Protein Interaction Data Sources

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Biotechnology Centre of Oslo
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MBV-INF 4410/9410
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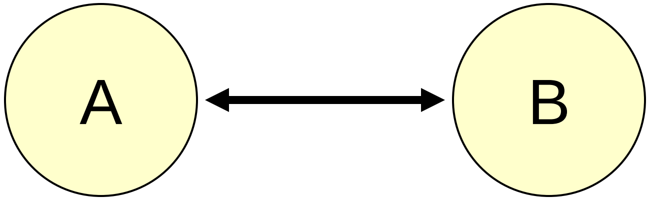
http://donaldson.uio.no/wiki/Protein_Interaction_Resources

http://irefindex.uio.no

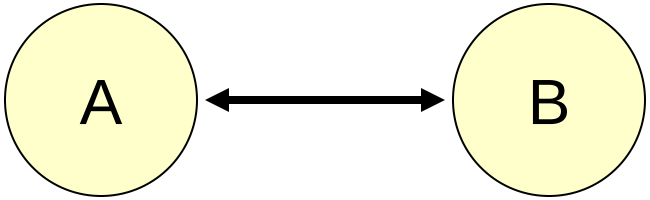
Overview

1. A simple interction record
2. Experimental methods
3. Representation of interactions
4. Interaction databases
5. Identifiers
6. Text mining sources
7. Predicted interaction sources
8. Consolidated databases
9. Visualization tools
10. Applications

A simple interaction record



A simple interaction record

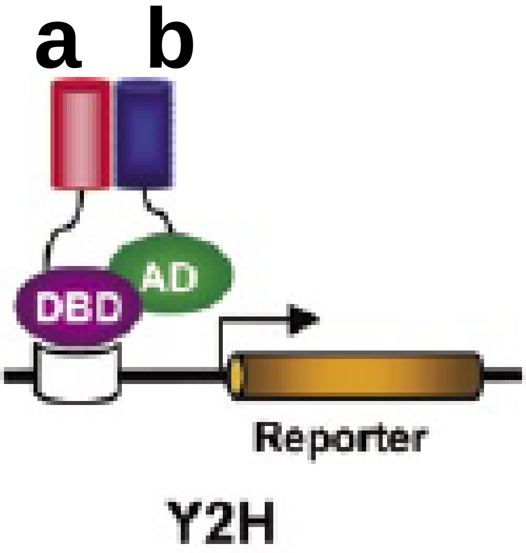


1. Short label
2. Type of molecule
3. Database identifier
4. Origin

5. Short label
6. Type of molecule
7. Database identifier
8. Origin

9. Publication reference

Experimental methods – Yeast Two Hybrid



http://en.wikipedia.org/wiki/Yeast_two-hybrid

Experimental methods
Two Hybrid family

Advantages

- an ”in vivo” binding assay
- easy to automate
- detects binary interactions

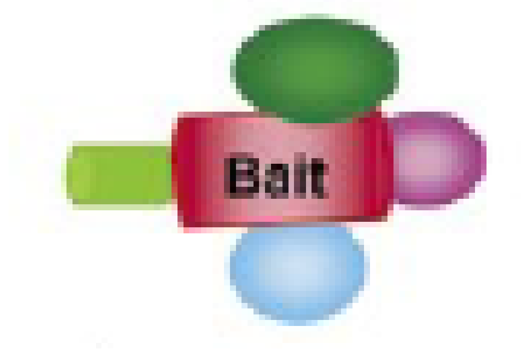
Experimental methods
Two Hybrid Family

Limitations

- false positives due to
  - sticky or activating bait or prey
  - overexpression
  - mis-localization (contextual specificity)
  - intermediary proteins

- false negatives due to
  - disruption of interaction by fusion construct
  - absence of intermediary proteins
  - absence of native taxon context

Experimental methods
Affinity purification



- interacting proteins are purified by mea of an affinity tag on a ”bait” protein
- proteins are detected via MS
- readout of this experiment type is a list of proteins that somehow interact with the bait protein
- note this is fundamentally different than readout of the Y2H family of experiments (more later)

Suter 2008, Biotechniques

Experimental methods
Affinity purification family

Limitations

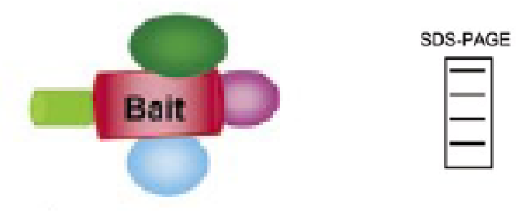
- false positives due to
  - sticky bait or prey
  - mis-identification during MS
  - non-native binding environment

- false negatives due to
  - mis-identification during MS
  - non-native binding environment

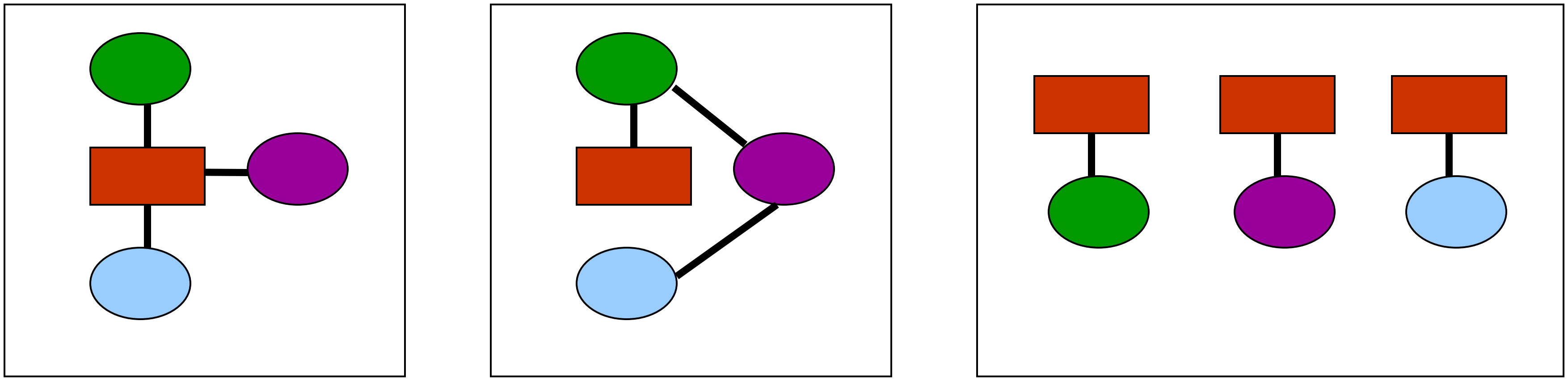
Experimental methods
Affinity purification family

Advantages

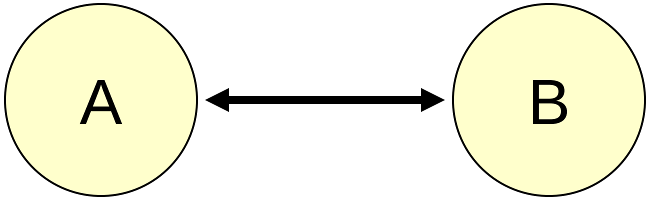
detection of protein complexes but no topology or stoichiometric data



This observation has multiple interpretations:



A simple interaction record



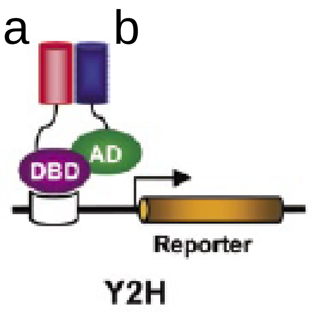
1. Short label
2. Type of molecule
3. Database identifier
4. Origin

5. Short label
6. Type of molecule
7. Database identifier
8. Origin

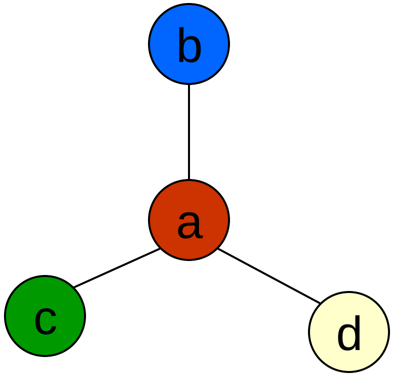
9. Publication reference

Representation of interaction data

binary data versus associative data



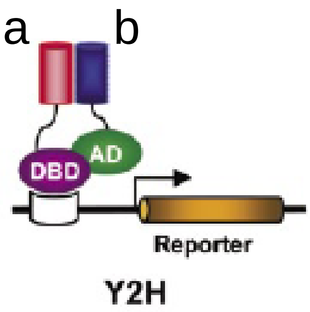
exp	bait	prey
1	a	b
2	a	c
3	a	d



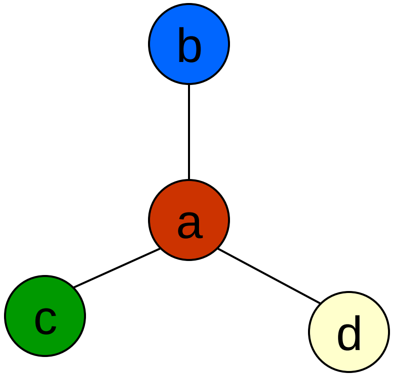
Suter 2008, Biotechniques

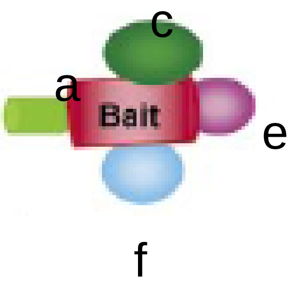
Representation of interaction data

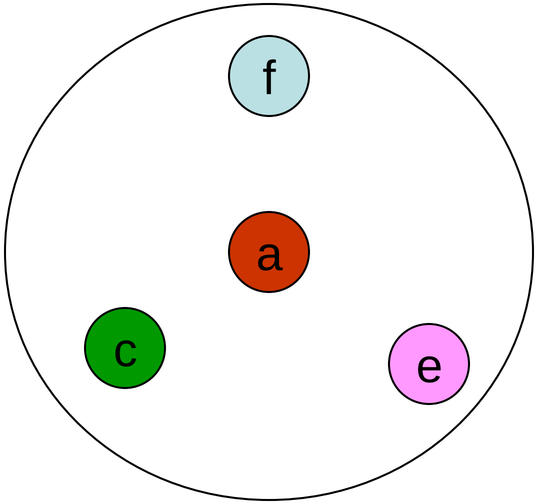
binary data versus associative data



exp	bait	prey
1	a	b
2	a	c
3	a	d



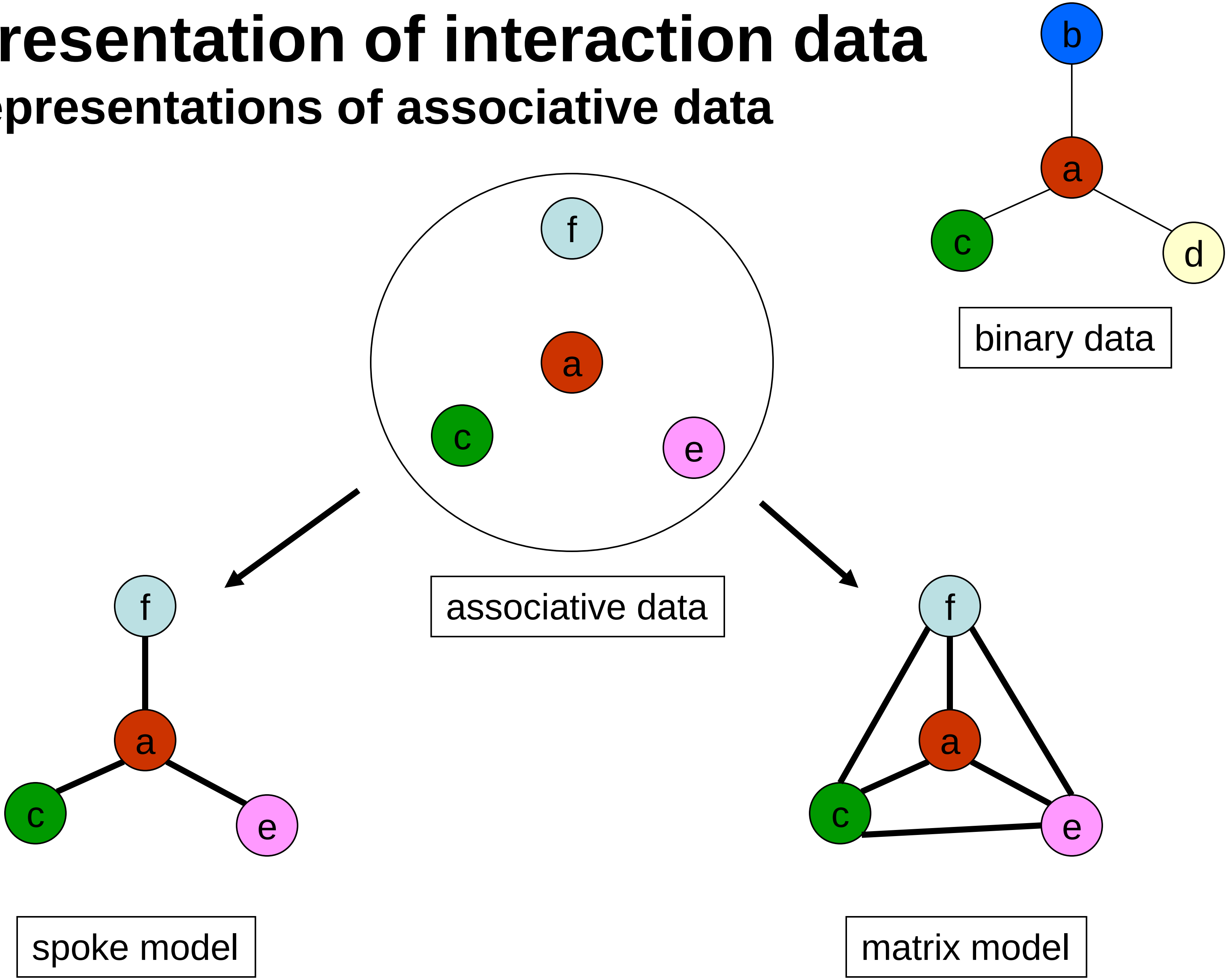




Suter 2008, Biotechniques

Representation of interaction data

misrepresentations of associative data



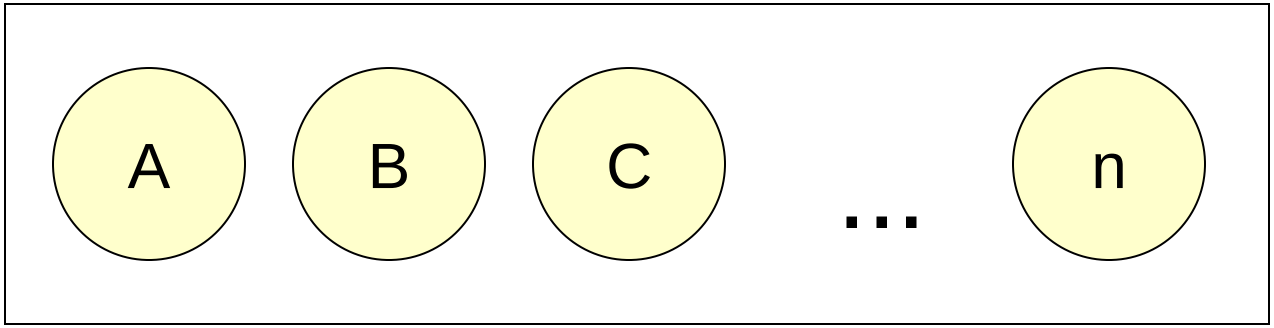
binary data

associative data

spoke model

matrix model

A simple interaction record

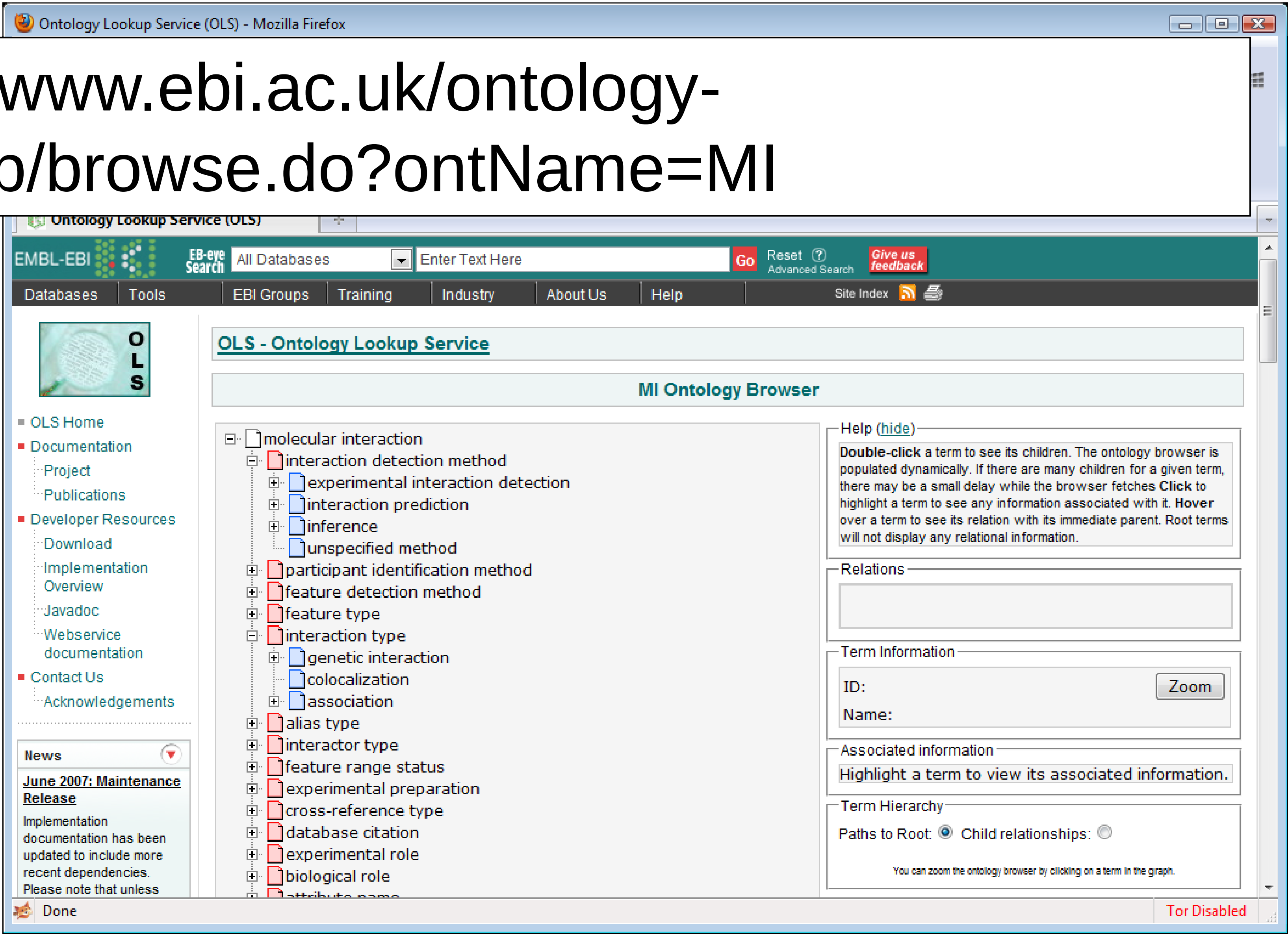


For each interactor
1. Short label
2. Type of molecule
3. Database identifier
4. Origin

For the interaction
5. Publication reference (method)

More about methods and interaction types that they support

http://www.ebi.ac.uk/ontology-lookup/browse.do?ontName=MI



June 2007: Maintenance Release

Implementation documentation has been updated to include more recent dependencies. Please note that unless

OLS - Ontology Lookup Service

MI Ontology Browser

- molecular interaction
  - interaction detection method
    - experimental interaction detection
    - interaction prediction
    - inference
    - unspecified method
  - participant identification method
  - feature detection method
  - feature type
  - interaction type
    - genetic interaction
    - colocalization
    - association
  - alias type
  - interactor type
  - feature range status
  - experimental preparation
  - cross-reference type
  - database citation
  - experimental role
  - biological role

Help (hide)

Double-click a term to see its children. The ontology browser is populated dynamically. If there are many children for a given term, there may be a small delay while the browser fetches **Click** to highlight a term to see any information associated with it. **Hover** over a term to see its relation with its immediate parent. Root terms will not display any relational information.

Relations

Term Information

ID:

Name:

Associated information

Highlight a term to view its associated information.

Term Hierarchy

Paths to Root: ● Child relationships: ○

You can zoom the ontology browser by clicking on a term in the graph.

Interaction databases

BIND	inactive
BioGRID	IMEX (Observer)
CORUM	complexes
DIP	IMEX (Archival)
HPRD	human resource
IntAct	IMEX (Archival)
MATRIX	extracellular matrix
MINT	IMEX (Topical)
MPACT	IMEX (Topical) yeast
MPIDB	IMEX (Observer) prokaryotic
MPPI	mammlian
OPHID/I2D	predicted
Many others	

See http://www.pathguide.org/ for URLs

Interaction databases

IMEx
International Molecular Exchange Consortium

IMEx partners exchange data and share curation tasks.

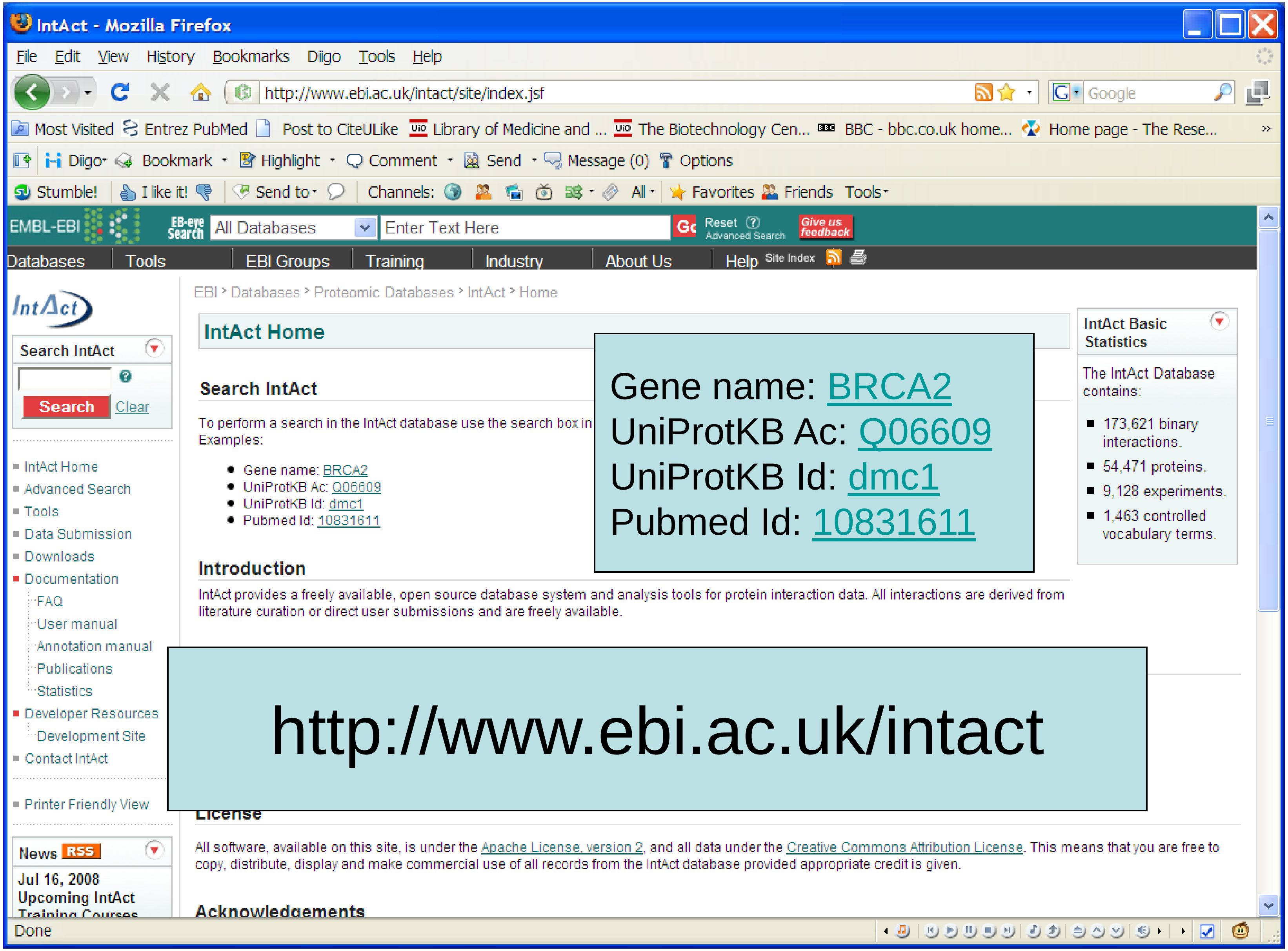
Set standards

They also accept interaction data submissions pre and post publication.

Data consolidation and exchange is an active area of research.

See http://www.imexconsortium.org/

Interaction databases: IntAct



EBI > Databases > Proteomic Databases > IntAct > Home

IntAct Home

Search IntAct

To perform a search in the IntAct database use the search box in
Examples:

- Gene name: BRCA2
- UniProtKB Ac: Q06609
- UniProtKB Id: dmc1
- Pubmed Id: 10831611

Introduction

IntAct provides a freely available, open source database system and analysis tools for protein interaction data. All interactions are derived from literature curation or direct user submissions and are freely available.

License

All software, available on this site, is under the Apache License, version 2, and all data under the Creative Commons Attribution License. This means that you are free to copy, distribute, display and make commercial use of all records from the IntAct database provided appropriate credit is given.

