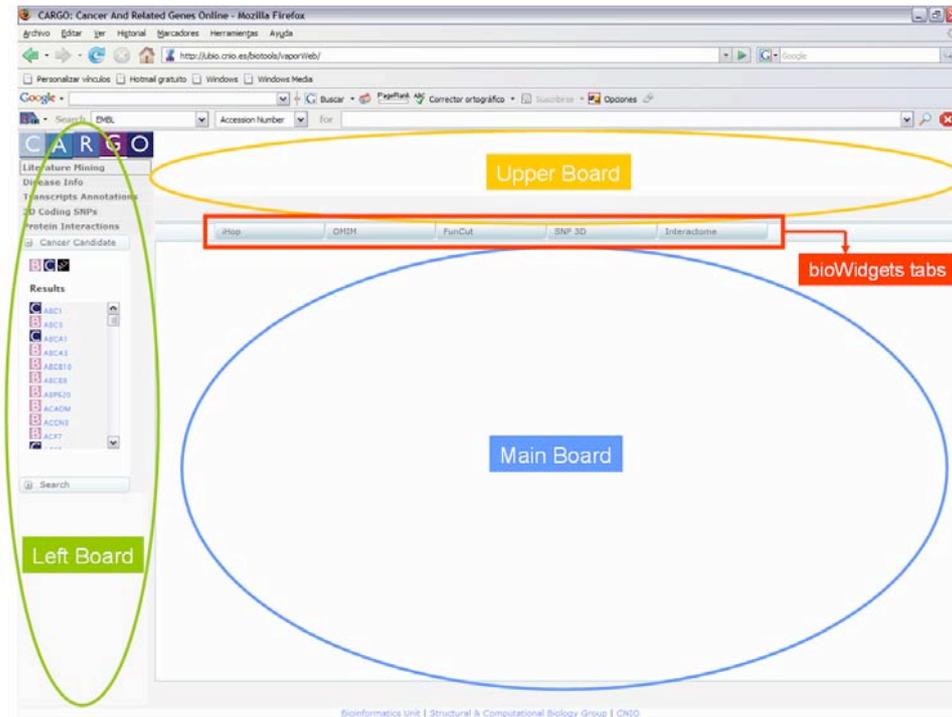
1. *3D Coding SNPs.*
2. *Literature Mining.*
3. *Transcripts Annotations.*
4. *Protein Interactions.*
5. *Disease Info.*

For more information about how to use bioWidgets go to “Using bioWidgets” Section.

## VII. How to use CARGO

Once you have opened CARGO, you'll find that the interface is organized in 3 boards (left, upper and main boards) as it is shown in Fig. 1.

Figure 1. CARGO interface arrangement.



Left board includes (from top to bottom): 1) bioWidget accession menu, 2) Cancer Candidate tab and 3) Search tab (see Fig. 2). By default, you'll notice Cancer Candidate tab is already opened showing the complete list of all Candidate Cancer Genes available (currently breast and colon). Search tab is closed by default. Upper and Main boards will contain query information and bioWidgets, respectively. In this sense, Main board contains minimized bioWidgets by default. Click on bioWidgets tabs to open those widgets of your interest ...

### **Searching for information related to Candidate Cancer Genes.**

**CARGO allows you to filter Candidate Cancer Genes List depending on a particular type of cancer you are interested in.** Suppose you want to have a look to a list of Candidate Genes related to breast cancer. Just clicking on B icon at Candidate Cancer Genes List options (Figure 2) you'll be able to filter candidate genes of your interest. Currently available options are: B=show breast related genes; C=show colon related genes; A=show all candidate genes.

