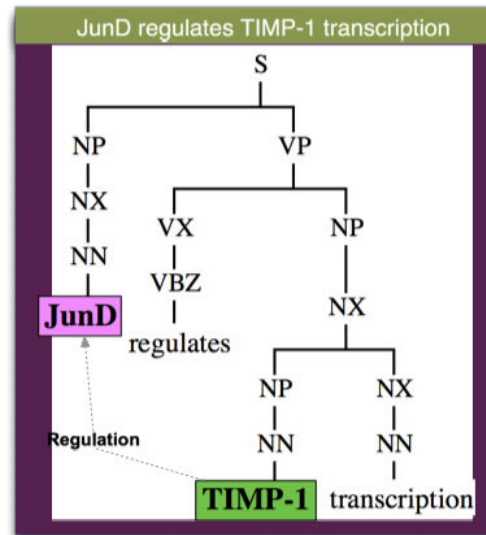




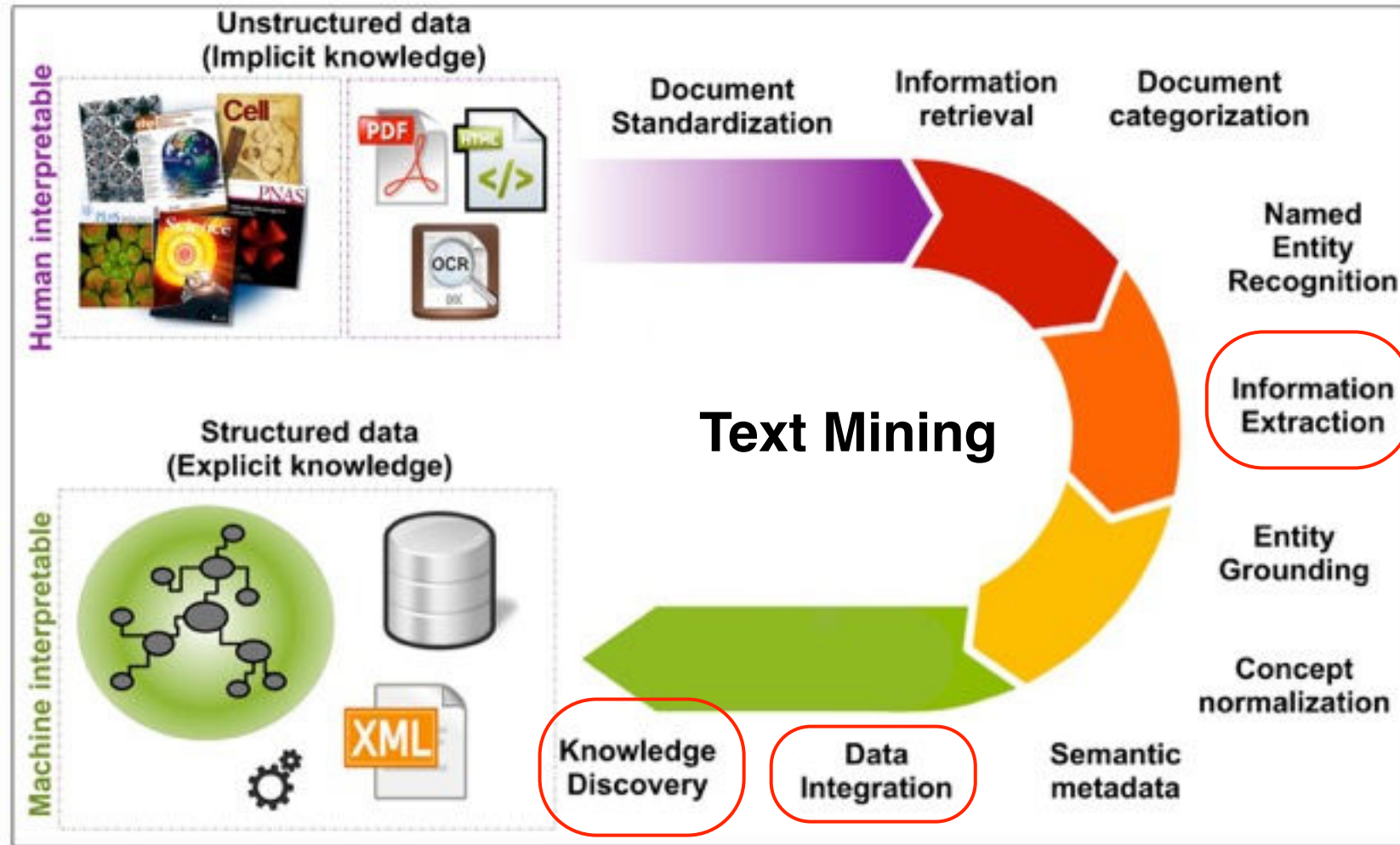
Information extraction and other NLP tasks

Martin Krallinger

Spanish National Cancer Centre (CNIO)



Text mining





Relation extraction

Interaction Network

BRCA1 & BRCA2

Retrieving synonyms...

Retrieving abstracts...
Performing linguistic analysis...

Analyzed 100 most recent abstracts out of 2335 available.
Found 23 interactive sentences and 170 parallel sentences.
[View all relevant sentences.](#)

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

However, non mutational functional suppression could result from various mechanisms, such as hypermethylation of the BRCA1 promoter or binding of BRCA2 by EMSY. [Ref: Mutations.2008](#)

- Resistance to mitomycin C and the repair of DNA double strand breaks by homologous recombination require the interaction of PALB2 with both BRCA1 and BRCA2. [Ref: Mol Cancer Res.2009](#)
- Using extracts from these cells, we find that PALB2 mediates the physical interaction of BRCA2 with a COOH terminal fragment of BRCA1. [Ref: Mol Cancer Res.2009](#)
- Restoration of BRCA1 and BRCA2 mediates resistance to platinum chemotherapy in recurrent BRCA1 and BRCA2 mutated hereditary ovarian carcinomas. [Ref: Mol Cancer Res.2009](#)
- EMSY gene amplification was a significantly less common event in BRCA2 mutation carriers as compared to BRCA1 mutation carriers (9 versus 24%, respectively). [Ref: Breast Cancer Res.2009](#)

PMID	Protein A	Protein B	Protein interaction evidence sentence
11689012	VSP1 AT5G24780	AGAMOUS AT4G18960	Coimmunoprecipitation, two-hybrid yeast, and affinity column assays show that the FLOR1-VSP1 complex interacts with AGAMOUS and that this transcription factor directly interacts with FLOR1.
11689012	FLOR1 AT3G12145	AGAMOUS AT4G18960	Coimmunoprecipitation, two-hybrid yeast, and affinity column assays show that the FLOR1-VSP1 complex interacts with AGAMOUS and that this transcription factor directly interacts with FLOR1.
16679456	SEU AT1G43850	AGAMOUS AT4G18960	Our data suggest that MADS box proteins are involved in the recruitment of the SEU-LUG repressor complex for regulation of AGAMOUS.
16679456	LUG AT4G32551	AGAMOUS AT4G18960	Our data suggest that MADS box proteins are involved in the recruitment of SEU-LUG repressor complex for regulation of AGAMOUS.

es are currently instable due to technical problems. We apologize for any inconvenience.

PMID	Protein A	Protein B	Protein interaction evidence sentence
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Experimental evidence

affinity column; affinity column assays; Coimmunoprecipitation; immunoprecipitation; two-hybrid

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Our data suggest that MADS box proteins are involved in the recruitment of SEU-LUG repressor complex for regulation of AGAMOUS.

Human Gene/Protein

BRCA1	5147
BRCA2	2150
p53	637
estrogen receptor	233
ATM	177
Rad51	160
HER2	127
BARD1	117
tumor suppressor	111
Chk2	110
hMLH1	101
progesterone receptor	85
p16	78
H2AX	74

4 locator

BRCA

is of the jon conte

ra recognize both in vitro-translated and recombinant, rived BRCA1, which co-migrate with BRCA1 from the human breast te, HBL100. [\[show abstract\]](#)

BRCA1 ↔ HS BRCA1 PMID:9662397

BRCA1 which interacts with RHA and, thus, the holoenzyme complex, subregions of the BRCT domain of BRCA1. [\[ref. \[show abstract\]](#)

ent

ment [1997]

Age penetrance is greater for BRCA1-linked than for BRCA2-linked cancers in this population. [2000]

Tumors lacking BRCA1 mRNA were more likely to lack BRCA2 mRNA than tumors expressing BRCA1 mRNA (P<0.01). [2002]

The rarity of these mutants in human cancer and their multiple occurrence in BRCA-associated breast tumours suggests that these novel p53 mutants are selected during malignant progression in the unique genetic background of BRCA1- and BRCA2-associated tumours. [1999]

MCF-7 cells transfected with a dominant negative mutant p53 (143 val->ala) required at least tenfold higher doses of adriamycin to down-regulate BRCA1 or BRCA2 mRNAs than did parental MCF-7 cells or control-transfected MCF-7 clones. [1998]

Silencing of BRCA1, BRCA2, or BRCA1/2-associated genes enhanced cisplatin cytotoxicity approximately 4- to 7-fold more in TP53-deficient cells than in matched TP53 wild-type cells. [2006]

METHODS: We determined the frequency of ATM IVS10-6T->G variants in a cohort of individuals affected by breast and/or ovarian cancer who underwent BRCA1 and BRCA2 genetic testing at four major Australian familial cancer clinics. [2004]

...DNA damage [2003]

...testing, 1,460 female mutation carriers (78% in BRCA1, 56% in BRCA2, 6% in BRCA1/2) were identified. The value of the resource has been greatly enhanced by determining the status of nearly 6,000 probands. at. 2009 Jul

Information about 'BRCA1'

Property Value

Name breast cancer 1, e...

Organism Homo sapiens

Article 937

PubGene Gene/Pro...

Extern. EG

Chrom. 17

Alt. Sy. BRCA1

Alt. Sy. BRCC1

Alt. Sy. IRIS

Alt. Sy. PSCP

Alt. Sy. RNF53

502 matches found in 324 documents. Search time: 2.308 seconds.

Global links/files: [all results in endnote](#) [all results in print version](#) [all results in xml](#)

Score: 62.00

Title: Identification of plant promoter constituents by analysis of local distribution of short sequences.

Authors: Yamamoto YY Ichida H Matsui M Obokata J Sakurai T Satou M Seki M Shinozaki K Abe T

Journal: BMC Genomics

Year: 2007

Bibliographic Information

Abstract

Matching Sentences

Match: [Sentence(s) appears to be scrambled. Click to see (opens new window)] [Field: body, subscore: 62.00]

Supplemental links/files: [reference in endnote](#) [reference in xml](#) [online text](#) [related articles](#) [PubMed citation](#)

breast cancers.

We report herein an infantile gynec immunohistochemistry of anti-BRCA1 and ar

We demonstrated that BRCA1 proteins, like BRCA2, are widely expressed in the nuclei of epithelial cells surrounding the lumen of the ducts in infantile gynecomastia.

The intensive nuclear staining of both proteins in the mammary tissues means that BRCA1 and BRCA2 proteins are largely expressed in infantile gynecomastia.

Science (2002).

p53, tumor suppressor protein p53 ● Brca1 ● Chk2 ...

[BRCA1 and genomic stability].

Al Zheng (2003).

tumor suppressor proteins ● p53, tumor suppressor proteins ● BRCA1, tumor suppressor proteins ● RAD50 ● RAD51 ...



Information Extraction

- Information extraction (IE): automatically extracting *structured information from unstructured* machine-readable documents
- IE approaches often focus on restricted domains (target domain)
- IE should facilitate logical reasoning to generate inferences from the structured output generated by those systems
- Assumption: *entities and events in documents are described in a similar way*, i.e. there are conventional, semantic, and syntactic constraints on how to express them



Information Extraction

- Typically IE systems simplify the problem by considering the events as a sort of *template*
- Templates are designed as a *case frame* or set of case frames, which in turn hold the information extracted from the documents
- Templates usually have *slots* for the entities and their relations
- IE systems need to understand the document at a level that allows filling the slots of the template with the correct information



Template: frames and slot filling

J Cell Biol. 2000 Jun 26;149(7):1405-18.
TPX2, A novel xenopus MAP involved in spindle pole organization.
 Wittmann T¹, Wilm M, Karsenti E, Vernos J.
 Author information
Abstract
 TPX2, the targeting protein for Xenopus kinesin-like protein 2 (Xklp2), was identified as a microtubule-associated protein that mediates the binding of the COOH-terminal domain of Xklp2 to microtubules (Wittmann, T., H. Boleti, C. Antony, E. Karsenti, and I. Vernos. 1998. J. Cell Biol. 143:673-685). Here, we report the cloning and functional characterization of Xenopus TPX2. TPX2 is a novel, basic 82.4-kD protein that is phosphorylated during mitosis in a microtubule-dependent way. TPX2 is nuclear during interphase and becomes localized to spindle poles in mitosis. Spindle pole localization of TPX2 requires the activity of the dynein-dynactin complex. In late anaphase TPX2 becomes relocalized from the spindle poles to the midbody. TPX2 is highly homologous to a human protein of unknown function and thus defines a new family of vertebrate spindle pole components. We investigated the function of TPX2 using spindle assembly in Xenopus egg extracts. Immunodepletion of TPX2 from mitotic egg extracts resulted in bipolar structures with disintegrating poles and a decreased microtubule density. Addition of an excess of TPX2 to spindle assembly reactions gave rise to monopolar structures with abnormally enlarged poles. We conclude that, in addition to its function in targeting Xklp2 to microtubule minus ends during mitosis, TPX2 also participates in the organization of spindle poles.