Acknowledgements

IntAct Basic Statistics

The IntAct Database contains:

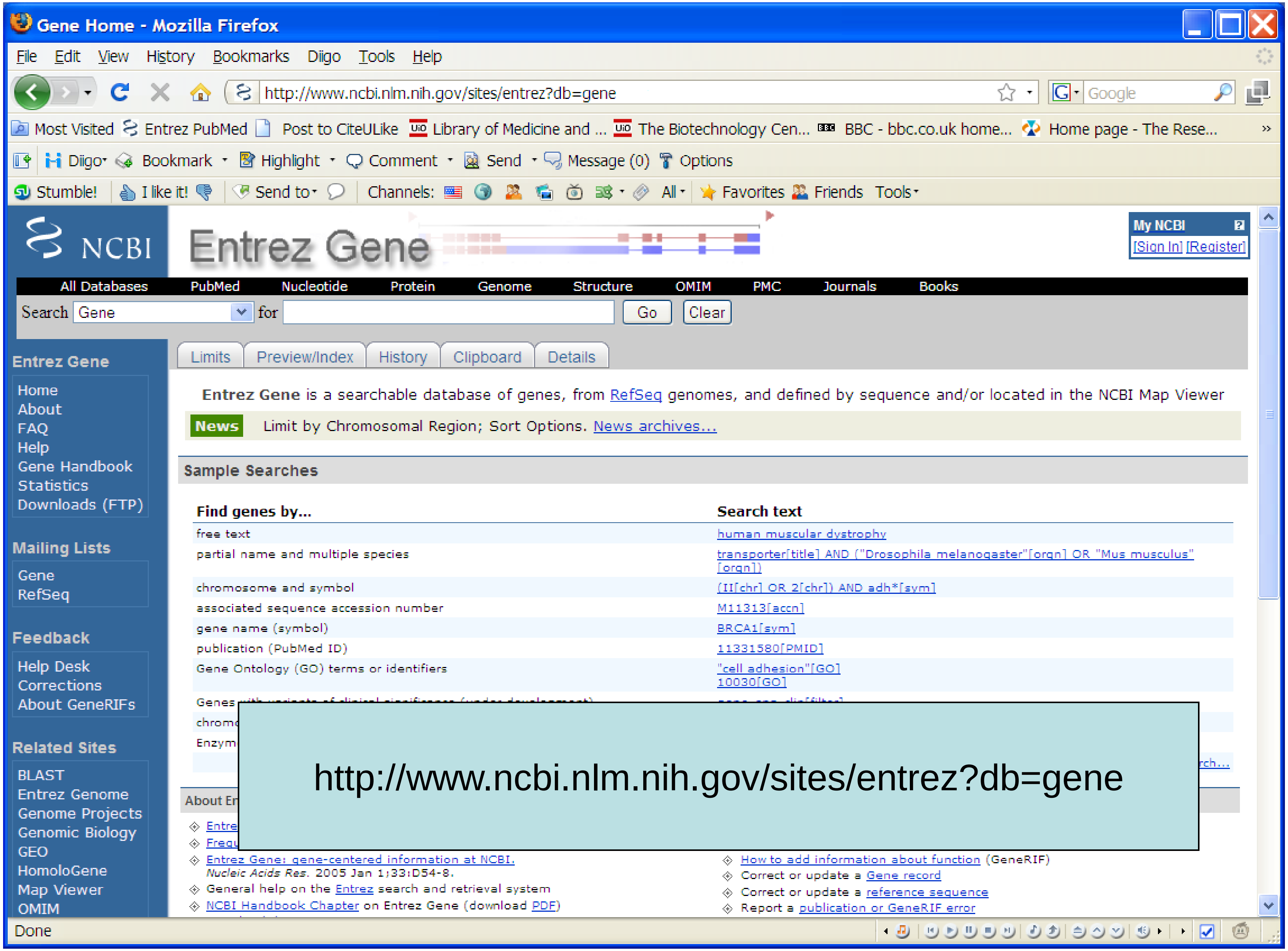
- 173,621 binary interactions.
- 54,471 proteins.
- 9,128 experiments.
- 1,463 controlled vocabulary terms.

Jul 16, 2008
Upcoming IntAct Training Courses

Gene name: BRCA2
UniProtKB Ac: Q06609
UniProtKB Id: dmc1
Pubmed Id: 10831611

http://www.ebi.ac.uk/intact

Identifiers: EntrezGene



Entrez Gene is a searchable database of genes, from RefSeq genomes, and defined by sequence and/or located in the NCBI Map Viewer

News Limit by Chromosomal Region; Sort Options. News archives...

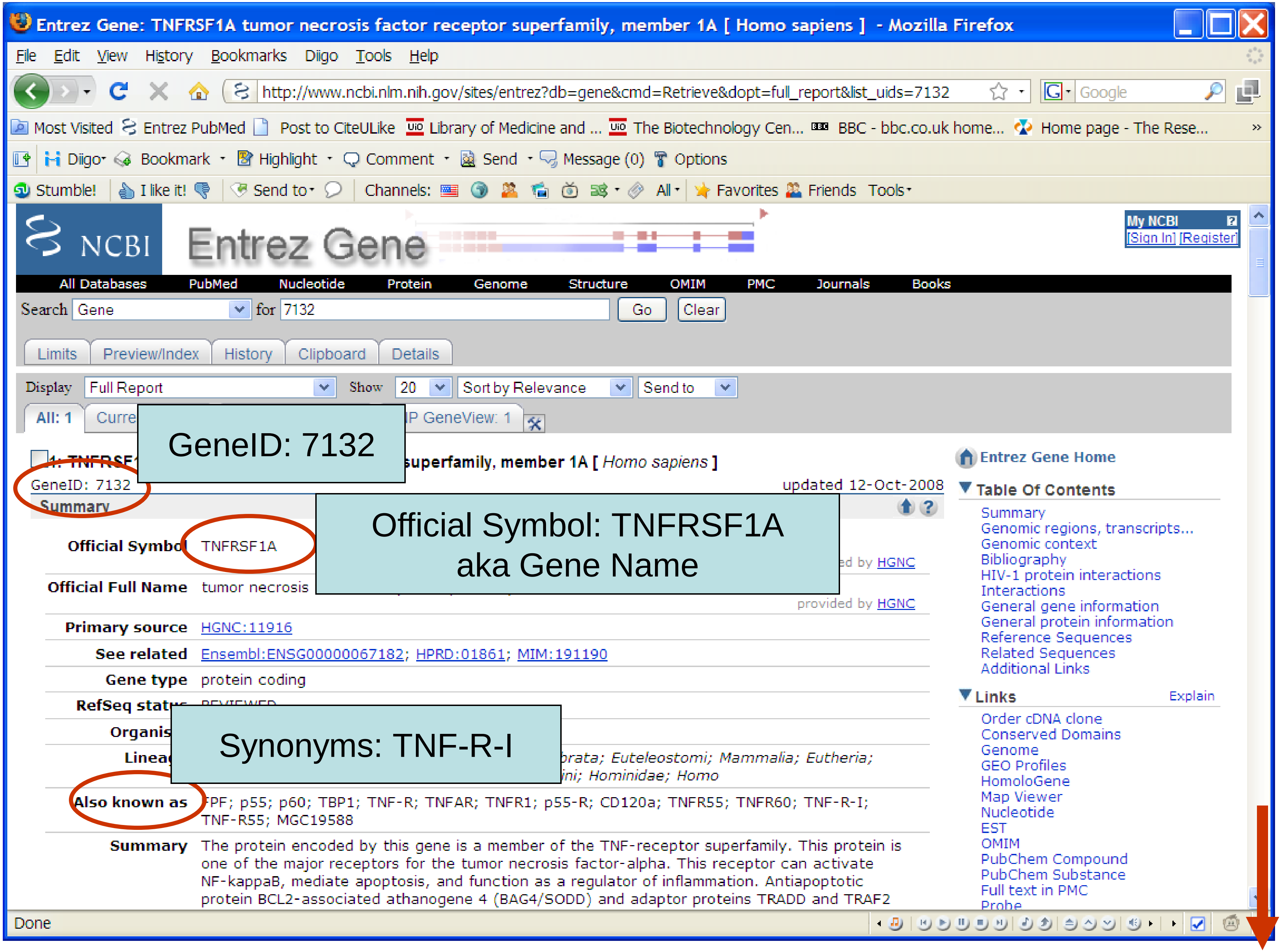
Sample Searches

Find genes by...	Search text
free text	human muscular dystrophy
partial name and multiple species	transporter[title] AND ("Drosophila melanogaster"[orgn] OR "Mus musculus"[orgn])
chromosome and symbol	(II[chr] OR 2[chr]) AND adh*[sym]
associated sequence accession number	M11313[accn]
gene name (symbol)	BRCA1[sym]
publication (PubMed ID)	11331580[PMID]
Gene Ontology (GO) terms or identifiers	"cell adhesion"[GO] 10030[GO]
Genes	
chrom	
Enzym	

About En

- Entre
- Frequ
- Entrez Gene: gene-centered information at NCBI. *Nucleic Acids Res.* 2005 Jan 1;33:D54-8.
- General help on the Entrez search and retrieval system
- NCBI Handbook Chapter on Entrez Gene (download PDF)
- How to add information about function (GeneRIF)
- Correct or update a Gene record
- Correct or update a reference sequence
- Report a publication or GeneRIF error

http://www.ncbi.nlm.nih.gov/sites/entrez?db=gene



1: TNFRSF superfamily, member 1A [*Homo sapiens*]

GeneID: 7132 updated 12-Oct-2008

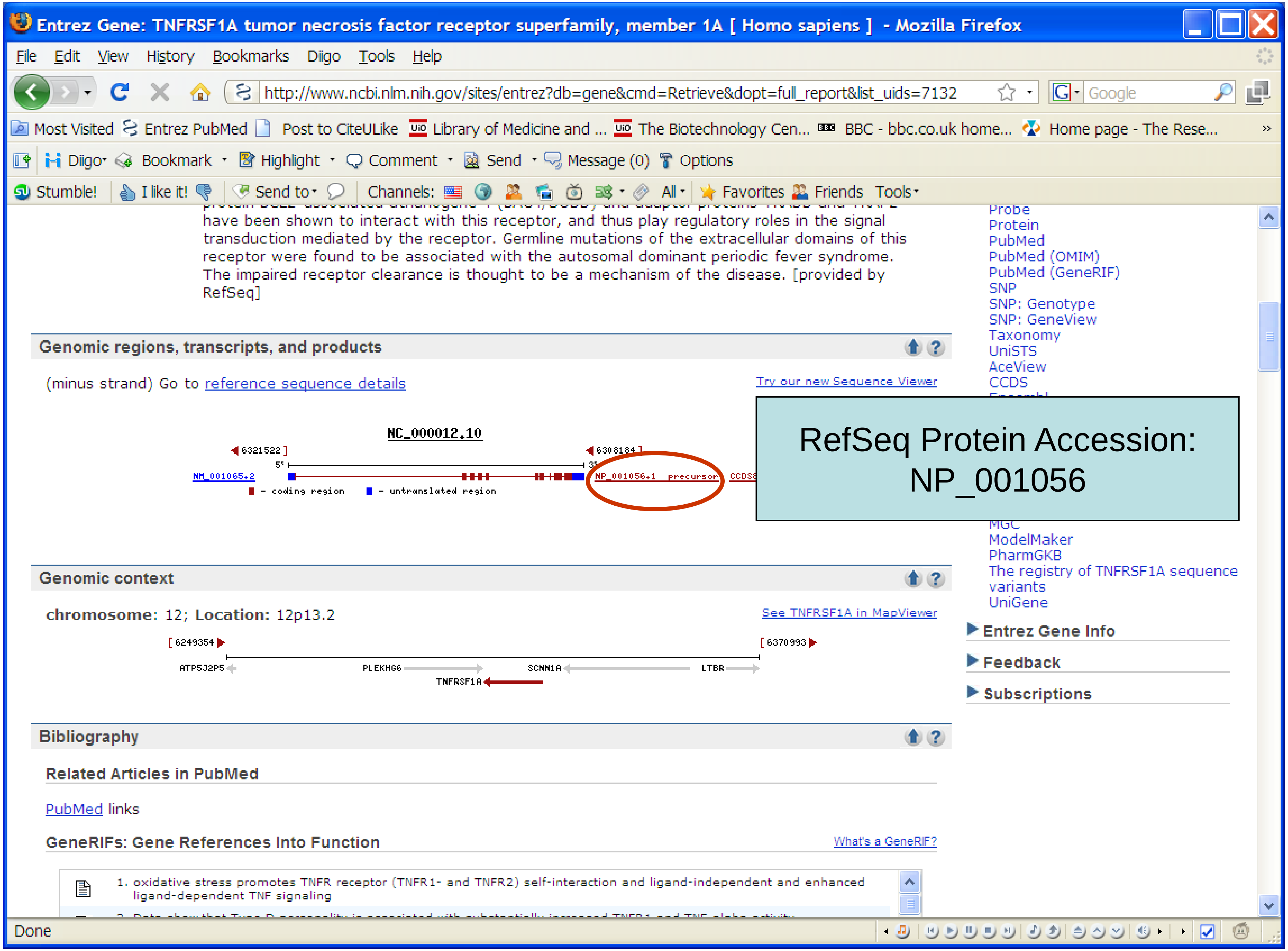
Summary

Official Symbol	TNFRSF1A ed by HGNC
Official Full Name	tumor necrosis provided by HGNC
Primary source	HGNC:11916
See related	Ensembl:ENSG00000067182; HPRD:01861; MIM:191190
Gene type	protein coding
RefSeq statu	
Organis	
Linea	brata; Euteleostomi; Mammalia; Eutheria; ini; Hominidae; Homo
Also known as	FPF; p55; p60; TBP1; TNF-R; TNFAR; TNFR1; p55-R; CD120a; TNFR55; TNFR60; TNF-R-I; TNF-R55; MGC19588
Summary	The protein encoded by this gene is a member of the TNF-receptor superfamily. This protein is one of the major receptors for the tumor necrosis factor-alpha. This receptor can activate NF-kappaB, mediate apoptosis, and function as a regulator of inflammation. Antiapoptotic protein BCL2-associated athanogene 4 (BAG4/SODD) and adaptor proteins TRADD and TRAF2

GeneID: 7132

Official Symbol: TNFRSF1A
aka Gene Name

Synonyms: TNF-R-I



have been shown to interact with this receptor, and thus play regulatory roles in the signal transduction mediated by the receptor. Germline mutations of the extracellular domains of this receptor were found to be associated with the autosomal dominant periodic fever syndrome. The impaired receptor clearance is thought to be a mechanism of the disease. [provided by RefSeq]

Genomic regions, transcripts, and products

(minus strand) Go to reference sequence details

Try our new Sequence Viewer

Genomic context

chromosome: 12; **Location:** 12p13.2

See TNFRSF1A in MapViewer

Bibliography

Related Articles in PubMed

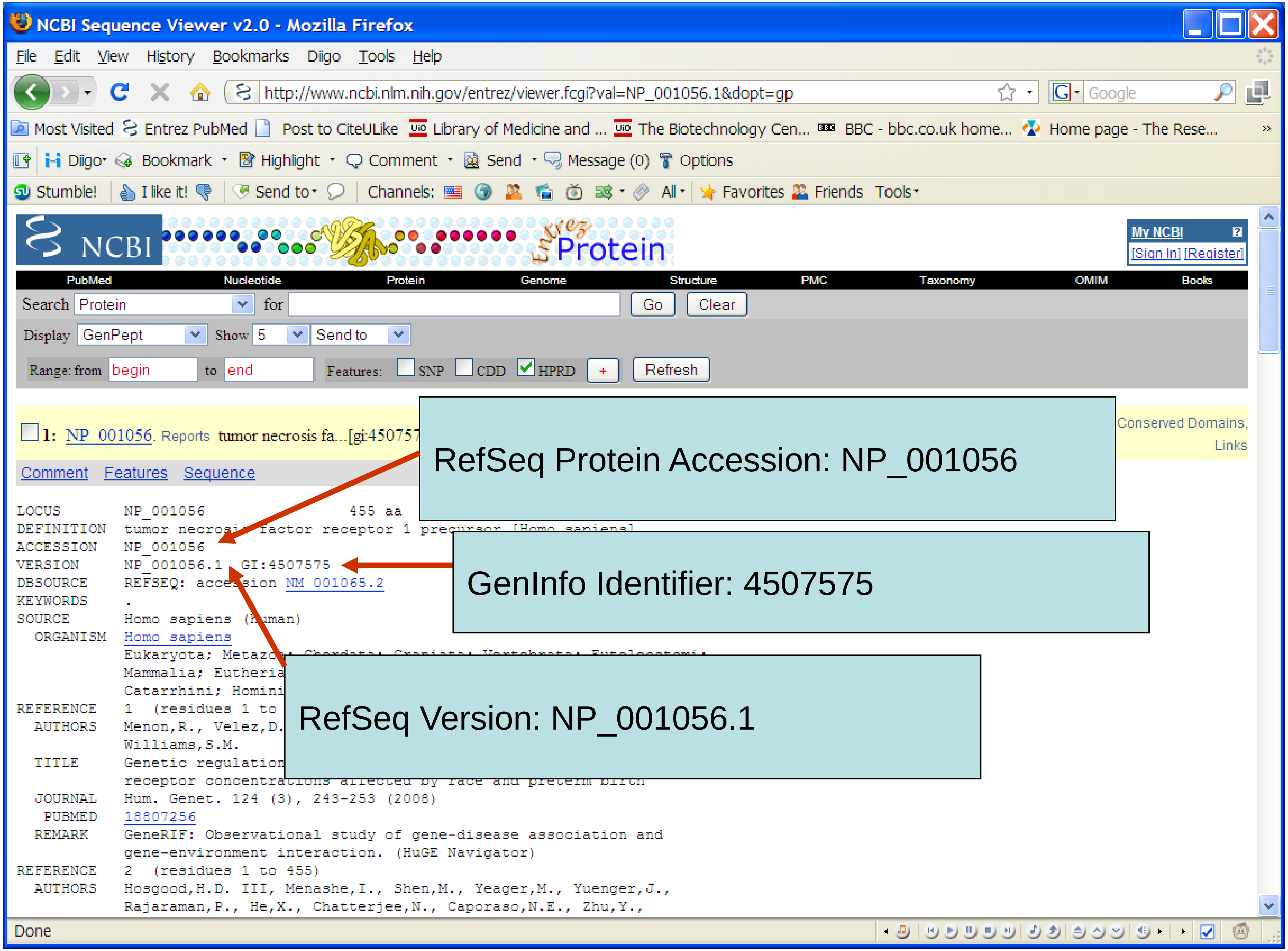
PubMed links

GeneRIFs: Gene References Into Function

What's a GeneRIF?

1. oxidative stress promotes TNFR receptor (TNFR1- and TNFR2) self-interaction and ligand-independent and enhanced ligand-dependent TNF signaling

RefSeq Protein Accession:
NP_001056



Search: Protein for

Display: GenPept Show: 5 Send to

Range: from begin to end Features: ☐ SNP ☐ CDD ☑ HPRD

☐ 1: NP_001056. Reports tumor necrosis fa...[gi:450757

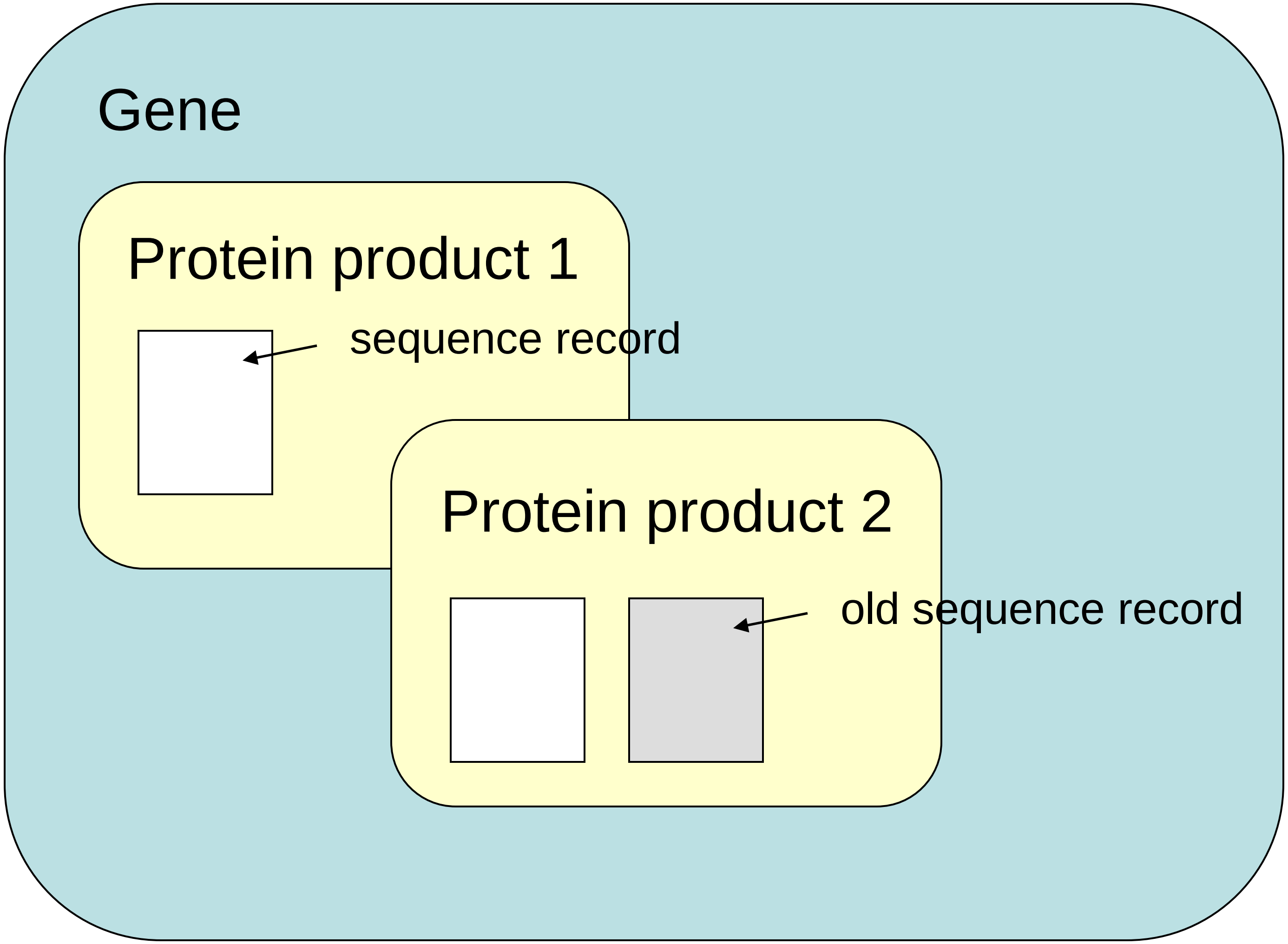
```
LOCUS       NP_001056               455 aa
DEFINITION  tumor necrosis factor receptor 1 precursor [Homo sapiens]
ACCESSION   NP_001056
VERSION     NP_001056.1  GI:4507575
DBSOURCE    REFSEQ: accession NM_001065.2
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria
            Catarrhini; Homini
REFERENCE   1  (residues 1 to
  AUTHORS   Menon,R., Velez,D.
            Williams,S.M.
  TITLE     Genetic regulation
            receptor concentrations affected by race and preterm birth
  JOURNAL   Hum. Genet. 124 (3), 243-253 (2008)
   PUBMED   18807256
  REMARK    GeneRIF: Observational study of gene-disease association and
            gene-environment interaction. (HuGE Navigator)
REFERENCE   2  (residues 1 to 455)
  AUTHORS   Hosgood,H.D. III, Menashe,I., Shen,M., Yeager,M., Yuenger,J.,
            Rajaraman,P., He,X., Chatterjee,N., Caporaso,N.E., Zhu,Y.,
```