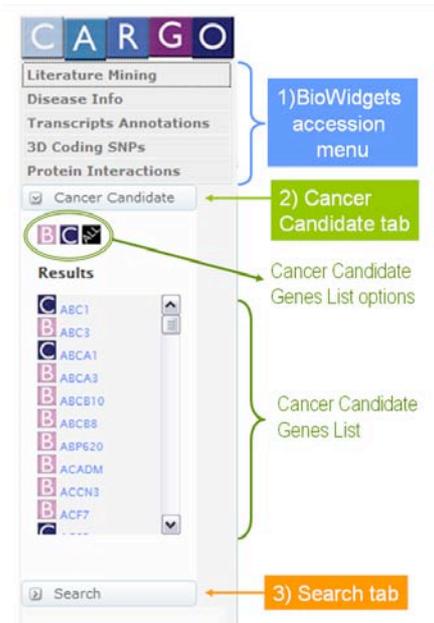
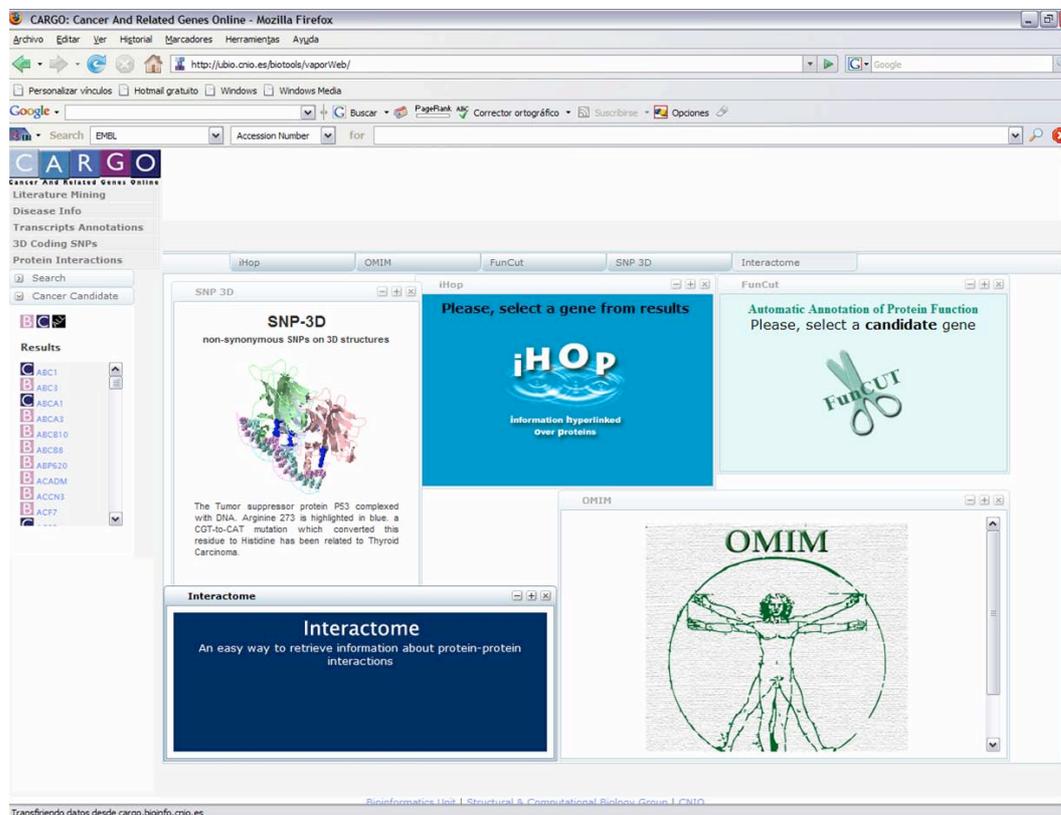


Figure 2. CARGO's Left board and Cancer Candidate tab organization.

You can access to individual gene descriptions of the Cancer Candidate Gene List rolling over gene names with your mouse pointer. This information will be localized under Search tab. At this point, you should activate those bioWidgets you are interested using bioWidgets Tabs. See Cargo's appearance after loading all bioWidgets in Figure 3. Once you have selected a particular gene make click on its gene symbol to display gene information in the bioWidgets. Loading bioWidgets after launching your query is also accepted.