TPX2 is nuclear during interphase and becomes localized to spindle poles in mitosis.

TPX2 is nuclear during interphase and becomes localized to spindle poles in mitosis.

(Type: _____, Theme: _____ ToLoc: _____, Temporal_attribute(_____))

(Type:Localization, Theme:TPX2, ToLoc:nuclear, Temporal_attribute(interphase))

(Type:Localization, Theme:TPX2, ToLoc:spindle poles, Temporal_attribute(mitosis))



IE historical view



- Dates back to late 1970s
- Commercial system (mid-1980s): JASPER for Reuters for providing real-time financial news to financial traders
- IE was strongly influenced by MUC*
- MUC: community challenge and conference focused:
 - MUC-1 (1987), MUC-2 (1989): Naval operations
 - MUC-3 (1991), MUC-4 (1992): Terrorism in Latin America
 - MUC-5 (1993): Joint ventures and microelectronics
 - MUC-6 (1995): News articles on management
 - MUC-7 (1998): Satellite launch

MUC*: Message Understanding Conferences



Main IE strategies

Statistical associations:

- Association statistics (Mutual information, Chi-square,..)

Hand-written regular expressions/rules:

- Use linguistic: syntactic/grammatical aspects
- Use semantic aspects
- Often define trigger terms relevant for relations (e.g. 'interact*', 'bind*' for PPIs)

Using machine learning:

- Flat features, sentence classifiers
- Linguistic kernels (syntactic trees or shallow parsing for features)



IE subtasks and components (I)

- Named entity recognition

BRAF is an oncogene. It is the target of **Nexavar**
Entity_type:Gene *Entity_type:Drug*

- Coreference resolution: detection of coreference and anaphoric relations between entities (associations between previously extracted named entities)

Relation_type:Anaphora
BRAF is an oncogene. **It** is the target of Nexavar.
Antecedent *Pronoun*

- Relationship extraction: identifying relations between entities/terms

Relation_type:Phosphorylation
CaMKII δ phosphorylates **titin**
Entity_type:Protein, role=kinase *Entity_type:Protein, role=substrate*

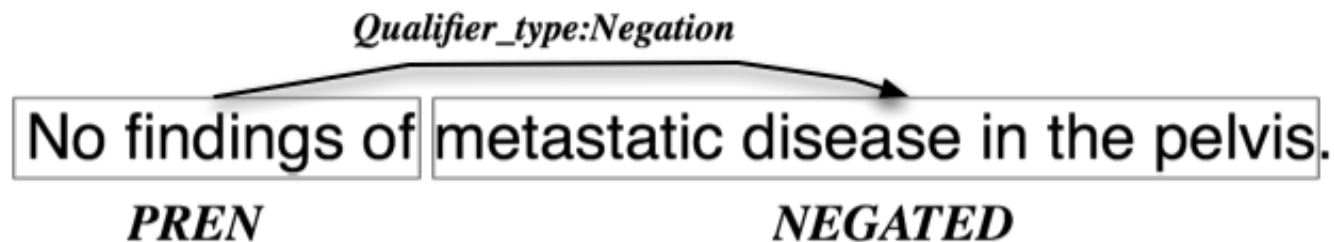


IE subtasks and components (II)

- Automatic term recognition (ATR): finding relevant terms from documents

The **V600E mutation** of BRAF is used in screening for **Lynch syndrome**.

- Negation detection: affirmed and negated phrases (e.g. NegEx)



no increase	[PSEU]
no suspicious change	[PSEU]
no significant change	[PSEU]
no change	[PSEU]
no interval change	[PSEU]
no definite change	[PSEU]

absence of	[PREN]
cannot	[PREN]
cannot see	[PREN]
checked for	[PREN]
declined	[PREN]
declines	[PREN]
denied	[PREN]

negative	[POST]
resolved	[POST]
ruled out	[POST]
not seen	[POST]
is absent	[POST]
is not seen	[POST]
are not seen	[POST]



Relation extraction

1

2

BRK: Q07666 (KHDR1_HUMAN)
Sam68: Q13882 (PTK6_HUMAN)

We show that BRK phosphorylates Sam68.					
WORD	BASE FORM	POS	CHUNK	NER	Phrase syntax
We	We	PRP	B-NP	O	nominal head, pro-nominal
show	show	VBP	B-VP	O	main verb, indicative present
that	that	IN	B-SBAR	O	reposed marker, clause marker
BRK	BRK	NN	B-NP	B-protein	nominal head, proper noun, single-word noun phrase
phosphorylates	phosphorylate	VBZ	B-VP	O	main verb, indicative present
Sam68	Sam68	NN	B-NP	B-protein	nominal head, noun, single-word noun phrase, sentence
.	.	.	O	O	boundary

3

LEFT-WALL we show.v that.c BRK phosphorylates[!].v Sam68 .

Constituent tree:
(S (NP We)
(VP show
(SBAR that
(S (NP BRK)
(VP phosphorylates
(NP Sam68))))))

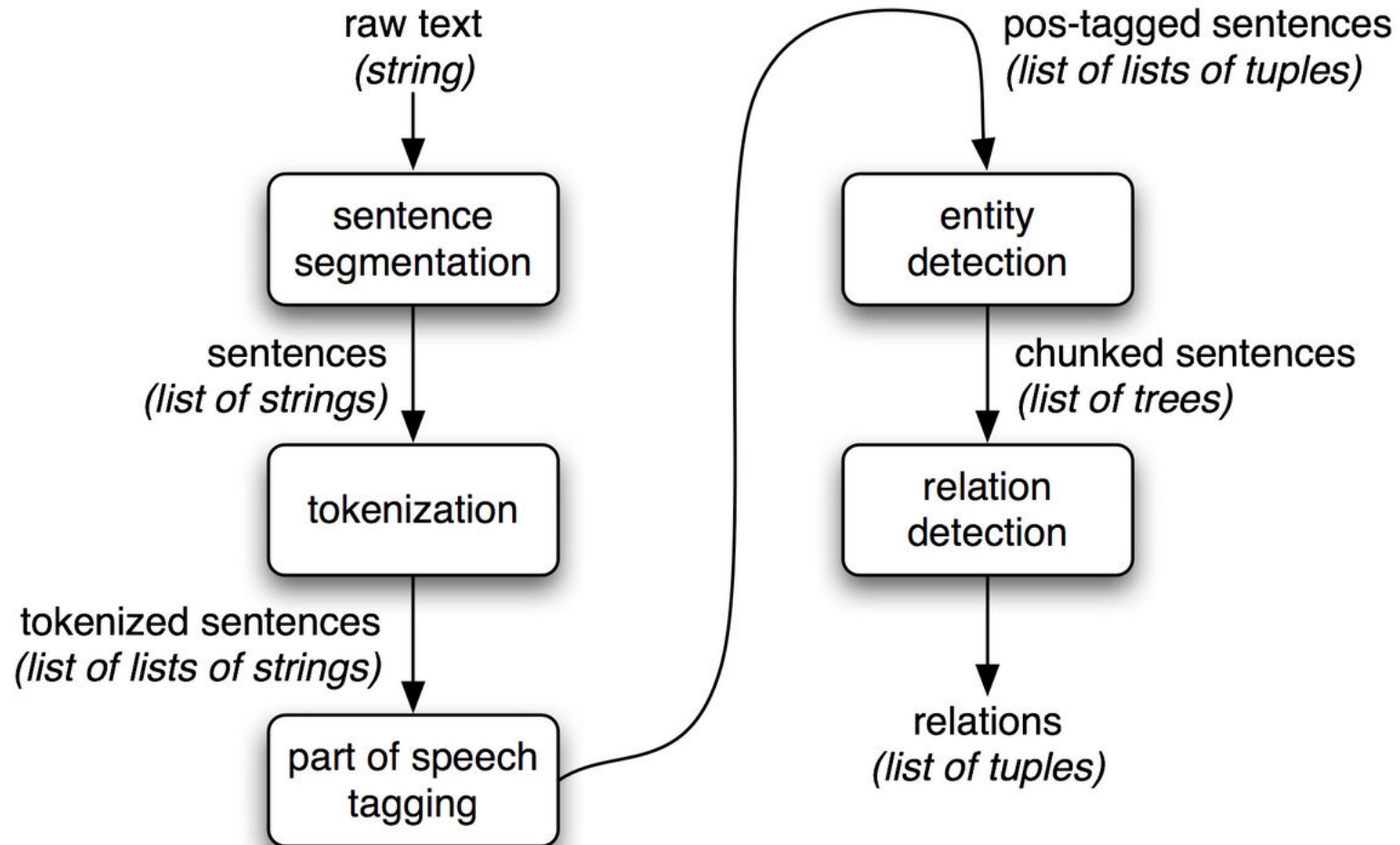
S connects subject-nouns to finite verbs

O connects transitive verbs to direct or indirect objects

Co-occurrence (frequency, M_i ,...), association rules, textual patterns (e.g. interaction verbs, frames), shallow parsing, full parsing, machine learning (sentence classifiers),...