RefSeq Protein Accession: NP_001056

GenInfo Identifier: 4507575

RefSeq Version: NP_001056.1

Identifiers: NCBI



Gene

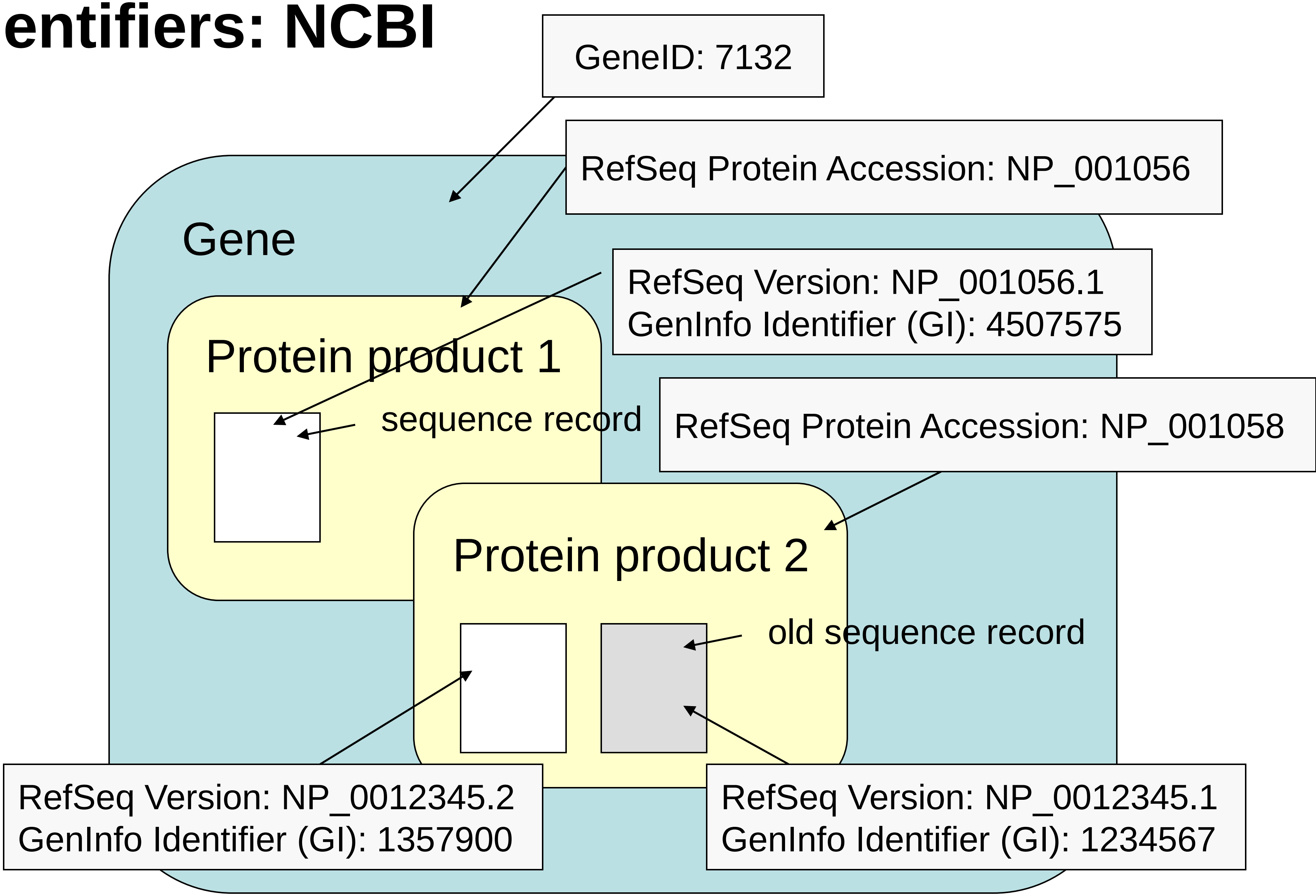
Protein product 1

sequence record

Protein product 2

old sequence record

Identifiers: NCBI



GeneID: 7132

RefSeq Protein Accession: NP_001056

Gene

RefSeq Version: NP_001056.1
GenInfo Identifier (GI): 4507575

Protein product 1

sequence record

RefSeq Protein Accession: NP_001058

Protein product 2

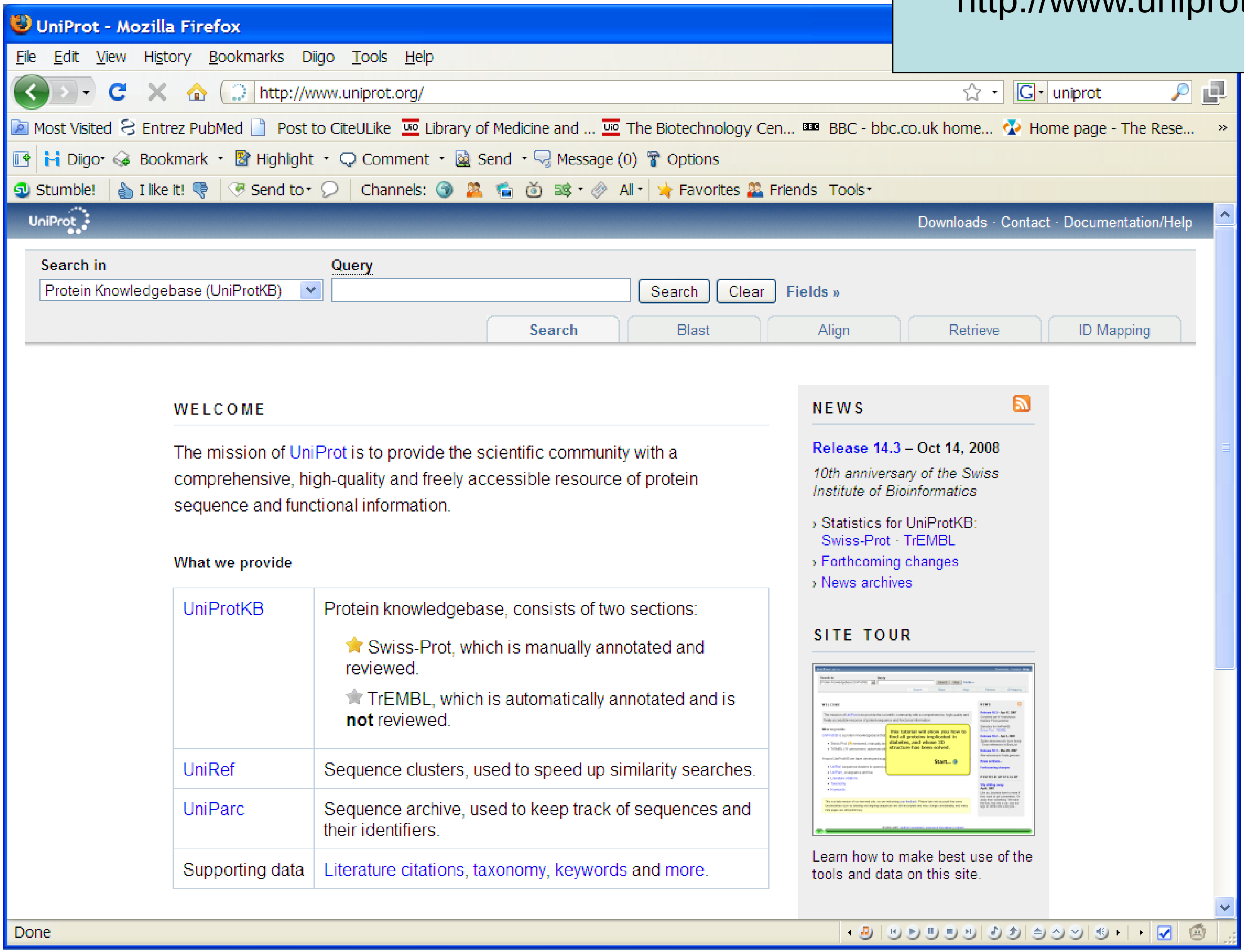
old sequence record

RefSeq Version: NP_0012345.2
GenInfo Identifier (GI): 1357900

RefSeq Version: NP_0012345.1
GenInfo Identifier (GI): 1234567

Identifiers: UniProtKB

http://www.uniprot.org/



WELCOME

The mission of UniProt is to provide the scientific community with a comprehensive, high-quality and freely accessible resource of protein sequence and functional information.

What we provide

UniProtKB	Protein knowledgebase, consists of two sections: ★ Swiss-Prot, which is manually annotated and reviewed. ★ TrEMBL, which is automatically annotated and is **not** reviewed.
UniRef	Sequence clusters, used to speed up similarity searches.
UniParc	Sequence archive, used to keep track of sequences and their identifiers.
Supporting data	Literature citations, taxonomy, keywords and more.

NEWS

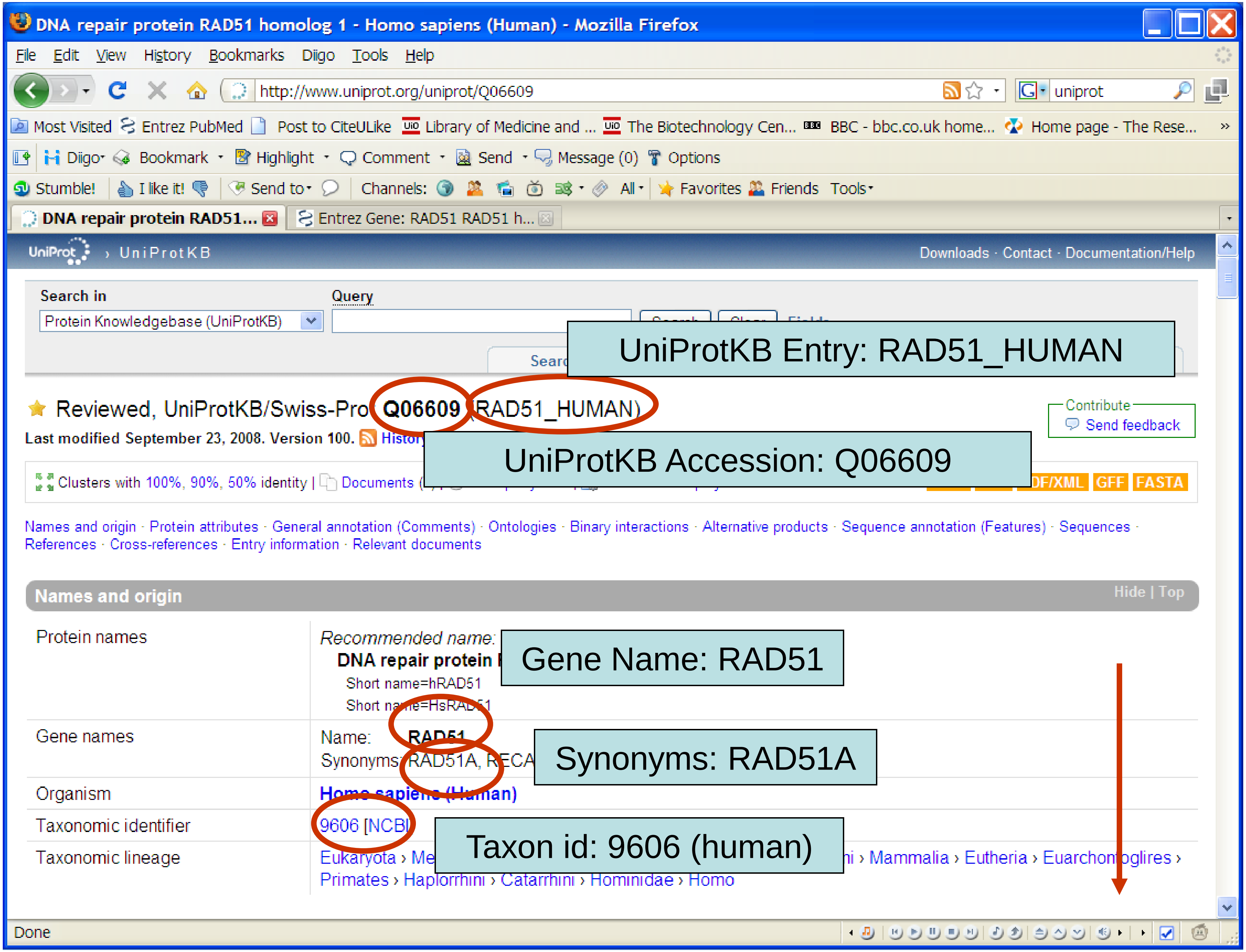
Release 14.3 – Oct 14, 2008

10th anniversary of the Swiss Institute of Bioinformatics

- Statistics for UniProtKB: Swiss-Prot · TrEMBL
- Forthcoming changes
- News archives

SITE TOUR

Learn how to make best use of the tools and data on this site.



UniProtKB Entry: RAD51_HUMAN

Reviewed, UniProtKB/Swiss-Pro Q06609 (RAD51_HUMAN)

Last modified September 23, 2008. Version 100. Histor

UniProtKB Accession: Q06609

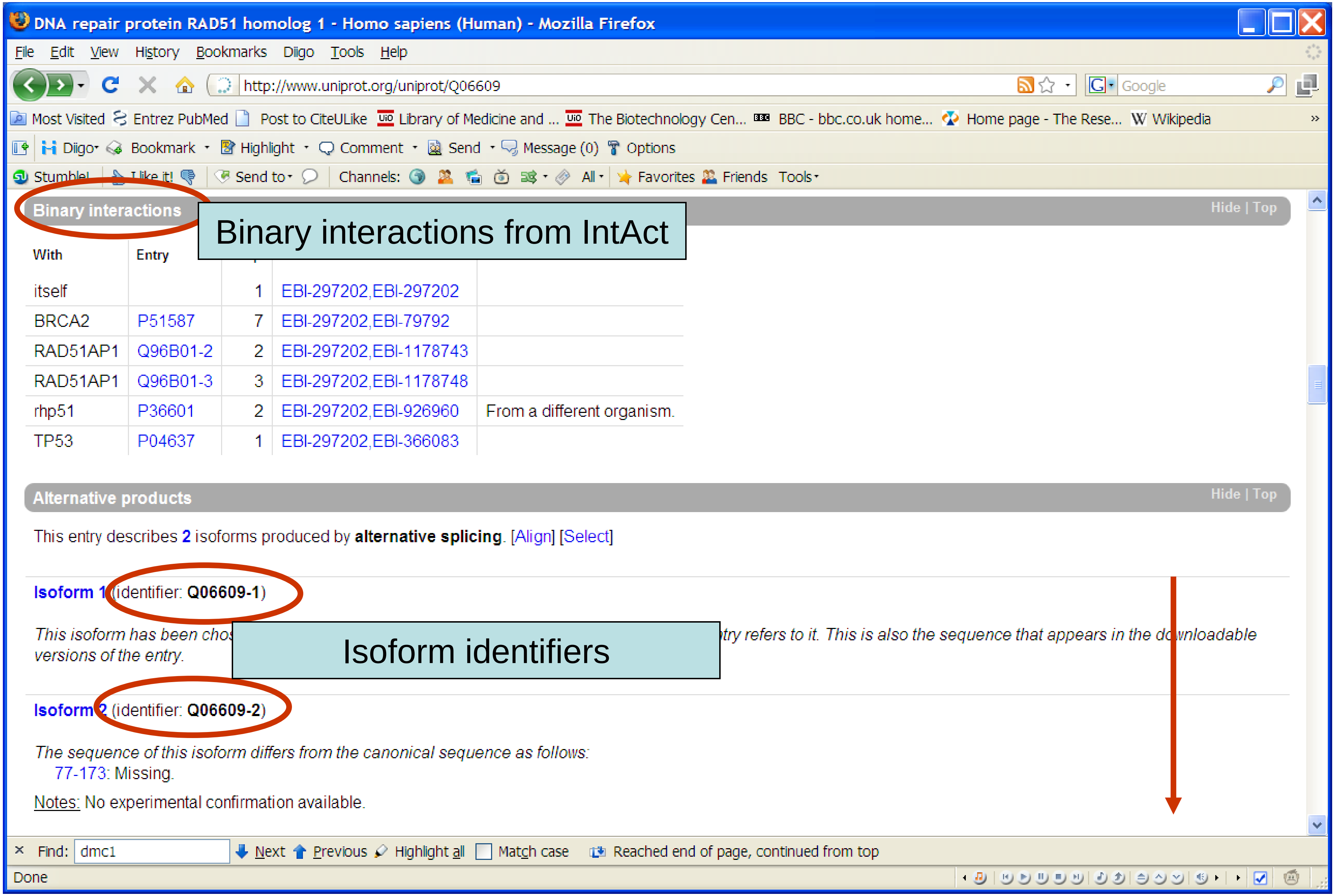
Names and origin

Protein names	*Recommended name:* **DNA repair protein** Short name=hRAD51 Short name=HsRAD51
Gene names	Name: **RAD51** Synonyms: RAD51A, RECA
Organism	**Homo sapiens (Human)**
Taxonomic identifier	9606 [NCBI
Taxonomic lineage	Eukaryota › Me … i › Mammalia › Eutheria › Euarchontoglires › Primates › Haplorrhini › Catarrhini › Hominidae › Homo

Gene Name: RAD51

Synonyms: RAD51A

Taxon id: 9606 (human)



Binary interactions

Binary interactions from IntAct

With	Entry		
itself		1	EBI-297202,EBI-297202
BRCA2	P51587	7	EBI-297202,EBI-79792
RAD51AP1	Q96B01-2	2	EBI-297202,EBI-1178743
RAD51AP1	Q96B01-3	3	EBI-297202,EBI-1178748
rhp51	P36601	2	EBI-297202,EBI-926960	From a different organism.
TP53	P04637	1	EBI-297202,EBI-366083

Alternative products

This entry describes **2** isoforms produced by **alternative splicing**. [Align] [Select]

Isoform 1 (identifier: **Q06609-1**)

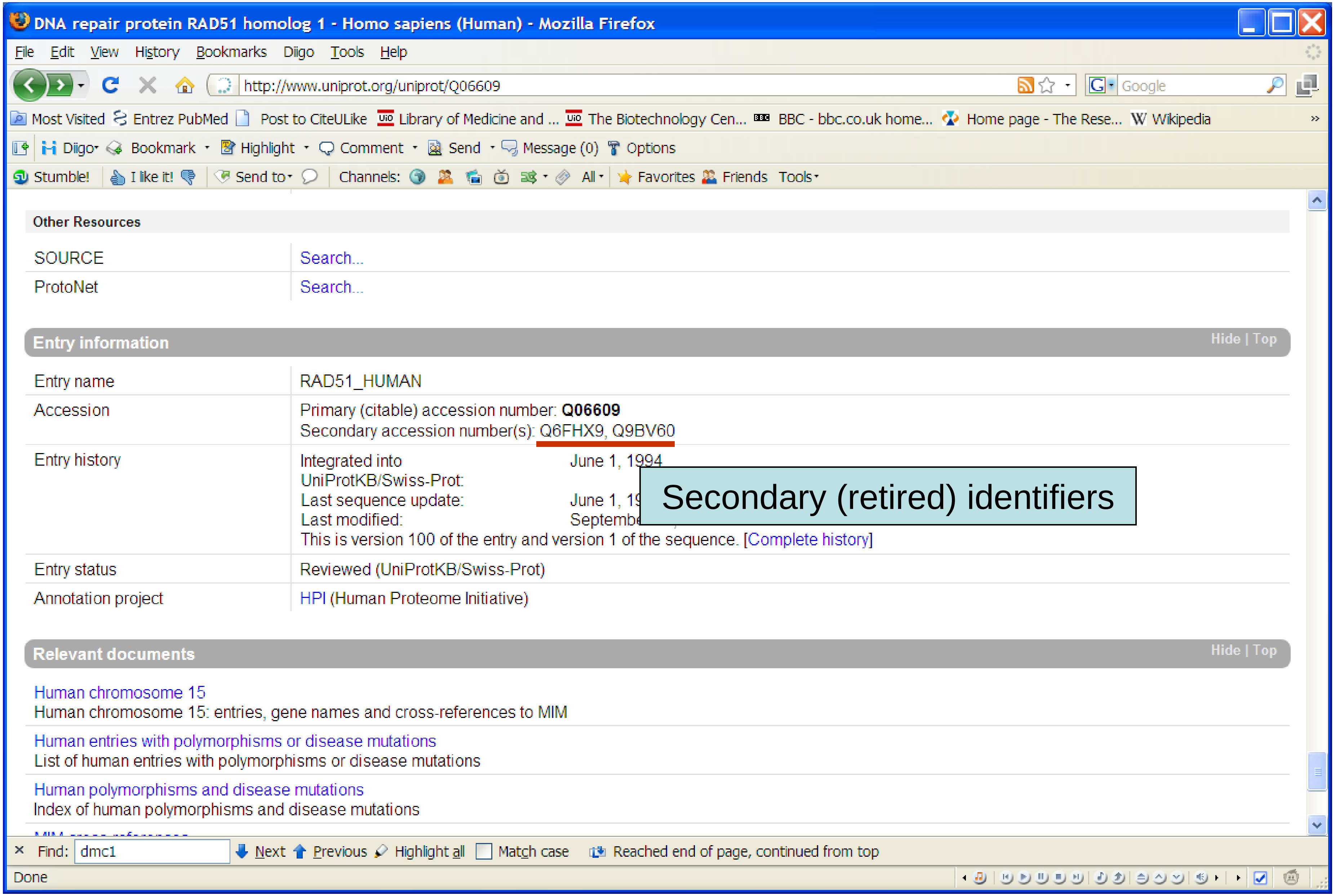
This isoform has been chos *try refers to it. This is also the sequence that appears in the downloadable versions of the entry.*

Isoform identifiers

Isoform 2 (identifier: **Q06609-2**)

The sequence of this isoform differs from the canonical sequence as follows:
77-173: Missing.

Notes: No experimental confirmation available.



Other Resources

SOURCE	Search...
ProtoNet	Search...

Entry information

Entry name	RAD51_HUMAN
Accession	Primary (citable) accession number: **Q06609** Secondary accession number(s): Q6FHX9, Q9BV60
Entry history	Integrated into UniProtKB/Swiss-Prot: June 1, 1994 Last sequence update: June 1, 19 Last modified: Septembe This is version 100 of the entry and version 1 of the sequence. [Complete history]
Entry status	Reviewed (UniProtKB/Swiss-Prot)
Annotation project	HPI (Human Proteome Initiative)

Secondary (retired) identifiers

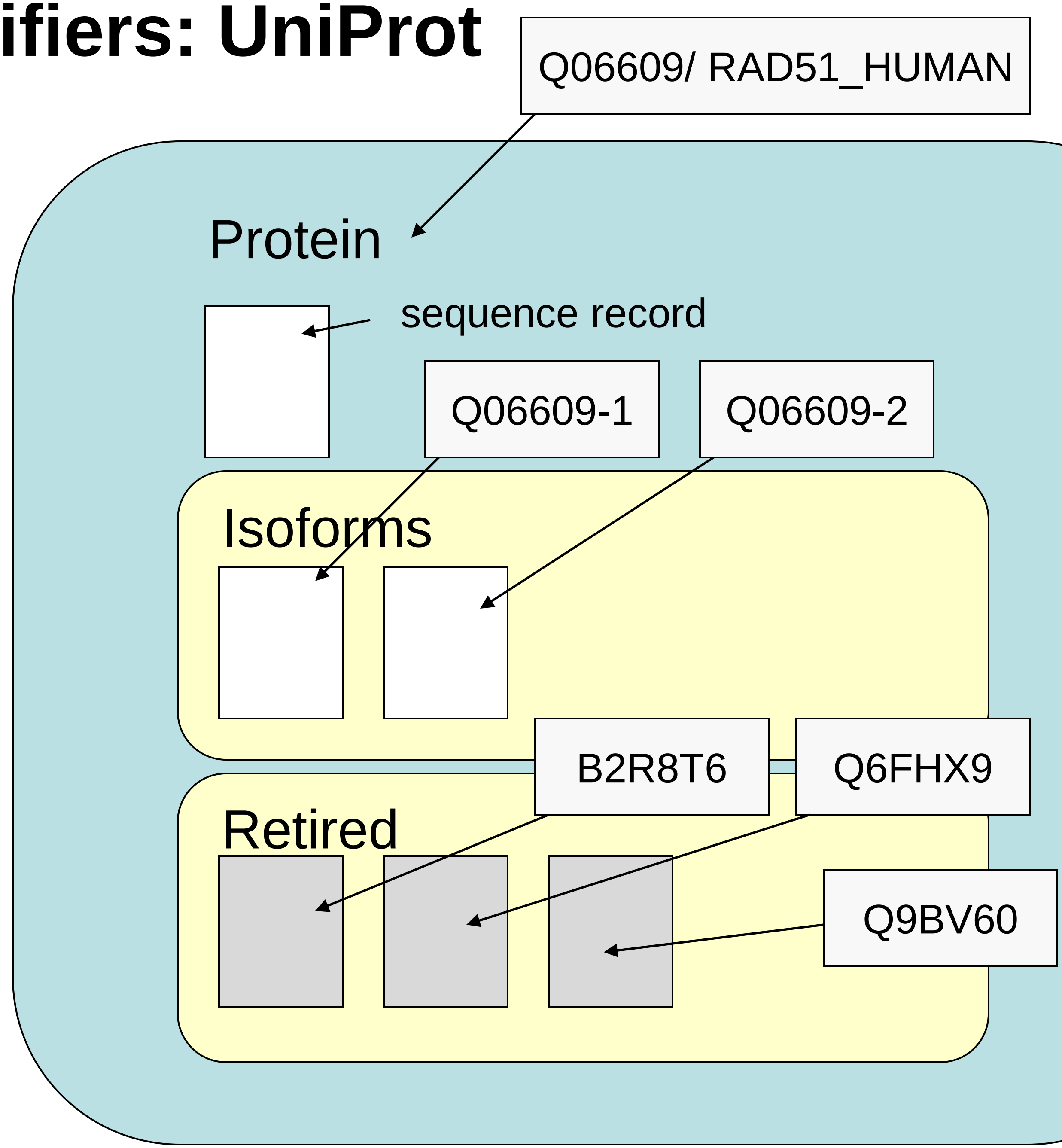
Relevant documents

Human chromosome 15
Human chromosome 15: entries, gene names and cross-references to MIM

Human entries with polymorphisms or disease mutations
List of human entries with polymorphisms or disease mutations

Human polymorphisms and disease mutations
Index of human polymorphisms and disease mutations

Identifiers: UniProt



Q06609/ RAD51_HUMAN

Protein

sequence record

Q06609-1

Q06609-2

Isoforms

B2R8T6

Q6FHX9

Retired

Q9BV60

For your information

Common Identifiers

Gene

Ensembl ENSG00000139618

Entrez Gene 675

Unigene Hs.34012

RNA transcript

GenBank BC026160.1

RefSeq NM_000059

Ensembl ENST00000380152

Protein

Ensembl ENSP00000369497

RefSeq NP_000050.2

UniProt BRCA2_HUMAN or A1YBP1_HUMAN

IPI IPI00412408.1

EMBL AF309413

PDB 1MIU

Species-specific

HUGO HGNC BRCA2

MGI MGI:109337

RGD 2219

ZFIN ZDB-GENE-060510-3

FlyBase CG9097

WormBase WBGene00002299 or ZK1067.1

SGD S000002187 or YDL029W

Annotations

InterPro IPR015252

OMIM 600185

Pfam PF09104

Gene Ontology GO:0000724

SNPs rs28897757

Experimental Platform

Affymetrix 208368_3p_s_at

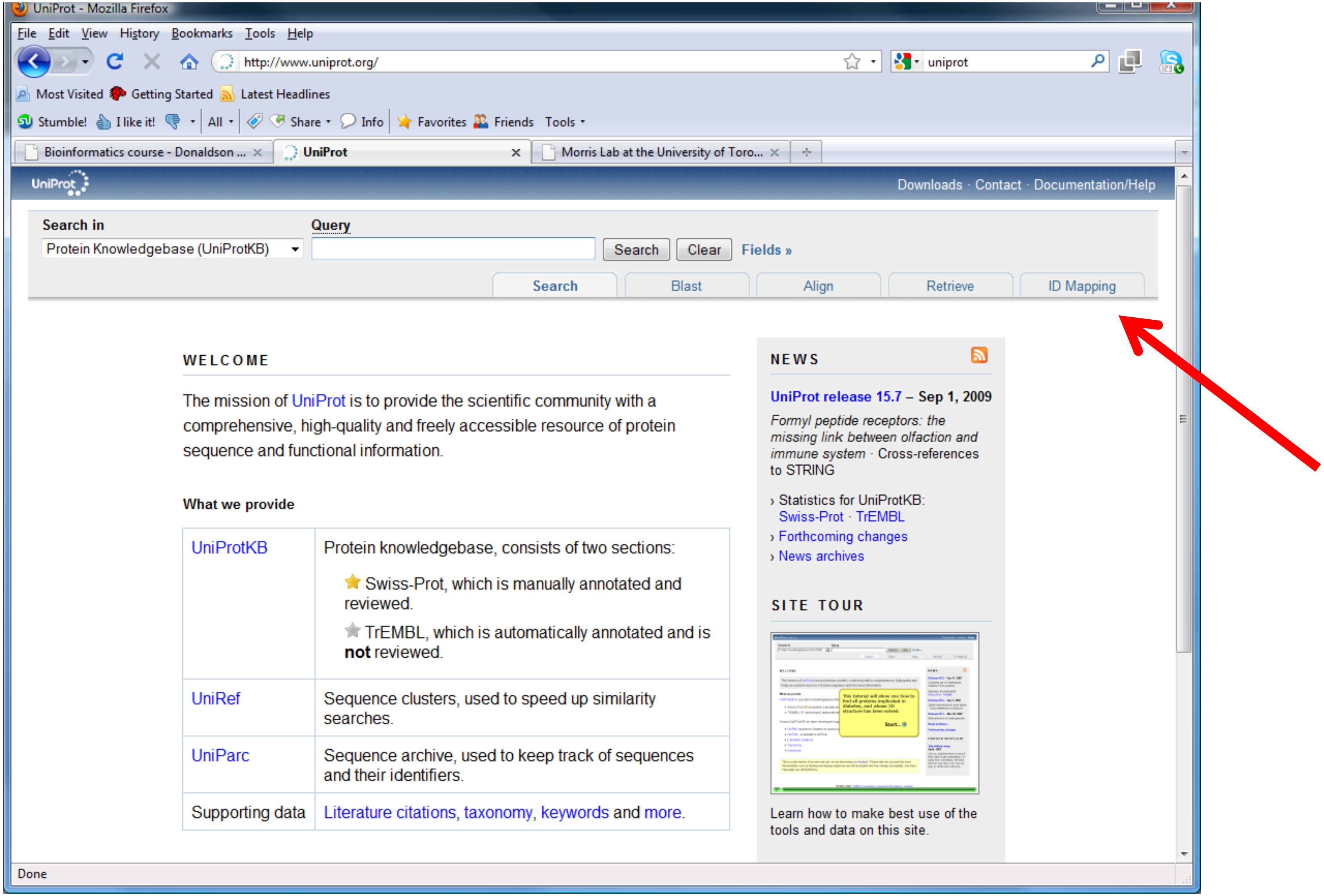
Agilent A_23_P99452

CodeLink GE60169

Illumina GI_4502450-S

Red = Recommended

UniProt ID Mapping Service



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UniRef	Sequence clusters, used to speed up similarity searches.
UniParc	Sequence archive, used to keep track of sequences and their identifiers.
Supporting data	Literature citations, taxonomy, keywords and more.