Figure 3. CARGO's bioWidgets loaded on Main Board

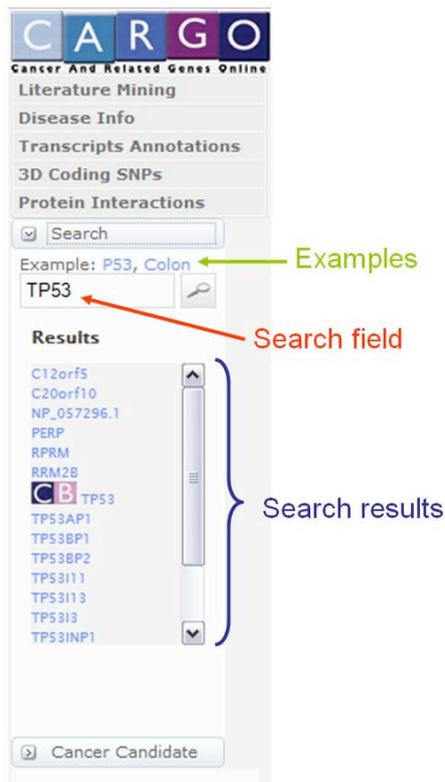


## Searching for information related to specified genes.

Typically, researcher is interested in information on a specific gene or protein. To launch a generic search simply click on Search tab (Fig. 4) to display the search field, next type a synonym (e.g. TP53), an Ensembl accession number (e.g. ENSG00000141510) or click on the available examples to start the query.

Search results will be listed below the search field providing all those genes related to your query. Rolling over gene names/identifiers you can access to individual gene descriptions. This information will be localized under Search tab. Note that those results described as Candidate Cancer Genes will be pointed out with icons (B icon for breast and C for colon cancer-related genes). Next, open those bioWidgets you are interested. Once you have selected a particular Search results, click on its gene symbol or identifier to display gene information in the bioWidgets. Of course, as mentioned before, you can open the bioWidgets after launch your query.

Figure 4. Search tab organization.



## Using bioWidgets

In this section, we'll see how to interpret biological data supplied by bioWidgets individually. Keep in mind that all this information corresponds to one gene selected a priori by the user. Ensembl accession number (ENSG00000141510), Gene symbol (e.g. TP53) and a brief description of this chosen gene will be available continuously in the Upper Board. Whether you change your gene of interest, information supplied by Upper Board and bioWidgets will be updated for the new selection.

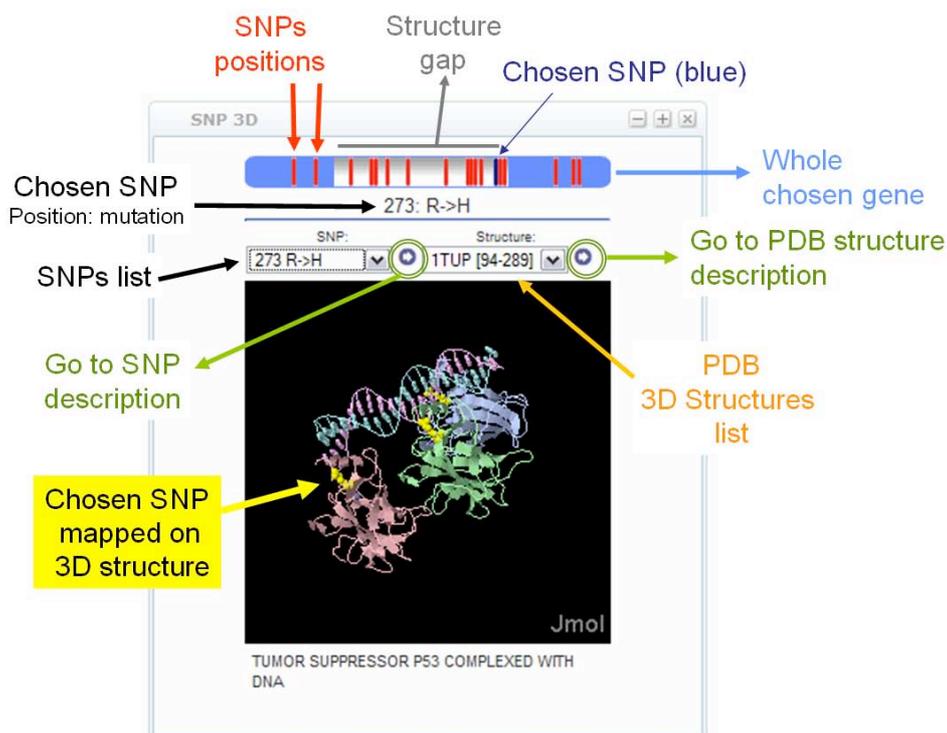
### 1. 3D CODING SNPS bioWIDGET.

This bioWidget integrates information concerning Single Nucleotide Polymorphisms (SNPs) and protein 3D structure obtained from Ensembl and Protein Data Bank (PDB), respectively.