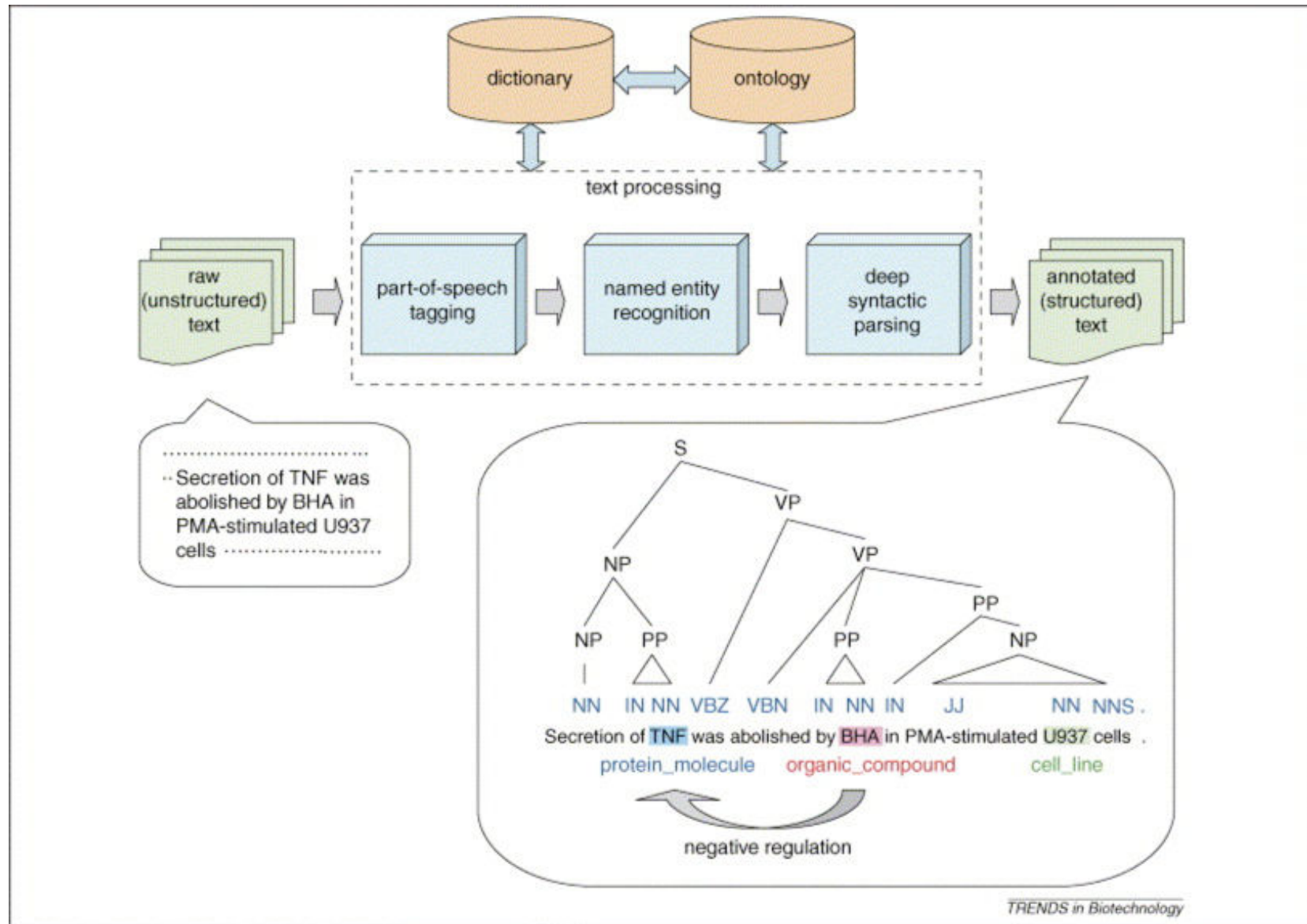


Simplified Information Extraction pipeline





Example IE pipeline: regulation



Text mining



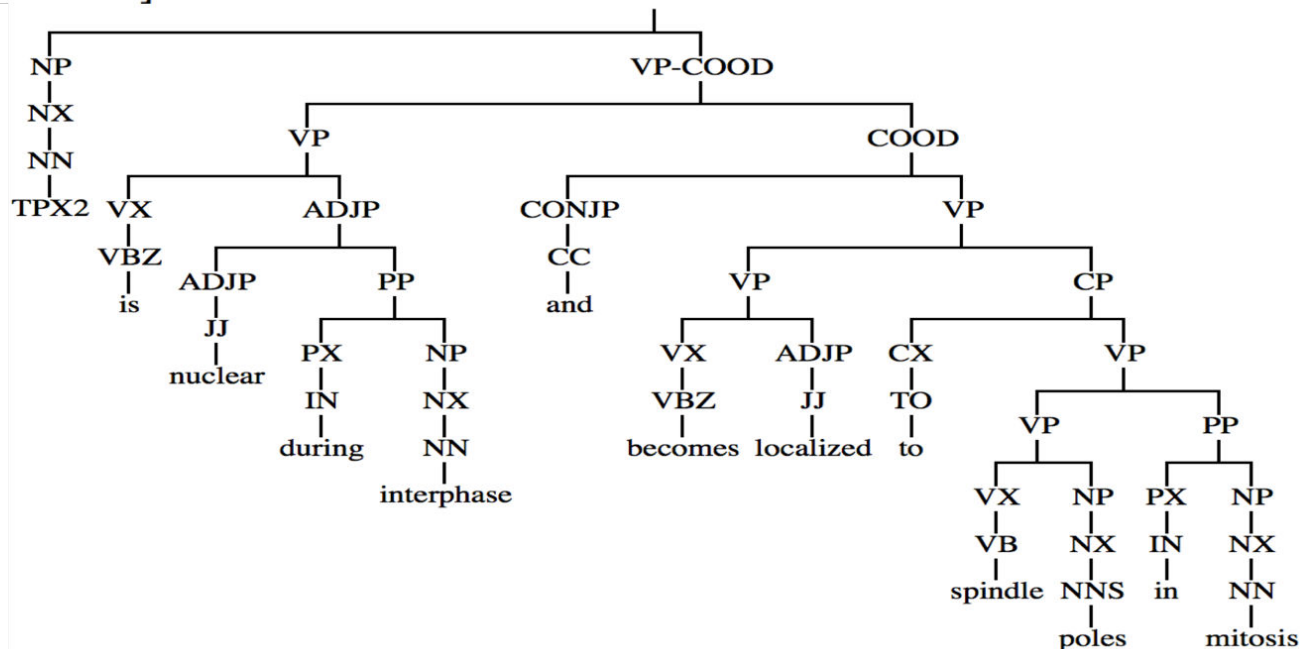
TPX2 is nuclear during interphase and becomes localized to spindle poles in mitosis.

(Type: _____, Theme: _____ ToLoc: _____, Temporal_attribute(_____))

(Type: Localization, Theme: TPX2, ToLoc: nuclear, Temporal_attribute(interphase))

(Type: Localization, Theme: TPX2, ToLoc: spindle poles, Temporal_attribute(mitosis))

[NP TPX2] [VP is] [ADJP nuclear] [PP during] [NP interphase] and
 [VP becomes] [ADJP localized] [VP to spindle] [NP poles] [PP in] [NP
 mitosis] .





Syntactic parser: Enju

Enju 2.4 online demo

Enter a sentence, and you will see a parse result in the XML format.

TPX2 is nuclear during interphase and becomes localized to spindle poles in mitosis

Parse

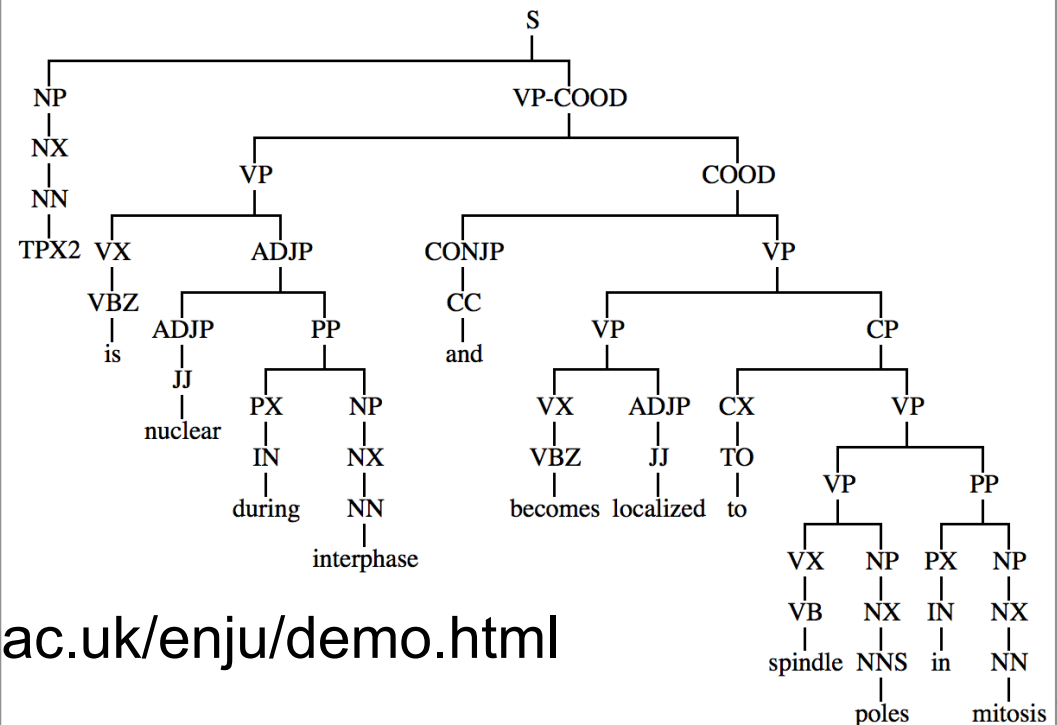
Domain: Newspaper Biomedical papers

Parse status: success

Click to change the view.

To understand the output of the Enju parser

- [Enju Output Specifications](#)
- [Enju XML Format](#)



<http://www.nactem.ac.uk/enju/demo.html>



Syntactic parsing

- Sentence (syntactic) parsing: divide sentence (string of words) into its constituents to generate a parse tree that displays syntactic relations between words
- Method of understanding the meaning of sentence
- Visualized with syntactic trees/diagrams



MEDIE: subject-verb-object relations

MEDIE — [See what causes cancer?](#) MEDIE is a demo system presented by [Tsuji Laboratory](#)

subject	verb	object
	inhibit	BRAF_HUMAN

[advance search](#)

Result 1 for inhibit 0.17 seconds (searched 100.00% of Medline)
[» show query](#)

Sort by Rank Date

show
subject **verb** object **gene disease**

[show next »](#)

1. [Overexpression of a calpastatin transgene in mdx muscle reduces dystrophic pathology.](#) [»XML](#)
 Melissa J Spencer, Ronald L Mellgren, pp. 2645-55, Volume 11, Issue 21, Human molecular genetics, 2002 [PMID:12354790]

Calpastatin (CS) is a specific, endogenous inhibitor of m- and micro -calpains that does not **inhibit calpain 3 (p94)**. [»sXML](#)

[show next »](#)

<http://www.nactem.ac.uk/medie/>



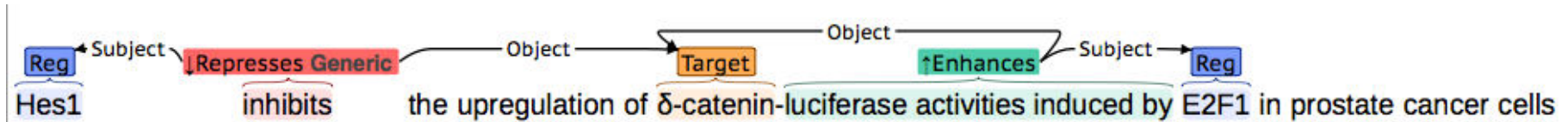
Example architecture: Relation extraction with NLP

- Tokenization
 - Entity recognition with synonyms list
 - Word boundaries (multi words)
 - Sentence boundaries (abbreviations)
- Part-of-speech tagging
 - TreeTagger trained on GENIA
- Semantic labeling
 - Dictionary of regular expressions
- Entity and relation chunking
 - Rule-based system implemented in CASS

From: Literature Mining and Systems Biology, by Lars Juhl Jensen



Gene regulation events: textual annotation

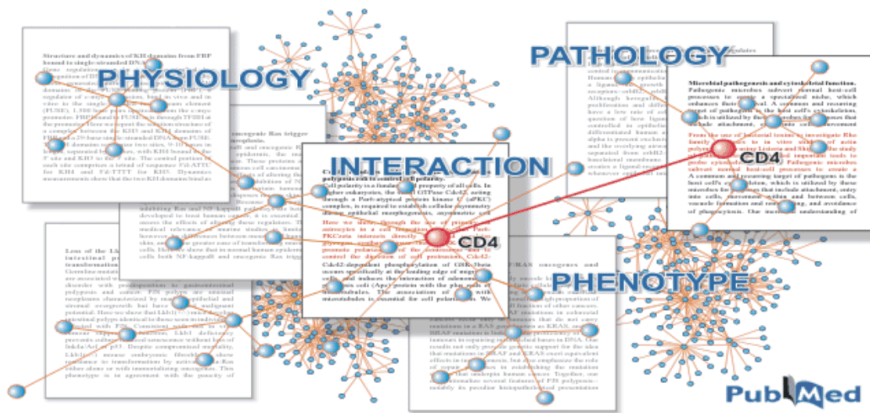


On the other hand, Hes1 was predicted to have several Regulates Direct _{binding sites} near the binding sites of E2F1 on delta-catenin promoter (Figure 1A).

As shown in Figure 1B, E2F1 induced dramatic increases in delta-catenin-luciferase activities in both cell lines with either BK1 or BK5 co-transfection.



Qualifying co-mentions: tri-co mentions



Information hyperlinked
over proteins

Symbol	Name	Synonyms	Organism
WNT1	Wnt-1 proto-oncogene protein precursor	INT1	Homo sapiens
UniProt	P04628		
OMIM	164820		
NCBI Gene	7471		
NCBI RefSeq	NP_005421		
NCBI Accession	CAA28874, X03072		

Homologues of WNT1 ... new

Definitions for WNT1 ...

Enhanced PubMed/Google query ... new

WARNING: Please keep in mind that gene detection is done automatically and can exhibit a certain error. Read more.

However, mAKT could act synergistically with **Wnt-1** or **Frat** to **activate LEF-1**.

Beta-catenin: a common target for the regulation of cell adhesion by **Wnt-1** and **Src** signaling pathways.

Wnt-1 regulates **Fgfb** expression in the adjacent metencephalon, most likely via a secondary mesencephalic signal.

Cultured cells transfected with a membrane-attached form of **Wnt-1** bind epitope-tagged **Frat-1** in the 10(-10) M range.

In mammalian cells, **Axin** inhibits **Wnt-1** stimulation of beta-catenin/lymphoid enhancer factor 1-dependent transcription.

Furthermore, **beta-catenin** is the target of two signal transduction pathways mediated by the proto-oncogenes **src** and **wnt-1**.

Ectopic expression of **Wnt-1** in 3T3-L1 preadipocytes stabilizes **beta-catenin**, activates TCF-dependent gene transcription, and blocks adipogenesis.

Wnt1 gene is a down-stream target gene of **Wnt1** in C57MG cells, and encodes a Cdc42-related GTPase with the potential to activate the JNK pathway.

Wnt1 induces morphological transformation of C57MG mammary epithelial cells and accumulation of cytosolic **beta-catenin** whereas **Wnt-5a** has no effect.

On the contrary, coexpressed **Wnt-1** and **Frat** activated **LEF-1** but did not show significant inhibition of GSK-mediated phosphorylation of a peptide substrate.

The specificity of the approach enabled us to identify an **Max1** consensus DNA site within the transcriptional control region of the developmental regulatory gene **Wnt-1**.

FraA efficiently inhibited the **Wnt-1** mediated increase in cytoplasmic (beta)catenin levels as well as the **Wnt-1** induction of transcription from a **Leftcf** reporter gene.

Furthermore, a similar phenotype is not observed in **Wnt1/RCAS**-infected brains, demonstrating that ectopic **Wnt1** is insufficient to mediate the effect of ectopic **Lmx1b** in our assay.

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[Developer's Zone](#)
[Help](#)

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Concept & Implementation by Robert Hoffmann

The **APC** tumor-suppressor protein **associates** with **beta-catenin**, a cell adhesion protein that is upregulated by the **WNT1** oncogene.