NEWS

UniProt release 15.7 – Sep 1, 2009

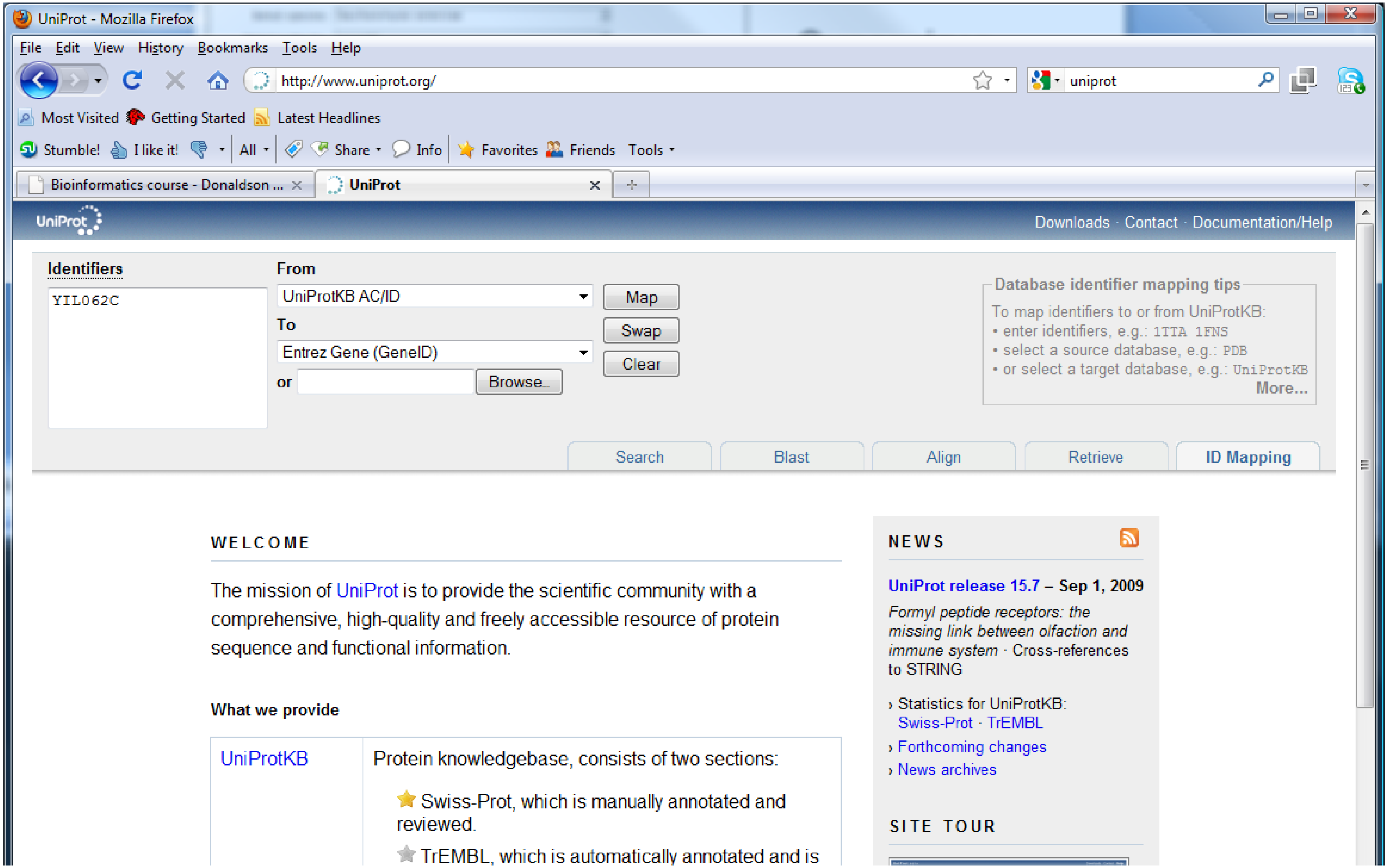
Formyl peptide receptors: the missing link between olfaction and immune system · Cross-references to STRING

- › Statistics for UniProtKB: Swiss-Prot · TrEMBL
- › Forthcoming changes
- › News archives

SITE TOUR

Learn how to make best use of the tools and data on this site.

UniProt ID Mapping Service



Identifiers

YIL062C

From

UniProtKB AC/ID

To

Entrez Gene (GeneID)

or

Database identifier mapping tips

To map identifiers to or from UniProtKB:
- enter identifiers, e.g.: `1TTA 1FNS`
- select a source database, e.g.: `PDB`
- or select a target database, e.g.: `UniProtKB`

More...

WELCOME

The mission of UniProt is to provide the scientific community with a comprehensive, high-quality and freely accessible resource of protein sequence and functional information.

What we provide

UniProtKB	Protein knowledgebase, consists of two sections: ★ Swiss-Prot, which is manually annotated and reviewed. ☆ TrEMBL, which is automatically annotated and is

NEWS

UniProt release 15.7 – Sep 1, 2009

Formyl peptide receptors: the missing link between olfaction and immune system · Cross-references to STRING

› Statistics for UniProtKB: Swiss-Prot · TrEMBL

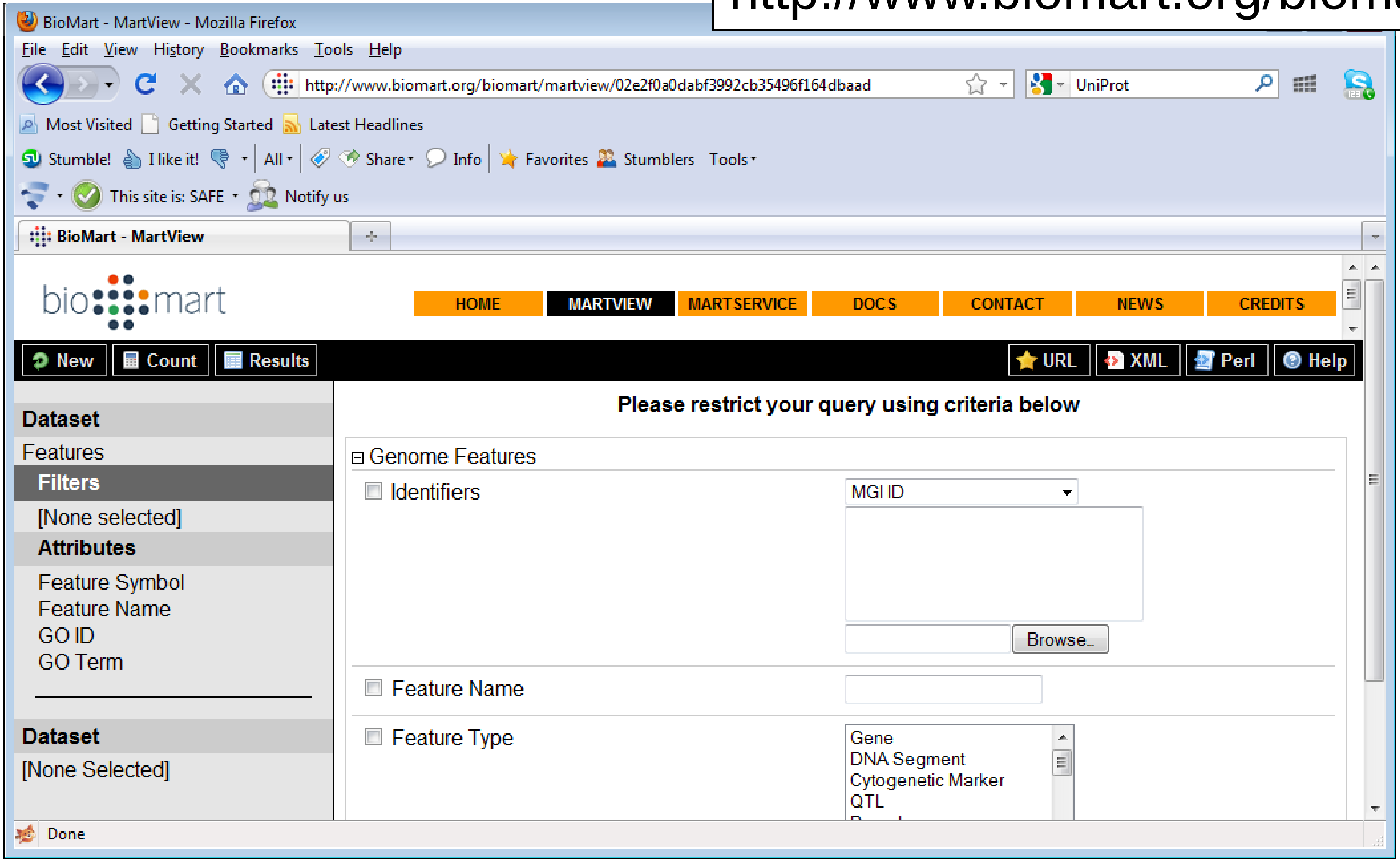
› Forthcoming changes

› News archives

SITE TOUR

Ensembl BioMart

http://www.biomart.org/biomart



http://www.biomart.org/biomart/martview/02e2f0a0dabf3992cb35496f164dbaad

Dataset

Features

Filters

[None selected]

Attributes

Feature Symbol
Feature Name
GO ID
GO Term

Dataset

[None Selected]

Please restrict your query using criteria below

⊟ Genome Features

☐ Identifiers — MGI ID

☐ Feature Name

☐ Feature Type — Gene, DNA Segment, Cytogenetic Marker, QTL

ID Mapping Challenges

- Avoid errors: map IDs correctly
- Gene name ambiguity – not a good ID
  - e.g. FLJ92943, LFS1, TRP53, p53
  - Better to use the standard gene symbol: TP53
- Excel error-introduction
  - OCT4 is changed to October-4
- Problems reaching 100% coverage
  - E.g. due to version issues
  - Use multiple sources to increase coverage

Zeeberg BR et al. Mistaken identifiers: gene name errors can be introduced inadvertently when using Excel in bioinformatics BMC Bioinformatics. 2004 Jun 23;5:80

ID Mapping Challenges

- Spot-test any ID mapping service you use.
- Check samples from first, last and middle of your list of identifiers to be converted.
- Ask for help if you are uncertain.

Identifiers: Why can’t I find my protein

Are you using a sequence record identifier?

Is the identifier retired?

Are you using the identifier for the correct organism?

Have you tried searching for identifiers for all products of the gene?

Try different identifier systems (Entrez Gene, UniProt)

Remember that only 10% to 50% of all proteins have interaction information.

You always have recourse to text-mining and predicted interactions.

Overview

1. A simple interction record
2. Experimental methods
3. Representation of interactions
4. Interaction databases
5. Identifiers
6. Text mining sources
7. Predicted interaction sources
8. Consolidated databases
9. Visualization tools
10. Applications

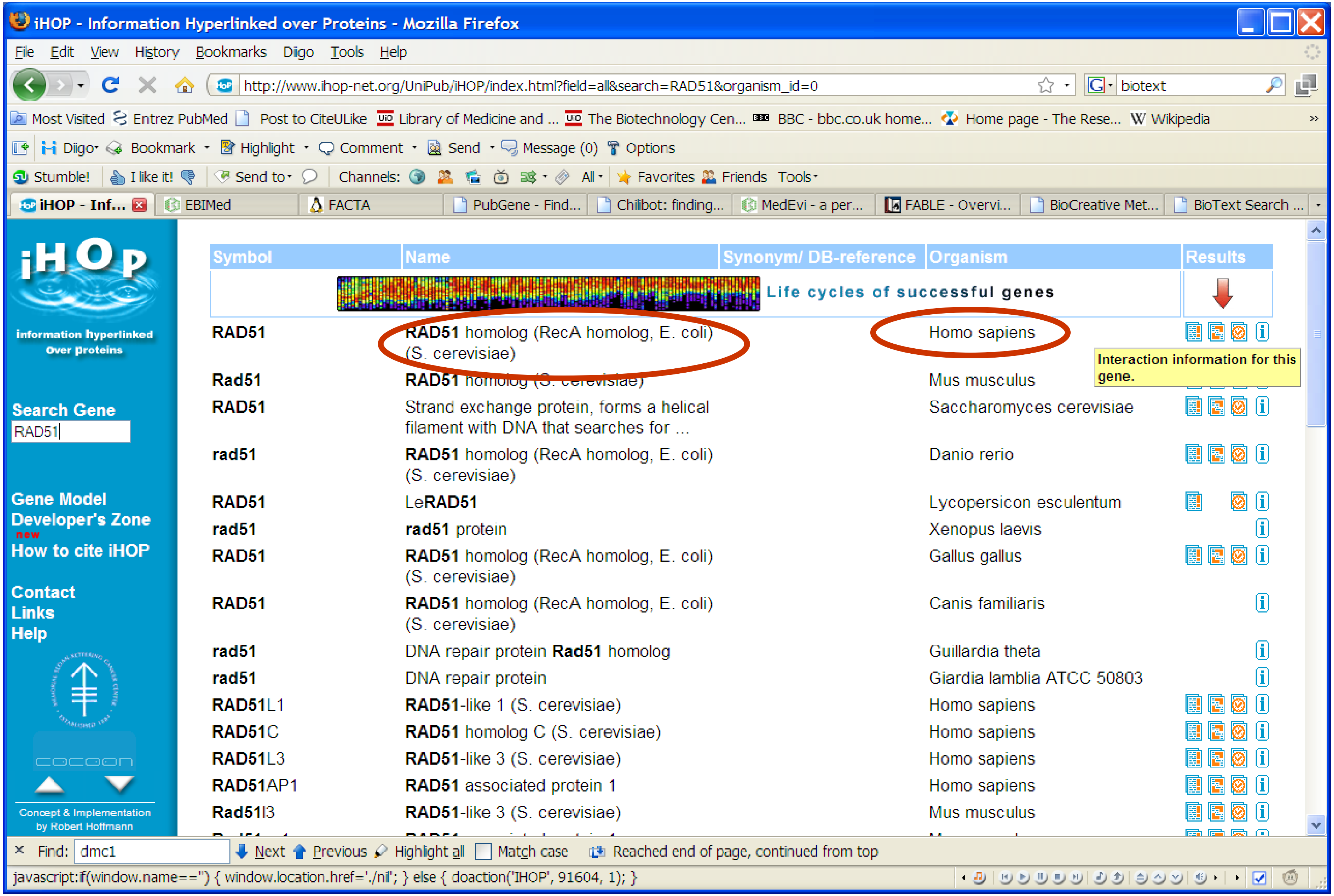
Text mining resources

Most are based on co-ocurrence of gene name mentions.

Start at http://zope.bioinfo.cnio.es/bionlp_tools

iHOP	http://www.ihop-net.org/UniPub/iHOP/
EBIMed	http://www.ebi.ac.uk/Rebholz-srv/ebimed/index.jsp
FACTA	http://text0.mib.man.ac.uk/software/facta/
PubGene	http://www.pubgene.org/
InfoPubMed	https://www-tsujii.is.s.u-tokyo.ac.jp/info-pubmed/
Chillibot	http://www.chilibot.net/
MedEvi	http://www.ebi.ac.uk/tc-test/textmining/medevi/
FABLE	http://fable.chop.edu/overview.jsp
BCMS	http://bcms.bioinfo.cnio.es/
BioText	http://biosearch.berkeley.edu/

Text mining resources: iHOP



http://www.ihop-net.org/UniPub/iHOP/index.html?field=all&search=RAD51&organism_id=0

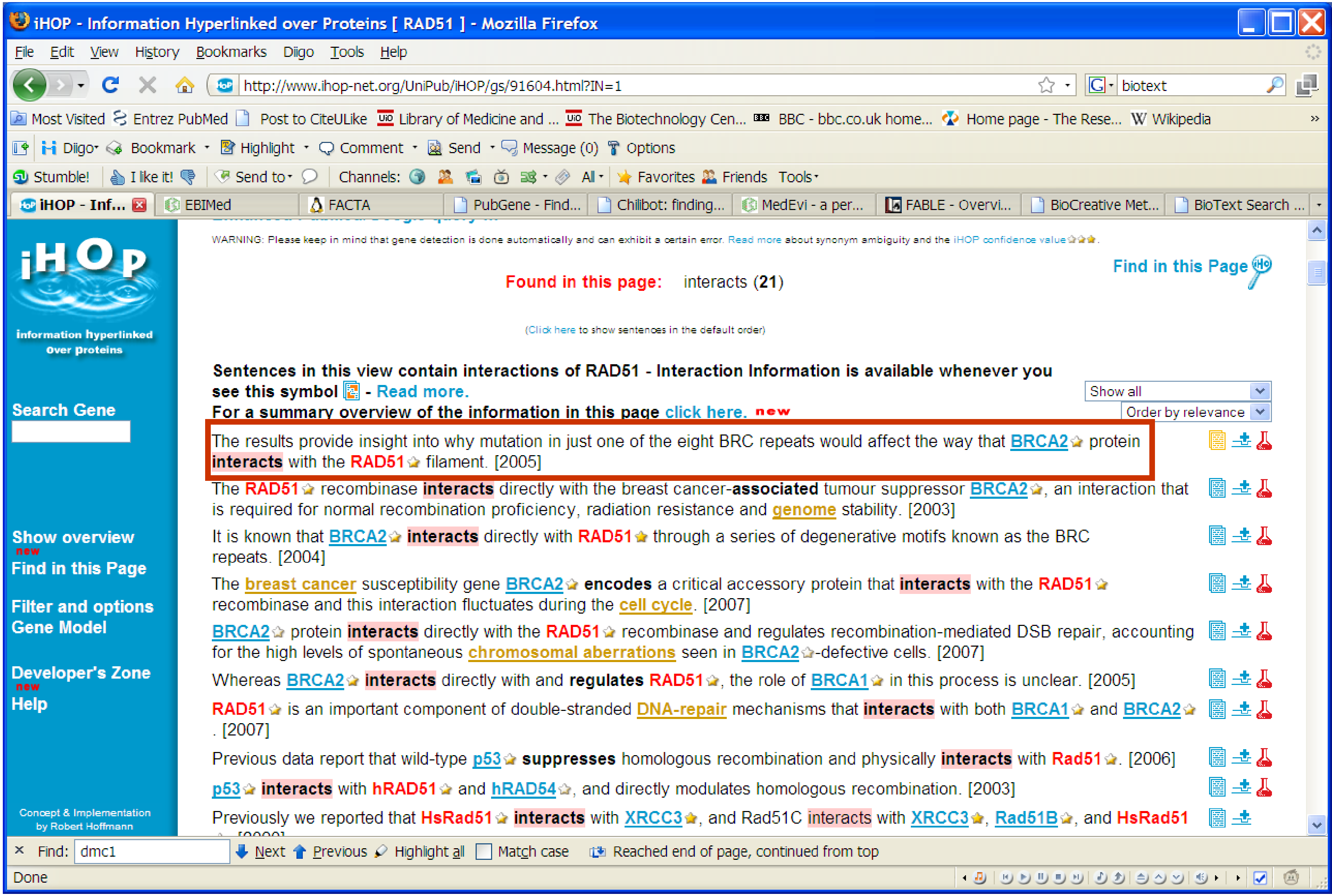
Search: biotext

Search Gene: RAD51

Find: dmc1

Symbol	Name	Synonym/ DB-reference	Organism	Results
RAD51	**RAD51** homolog (RecA homolog, E. coli) (S. cerevisiae)		Homo sapiens	
Rad51	**RAD51** homolog (S. cerevisiae)		Mus musculus	
RAD51	Strand exchange protein, forms a helical filament with DNA that searches for …		Saccharomyces cerevisiae	
rad51	**RAD51** homolog (RecA homolog, E. coli) (S. cerevisiae)		Danio rerio	
RAD51	Le**RAD51**		Lycopersicon esculentum	
rad51	**rad51** protein		Xenopus laevis	
RAD51	**RAD51** homolog (RecA homolog, E. coli) (S. cerevisiae)		Gallus gallus	
RAD51	**RAD51** homolog (RecA homolog, E. coli) (S. cerevisiae)		Canis familiaris	
rad51	DNA repair protein **Rad51** homolog		Guillardia theta	
rad51	DNA repair protein		Giardia lamblia ATCC 50803	
RAD51L1	**RAD51**-like 1 (S. cerevisiae)		Homo sapiens	
RAD51C	**RAD51** homolog C (S. cerevisiae)		Homo sapiens	
RAD51L3	**RAD51**-like 3 (S. cerevisiae)		Homo sapiens	
RAD51AP1	**RAD51** associated protein 1		Homo sapiens	
Rad51l3	**RAD51**-like 3 (S. cerevisiae)		Mus musculus	

javascript:if(window.name=='') { window.location.href='./nil'; } else { doaction('IHOP', 91604, 1); }



http://www.ihop-net.org/UniPub/iHOP/gs/91604.html?IN=1

WARNING: Please keep in mind that gene detection is done automatically and can exhibit a certain error. Read more about synonym ambiguity and the iHOP confidence value.