Using 3D Coding SNPs bioWidget you can:

- Display an interactive protein 3D structural model of a particular gene/protein choosing an option in PDB 3D Structures pull down list (See Fig. 5). Gene sequence included in 3D structure is showed in Structure gap included in the upper blue bar representing the whole chosen gene.
- Obtain information concerning SNPs described in the gene of interest. Look at whole chosen gene schema, red lines corresponds to SNPs positioning in the gene sequence, clicking on them you can select a particular SNP. Position and amino acid change is described just below the schema and in the SNPs drop down list. You can also access directly to NCBI SNP information clicking on arrow button next to SNPs list.
- Map SNPs on the 3D protein model. Just click on the SNP you want to map. SNP position in the 3D structure will be highlighted by yellow dots.

Figure 5. 3D Coding SNPs bioWidget appearance and options.

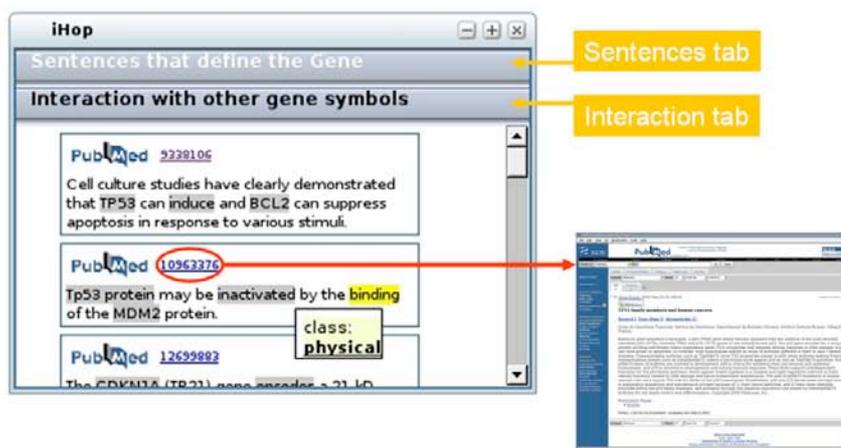


## 2. LITERATURE MINING bioWIDGET.

You should load the text-mining tool iHOP (Information Hiperlinked over Proteins) whether you want to track specific query-related information in PubMed abstracts.

This bioWidget contains 2 main tabs: a) Open Sentences tab you'll access to **all sentences found in the literature that mention your queried gene** together with relevant biomedical terms (Fig. 6). b) Interaction tab shows **literature-described interactions for your query** with another gene symbols. Clicking on PubMed IDs you'll access directly to PubMed abstracts related with your queried gene/protein.

Figure 6. Literature bioWidget appearance and options.



### 3. TRANSCRIPTS ANNOTATIONS bioWIDGET.

Transcripts Annotations bioWidget uses FUNCut algorithm (Abascal & Valencia, Proteins, 2003, vol. 53, nº3, pp.683-692) to generate **automatic functional annotations for Candidate Cancer Genes** from SwissProt y TrEMBL. Use the List of Transcripts drop-down menu (red circle in Fig. 7) to select the transcript you are interested in and explore the annotations on the underneath panel. Click on annotations for direct accession to the biological database source.

Note: Transcripts Annotations bioWidget works for Candidate Cancer Genes only.

Figure 7. Transcript Annotations bioWidget.

The screenshot shows the FunCut web interface for the P53 gene. The main window is titled "FunCut" and "Transcript Annotations from P53 gene". It features a dropdown menu labeled "List of transcripts (order-numAminoAcids):" with "0-341" selected. Below this, there are three main annotations:

- Consensus annotated description: **Cellular tumor antigen p53 (Tumor suppressor p53) (Phosphoprotein p53) (Antigen NY-CO-13)**
- Closer protein in the family: **P04637**
- Consensus key words: **Nuclear protein, Cell cycle, Metal-binding, Transcription**

Green arrows point from these annotations to other parts of the interface: from the dropdown menu to a UniProt entry for P53, from the "P04637" link to a UniProt entry for P04637, and from the key words to a KEGG pathway diagram. A separate window shows "BLAST info" results. At the bottom, a FASTA sequence for TP53 is provided:

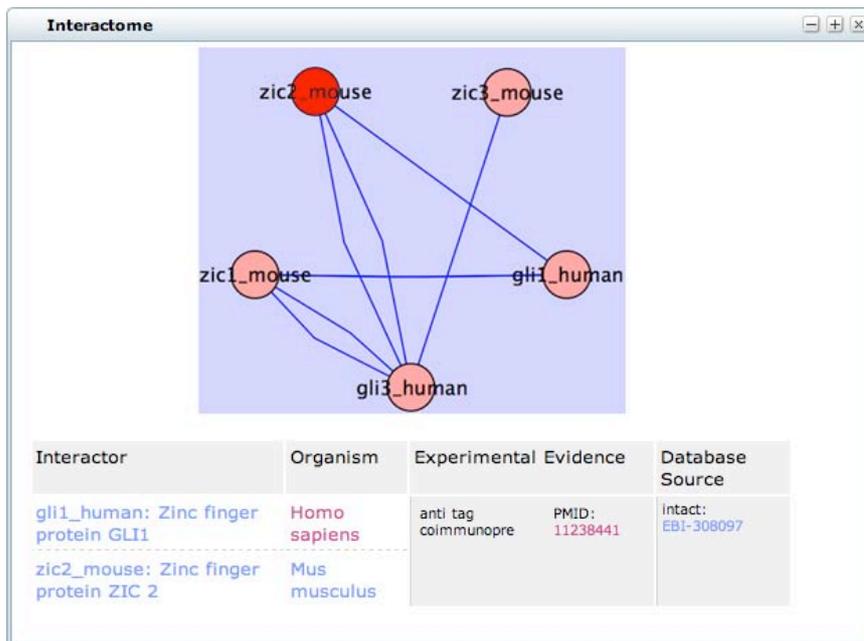
```
>TP53_ENSP00000352610
MEEPQSDPSVEPPLSQETFSDLWKLLPENNVLSPLP
SQAMDDLMLSPDDIEQWFTEDPGPDEAPRMPEAAP
PVAPAPAAPTAPAPAPAPSWPLSSSVPSQKTYQGSY
GFRLGFLHSGTAKSVTCTYSPALNKMFCQLAKTCPVQ
LWVDSTPPPGRVRA
```

#### 4. PROTEIN INTERACTIONS bioWIDGET.

Taking cPath as main source, this bioWidget **supplies entire information for direct interaction relationships** regarding the gene/protein of interest and other proteins. Inside the Protein Interactions widget also you will get:

- A graph with the existing protein-protein interactions of a given one (see Fig. 8)
- The experimental evidences of the interaction, links to literature abstracts (PMID) describing interactions and accession to source database (IntAct).

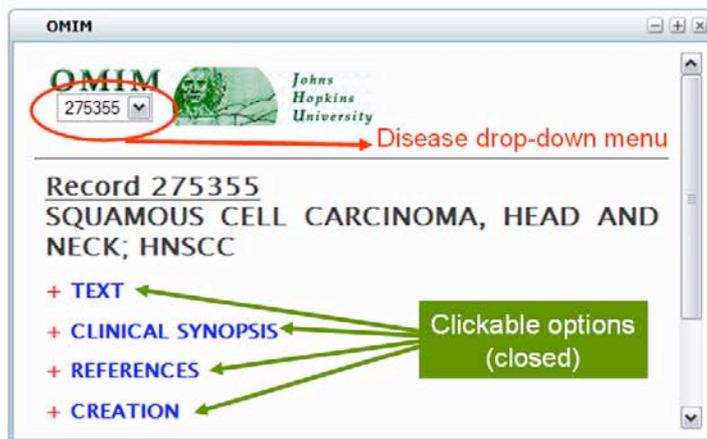
Figure 8. Protein Interactions bioWidget. Graph, interaction information and links.



## 5. DISEASE INFO bioWIDGET.

This widget reports a drop-down menu including NCBI OMIM [annotations for diseases in which provided gene/protein is implicated](#). Use Disease drop-down menu (Fig. 9) for disease selection. Clickable options are available for independent to accession to OMIM contents (text, clinical synopsis, references, creation, edit history, etc).

Figure 8. Disease Info bioWidget. Disease drop down menu and options.



## VII. Acknowledgments

CARGO displays information from different sources. We are thankful to the developers and Institutions that put their information and services freely available for the scientific community. Enter here to view [the full list](#).

## VIII. Contact

This CARGO website is powered by the **Bioinformatics Unit** and **Protein Design Group** Spanish National Cancer Research Centre (CNIO), Madrid, Spain.

This tutorial has been prepared by [Gonzalo Gómez](#).  
If you have questions or comments, please write to [Ana Rojas](#).

Last modified: December 2006.