Wntch1 gene is a down-stream **target** gene of **Wnt1** in C57MG cells, and encodes a Cdc42-related GTPase with the potential to activate the JNK pathway.

On the contrary, coexpressed **Wnt-1** and **Frat** **activated** **LEF-1** but did not show significant inhibition of GSK-mediated phosphorylation of a peptide substrate.

Wnt-1 **regulates** **Fgfb** expression in the adjacent metencephalon, most likely via a secondary mesencephalic signal.

Moreover, we demonstrate that activation of beta-catenin/LeF-1 signaling by **Wnt-1** or by overexpression of **beta-catenin** itself is **inhibited** by **caveolin-1** expression.

Information hyperlinked
over proteins

Symbol	Name	Synonyms	Organism
LEF1	Lymphoid enhancer binding factor 1	LEF-1, lymphoid enhancer-binding factor 1, T cell-specific transcription factor 1-alpha, TCF-1ALPHA, TCF1-alpha	Homo sapiens
UniProt	Q9HAZ0, Q9LUJ2		
OMIM	163245		
NCBI Gene	51176		
NCBI RefSeq	NP_057353		
NCBI Accession	AAF13268, AAG01022, AAG26886		

Homologues of LEF1 ... new

Definitions for LEF1 ...

Enhanced PubMed/Google query ... new

WARNING: Please keep in mind that gene detection is done automatically and can exhibit a certain error. Read more.

However, mAKT could act synergistically with **Wnt-1** or **Frat** to **activate LEF-1**.

On the contrary, coexpressed **Wnt-1** and **Frat** **activated** **LEF-1** but did not show significant inhibition of GSK-mediated phosphorylation of a peptide substrate.

Addition of **Wnt-1** to normal **epithelial cell** lines **stabilizes** cytoplasmic **beta-catenin** that **LEF-1** then transports to nuclei, causing a small amount of EMT.

Here we study the mechanism of transcriptional regulation by **LEF-1** in response to a **Wnt-1** signal under conditions of endogenous **beta-catenin** in NIH 3T3 cells, and we examine whether association with **beta-catenin** is obligatory for the function of **LEF-1**.

In **Wnt-1**-transfected C57MG cells, free **beta-catenin** accumulated and was able to **associate** with **LEF-1**.

Beta-catenin forms **complexes** with **Tcf** and **LeF-1** and functions as a transcriptional activator in the Wnt signaling pathway.

Thus, the apoptotic effects of overexpressed exogenous **beta-catenin** do not rely on its transactivating function with nuclear **LEF-1**.

Beta-catenin forms **complexes** with **Tcf** and **LeF-1** and functions as a transcriptional activator downstream of the Wnt signaling pathway.

NCID stimulation of **LEF-1** activity was context dependent and occurred on a subset of promoters distinct from those **activated** by **beta-catenin**.

The **Wnt**-responsive **transcription factor** **LEF1** can **activate** transcription in association with **beta-catenin** and repress transcription in association with Groucho.

Among others, **LEF-1** **regulates** expression of cyokeratin genes involved in formation of hair follicles and the gene encoding the cell-adhesion molecule **E-cadherin**.

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Concept & Implementation by Robert Hoffmann



iHOP

PHYSIOLOGY

PATHOLOGY

INTERACTION

PHENOTYPE

CD4

PubMed

Hoffmann, R., Valencia, A. A Gene Network for Navigating the Literature. *Nature Genetics* 36, 664
 more than **1,500 organisms**. **80,000 genes**. **12 million sentences**.
 ...always up-to-date.

Search for a gene **synonym** or **accession number**... [\(Click here for an example: SNF1\)](#)

in


[\[SEARCH\]](#)


<http://www.ihop-net.org/UniPub/iHOP/>









iHOP system: Defining information









Find in this Page 




Sentences in this view contain definitions for BRCA2 - Definitions are available whenever you see this symbol  - [Read more](#).
 For a summary overview of the information in this page [click here](#). **new**




PALB2, which encodes a **BRCA2** -interacting protein, is a [breast cancer](#) susceptibility gene. [2007]  




Inheritance of one defective **BRCA2**  allele predisposes humans to [breast cancer](#). [2001]  




A common variant in **BRCA2**  is associated with both [breast cancer](#) risk and prenatal viability. [2000]  




Inherited mutations in the gene **BRCA2**  predispose carriers to early onset [breast cancer](#), but such mutations account for fewer than 2% of all cases in East Anglia. [2000]  




Mutations in **BRCA2**  are thought to account for as much as 35% of all inherited [breast cancer](#) as well as a proportion of inherited [ovarian cancer](#). [1996]  




Two of the five **BRCA2**  mutation carriers reported a family history of [breast cancer](#), and none reported a family history of [ovarian cancer](#). [2002]  

Our results indicate that **BRCA2**  confers a very high risk of [breast cancer](#) and is responsible for a substantial fraction of breast and [ovarian cancer](#) in Iceland, but only a small proportion of other cancers. [1996]  

Recent studies have identified mutations in the breast and ([ovarian cancer](#) susceptibility gene 2 (**BRCA2** )), one which has been found in the germline of several males and one female affected with [breast cancer](#). [1996]  

The [breast cancer](#) susceptibility gene **BRCA2**  on [chromosome](#) 13q12-13 has recently been identified. [1997]  

The [breast cancer](#) susceptibility gene, **BRCA2**  on [chromosome](#) 13q12-13, was recently isolated. [1996]  

The **BRCA2**  gene on [chromosome](#) 13 has been shown to be associated with familial male and female [breast cancer](#). [1996]  

Colour legend	Main gene
	Associated genes
	Relevant Biomedical terms
	Compounds

Defining Information for this Gene






iHOP system: interaction information

Sentences in this view contain interactions of BRCA2 - Interaction Information is available whenever you see this symbol  - [Read more.](#)



For a summary overview of the information in this page [click here.](#) **new**

Show all




Order by relevance

RESULTS: Definite **BRCA2**  mutations were found in 2 of the 73 women with early-onset **breast cancer** (2.7 percent; 95 percent **confidence interval**, 0.4 to 9.6 percent), suggesting that **BRCA2**  is **associated** with fewer cases than **BRCA1**  (P=0.03). [1997]







Age **penetrance** is greater for **BRCA1** -**linked** than for **BRCA2** -linked cancers in this population. [2000]






Tumors lacking **BRCA1**  mRNA were more likely to lack **BRCA2**  mRNA than tumors **expressing BRCA1**  mRNA (P<.001). [2002]





We evaluate current knowledge of **BRCA1**  and **BRCA2**  **functions** to explain why mutations in **BRCA1**  and **BRCA2**  lead specifically to breast and **ovarian cancer**. [2001]





PURPOSE: Morphologic and immunohistochemical studies of familial breast cancers have identified specific characteristics associated with **BRCA1**  mutation-**associated** tumors when compared with **BRCA2**  and non-BRCA1/2 tumors, but have not identified differences between **BRCA2**  and non-BRCA1/2 tumors. [2005]





What you don't know can hurt you: adverse psychologic effects in members of **BRCA1** -**linked** and **BRCA2** -linked families who decline genetic testing. [1998]





Here we report the chromosomal gains and losses as measured by CGH in 25 **BRCA2** -**associated breast tumors** and compared them with our existing 36 **BRCA1**  and 30 control profiles. [2005]



Germline mutations of **BRCA1**  are also **associated** with **ovarian cancer** and mutations of **BRCA2**  are associated with an increased risk of **male breast cancer**, **ovarian cancer**, **prostate cancer** and **pancreatic cancer**. [1997]





As these studies concerned sporadic cancer cases, we investigated whether N372H and another common variant located in the 5'-untranslated region (203G > A) of the **BRCA2**  gene **modify** breast or **ovarian cancer** risk in **BRCA1**  mutation carriers. [2005]



The identification of molecules that interact with **Brcal**  and **Brc2**  has greatly **enhanced** our knowledge of how **BRCA1**  and **BRCA2**  may function as tumor suppressors. [1998]



BRCA1  mutations are more commonly **associated** with **ovarian cancer** than **BRCA2**  mutations. [2001]



Text mining



Info-PubMed: PPI

Gene Dictionary

Search for gene / protein / disease names

Pax3

>> EntityType >> Fields >> Help

1 -- 2 (2 entities hit)

You can drag symbol names into other windows.

Symbol	Name	Synonym	Product	DB
HS NCOA1	nuclear receptor coactivator 1		PAX3/NCOA1 fusion protein	DB
HS PAX3	paired box gene 3 (Waardenburg syndrome 1)		PAX3/FKHR fusion gene Paired box protein Pax-3	DB

1 -- 2 (2 entities hit)



Content Viewer 1

Settings Help

Symbol HS PAX3

Name paired box gene 3 (Waardenburg syndrome 1)

Organism Homo sapiens

Link DB

Synonym CDHS / HuP2 / PAIRED BOX GENE 3 / PAIRED DOMAIN GENE HuP2 / WS1 / paired box homeotic gene 3 (Waardenburg syndrome 1)

Product HUP2 / HUP2-A / PAX3/FKHR fusion gene / Paired box protein Pax-3 / paired box gene 3 / paired box homeotic gene 3 / paired domain gene 3 / paired domain gene HuP2

Content Viewer 1

Settings Help

RELATION ALL 588 / 588 HS PAX3 HS PAX3 all types of relation

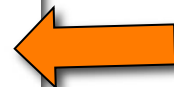
HS PAX3 is HS PAX3 is

Prev 1 -- 30 (588 locations hit) Next

- SENT ENCE PPI HS PAX3 ↔ HS PAX3 PMID:9500554

We further show that **Pax3** proteins associated with **WS1** in either the paired domain or the **homeodomain** fail to recognize and transactivate the MITF promoter. [\[show abstract\]](#)
- SENT ENCE PPI HS PAX3 ↔ HS PAX3 PMID:16280008

Within this lineage, **Pax3** has been shown to regulate the genes encoding **microphthalmia-associated transcription factor** (Mitf) and **tyrosinase-related protein-1** (**Trp-1**), despite each having dissimilar **Pax3** recognition sequences. [\[show abstract\]](#)



Relation Viewer

Settings Help

Queried entity HS PAX3 *Drop an entity here to obtain its relation partners*

Relation type all types of relation

Target entity Homo sapiens

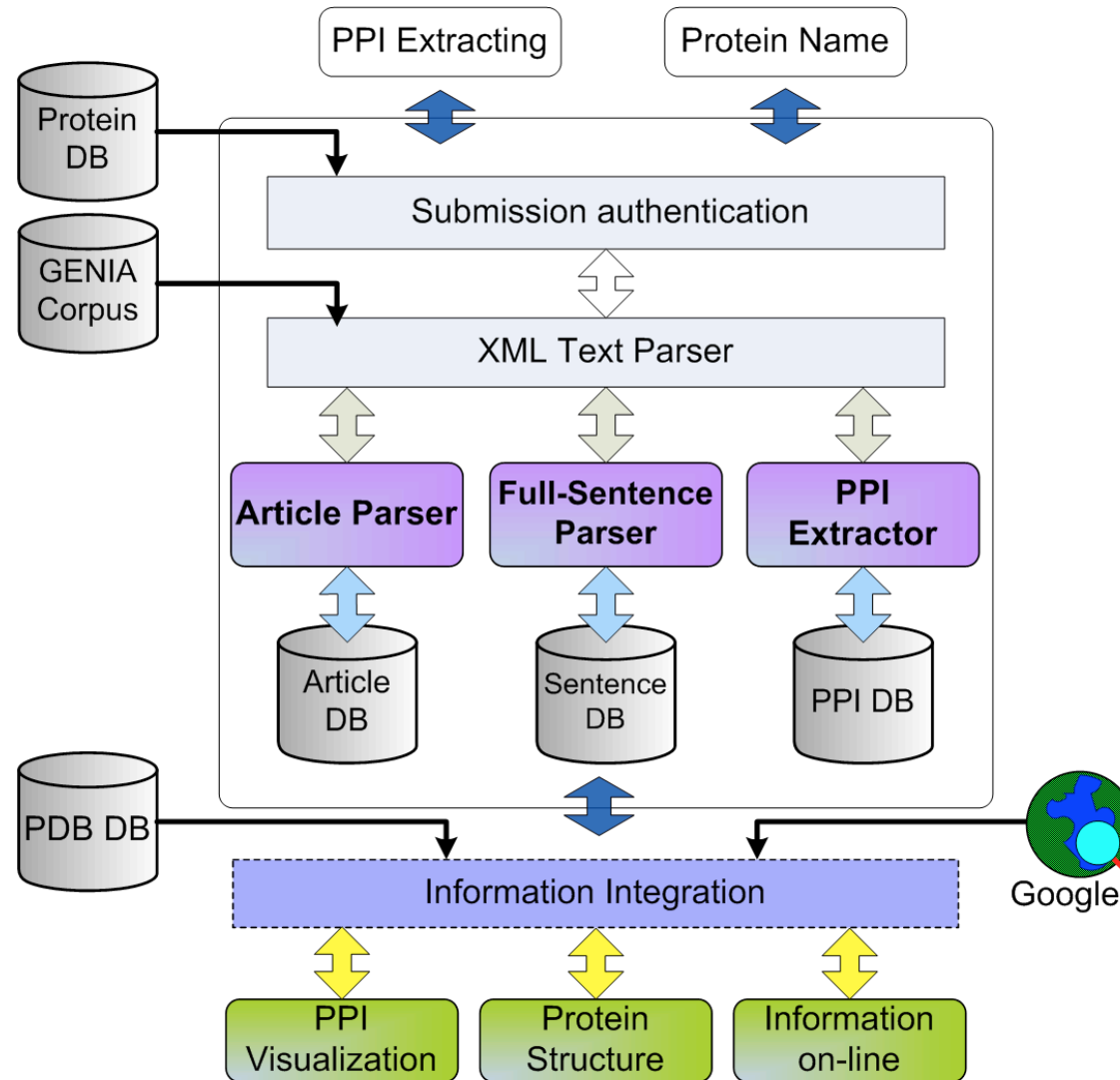
You can drag symbol names and relations into other windows.