Found in this page: interacts (**21**)

(Click here to show sentences in the default order)

Sentences in this view contain interactions of RAD51 - Interaction Information is available whenever you see this symbol - Read more.
For a summary overview of the information in this page click here. new

The results provide insight into why mutation in just one of the eight BRC repeats would affect the way that BRCA2 protein **interacts** with the RAD51 filament. [2005]

The RAD51 recombinase **interacts** directly with the breast cancer-**associated** tumour suppressor BRCA2, an interaction that is required for normal recombination proficiency, radiation resistance and genome stability. [2003]

It is known that BRCA2 **interacts** directly with RAD51 through a series of degenerative motifs known as the BRC repeats. [2004]

The breast cancer susceptibility gene BRCA2 **encodes** a critical accessory protein that **interacts** with the RAD51 recombinase and this interaction fluctuates during the cell cycle. [2007]

BRCA2 protein **interacts** directly with the RAD51 recombinase and regulates recombination-mediated DSB repair, accounting for the high levels of spontaneous chromosomal aberrations seen in BRCA2-defective cells. [2007]

Whereas BRCA2 **interacts** directly with and **regulates** RAD51, the role of BRCA1 in this process is unclear. [2005]

RAD51 is an important component of double-stranded DNA-repair mechanisms that **interacts** with both BRCA1 and BRCA2 . [2007]

Previous data report that wild-type p53 **suppresses** homologous recombination and physically **interacts** with Rad51. [2006]

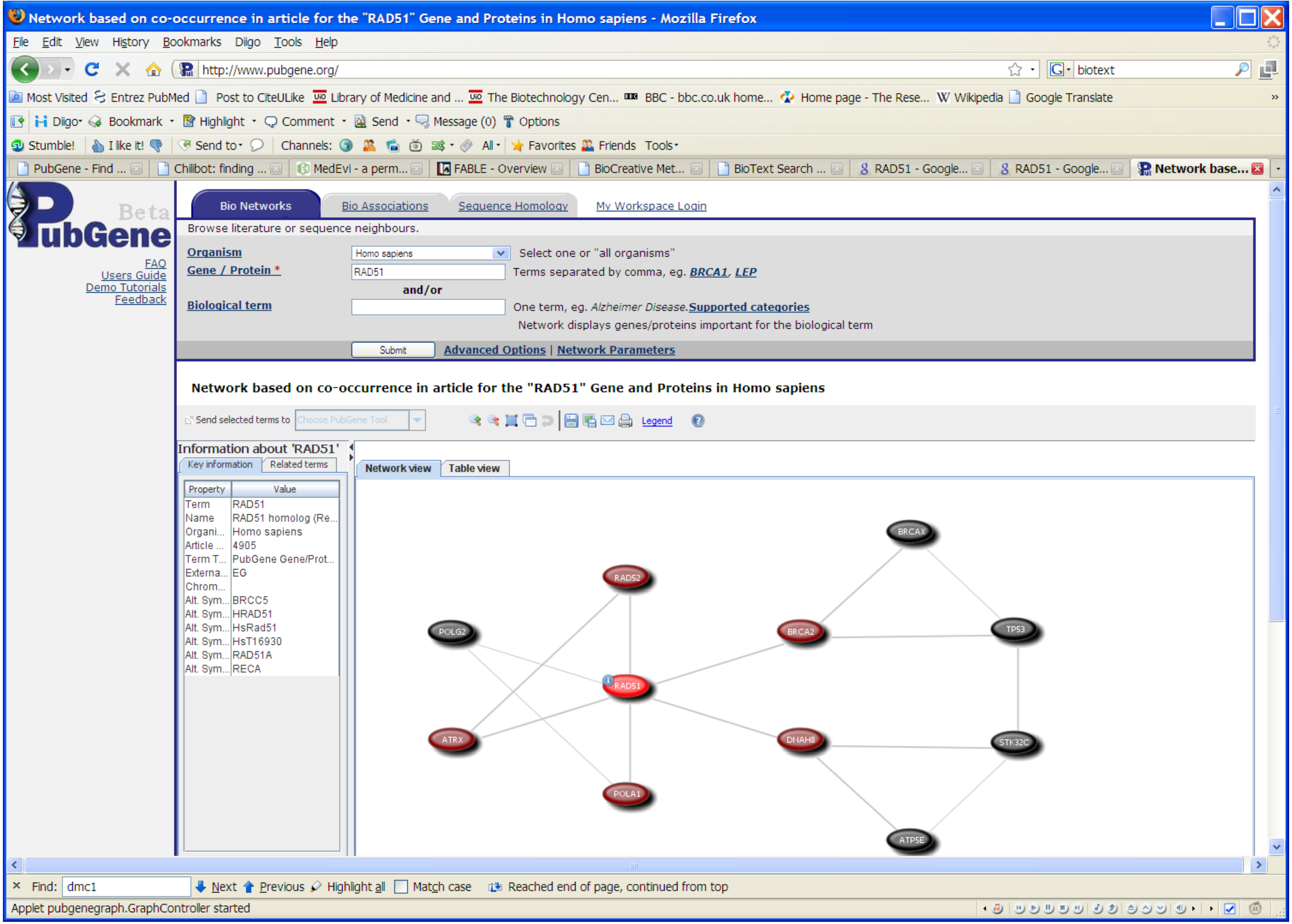
p53 **interacts** with hRAD51 and hRAD54, and directly modulates homologous recombination. [2003]

Previously we reported that HsRad51 **interacts** with XRCC3, and Rad51C interacts with XRCC3, Rad51B, and HsRad51

dmc1

Reached end of page, continued from top

Text mining resources: PubGene



Network based on co-occurrence in article for the "RAD51" Gene and Proteins in Homo sapiens - Mozilla Firefox

http://www.pubgene.org/

Browse literature or sequence neighbours.

Organism Homo sapiens Select one or "all organisms"

Gene / Protein * RAD51 Terms separated by comma, eg. **BRCA1**, **LEP**

and/or

Biological term One term, eg. *Alzheimer Disease*. **Supported categories**

Network displays genes/proteins important for the biological term

Network based on co-occurrence in article for the "RAD51" Gene and Proteins in Homo sapiens

Information about 'RAD51'

Property	Value
Term	RAD51
Name	RAD51 homolog (Re...
Organi...	Homo sapiens
Article ...	4905
Term T...	PubGene Gene/Prot...
Externa...	EG
Chrom...	
Alt. Sym...	BRCC5
Alt. Sym...	HRAD51
Alt. Sym...	HsRad51
Alt. Sym...	HsT16930
Alt. Sym...	RAD51A
Alt. Sym...	RECA

Find: dmc1

Reached end of page, continued from top

Applet pubgenegraph.GraphController started

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Predicted interaction resources

STRING	http://string.embl.de/
OPHID/I2D	http://ophid.utoronto.ca/ophidv2.201/
FunCoup	http://FunCoup.sbc.su.se

Finding interaction information

The take home message:

There is no single place to collect interaction information.

Users are placed in a ”go-fish” position and are responsible for distinguishing and sorting through multilple data sources.

There are a few reources that are focusing on providing an integrated data resource...

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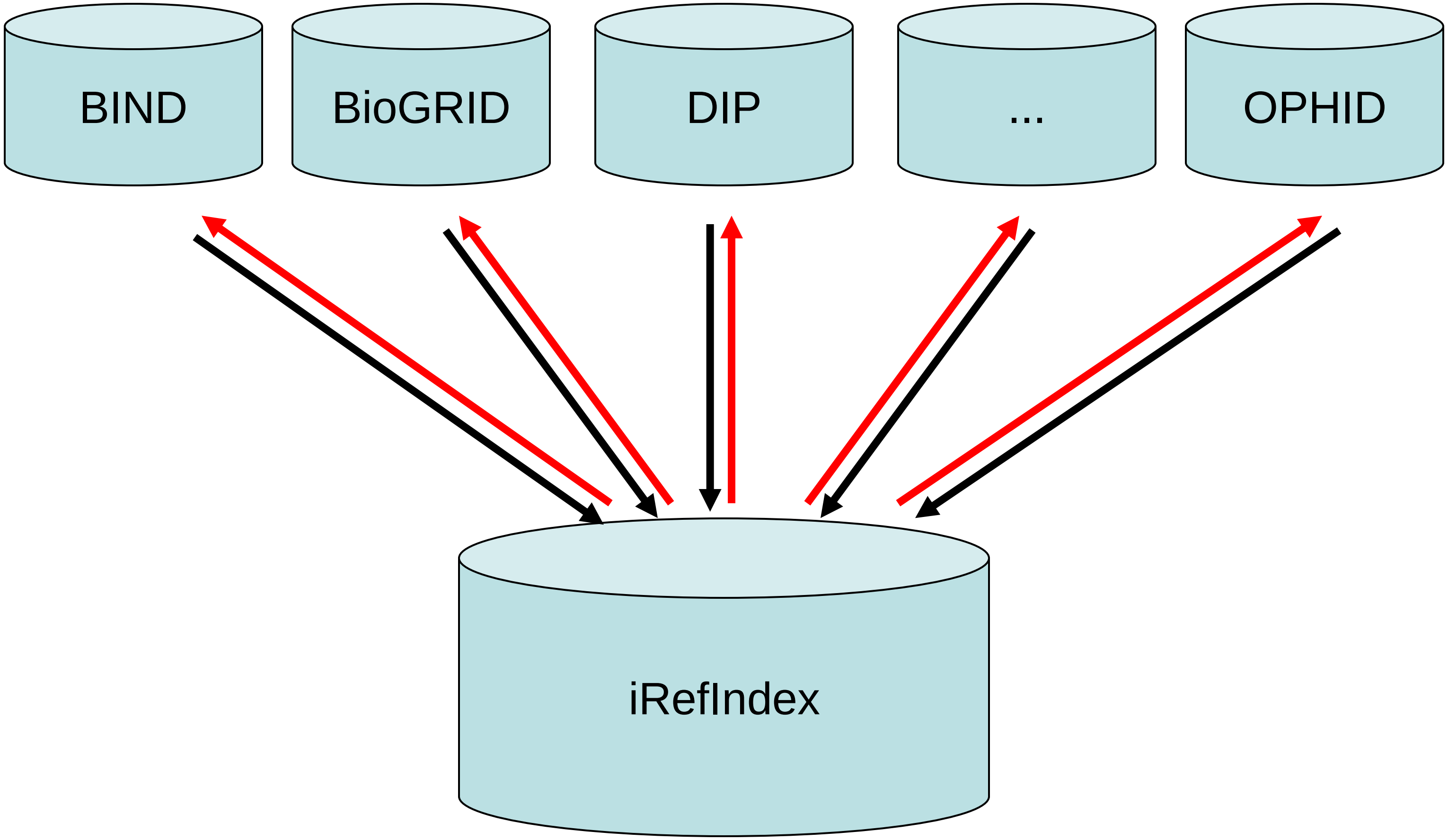
Consolidated databases

APID2NET	http://bioinfow.dep.usal.es/apid/apid2net.html
Pathway Commons	http://www.pathwaycommons.org/pc/
MiMI	http://mimi.ncibi.org/MimiWeb/main-page.jsp
iRefIndex	http://irefindex.uio.no/wiki/iRefIndex

iRefIndex: Integration and feedback



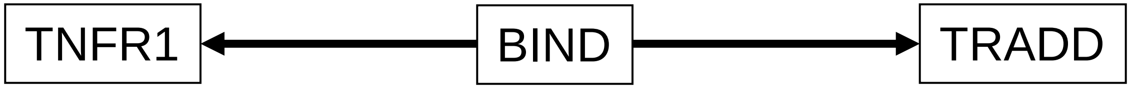
The problem

TNFR1

TRADD

An interaction.

The problem



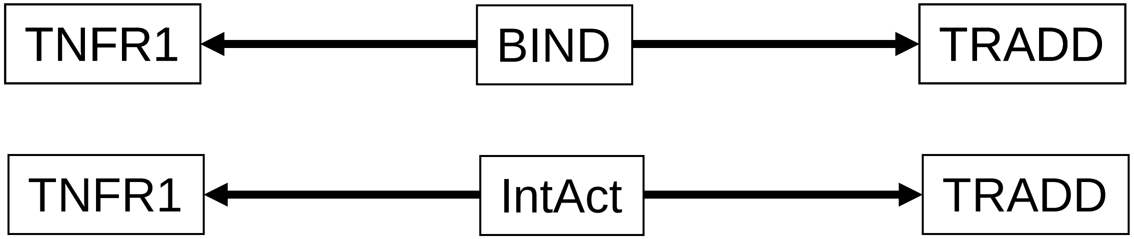
TNFR1

BIND

TRADD

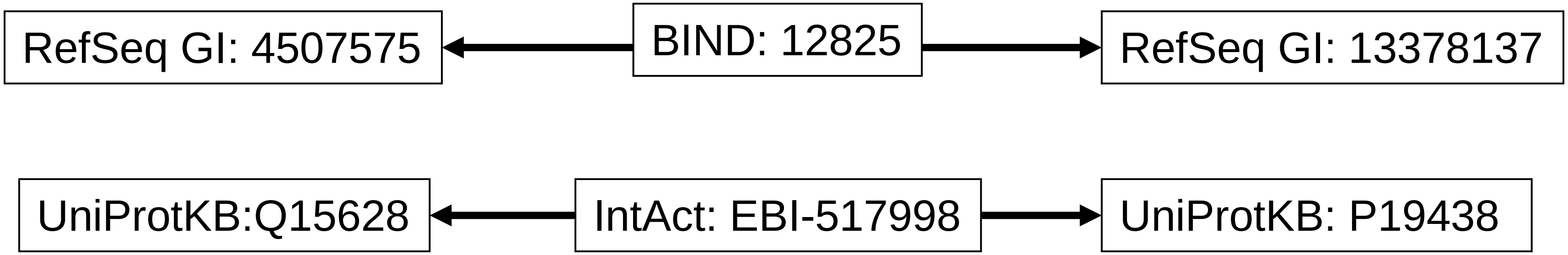
An interaction described in a database.

The problem



An interaction described in two databases.

The problem

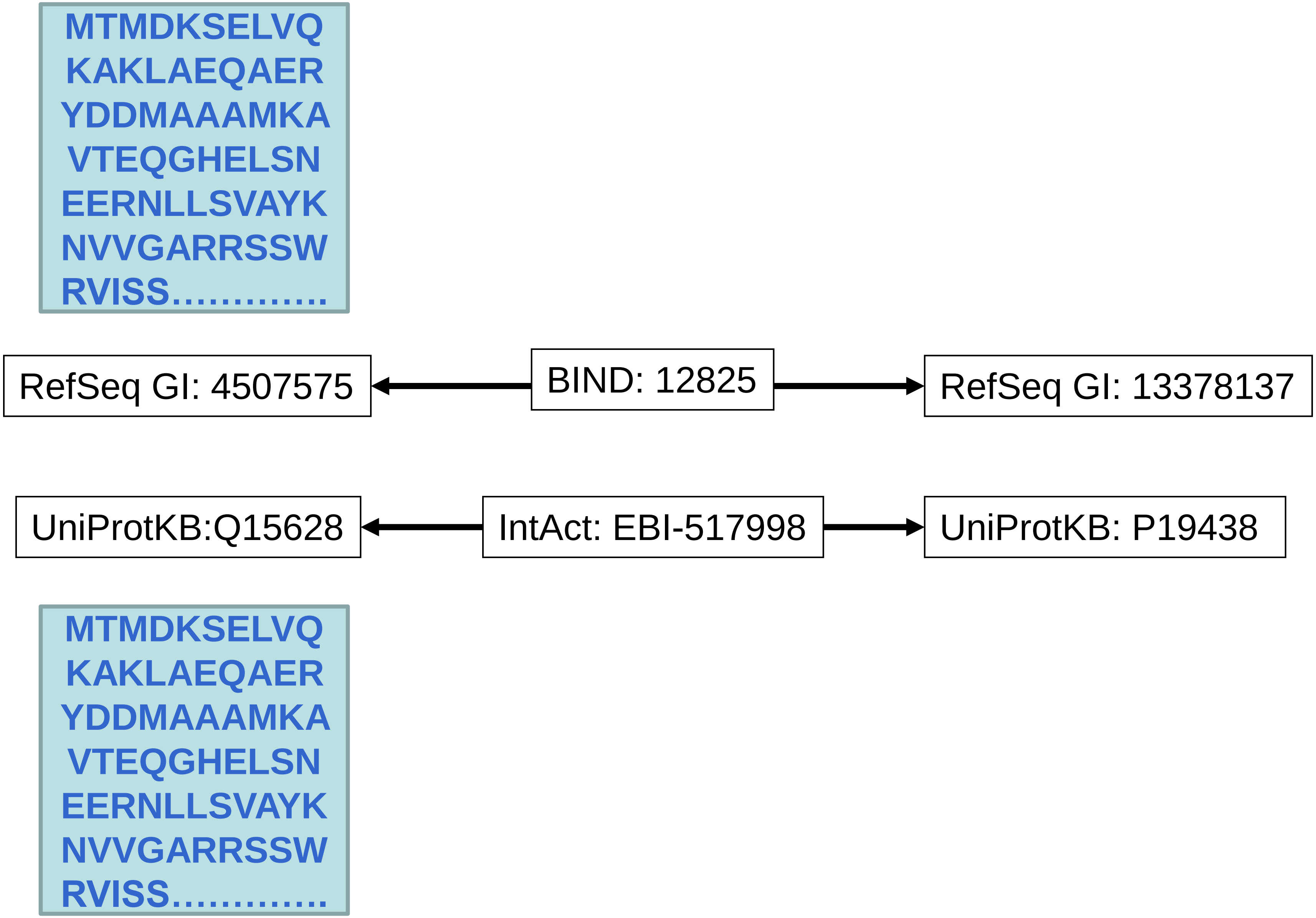


RefSeq GI: 4507575 ← BIND: 12825 → RefSeq GI: 13378137

UniProtKB:Q15628 ← IntAct: EBI-517998 → UniProtKB: P19438

Different protein accessions are used to describe the same thing.

The solution



MTMDKSELVQ
KAKLAEQAER
YDDMAAAMKA
VTEQGHELSN
EERNLLSVAYK
NVVGARRSSW
RVISS………….

RefSeq GI: 4507575 ← BIND: 12825 → RefSeq GI: 13378137

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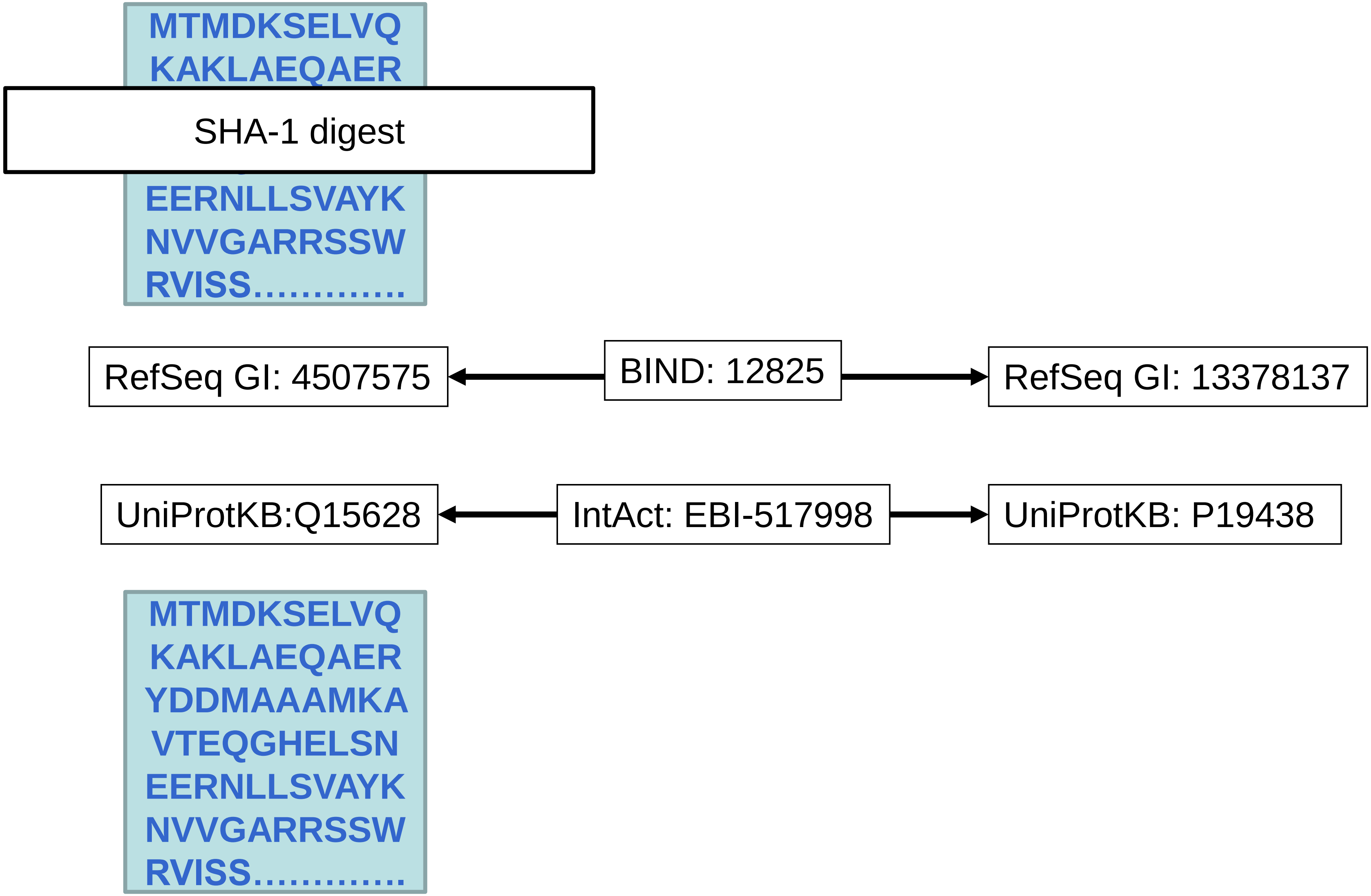

MTMDKSELVQ
KAKLAEQAER

SHA-1 digest

EERNLLSVAYK
NVVGARRSSW
RVISS.............

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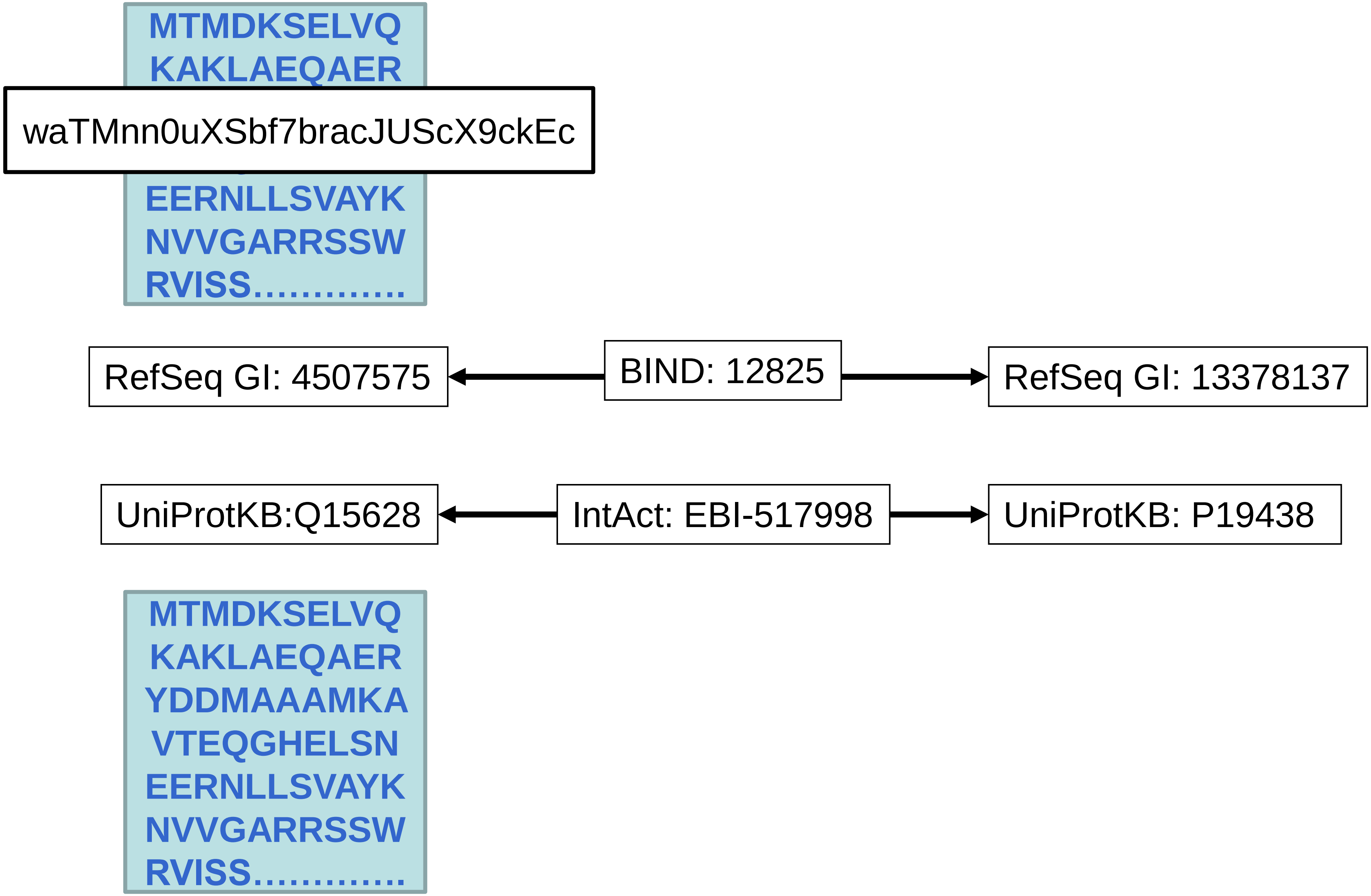
The solution



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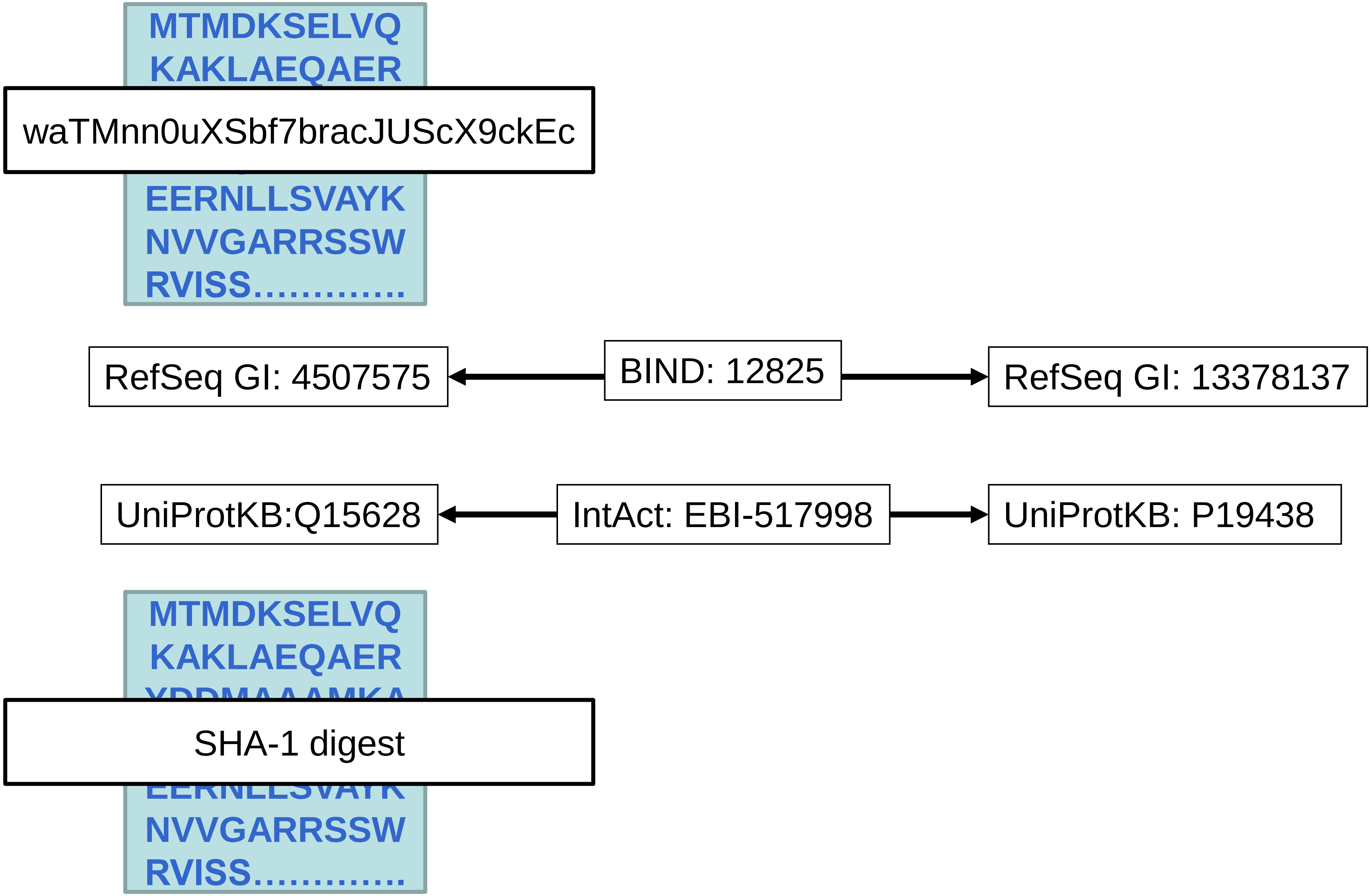