Prev 1 -- 10 (275 entities hit) Next

HS PAX3	RELATION ALL 588 / 588 HS PAX3 HS PAX3
HS PAX7	RELATION ALL 59 / 59 HS PAX3 HS PAX7
HS PAX6	RELATION ALL 38 / 38 HS PAX3 HS PAX6
HS MYF5	RELATION ALL 35 / 35 HS PAX3 HS MYF5
HS WS2A	RELATION ALL 32 / 32 HS PAX3 HS WS2A
HS MYOG	RELATION ALL 22 / 22 HS PAX3 HS MYOG



IE for protein interactions: PPLook



<http://meta.usc.edu/softs/PPLook/>

Text mining



STRING: Data integration: from literature to databases to experiments

a

search by name | search by protein sequence | multiple names | multiple sequences

protein name: (examples: #1 #2 #3)
CagA

(STRING understands a variety of protein names and accessions; you can also try a [random entry](#))

organism:
Helicobacter

interactors wanted:
COGs | Proteins

Reset GO!

b

There are several proteins named 'CagA'. Please select one from the list below and press Continue to proceed.

<- Back Continue ->

Select bio-entity of interest

organism	protein
<input checked="" type="radio"/> Helicobacter pylori HPAG1	cagA - Cytotoxicity-associated immunodominant antigen; May be necessary for the transcription, folding, export, or function of the cytotoxin
<input type="radio"/> Helicobacter pylori J99	cagA - Cytotoxicity-associated immunodominant antigen; May be necessary for the transcription, folding, export, or function of the cytotoxin
<input type="radio"/> Helicobacter pylori 26695 0547	cagA - Cytotoxicity-associated immunodominant antigen; May be necessary for the transcription, folding, export, or function of the cytotoxin

<- Back Continue ->

c

Your Input:

- cagA Cytotoxicity-associated immunodominant antigen; May be necessary for the transcription, folding, export, or function of the cytotoxin (1200 aa) (*_unassigned*)

Predicted Functional Partners:

- cag-Y cag pathogenicity island protein Y (662 aa)
- cag3 cag pathogenicity island protein 3 (481 aa)
- cagM cag pathogenicity island protein M (376 aa)
- picB Cag pathogenicity island protein (Cag pathogenicity island protein E); Involved in DNA transfer [...] (534 aa)
- virB10 cag pathogenicity island protein Y (1295 aa)

Neighborhood	Gene Fusion	Cooccurrence	Coexpression	Experiments	Databases	Textmining	[Homology]	Score
●	●	●	●	●	●	●	●	0.912
●	●	●	●	●	●	●	●	0.899
●	●	●	●	●	●	●	●	0.879
●	●	●	●	●	●	●	●	0.860
●	●	●	●	●	●	●	●	0.856
●	●	●	●	●	●	●	●	0.854
●	●	●	●	●	●	●	●	0.812
●	●	●	●	●	●	●	●	0.800
●	●	●	●	●	●	●	●	0.800
●	●	●	●	●	●	●	●	0.800

d

Relation network

e

Relevant abstracts mentioning other species:

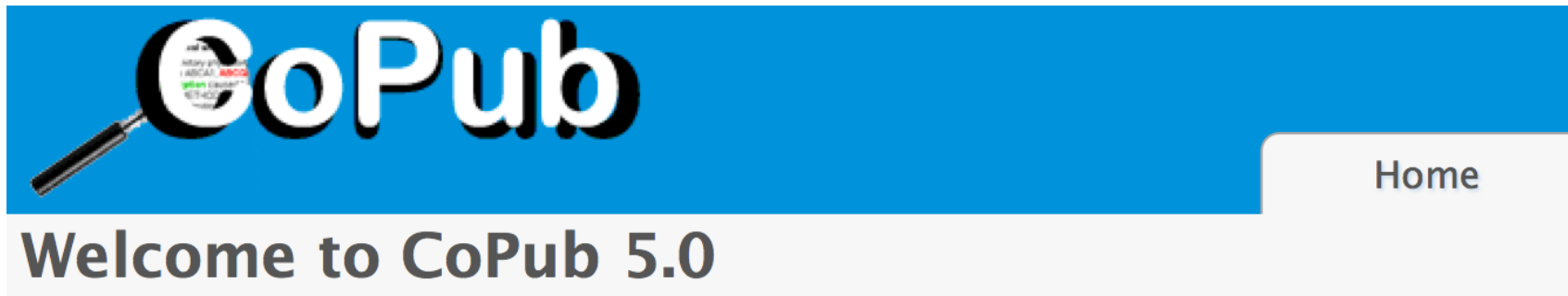
- Translocation of the Helicobacter pylori CagA protein in gastric epithelial cells by a type IV secretion apparatus. Cell Microbiol (2000). PubMed
- Identification of a tyrosine-phosphorylated 35 kDa carboxy-terminal fragment (p35CagA) of the Helicobacter pylori CagA protein in phagocytic cells: processing or breakage? Proteomics (2001). PubMed
- The role of CagA status in gastric and extragastric complications of Helicobacter pylori. J Physiol Pharmacol (1999). PubMed

Evidence sentences

Interaction summary table & evidence types



Bio-entities to terms: CoPub Mapper



CoPub is a text mining tool that detects co-occurring biomedical concepts in abstracts from the MedLine
Please use one of the modes below to access the CoPub technology.

- [Search for a term](#)
 - Publications of a term
 - Co-publications of term with category of other terms
 - Hidden relations
- [Search for pair of terms](#)
 - Co-publications of 2 terms
 - Hidden relations
- [Set of terms](#)
 - Enrich
 - Annotate
 - Network

<http://services.nbic.nl/copub5>



Search for terms

Query: ✕ 🔍

Examples: [CXCR4](#) or [rheumatoid arthritis](#) or [cell proliferation](#)

Type: ▼

Category:

Abstract count threshold:

Preferred name	Species	Gene ID	Abstract count	Alternative names	Alias
CD63 antigen	mouse gene	CD63	569	melanoma 1 antigen	ME491, TSPAN...
actin, beta, cytoplasmic	mouse gene	ACTB	66	melanoma X actin, ...	Actx, E430023...
interleukin 24	human gene	IL24	344	melanoma differenti...	FISP, MDA7, S...
interleukin 19	human gene	IL19	104	melanoma differenti...	MDA1, ZMDA1,...
cyclin dependent kinase inhibitor 1A	human gene	CDKN1A	12694	CDK interaction pro...	P21, CIP1, SDI...
cyclin dependent kinase 4	human gene	CDK4	3379	cell division kinase ...	CMM3, PSKJ3, ...
chemokine ligand 3	human gene	CXCL3	219	GRO3 oncogene, m...	MGSA, GRO3, ...
chemokine ligand 1	human gene	CXCL1	809	melanoma growth s...	GRO1, GROa, ...
chemokine ligand 2	human gene	CXCL2	1306	GRO2 oncogene, m...	MGSA, GRO2, ...
melan A	mouse gene	MLANA	1194	melanoma associat...	MART1, A9300...



Bio-entities to terms: CoPub Mapper

Term details

Preferred name	v raf murine sarcoma viral oncogene homolog B1
Alternative names	94 kDa B raf protein Murine sarcoma viral oncogene homolog B1
Preferred symbol	BRAF
Alternative symbols	BRAF1, MGC126806, MGC138284, RAFB1
Categories	human gene
Nr of abstracts	408



Bio-entities to terms: CoPub Mapper

disease		
Name	Score	Count
costello syndrome	59	7
Adenoma,follicular		
Cancer of thyroid		
Carcinoma,anaplastic		
melanoma		
Turner syndrome,male		
thyroid nodule		
Carcinoma,undifferentiated		
Carcinoma,non-small-cell lung		
adenomatous polyposis coli		

celltype		
Name	Score	Count
Melanoma cell	49	47
melanocyte		
Cancer cell		
Neoplastic cell		
Renal cell		
Reproductive cell		
fibroblast		
Squamous cell		
Stem cell		
hepatocyte		

GO molecular function		
Name	Score	Count
oncogene	52	220
MAP kinase	48	33
platelet derived growth factor receptor	47	4
vascular endothelial growth factor receptor	46	3
kinase	43	222
protein kinase	43	87
epidermal growth factor receptor	43	13
DNA methyltransferase	43	3
tyrosine kinase	42	30
tumor suppressor	42	20



CoPub Mapper

metabolite		
Name	Score	Count
3,5-dihydro-4h-imidazol-4-one	55	3
sodium iodide		
threonine		
valine		
thymine		
rapamune		
serine		
glutamic acid		
2-amino-3-(4-hydroxyphenyl)propanoic acid		
iodide ion		

tissue		
Name	Score	Count
thyroid tumor		
thyroid carcinoma		
colorectal tumor		
melanocyte		
melanoma		
colorectal adenocarcinoma		
colorectal carcinoma		
colon tumor		
colon cancer		
lung adenocarcinoma		

human gene		
Name	Score	Count
v raf murine sarcoma 3611 viral oncogene homolog	69	6
neuroblastoma RAS viral oncogene homolog	67	47
small nuclear ribonucleoprotein polypeptide E	66	13
two pore segment channel 1	62	7
v Ha ras Harvey rat sarcoma viral oncogene homolog	61	122
A kinase anchor protein 9	61	3
nuclear receptor coactivator 4	59	8
v Ki ras2 Kirsten rat sarcoma viral oncogene homolog	58	99
mitogen activated protein kinase kinase 2	58	9
paired box gene 8	57	9



COREMINE

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Category filter Network tools

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+ melanoma

... we found the following information

melanoma (Disease)
 ☆ | [Set alert!](#) | [Add to project](#)

Synonyms (11)

A malignant neoplasm derived from cells that are capable of forming melanin, which may occur in the skin of any part of the body, in the eye, or, rarely, in the mucous membranes of the genitalia, anus, oral cavity, or other sites. It occurs mostly in adults and may originate de novo or from a pigmented nevus or malignant lentigo. Melanomas frequently metastasize widely, and the regional lymph nodes, liver, lungs, and brain are likely to be involved. The incidence of malignant skin melanomas is rising rapidly in all parts of the world. (Stedman, 25th ed; from Rook et al., Textbook of Dermatology, 4th ed, p2445) [MSH]
 malignant neoplasm derived from cells that are capable of forming melanin, which may occur in the skin of any part of the body, in the eye, or, rarely, in the mucous membranes of the genitalia, anus, oral cavity, or other sites; occurring mostly in adults and may originate de novo or from a pigmented nevus or malignant lentigo; frequently metastasize widely, and the regional lymph nodes, liver, (UMLS) ↗

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Extracted associations [Collapse all](#)

- ▶ **Biomedical experts (100)**
- ▶ **Disease (2837)**
- ▶ **Drug (2320)**
- ▶ **Symptom (443)**
- ▶ **Procedure (3749)**
- ▶ **Anatomy (3646)**

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▶ Biomedical experts (100)	
▶ Disease (2837)	
▶ Drug (2320)	
▶ Symptom (443)	
▶ Procedure (3749)	
▶ Anatomy (3646)	
▶ Food (214)	
▶ Gene/Protein (5539)	
▶ MeSH (6733)	
▶ Chemical (11877)	
▶ Cellular component (337)	
▶ Biological process (1164)	
▶ Molecular function (384)	
▶ Traditional chinese medicine (280)	
▶ All categories (39523)	
▶ Found in the same articles	

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Highly specialized IE: eGIFT

<http://biotm.cis.udel.edu/eGIFT/index.php>
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eGIFT (Extracting Gene Information From Text)

identifies terms and documents that are relevant to a gene and its products.