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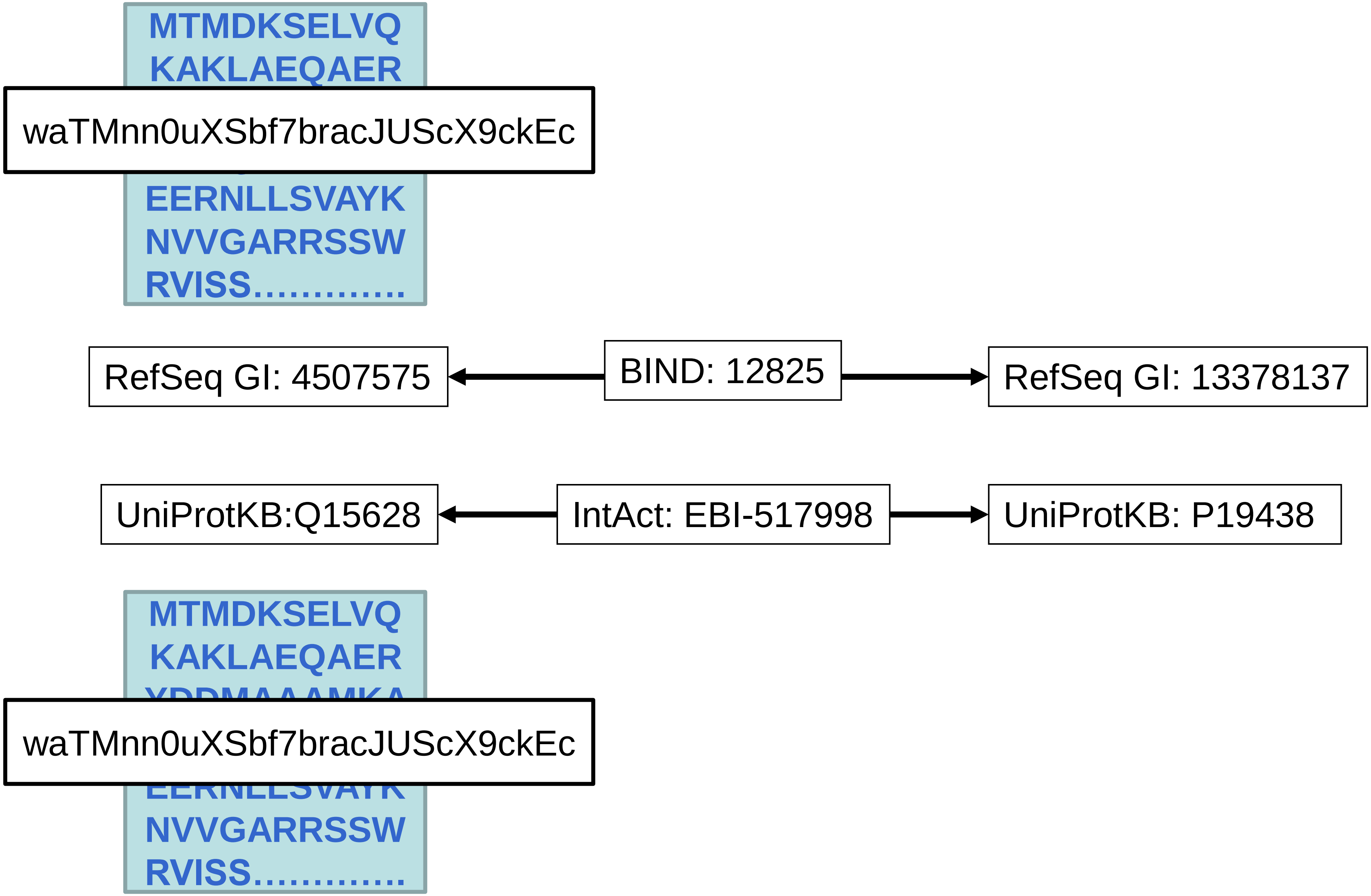
SHA-1 digest

NVVGARRSSW
RVISS............

The solution



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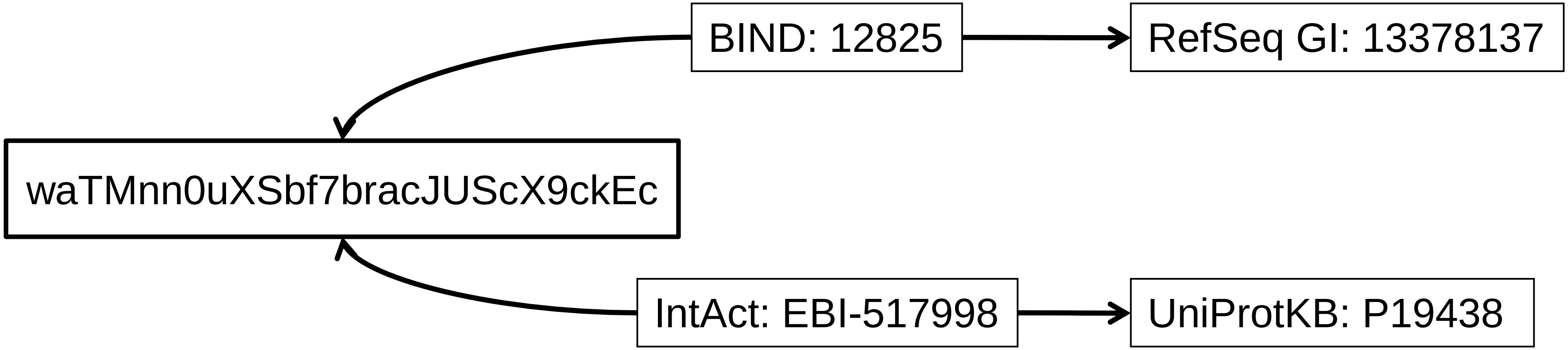
NVVGARRSSW
RVISS.............

The solution



BIND: 12825

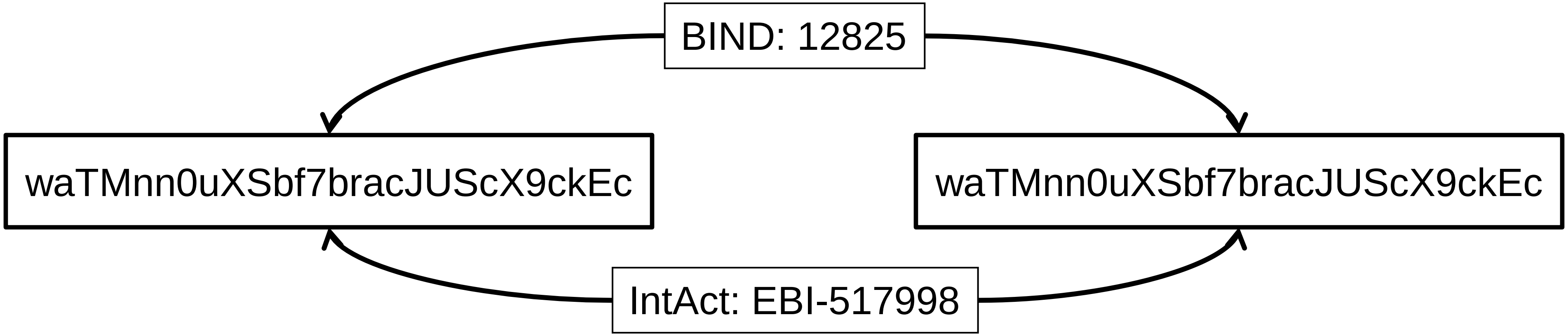
RefSeq GI: 13378137

waTMnn0uXSbf7bracJUScX9ckEc

IntAct: EBI-517998

UniProtKB: P19438

The solution



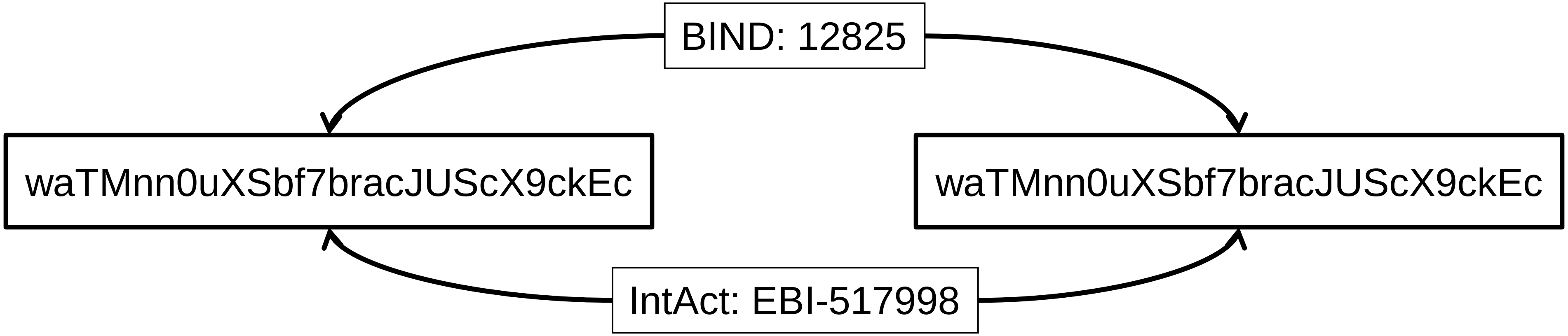
BIND: 12825

waTMnn0uXSbf7bracJUScX9ckEc

waTMnn0uXSbf7bracJUScX9ckEc

IntAct: EBI-517998

The solution



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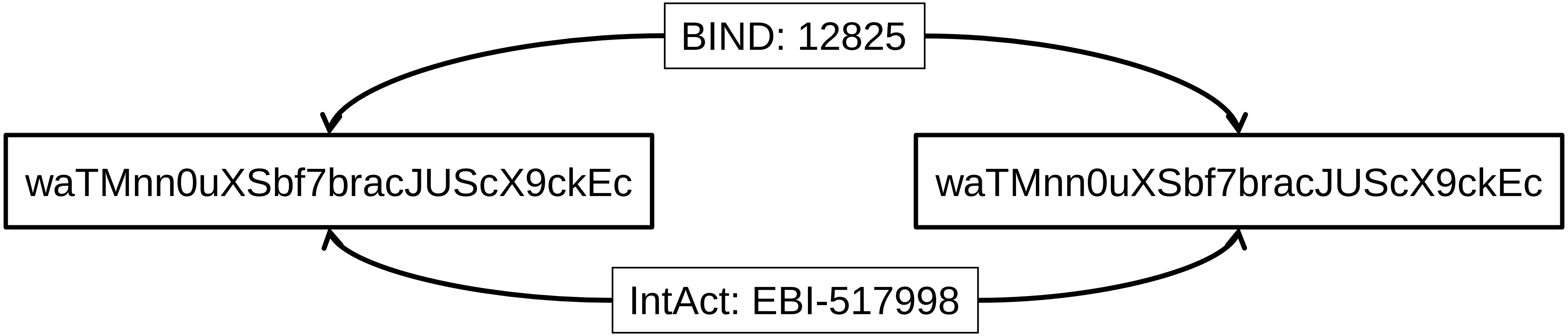


BIND: 12825

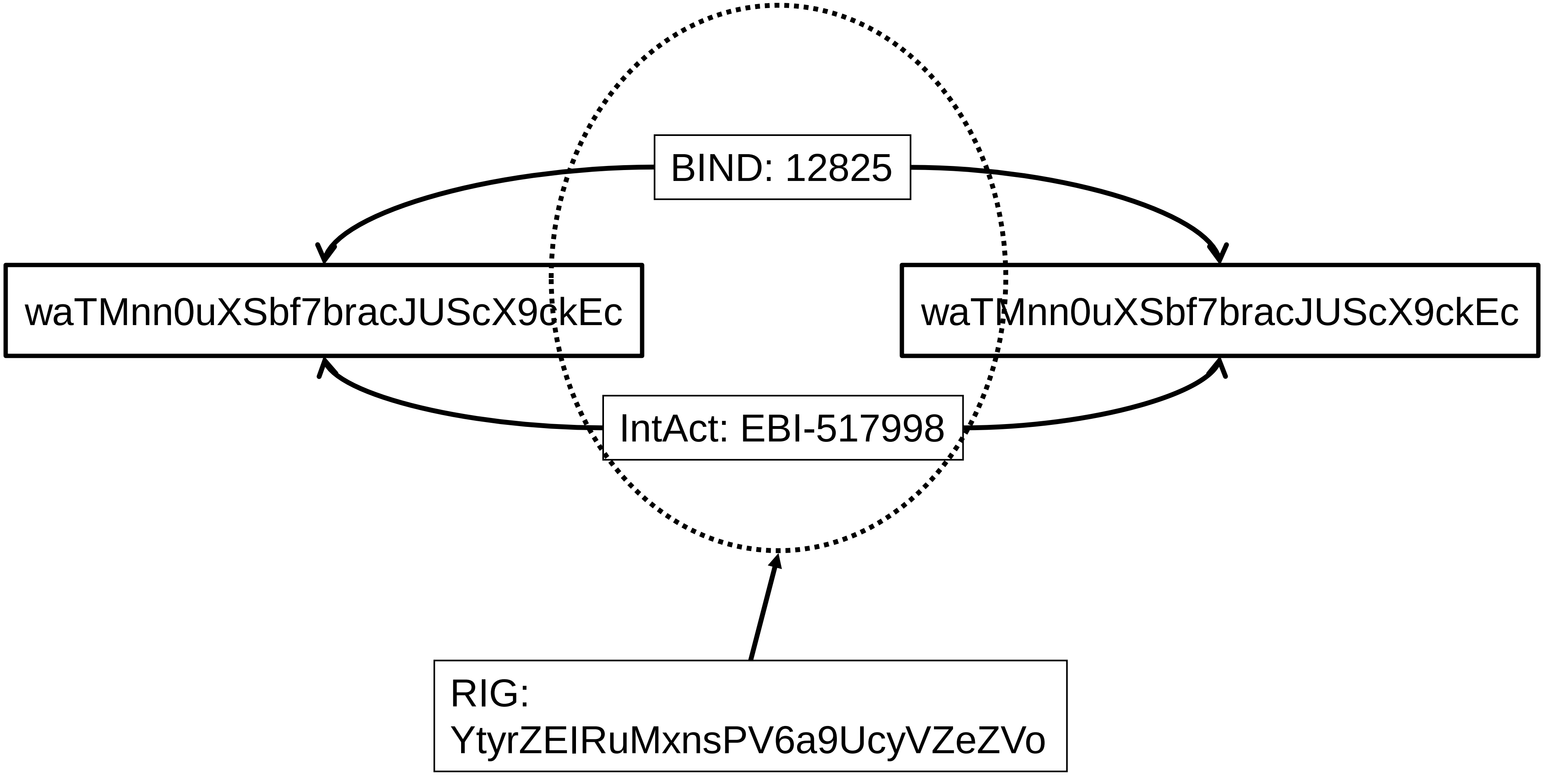
waTMnn0uXSbf7bracJUScX9ckEc

waTMnn0uXSbf7bracJUScX9ckEc

IntAct: EBI-517998

So the solution is based on **exact sequence matches** between interaction records

The solution



BIND: 12825

waTMnn0uXSbf7bracJUScX9ckEc

waTMnn0uXSbf7bracJUScX9ckEc

IntAct: EBI-517998

RIG:
YtyrZEIRuMxnsPV6a9UcyVZeZVo

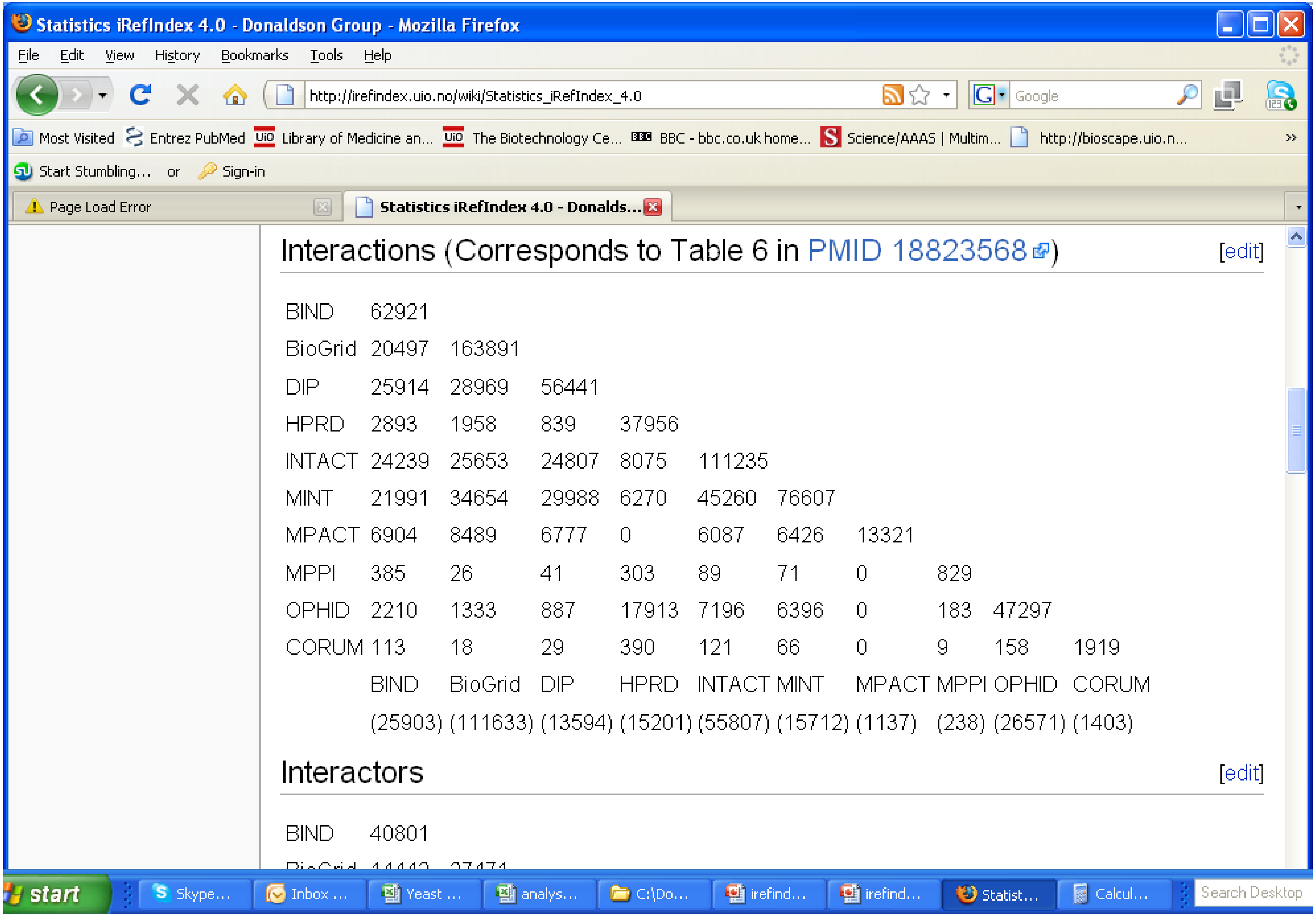
Hash keys allow consolidated of interaction data

Protein A reference

Interaction record

Protein B reference

Results: RIG redundancy between source databases.



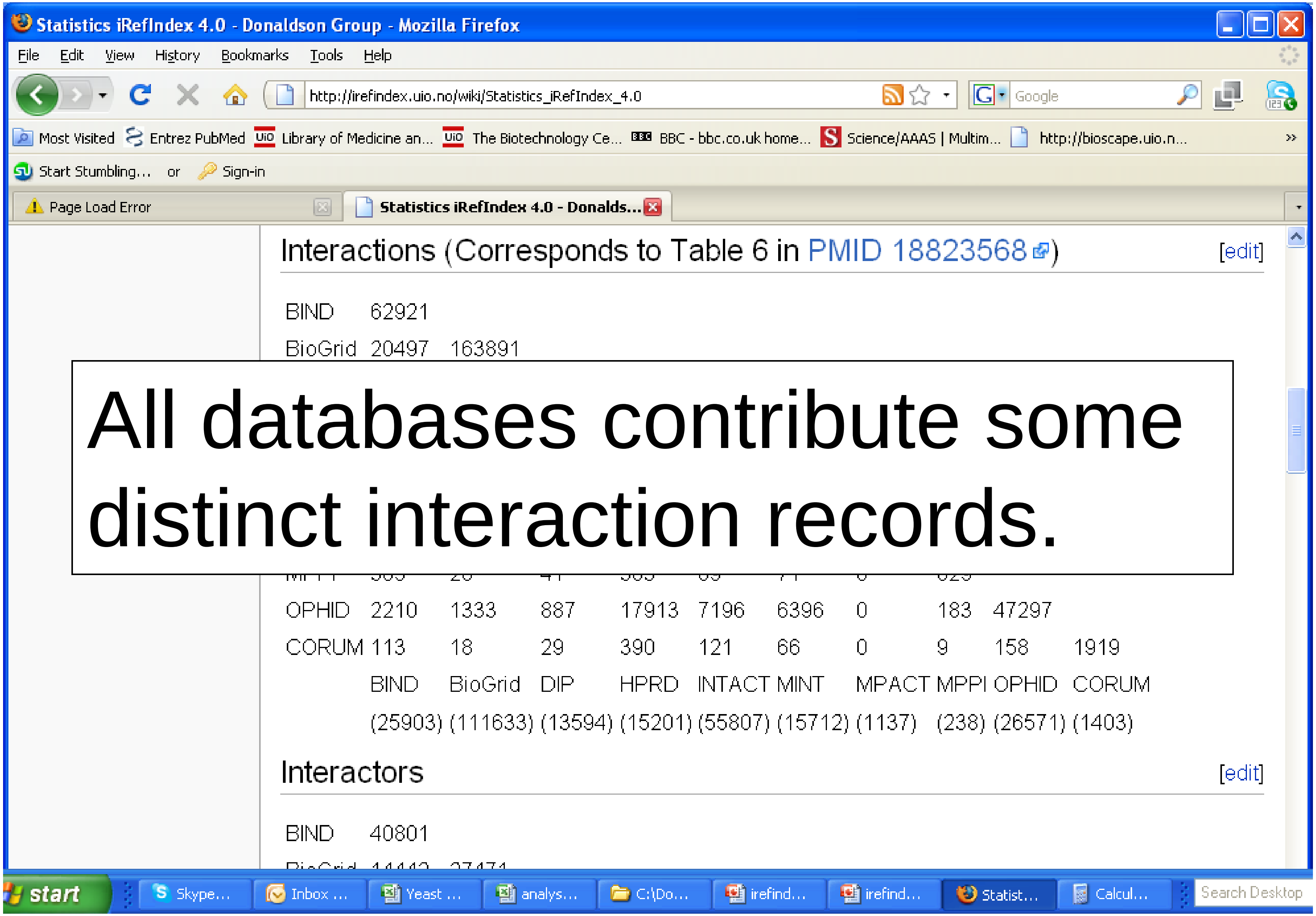
Interactions (Corresponds to Table 6 in PMID 18823568) [edit]

BIND	62921									
BioGrid	20497	163891								
DIP	25914	28969	56441							
HPRD	2893	1958	839	37956						
INTACT	24239	25653	24807	8075	111235					
MINT	21991	34654	29988	6270	45260	76607				
MPACT	6904	8489	6777	0	6087	6426	13321			
MPPI	385	26	41	303	89	71	0	829		
OPHID	2210	1333	887	17913	7196	6396	0	183	47297	
CORUM	113	18	29	390	121	66	0	9	158	1919
	BIND	BioGrid	DIP	HPRD	INTACT	MINT	MPACT	MPPI	OPHID	CORUM
	(25903)	(111633)	(13594)	(15201)	(55807)	(15712)	(1137)	(238)	(26571)	(1403)

Interactors [edit]

BIND 40801

Results: RIG redundancy between source databases.



Interactions (Corresponds to Table 6 in PMID 18823568) [edit]

BIND	62921									
BioGrid	20497	163891								
OPHID	2210	1333	887	17913	7196	6396	0	183	47297	
CORUM	113	18	29	390	121	66	0	9	158	1919
	BIND	BioGrid	DIP	HPRD	INTACT	MINT	MPACT	MPPI	OPHID	CORUM
	(25903)	(111633)	(13594)	(15201)	(55807)	(15712)	(1137)	(238)	(26571)	(1403)

Interactors [edit]

BIND 40801

All databases contribute some distinct interaction records.

http://irefindex.uio.no/

iRefIndex

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2 A reference index for protein interaction data
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4 Data availability via download
5 Data availability via web interface
6 Data availability via Cytoscape
7 Data availability via Web services
8 Feedback files
9 License
10 Disclaimer
11 Statistics
12 Credits
13 Citation
14 References
15 Contact
16 iRefIndex Google Group

Please take the biolibrarian survey

[edit]

See http://irefindex.uio.no/wiki/The_Biolibrarian_Proposal

A reference index for protein interaction data

[edit]

iRefIndex provides an index of protein interactions available in a number of primary interaction databases including BIND, BioGRID, CORUM, DIP, HPRD, IntAct, MINT, MPact, MPPI and OPHID. This index allows the user to search for a protein and retrieve a non-redundant list of interactors for that protein.

iRefIndex uses the Sequence Global Unique Identifier (SEGUID) to group proteins and interactions into redundant groups. This method allows users to integrate their own data with the iRefIndex in a way that ensures proteins with the exact same sequence will be represented only once.

The iRefIndex paper has been published and is available here.

Finding interaction information

The take home message:

There is no single place to collect interaction information.

Users are placed in a ”go-fish” position and are responsible for distinguishing and sorting through multilple data sources.

There are a few reources that are focusing on providing an integrated data resource...

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Visualization Tools

Cytoscape	http://www.cytoscape.org/
VisAnt	http://visant.bu.edu/

There are over 30 visualization tools listed in a recent review

Suderman M, Hallett M: Tools for visually exploring biological networks. *Bioinformatics* 2007, 23(20):2651-2659.

Cytoscape will be covered in a following talk.

Conclusions

Interaction data is an important bioinformatics data source.

Interaction detection techniques have evolved past the simple Y2H and coimmpunoprecipitation methods.

Finding data is still a non-trivial task.

There is no de facto source of data and users are faced with doing their own collection and curation.

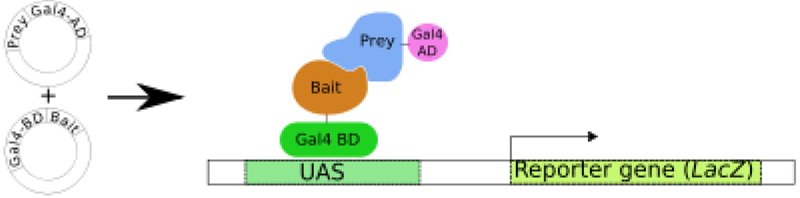
Data integration and accessibility is an ongoing area of research.

Experimental methods – Yeast Two Hybrid

A. Regular transcription of the reporter gene

B. One fusion protein only (Gal4-BD + Bait) - no transcription

C. One fusion protein only (Gal4-AD + Prey) - no transcription

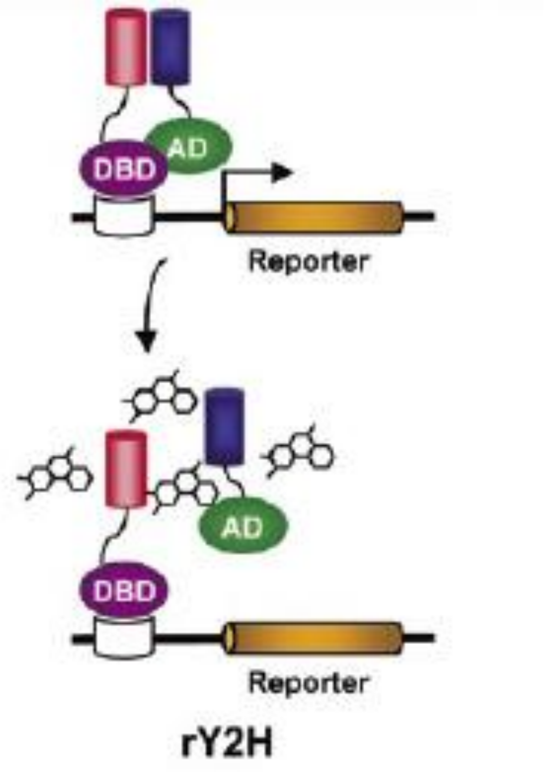


D. Two fusion proteins with interacting Bait and Prey

http://en.wikipedia.org/wiki/Yeast_two-hybrid

Experimental methods – reverse Two Hybrid

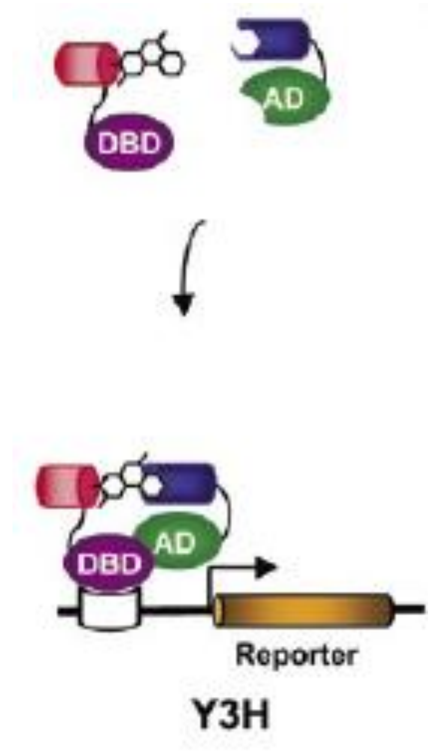
- screens for small molecules that can disrupt an interaction
- uses a counter-selective strategy



Suter 2008, Biotechniques

Experimental methods – Yeast 3 Hybrid

- screens for small molecules or other components that mediate an interaction

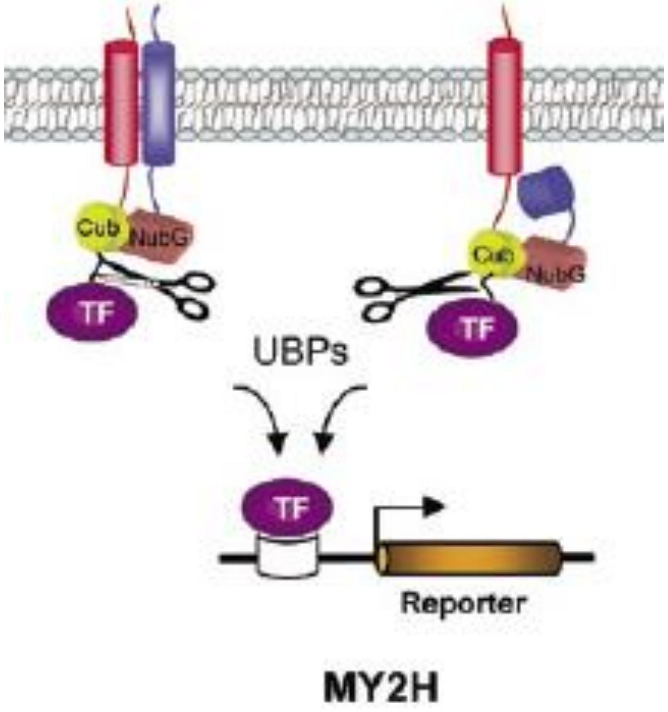


Suter 2008, Biotechniques

Experimental methods – membrane Yeast Two-Hybrid (mY2H)

- screens for proteins that interact within or near the membrane
- nearly one third of all proteins are integral membrane proteins not amenable to Y2H

Cub: C-terminus of Ubiquitin
Nub: N-terminus of Ubiquitin

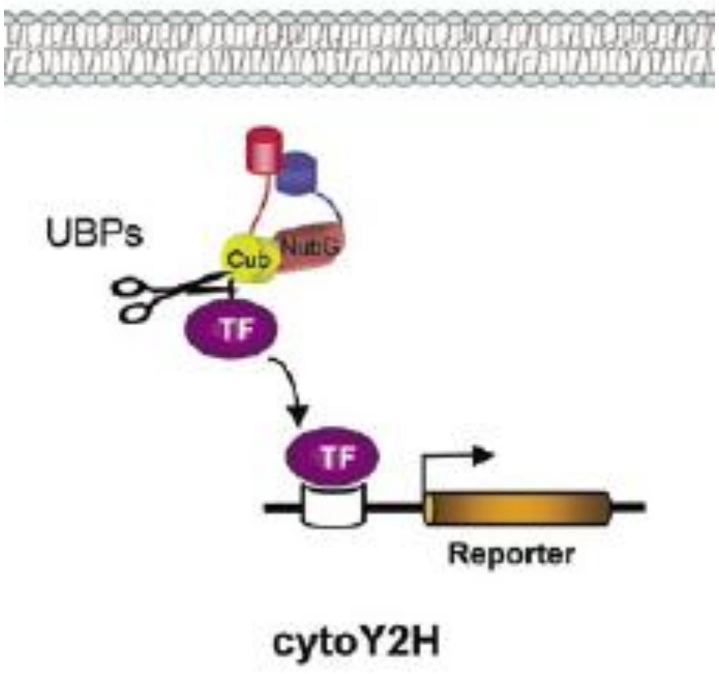


Suter 2008, Biotechniques

Experimental methods – cytosolic Yeast Two-Hybrid (cY2H)

- screens for proteins that interact within cytosol
- alternative for studying proteins in proper context
- alternative for studying proteins that may self activate in Y2H

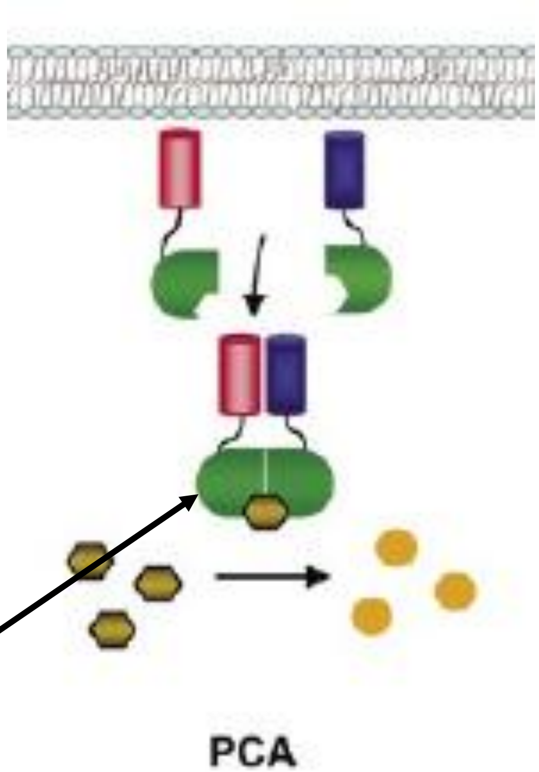
Cub: C-terminus of Ubiquitin
Nub: N-terminus of Ubiquitin



Suter 2008, Biotechniques

Experimental methods – PCA
Protein Complementation assay

- based on reconstitution of some protein activity
- fusion protein design must prevent spontaneous refolding
- independent of transcription based reporter
- alternatives include assays for luminescence or fluorescence
- useful in a variety of organisms
- other variants of this assay are split TEV protease assay



e.g. Reconstituted DHFR activity allows growth on trimethoprim

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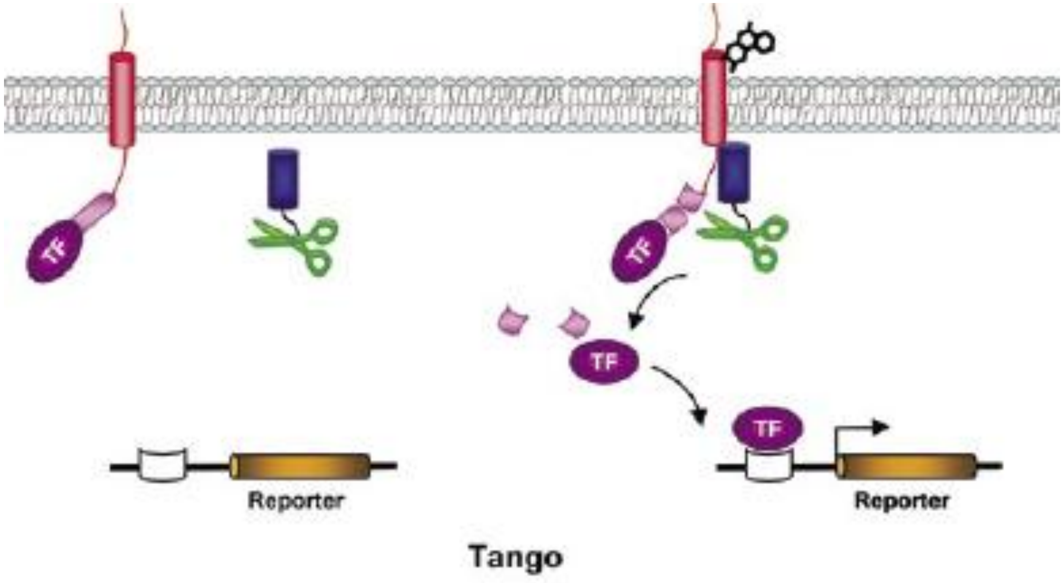
Experimental methods – Tango
State-specific binding assay

TEV protease is juxtaposed to reporter construct under specific conditions (presence of a ligand).



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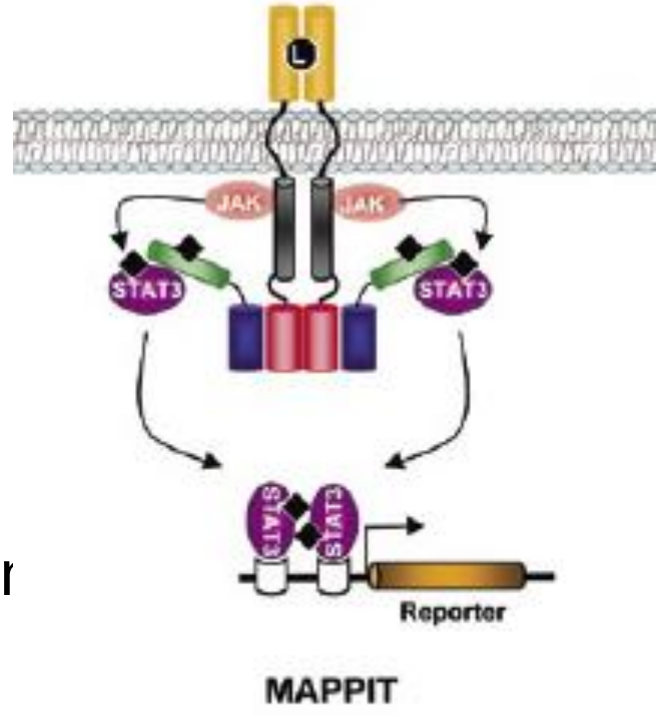
Experimental methods – MAPPIT
Mammalian protein interaction trap

- interaction between bait and prey restores ligand-dependent cytokine receptor signalling

- especially applicable to analysis of cell signalling pathways due to native context of tested bait and prey

- rMAPPIT is used to screen for compounds that disrupt an interaction



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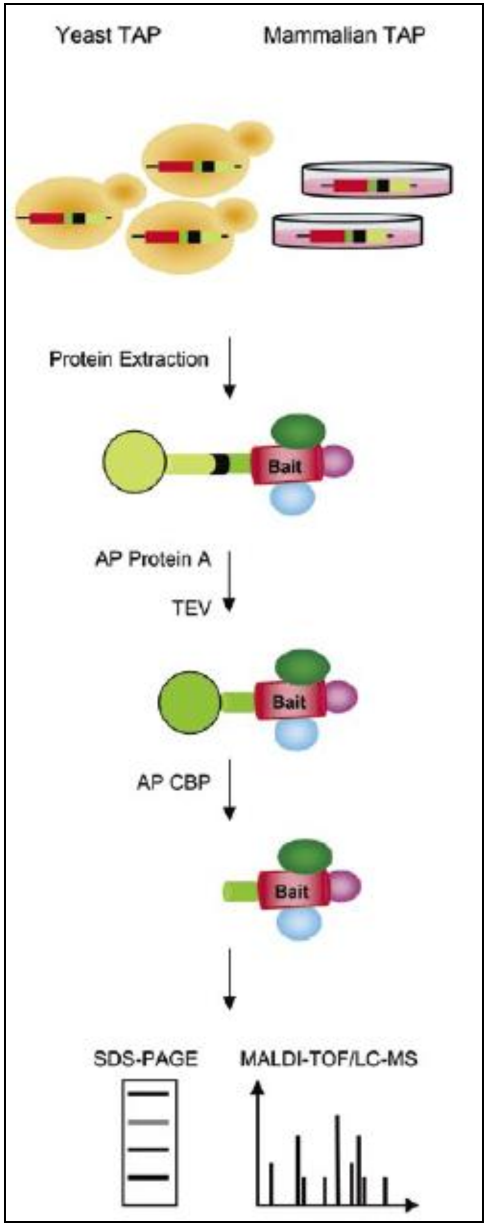
Experimental methods
Affinity purification

- interacting proteins are purified by means of an affinity tag on a ”bait” protein

- proteins are detected via MS

- readout of this experiment type is a list of proteins that somehow interact with the bait protein

- note this is fundamentally different than readout of the Y2H family of experiments (more later)



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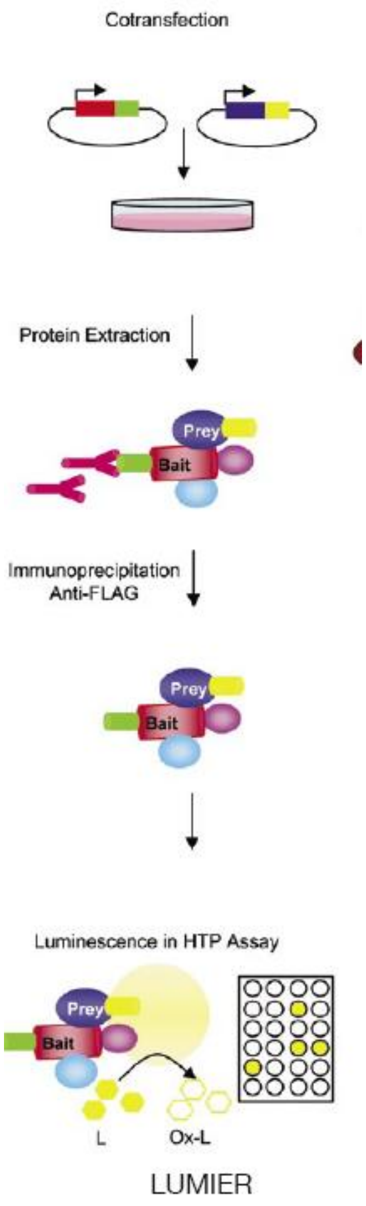
Experimental methods – LUMIER
Luminescent mammlian interaction assay

- bait is tagged with FLAG epitope
- prey fused to luciferase
- expression in mammlian cells
- pairwise screening in a high-troughput screen
- pre-tagging of prey aids in non-ambiguous identification



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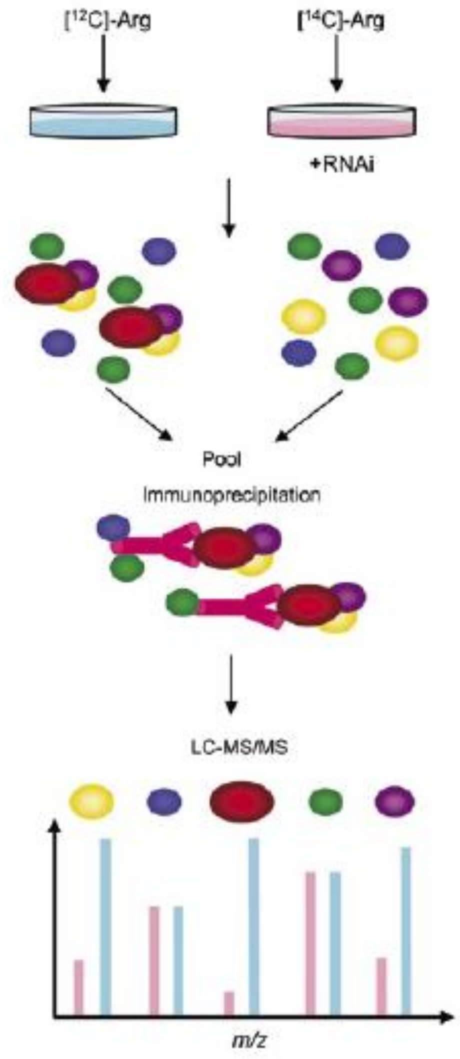
Experimental methods – QUICK

Quantitative IP combined with knockdown

- ”bait” is knocked down in heavy-labelled sample
- requires antibodies specific to bait (not high throughput)
- reduces noises from non-specifically binding proteins found in IP sample
- no tags, represents native-like cell



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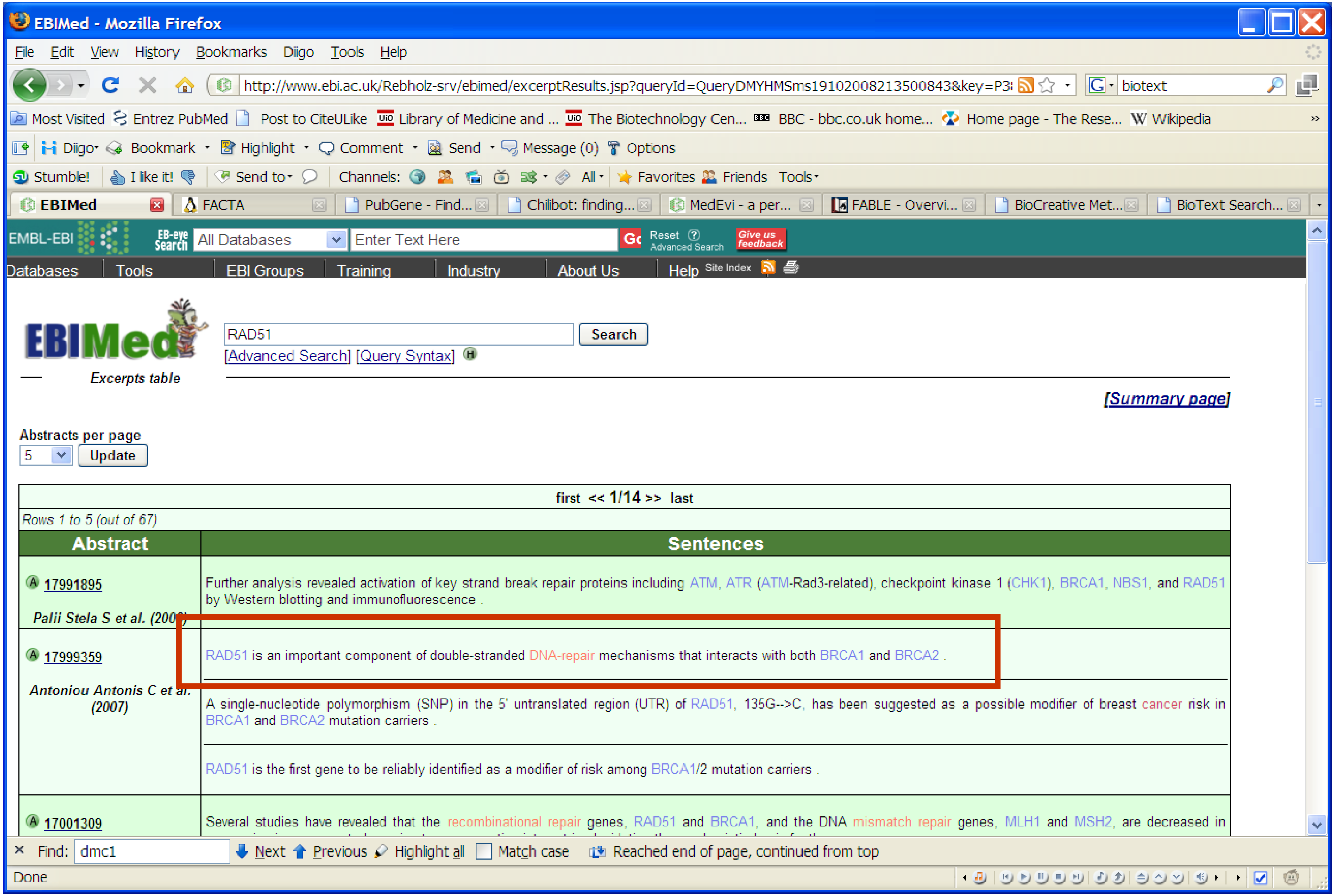
Text mining resources: EBIMed

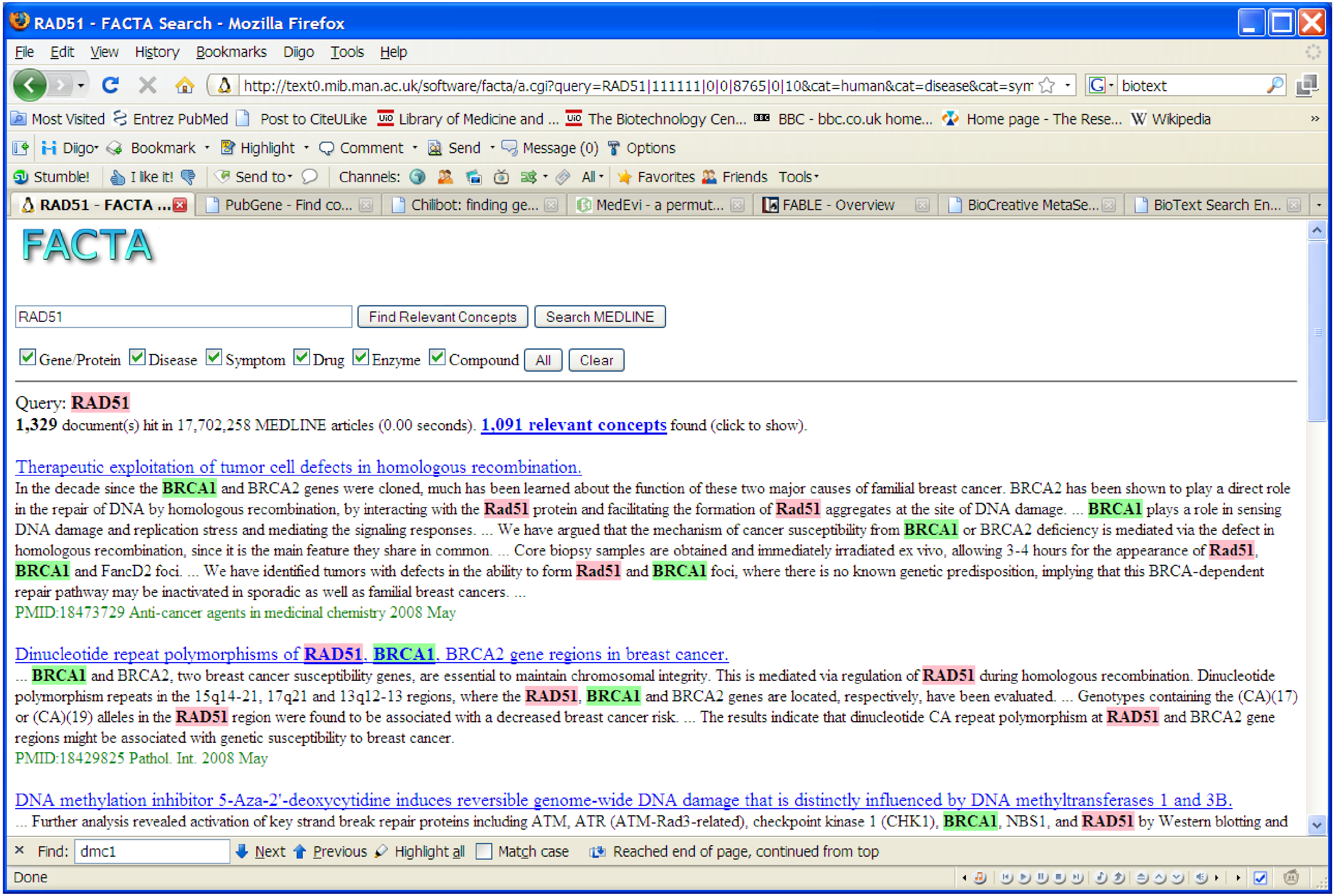


first << 1/14 >> last

Rows 1 to 5 (out of 67)

Abstract	Sentences
17991895 *Palii Stela S et al. (2007)*	Further analysis revealed activation of key strand break repair proteins including ATM, ATR (ATM-Rad3-related), checkpoint kinase 1 (CHK1), BRCA1, NBS1, and RAD51 by Western blotting and immunofluorescence .
17999359 *Antoniou Antonis C et al. (2007)*	RAD51 is an important component of double-stranded DNA-repair mechanisms that interacts with both BRCA1 and BRCA2 .
	A single-nucleotide polymorphism (SNP) in the 5' untranslated region (UTR) of RAD51, 135G-->C, has been suggested as a possible modifier of breast cancer risk in BRCA1 and BRCA2 mutation carriers .
	RAD51 is the first gene to be reliably identified as a modifier of risk among BRCA1/2 mutation carriers .
17001309	Several studies have revealed that the recombinational repair genes, RAD51 and BRCA1, and the DNA mismatch repair genes, MLH1 and MSH2, are decreased in

Text mining resources: FACTA



RAD51

☑ Gene/Protein ☑ Disease ☑ Symptom ☑ Drug ☑ Enzyme ☑ Compound

Query: **RAD51**

1,329 document(s) hit in 17,702,258 MEDLINE articles (0.00 seconds). **1,091 relevant concepts** found (click to show).