Additional functionalities of eGIFT include:

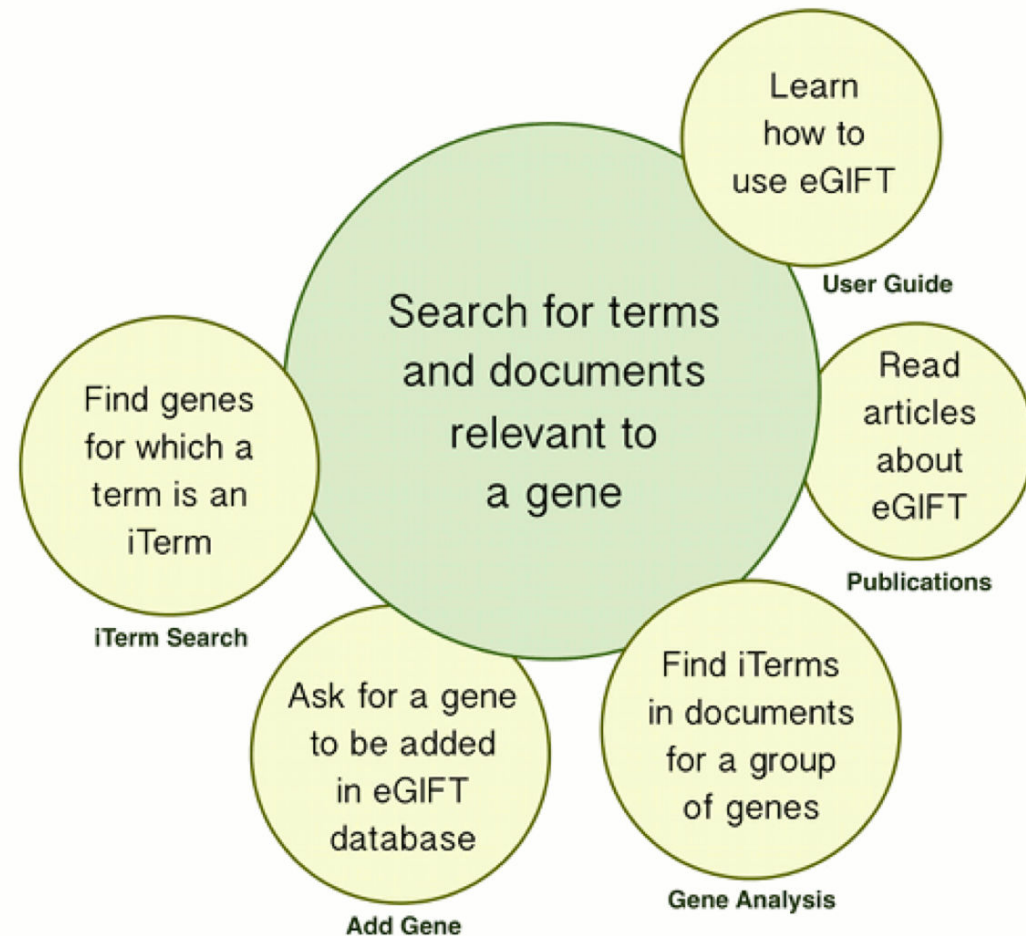
- finding terms in documents for a group of genes
- finding genes sharing a specific term
- finding related terms and related genes

1 8 4 5 8

genes linked to documents currently in eGIFT

Additional genes are included in the database on a daily basis. eGIFT's users can also request that a particular gene be added to the database.

The genes in eGIFT are not species-specific. The literature for many gene-species pairs is sparse, and because eGIFT uses a frequency-based approach, the results will be misleading if too few documents are used. The core properties of a gene are likely to be common to many species, and these will be captured as top-ranking terms in a species-





Highly specialized IE: eGIFT

8 of 9 provided genes were found in eGIFT

Add genes that were not found

See documents for all genes

See CSV file

Choose category for display

Submit

Apply analysis for selected genes

iTERM	SCORE	CATEGORY	COUNT	GENES	Select genes
3-kinase	3.1769	gene/protein	6	bad (9) pten (1) raf1 (25) bcl2l1 (62) ptk2 (17) grb2 (11)	<input type="checkbox"/>
proapoptosis protein	3.0491	gene/protein	3	bax (52) bcl2l1 (63) bad (22)	<input type="checkbox"/>
erk	2.9317	function/process	5	raf1 (8) bad (65) braf (30) grb2 (76) ptk2 (39)	<input type="checkbox"/>
proapoptosis	2.8716	function/process	3	bad (4) bax (13) bcl2l1 (9)	<input type="checkbox"/>
pro-apoptosis protein	2.8270	gene/protein	3	bcl2l1 (38) bax (33) bad (21)	<input type="checkbox"/>
bh3-only	2.7872	gene/protein	3	bad (31) bcl2l1 (52) bax (87)	<input type="checkbox"/>
tunel	2.6877	technique	3	bad (67) bax (16) bcl2l1 (49)	<input type="checkbox"/>
antiapoptosis protein	2.6333	gene/protein	3	bad (53) bax (36) bcl2l1 (4)	<input type="checkbox"/>
pro-apoptosis	2.6333	function/process	3	bax (8) bcl2l1 (6) bad (8)	<input type="checkbox"/>



IE: GoPubMed



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 - M Male 3.7 million
 - M Female 3.7 million
 - M Middle Aged 1.8 million
 - M Research Report 1.4 million
 - M Adolescent 0.9 million
 - M Medicalization 0.6 million
 - M Time Factors 0.5 million
 - M General Surgery 473,111
 - M Risk Factors 433,166
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- ▶ K All related concepts
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- ▶ 🌐 Locations
- ▶ 📁 Journals
- ▶ 🕒 Publication Dates
- ▶ 🔍 Find concepts in Knowledge Base
- ▶ ? Previous queries
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Bioinformatics Tools



IE: GoPubMed



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refine search

- ★ Favorite concepts
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 - Proto-Oncogene Proteins B-raf 1,241
 - Humans 2,939
 - Survival 718
 - Female 1,513
 - Carcinogens 502
 - Middle Aged 1,007
 - Male 1,364
 - Thyroid Gland 448
 - Thyroiditis 443
 - DNA Mutational Analysis 339
 - more
- ▶ All related concepts
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★ BRAF

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Serrated colorectal cancer: Molecular classification, prognosis, and response to chemotherapy.

Authors: Murcia, Oscar, et.al.

Journal: World journal of gastroenterology (World J Gastroenterol), Vol. 22 (13): 3516-30, 2016

New classifications for colorectal cancer (CRC) were proposed recently based on genetic profiles that show four types of molecular alterations: **BRAF** gene mutations, KRAS gene mutations, microsatellite instability, and hypermethylation of CpG islands.

[27053844](#) [Related Articles](#) [Read Full Text](#)

Affiliation: Oscar Murcia, Miriam Juárez, Eva Hernández-Illán, Cecilia Egoavil, Mar Giner-Calabuig, Marí ... ▶

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Suppression of Type I Interferon Signaling Overcomes Oncogene-Induced Senescence and Mediates Melanoma Development and Progression.

Authors: Katlinskaya, Yuliya V, et.al.



Serrated colorectal cancer: Molecular classification, prognosis, and response to chemotherapy.

Authors: Murcia, Oscar, et.al.

Journal: World journal of gastroenterology (World J Gastroenterol), Vol. 22 (13): 3516-30, 2016

New classifications for colorectal cancer (CRC) were proposed recently based on genetic profiles that show four types of molecular alterations: BRAF gene mutations, KRAS gene mutations, microsatellite instability, and hypermethylation of C

PubMed 27053844

Affiliation: Oscar Murcia

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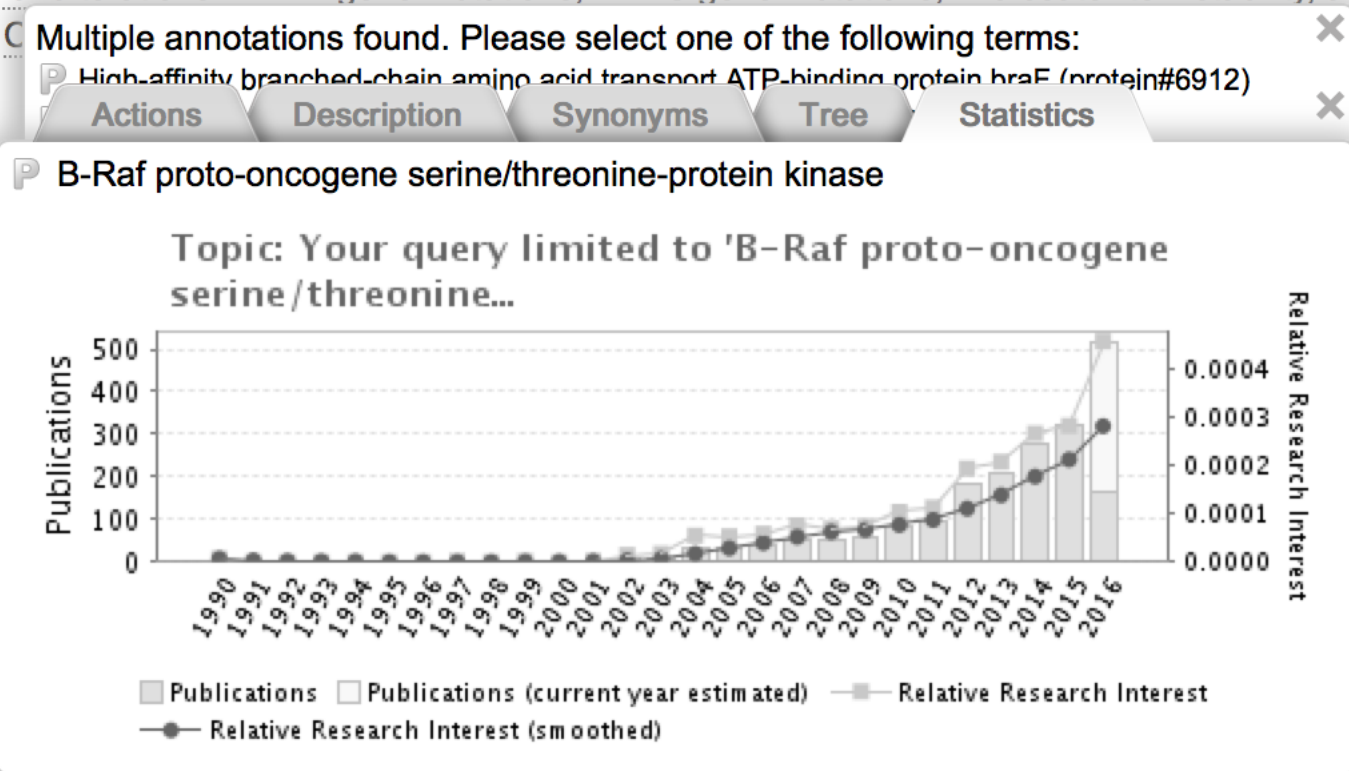


Suppression of Senescence

Authors: Katlinskaya

Journal: Cell reports

Mice harboring an I development, suppr





PolySearch

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[View sample results on query "Given Toxin *Bisphenol A* Find associated Diseases"](#)

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PolySearch

Choose your search type and enter query keyword

Given **Find ALL associated**

Query Keyword

Please cite:
Liu Y., Liang Y., Wishart D

Search 2.0: A significantly improved text-mining system for discovering associati
All Match Case 1 of 14 matches
biological terms and exploits the latest search engine technology to rapidly retrieve releve

- Disease
- Drug
- Food Metabolite
- Gene Family
- Genes/Protein
- Human Metabolite
- Organ
- Pathway
- SNP (rs#/ss#)
- Species
- Subcell Location
- Text
- Tissue
- Toxin

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PolySearch

ZScore	RScore	Entity ID	Name	Synonyms	Hits	Details
9.88	240	PS07536	B-Raf	B-Raf; B-Raf proto-oncogene serine/threonine-protein kinase; B-raf 1; BRAF; BRAF-1; BRAF1; Oncogene BRAF; RAFB-1; RAFB1; Rmil; v-RAF murine sarcoma viral oncogene homolog B1; B-Raf proto-oncogene seri... (Read More)	19 [0, 1, 5, 13]	Details
9.14	225	PS17397	MTS-1	MTS-1; MTS1; CDK4 inhibitor; CDK4I; CDKN-2; CDKN2; CDKN2A; CMM-2; CMM2; Cyclin dependent kinase inhibitor 2A; Cyclin-dependent kinase 4 inhibitor A; INK-4; INK4; INK4a; Multiple tumor suppressor 1; TP... (Read More)	16 [0, 1, 5, 10]	Details
8.65	215	PS00895	CLL associated antigen KW 1	CLL associated antigen KW 1; CLL-associated antigen KW-1 splice variant 1; CLL-associated antigen KW-1 splice variant 2; Melanoma-associated antigen; CLL-associated antigen KW-1 splice variant 1s; CLL... (Read More)	15 [0, 0, 7, 8]	Details

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PolySearch

RScore	Document	Snippets	Details
50 - [0, 1, 0, 0]	<p>Adjuvant treatment of melanoma. [MEDLINE : 23476798]</p>	<p>Moreno Nogueira JA, Valero Arbizu M, Pérez Temprano R (2013) Adjuvant treatment of melanoma. ISRN dermatology;ISRN Dermatol;2013 ;2013:545631 (PMID: 23476798)</p> <ul style="list-style-type: none"> - Several oncogenes have been identified in melanoma as BRAF, NRAS, c-Kit, and GNA11 GNAQ, each capable of activating MAPK pathway that increases cell proliferation and promotes angiogenesis, although NRAS and c-Kit also activate PI3 kinase pathway, including being more commonly BRAF activated oncogene. 	<p>Details</p>
35 - [0, 0, 1, 2]	<p>Targeted therapy in melanoma. [MEDLINE : 23438383]</p>	<p>Kudchadkar RR, Smalley KS, Glass LF, Trimble JS, Sondak VK (2013) Targeted therapy in melanoma. Clinics in dermatology;Clin. Dermatol.;2013 Mar-Apr;31(2):200-8 (PMID: 23438383)</p> <ul style="list-style-type: none"> - Strategies for the management of the vexing clinical problem of BRAF inhibitor resistance, primarily via combination therapy, are outlined. - Since the discovery of activating mutations in the BRAF oncogene in melanoma, there has been remarkable progress in the development of targeted therapies for unresectable and metastatic melanoma. - With the recent approval of the BRAF inhibitor vemurafenib for stage IV metastatic melanoma, use of this agent is expanding in the United States. 	<p>Details</p>

<http://polysearch.cs.ualberta.ca/>



Highly specialized IE: E3Miner



[Home](#) [E3DB](#) [Advanced Search](#) [Pathway Browser](#) [Contact](#)

[Help](#)

Quick Search:



E3Miner: a text mining tool specialized for ubiquitin-protein ligases

E3Miner is a web-based text mining tool that extracts and incorporates comprehensive knowledge about E3s with their underlying mechanisms. This tool integrates available E3 data not only from the published literature but also from the biological databases, using natural language processing techniques.

1. Copy & paste your text, or input comma (,) separated PMID(s).
e.g.) 17646408, 17682061, 18042044
2. Click 'Mining' button.

Clear

Mining

E3 File

Browse...

No file selected.

Open

<http://e3miner.biopathway.org/e3miner.html>



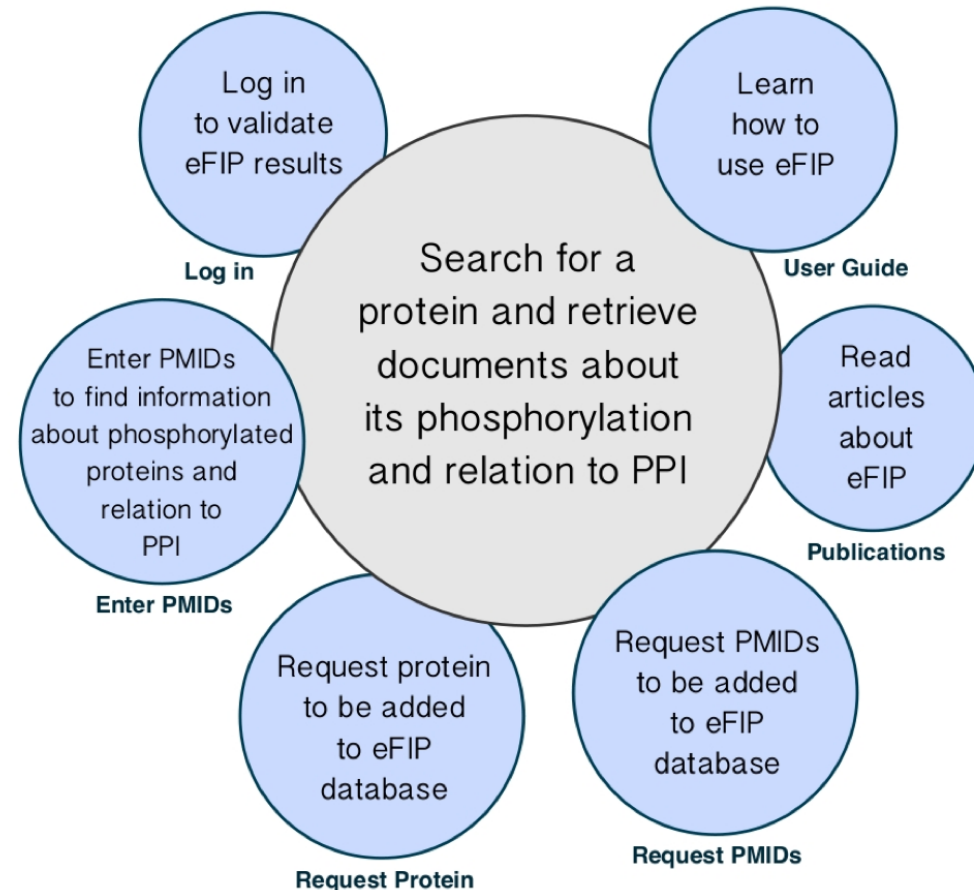
Highly specialized IE: eFIP

eFIP

Home Protein Search Enter PMIDs Request Protein/PMIDs User Guide Feedback

eFIP (Extracting Functional Impact of Phosphorylation) is a tool to support article selection and information extraction of functional impact of phosphorylated proteins. The current version focuses on protein-protein interactions (**PPIs**) as functional impact. In **eFIP**, PPIs refer to interactions between protein elements, including protein complexes and classes of proteins. **Impact is defined as any direct relation between protein phosphorylation and PPI**. The relation could be positive (phosphorylation of A increases binding to B), negative (when phosphorylated A dissociates from B) or neutral (phosphorylated A binds B).

eFIP combines information provided by applications such as eGRAB, RLIMS-P, eGIFT, and our internal PPI tool to rank abstracts based on the information content related to protein phosphorylation, phosphorylation site information, PPI, and phosphorylation-PPI relation. Results for each abstract are displayed in a tabular format with links



<http://biotm.cis.udel.edu/eFIP/index.php>



Highly specialized IE: eFIP

BRAF - V-raf murine sarcoma viral oncogene homolog b1

The PMIDs are ranked based on information contained in the abstract: phosphorylation information [Site](#), protein-protein interaction information [PPI](#), and impact of phosphorylation on the PPI [Impact](#).

Download PMIDS:

[Impact](#)

1.

[PPI](#)

[Site](#)

Summary of extracted information:

Raf-1 ↔ most SH2 domain (interaction → dependent on → phosphorylation)

Raf-1 ↔ Raf-1 (phosphorylation → dependent on → association)

Raf-1 ↔ Fyn/Src (phosphorylation → by → complex)

Fyn SH2 domain (phosphorylation → association)

PMID 7517401 | [see in PubMed](#) | [read abstract here](#) | [view evidence](#)

[Impact](#)

2.

[PPI](#)

Summary of extracted information:

Raf kinase inhibitory protein (RKIP) ↔ Raf-1 (phosphorylation → upon → association)

Raf kinase inhibitory protein (RKIP) ↔ GRK2 (phosphorylation → upon → association)

PMID 17170028 | [see in PubMed](#) | [read abstract here](#) | [view evidence](#)



Highly specialized IE: miRTex

miRTex [RESTful APIs](#) [Contact](#)

177 of 462 abstracts from PubMed contain miRNA-gene relations.
 261 miRNA-target pairs, 265 miRNA-gene regulation pairs and 54 gene-miRNA regulation pairs are extracted.
 Download ▾

Filter: < 1 2 3 4 5 ... 24 >

PMID	miRNA	Gene	Relation Type	Direct	Text Evidence	
					Sentence	Abstract
26116372	MiR-21	APAF1	miRNA → gene	✓	1	
26104682	miR-9	YY1	gene → miRNA	N/A	1	
21435193	miR-211	BRN2 transcription factor	miRNA → gene	✗	1	
25242509	miR96	NUAK1	miRNA → gene	✓	1	
24767210	miR-224	HIF1A	miRNA → gene	✗	1	
24762088	miR-125b	p21	miRNA → gene	✗	1	
19074879	miR-34c	MET	miRNA → gene	✗	1	
26287415	miR-664	cyclin D1	miRNA → gene	✗	1	

<http://research.bioinformatics.udel.edu/miRTex/>



Highly specialized IE



PESCADOR

Platform for Exploration of Significant Concepts AssociateD to co-Occurrences Relationships.

[Input](#) | [Concepts](#) | [Retrieval](#) | [Development](#) | [Help](#)

Resurrected!

INPUT [Required]

Retrieve PMIDs that match a PubMed query, paste below you query:

Query PubMed

OR

Choose a PubMed ID list file to upload:

Browse... No file selected.

PMID list matched for query: **melanoma**

```
27007961
26977479
26962743
26962742
26962741
26962740
26940869
26939188
```

Total: 1000

<http://cbdm.mdc-berlin.de/tools/pescador/index.php>



Highly specialized IE



PESCADOR

Platform for Exploration of Significant Concepts Associated to co-Occurrences Relationships.

Your request ID is: **1460126042**. Click in the below links to access the results of your analysis.

Browse results

- Biological [terms](#) and their identified co-occurrences within the loaded scientific literature;
- List of identified [concepts](#) along with biological terms within the loaded text;
- Highlighted [abstracts](#) with term co-occurrences and relationships;
- Visualize a co-occurrence [network](#) using EMBL Medusa ([Hooper and Bork, 2005](#)) for the biological terms identified;
- Access the pairs [validations](#) for this project;

Download files

- Click [here](#) for NLPROT tagged abstracts;
- Click [here](#) for LAITOR co-occurrence analysis;
- Click [here](#) for MEDUSA global network (last updated main file);
- Click [here](#) for EVALUATION table;
- Click [here](#) for TERMS identified in the project;
- Click [here](#) for CONCEPTS identified in the project;



Chilibot

Mining PubMed for relationships

Chilibot searches PubMed literature database (abstracts) about specific relationships between **proteins, genes, or keywords**. The results are returned as a graph ([see examples](#)). We use several different search methods.

Search for relationship between **two** genes, proteins or keywords

Examples:

BDNF & TRKB
BDNF & polymorphism
BDNF & [modulate](#)

&

Search for relationships between **many** genes, proteins, or keywords

Example:

Apoptosis
TrkB
BDNF
Nur77



<http://www.chilibot.net/>



Chilibot

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

- BFD 22 a new potential inhibitor of **BRAF** inhibits the metastasis of B16F10 **melanoma** cells and simultaneously increase the tumor immunogenicity. [Ref: Toxicol Appl Pharmacol, 2016, PMID: 26876618](#)
- BFD 22 a new potential inhibitor of **BRAF** inhibits the metastasis of B16F10 **melanoma** cells and simultaneously increase the tumor immunogenicity. [Ref: Toxicol Appl Pharmacol, 2016, PMID: 26876618](#)
- The natural genetic progression of **melanoma** can be modified by targeted (**BRAF** or MEK inhibitor) or immunotherapy. [Ref: Cancer Metastasis Rev, 2016, PMID: 26970965](#)
- Inhibition of oncogenic **BRAF** activity by indole 3 carbinol disrupts microphthalmia associated transcription factor expression and arrests **melanoma** cell proliferation. [Ref: Mol Carcinog, 2016, PMID: 26878440](#)
- Inhibition of oncogenic **BRAF** activity by indole 3 carbinol disrupts microphthalmia associated transcription factor expression and arrests **melanoma** cell proliferation. [Ref: Mol Carcinog, 2016, PMID: 26878440](#)
- Moreover, nelfinavir is effective in **BRAF** and NRAS mutant **melanoma** cells isolated from patients progressed on MAPK inhibitor (MAPKi) therapy and in **BRAF** NRAS PTEN mutant tumors. [Ref: Cancer Cell, 2016, PMID: 26977879](#)



Knowledge Discovery (KD)

A

C

B



Arrowsmith

Start	A-Literature	C-Literature	B-list	Filter	Literature
--------------	--------------	--------------	--------	--------	------------

Start ARROWSMITH

This search mode will assist you in looking for items or concepts that may be present in common between two distinct sets of articles. Another context for using this search mode is when you want to find information that is present in one field that may be relevant to another field of inquiry. You will be guided through two PubMed searches to retrieve biomedical articles from the Medline database: the first search defines "literature A" and the second defines "literature C." The program then generates a "B-list" of words and phrases found in the titles of both literatures.

The B-list is displayed ranked by relevance, and can be restricted to certain semantic categories (e.g. anatomical regions, or disorders, or drugs). For each B-term of interest, one can view the titles containing A and B ("AB titles") juxtaposed to the titles containing B and C ("BC titles"). In this manner, one can readily assess whether there appears to be a biologically significant commonality or relationship between the two sets of articles.

TUTORIAL: Smalheiser NR, Torvik VI, Zhou W. [Arrowsmith two-node search interface: A tutorial on finding meaningful links between two disparate sets of articles in MEDLINE](#). *Comput Meth Program Biomed.* 2009; 94(2): 190-197. *A preprint version of this paper is available [here](#).*

Basic - provides a list of B-terms ranked by relevance.
 Advanced - provides a list of B-terms with multiple options for manual filtering.

Or enter an existing search id #

http://arrowsmith.psych.uic.edu/cgi-bin/arrowsmith_uic/start.cgi

Text mining



Start A-Literature C-Literature **B-list** Filter Literature

A: 19766 C: 50000 Overlap: 1187
A-query: gastrin
C-query: gastric cancer

The B-list contains title words and phrases (terms) that appeared in both the A and the C literature. **1187** articles appeared in both literatures and were not included in the process of computing the B-list but can be viewed [here](#). The results of this search are saved under id # **17972** and can be accessed from the start page after you leave this session. There are **19576** terms on the current B-list (**5465** are predicted to be relevant), which is shown ranked according to predicted relevance. The list can be further trimmed down using the filters listed in the left margin.