Therapeutic exploitation of tumor cell defects in homologous recombination.

In the decade since the **BRCA1** and BRCA2 genes were cloned, much has been learned about the function of these two major causes of familial breast cancer. BRCA2 has been shown to play a direct role in the repair of DNA by homologous recombination, by interacting with the **Rad51** protein and facilitating the formation of **Rad51** aggregates at the site of DNA damage. ... **BRCA1** plays a role in sensing DNA damage and replication stress and mediating the signaling responses. ... We have argued that the mechanism of cancer susceptibility from **BRCA1** or BRCA2 deficiency is mediated via the defect in homologous recombination, since it is the main feature they share in common. ... Core biopsy samples are obtained and immediately irradiated ex vivo, allowing 3-4 hours for the appearance of **Rad51**, **BRCA1** and FancD2 foci. ... We have identified tumors with defects in the ability to form **Rad51** and **BRCA1** foci, where there is no known genetic predisposition, implying that this BRCA-dependent repair pathway may be inactivated in sporadic as well as familial breast cancers. ...

PMID:18473729 Anti-cancer agents in medicinal chemistry 2008 May

Dinucleotide repeat polymorphisms of **RAD51**, **BRCA1**, BRCA2 gene regions in breast cancer.

... **BRCA1** and BRCA2, two breast cancer susceptibility genes, are essential to maintain chromosomal integrity. This is mediated via regulation of **RAD51** during homologous recombination. Dinucleotide polymorphism repeats in the 15q14-21, 17q21 and 13q12-13 regions, where the **RAD51**, **BRCA1** and BRCA2 genes are located, respectively, have been evaluated. ... Genotypes containing the (CA)(17) or (CA)(19) alleles in the **RAD51** region were found to be associated with a decreased breast cancer risk. ... The results indicate that dinucleotide CA repeat polymorphism at **RAD51** and BRCA2 gene regions might be associated with genetic susceptibility to breast cancer.

PMID:18429825 Pathol. Int. 2008 May

DNA methylation inhibitor 5-Aza-2'-deoxycytidine induces reversible genome-wide DNA damage that is distinctly influenced by DNA methyltransferases 1 and 3B.

... Further analysis revealed activation of key strand break repair proteins including ATM, ATR (ATM-Rad3-related), checkpoint kinase 1 (CHK1), **BRCA1**, NBS1, and **RAD51** by Western blotting and

Text mining resources: Chillibot

Chilibot

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Last update: 08/04/07

We recommend FireFox browser.

RAD51 & BRCA2

Retrieving synonyms..

Retrieving abstracts .. |RAD51/BRCA2 ....

Performing linguistic analysis ..

.

Analyzed **100** *most recent* abstracts out of **207** available.

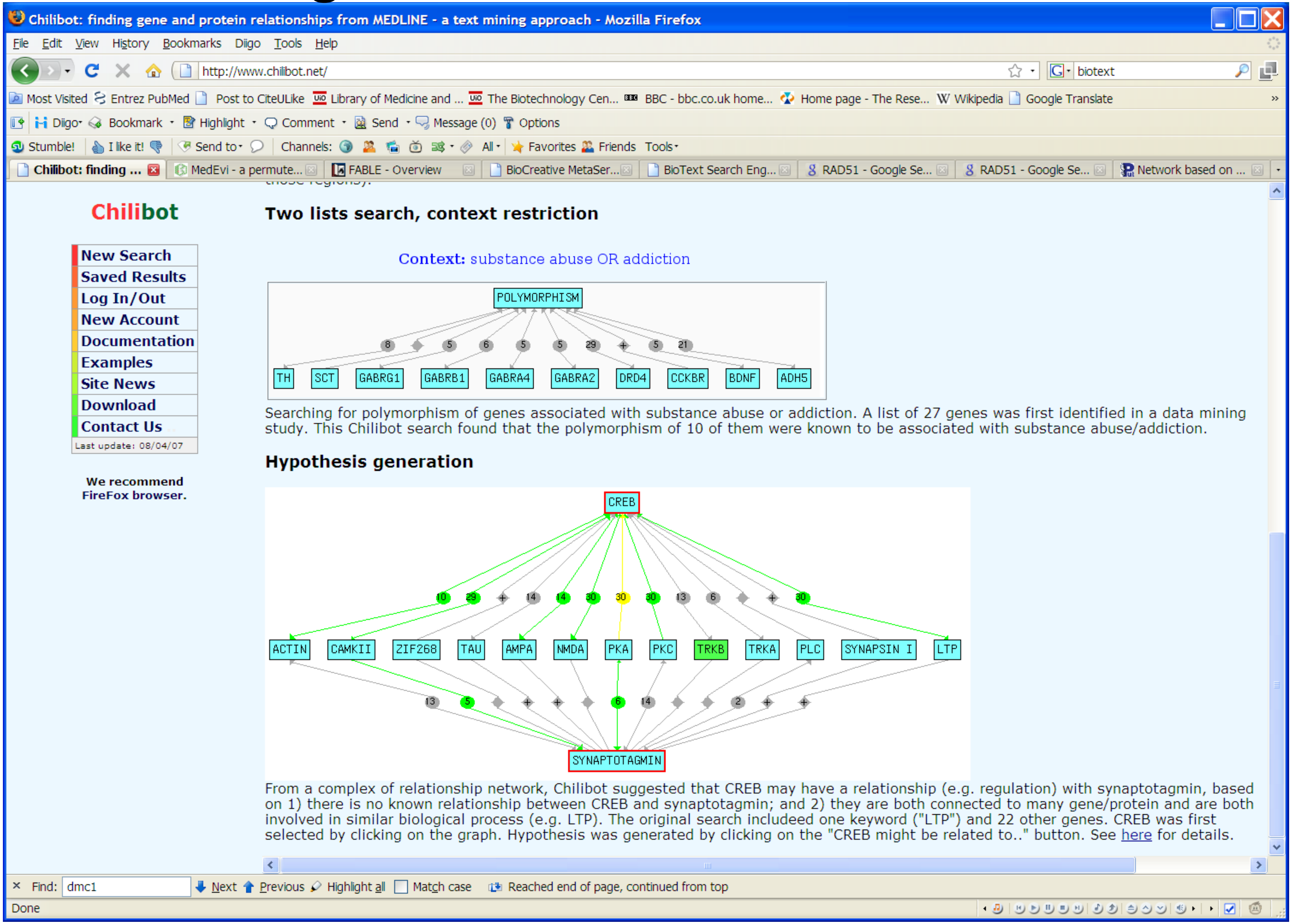
Found **103** interactive sentences and **70** parallel sentences.

`View all relevant sentences.`

Interactive relationship (e.g. stimulation, inhibition, etc)

- These findings indicate that **BRCA2** inhibits **Rad51** cleavage and subsequent apoptosis. Ref: Radiat Res, 2008
- Similarly, reducing **BRCA2** by 50% reduces **RAD51** and BCCIP foci. Ref: Mol Cell Biol, 2005
- **BRCA2** expression also modulates **Rad51** protein levels such that **Rad51** protein is relatively decreased in **BRCA2** defective cancer cells. Ref: Mol Carcinog, 2008
- **BRCA2** is essential for homologous recombination in vivo, but isolated BRC repeat peptides can prevent the assembly of **RAD51** into active nucleoprotein filaments in vitro, suggesting a model in which **BRCA2** sequesters **RAD51** in undamaged cells, and promotes recombinase function after DNA damage. Ref: Nucleic Acids Res, 2006
- The interactions of **BRCA2** with **RAD51** and DMC1 lead us to suggest that the **BRCA2** tumour suppressor is a universal regulator of recombinase actions. Ref: Oncogene, 2007
- The **BRCA2** tumour suppressor regulates the RAD 51 [**RAD51**] recombinase during double strand break (DSB) repair by homologous recombination (HR) but how **BRCA2** executes its functions is not well understood. Ref: J Mol Biol, 2006
- The crystallographic analysis shows that the BRC motif of the **BRCA2** tumor suppressor is in contact with the subunit subunit interface of **Rad51** and could thus prevent filament formation of **Rad51** . Ref: Genes Cells, 2008
- From these results, we conclude that (i) **BRCA2** regulates **RAD51** recombination in response to the type of DNA damage and (ii) **BRCA2** suppresses SCRS, suggesting a role for **BRCA2** in sister chromatids cohesion and or alignment. Ref: Cancer Res, 2005
- Inhibition of filament formation of human **Rad51** protein by a small peptide derived from the BRC motif of the **BRCA2** protein. Ref: Genes Cells, 2008
- Brh2, the ortholog of the **BRCA2** tumor suppressor in Ustilago maydis, works hand in hand with **Rad51** to promote repair of DNA by homologous recombination. Ref: Proc Natl Acad Sci U S A, 2008
- The **BRCA2** tumor suppressor functions in repair of DNA by homologous recombination through regulating the action of **Rad51** . Ref: DNA Repair (Amst) , 2007

Text mining resources: Chillibot



Two lists search, context restriction

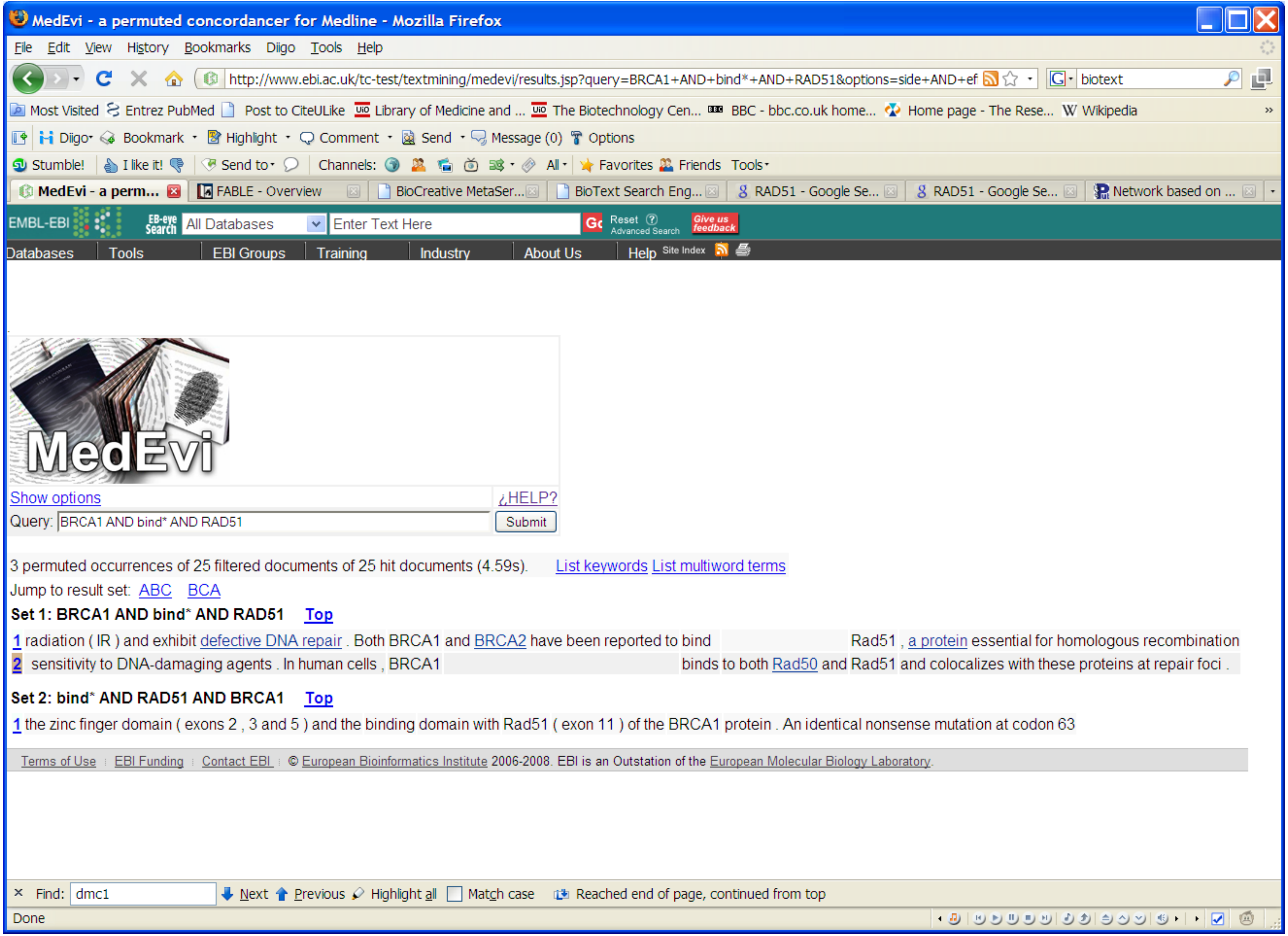
Context: substance abuse OR addiction

Searching for polymorphism of genes associated with substance abuse or addiction. A list of 27 genes was first identified in a data mining study. This Chilibot search found that the polymorphism of 10 of them were known to be associated with substance abuse/addiction.

Hypothesis generation

From a complex of relationship network, Chilibot suggested that CREB may have a relationship (e.g. regulation) with synaptotagmin, based on 1) there is no known relationship between CREB and synaptotagmin; and 2) they are both connected to many gene/protein and are both involved in similar biological process (e.g. LTP). The original search includeed one keyword ("LTP") and 22 other genes. CREB was first selected by clicking on the graph. Hypothesis was generated by clicking on the "CREB might be related to.." button. See here for details.

Text mining resources: MedEvi



Query: BRCA1 AND bind* AND RAD51

3 permuted occurrences of 25 filtered documents of 25 hit documents (4.59s). List keywords List multiword terms

Jump to result set: ABC BCA

Set 1: BRCA1 AND bind* AND RAD51 Top

1 radiation (IR) and exhibit defective DNA repair . Both BRCA1 and BRCA2 have been reported to bind Rad51 , a protein essential for homologous recombination

2 sensitivity to DNA-damaging agents . In human cells , BRCA1 binds to both Rad50 and Rad51 and colocalizes with these proteins at repair foci .

Set 2: bind* AND RAD51 AND BRCA1 Top

1 the zinc finger domain (exons 2 , 3 and 5) and the binding domain with Rad51 (exon 11) of the BRCA1 protein . An identical nonsense mutation at codon 63

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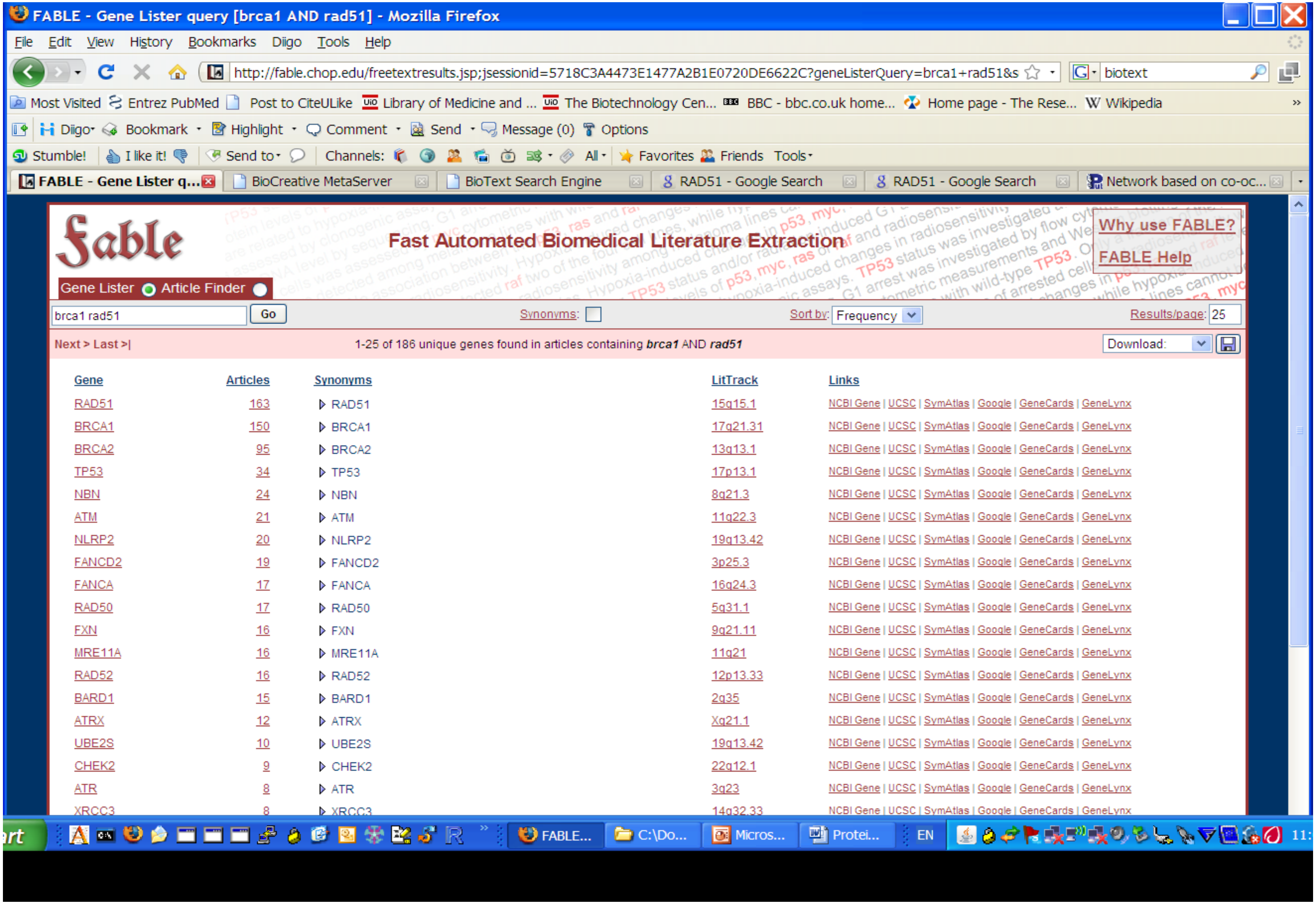
Text mining resources: FABLE



FABLE - Gene Lister query [brca1 AND rad51] - Mozilla Firefox

http://fable.chop.edu/freetextresults.jsp;jsessionid=5718C3A4473E1477A2B1E0720DE6622C?geneListerQuery=brca1+rad51&s

fable

Fast Automated Biomedical Literature Extraction

Gene Lister ● Article Finder ○

brca1 rad51 | Go

Synonyms: ☐ Sort by: Frequency Results/page: 25

Next > Last >|

1-25 of 186 unique genes found in articles containing ***brca1*** AND ***rad51***

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Gene	Articles	Synonyms	LitTrack	Links
RAD51	163	▷ RAD51	15q15.1	NCBI Gene | UCSC | SymAtlas | Google | GeneCards | GeneLynx
BRCA1	150	▷ BRCA1	17q21.31	NCBI Gene | UCSC | SymAtlas | Google | GeneCards | GeneLynx
BRCA2	95	▷ BRCA2	13q13.1	NCBI Gene | UCSC | SymAtlas | Google | GeneCards | GeneLynx
TP53	34	▷ TP53	17p13.1	NCBI Gene | UCSC | SymAtlas | Google | GeneCards | GeneLynx
NBN	24	▷ NBN	8q21.3	NCBI Gene | UCSC | SymAtlas | Google | GeneCards | GeneLynx
ATM	21	▷ ATM	11q22.3	NCBI Gene | UCSC | SymAtlas | Google | GeneCards | GeneLynx
NLRP2	20	▷ NLRP2	19q13.42	NCBI Gene | UCSC | SymAtlas | Google | GeneCards | GeneLynx
FANCD2	19	▷ FANCD2	3p25.3	NCBI Gene | UCSC | SymAtlas | Google | GeneCards | GeneLynx
FANCA	17	▷ FANCA	16q24.3	NCBI Gene | UCSC | SymAtlas | Google | GeneCards | GeneLynx
RAD50	17	▷ RAD50	5q31.1	NCBI Gene | UCSC | SymAtlas | Google | GeneCards | GeneLynx
FXN	16	▷ FXN	9q21.11	NCBI Gene | UCSC | SymAtlas | Google | GeneCards | GeneLynx
MRE11A	16	▷ MRE11A	11q21	NCBI Gene | UCSC | SymAtlas | Google | GeneCards | GeneLynx
RAD52	16	▷ RAD52	12p13.33	NCBI Gene | UCSC | SymAtlas | Google | GeneCards | GeneLynx
BARD1	15	▷ BARD1	2q35	NCBI Gene | UCSC | SymAtlas | Google | GeneCards | GeneLynx
ATRX	12	▷ ATRX	Xq21.1	NCBI Gene | UCSC | SymAtlas | Google | GeneCards | GeneLynx
UBE2S	10	▷ UBE2S	19q13.42	NCBI Gene | UCSC | SymAtlas | Google | GeneCards | GeneLynx
CHEK2	9	▷ CHEK2	22q12.1	NCBI Gene | UCSC | SymAtlas | Google | GeneCards | GeneLynx
ATR	8	▷ ATR	3q23	NCBI Gene | UCSC | SymAtlas | Google | GeneCards | GeneLynx
XRCC3	8	▷ XRCC3	14q32.33	NCBI Gene | UCSC | SymAtlas | Google | GeneCards | GeneLynx

Text mining resources: BioText

RAD51 AND BRCA2

Search Over: ○ Full Text & Abstracts ● Figure Captions (List) ○ Figure Captions (Grid) ○ Tables **Sort By:** Relevance

Results **1-1** of **1**

γ-H2AX in recognition and signaling of DNA double-strand breaks in the context of chromatin

Kinner, A., Wu, W., Staudt, C., Iliakis, G. (2008) *Nucleic Acids Research.*

FIGURE CAPTION

Figure 2.. DSB repair pathways. (A) Homologous recombination repair (HRR). After the initial sensing of the DSB by MRN and the activation of ATM, H2AX is phosphorylated, which in turn elicits a sequence of signaling events thought to ultimately cause the activation of nucleases such as Mre11 and CtIP to process the DNA ends and generate ssDNA with 3′ overhangs. ssDNA is bound by RPA, which is subsequently exchanged by **Rad51** and **Rad51** paralogs. This exchange is facilitated by Rad52, Rad54 and **BRCA2**. The Rad51-decorated DNA fiber initiates strand invasion into an intact homologous DNA molecule that leads to the formation of a Holiday junction. The DNA sequence around the DSB is copied by DNA synthesis associated with branch migration, and the process is completed by resolution of the Holiday junction. HRR is a templated repair process and is therefore error free (15–17). (B) DNA-PK-dependent nonhomologous end joining (D-NHEJ). DNA ends are recognized by Ku, which recruits, after processing by Tdp1 or PNKP, DNA-PKcs. Upon end-binding, DNA-PKcs is activated and phosphorylates itself and possibly also other proteins (like H2AX on an adjacent nucleosome). Phosphorylated DNA-PKcs is thought to be released from the DNA end, which allows the DNA ligase IV/XRCC4/XLF complex to mediate end-ligation possibly with the help of a DNA polymerase that catalyzes gap filling (19,149,150). (C) Back up pathway of nonhomologous end joining (B-NHEJ). There is evidence that cells of higher eukaryotes with defects in D-NHEJ rejoin the majority of DSBs using an alternative repair pathway that is not utilizing any of the HRR-associated activities (19). This pathway is therefore termed backup NHEJ (B-NHEJ). Although details of this pathway remain to be elucidated, there is evidence that it utilizes the PARP-1/DNA Ligase III/XRCC1 repair module known to be involved in the repair of SSB and base damages (151–155), and that its function is facilitated by the linker histone H1 (156). (D) Single strand annealing (SSA). This repair pathway shares features of HRR and NHEJ, and is best described in yeast (17). After the initial sensing of the DSBs