To assess whether there appears to be a biologically significant relationship between the AB and BC literatures for specific B-terms, please select one or more B-terms and then click the button to view the corresponding AB and BC literatures. Use Ctrl to select multiple B-terms.

Rank	Prob	B-term
1	0.97	pylori eradication
2	0.97	cox-2
3	0.97	helicobacter pylori eradication
4	0.97	h pylori
5	0.97	eradication helicobacter pylori
6	0.97	lansoprazole
7	0.96	cyp2c19
8	0.96	wnt
9	0.96	c erbb-2
10	0.96	helicobacter pylori gastric
11	0.96	diagnosis helicobacter pylori
12	0.96	campylobacter pylori
13	0.96	treatment helicobacter
14	0.96	--treatment helicobacter pylori
15	0.96	helicobacter pylori associated
16	0.96	pantoprazole
17	0.96	helicobacter pylori infection
18	0.96	pylori gastric
19	0.96	therapy helicobacter
20	0.96	proton pump inhibitor

Restrict by semantic categories?



Arrowsmith

Start	A-Literature	C-Literature	B-list	Filter	Literature
AB literature		B-term		BC literature	
gastrin		cox-2		gastric cancer	
<p>1: Probiotics regulate the expression of COX-2 in intestinal epithelial cells. 2009 Add to clipboard</p> <p>2: The CCK-2/gastrin splice variant receptor retaining intron 4 transactivates the COX-2 promoter in vitro. 2007 Add to clipboard</p> <p>3: Growth inhibition of non-small-cell lung carcinoma by BN/GRP antagonist is linked with suppression of K-Ras, COX-2, and pAkt. 2007 Add to clipboard</p> <p>4: Activation of NFkappaB represents the central event in the neoplastic progression associated with Barrett's esophagus: a possible link to the inflammation and overexpression of COX-2, PPARgamma and growth factors. 2004 Add to clipboard</p> <p>5: Regulation and function of COX-2 gene expression in isolated gastric parietal cells. 2002 Add to clipboard</p> <p>6: COX-2 selective inhibition reverses the trophic properties of gastrin in colorectal cancer. 2002 Add to clipboard</p> <p>7: Classic NSAID and selective cyclooxygenase (COX)-1 and COX-2 inhibitors in healing of chronic gastric ulcers. 2001 Add to clipboard</p>		<p>1: Anti-gastric cancer effects of celecoxib, a selective COX-2 inhibitor, through inhibition of Akt signaling. 2009 Add to clipboard</p> <p>2: Anticancer effect of celecoxib via COX-2 dependent and independent mechanisms in human gastric cancer cells. 2009 Add to clipboard</p> <p>3: Effect of Helicobacter pylori infection on IL-8, IL-1beta and COX-2 expression in patients with chronic gastritis and gastric cancer. 2009 Add to clipboard</p> <p>4: Polymorphism in COX-2 modifies the inverse association between Helicobacter pylori seropositivity and esophageal squamous cell carcinoma risk in Taiwan: a case control study. 2009 Add to clipboard</p> <p>5: Involvement of Ras and AP-1 in Helicobacter pylori-Induced Expression of COX-2 and iNOS in Gastric Epithelial AGS Cells. 2009 Add to clipboard</p> <p>6: COX-2 and CCR2 induced by CD40 ligand and MCP-1 are linked to VEGF production in endothelial cells. 2008 Add to clipboard</p>			



FACTA+

- Finding Associated Concepts with Text Analysis -

Melanoma [Help](#)
e.g. "apoptosis", "p53" or "diabetes GENIA:Gene_expression"

- Gene/Protein Disease Symptom Drug Enzyme Compound

Pivot Concepts: Target Concepts:

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

<http://www.nactem.ac.uk/facta/>



FACTA+

Gene/Protein
 Disease
 Symptom
 Drug
 Enzyme
 Compound

Pivot Concepts:
 Target Concepts:

Query: **Melanoma**

79,002 document(s) hit in 21,030,264 MEDLINE articles (0.07 seconds)

Concepts found in the documents ranked by [[Frequency](#) | [Pointwise Mutual Information](#) | [Symmetric Conditional Probability](#)] .

Human Gene/Protein		Disease		Symptom		Drug		Enzyme		Compound	
Polymerase	2547	melanoma	76217	pain	379	IFN-gamma	784	tyrosinase	1786	DNA	6724
Interleukin-2	2098	Melanoma	59668	nausea	268	IL-2	769	mitogen-activated protein kinase	675	Interleukin-2	1894
tyrosinase	1812	tumor	40361	vomiting	220	Gel	745	ERK	656	phenol	1561
CD8	1509	Skin Neoplasms	25355	erythema	216	Fluorescein	537	MAP	429	Dacarbazine	1307
cytokine	1426	cancer	14913	fatigue	189	Fluorescein	534	protein kinase	378	Tyrosine	1235
interferon	1381	metastases	11992	Anesthesia	171	Progesterone	518	DCF	338	Tumor Necrosis Factor	1026
Interferon-gamma	1307	Melanoma, Experimental	6639	diarrhea	139	Cyclophosphamide	476	protein kinase C	331	Iodine	864
HLA	1082	Neoplasms	5380	headache	129	CSF	356	reverse transcriptase	269	Cisplatin	858
p53	1039	mole	4748	nausea and vomiting	127	Glutathione	321	MEK	241	Tyrosine	835
CD4	1029	Lymphatic Metastasis	4490	anorexia	100	Tretinoin	257	caspase-3	235	oxygen	823
S100	1006	Lung Neoplasms	4358	abdominal pain	91	Tretinoin	255	ABL	235	calcium	672
MART-1	874			chills	81	Nitric Oxide	221			Hydrogen	606
F10	842					Albumin	203				

Direct relations: co-occurrences

<http://www.nactem.ac.uk/facta/>



FACTA+

Diseases found indirectly associated with the query through Human Gene/Proteins.

Exp. Info.	Info.	Target Concepts	<-->	Pivot Concepts	<-->	Query Concept
14.3444	17.27	OCA3	☰	0.955 tyrosinase-related protein-1	☰ 0.514	Melanoma
				0.818 tyrosinase	☰ 0.342	
				0.545 MATP	☰ 0.250	
13.8260	17.27	OCA4	☰	0.650 tyrosinase-related protein-1	☰ 0.514	Melanoma
				0.800 tyrosinase	☰ 0.342	
				0.950 MATP	☰ 0.250	
11.7406	17.27	OCA1B	☰	0.889 tyrosinase	☰ 0.342	Melanoma
				0.778 Tyrosinase	☰ 0.350	
				0.333 tyrosinase-related protein-1	☰ 0.514	
11.3947	17.27	autism	☰	0.500 SEC23IP	☰ 0.500	Melanoma
				0.250 MAGE-G1	☰ 0.500	
				0.250 MAGE-Xp	☰ 0.250	
10.8429	12.95	schizophrenia	☰	0.500 GALNT7	☰ 0.500	Melanoma
				0.500 KPNA3	☰ 0.250	
				0.286 Syntaxin-7	☰ 0.286	

Indirect relations

<http://www.nactem.ac.uk/facta/>



Question Answering (QA)

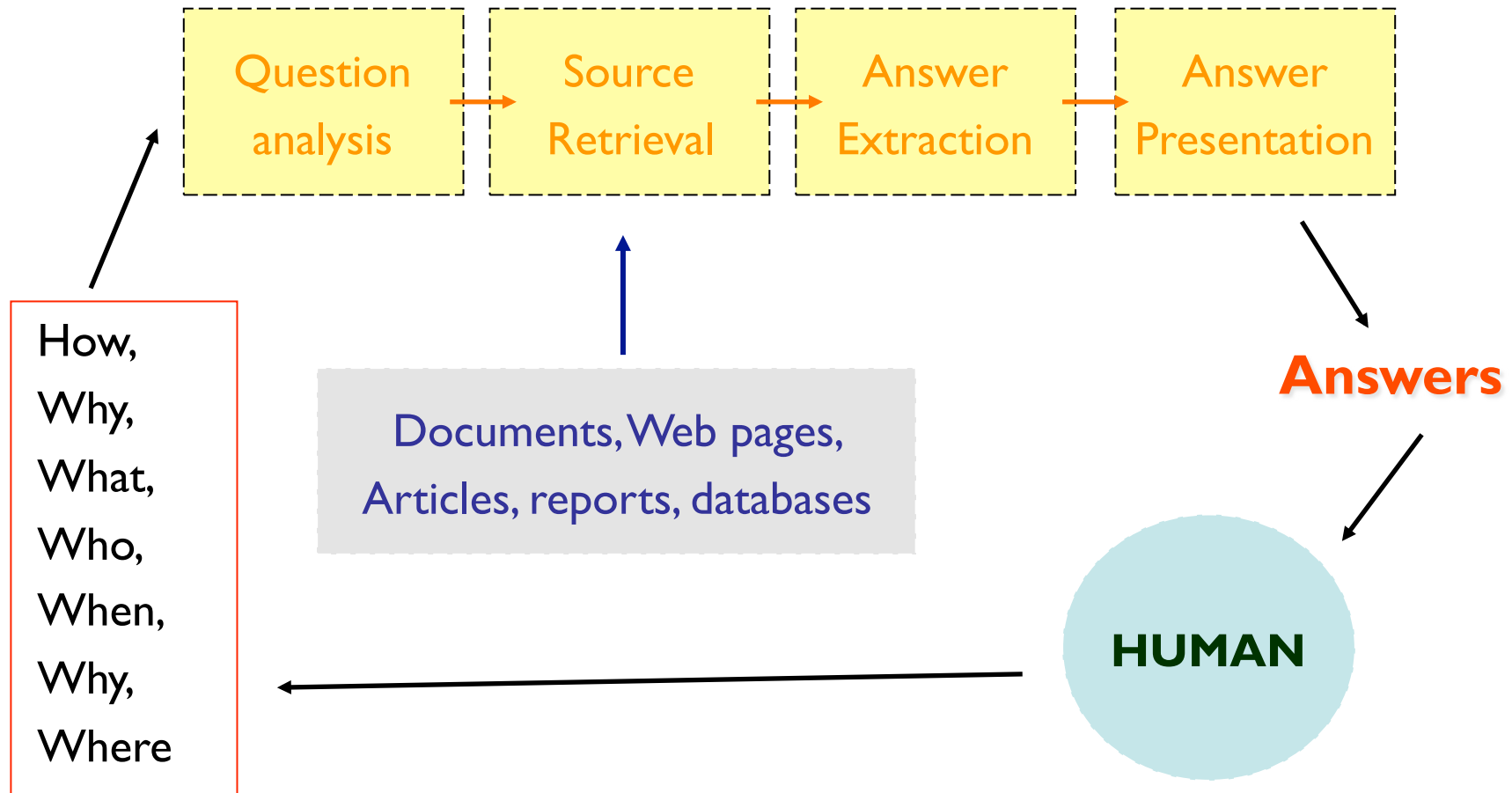


Question Answering

- Humans formulate questions using natural language.
- Example: What are the molecular functions of Glycogenin?.
- QA: automatic generation of answers to queries in form NL expressions from document collections.
- Most systems limited to generic literature or newswire.
- QA difficult: heterogeneous, poorly formalized domain, new scientific terms
- Ad hoc retrieval task of the TREC Genomics Track 2005.
- Galitsky system (semantic skeletons (SSK), logical programming).



Question Answering simplified architecture



New directions in Question Answering, Mark Maybury



Question Answering for Alzheimer domain

QA4MRE

Question Answering for Machine Reading Evaluation
at CLEF 2012



- Home
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- Pilot Tasks
 - Modality and Negation
 - Biomedical about Alzheimer
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- Links

News

QA @ CLEF Repository

MACHINE READING OF BIOMEDICAL TEXTS ABOUT THE ALZHEIMER DISEASE

Task Description

This pilot task aims at exploring the ability of a machine reading system to answer questions about a scientific topic. The task will focus on biomedical texts about the Alzheimer disease. It is well known that scientific language poses additional challenges to natural language processing, since domain knowledge (from ontologies and databases) is essential to reach deep understanding. There exist NLP tools to process scientific text at several levels of analysis, and several tasks have been organised to extract different types of information from scientific texts. With this task we aim at going a step further, by proposing a task where inference plays a main role.

As in the main task, this task focuses on the reading of single documents and the identification of the answers to a set of questions about information that is stated or implied in the text. Questions are in the form of multiple choice, each having five options, and only one correct answer. The detection of correct answers is specifically designed to require various kinds of inference and the consideration of previously acquired background knowledge from reference document collections provided by the organization. Although the additional knowledge obtained through the background collection may be used to assist with answering the questions, the principal answer is to be found among the facts contained in the test documents given.

<http://celct.fbk.eu/QA4MRE/index.php?page=Pages/biomedicalTask.html>



askMEDLINE [[Back to Home Page](#)]

Your question: *What is cutaneous melanoma?*

Your question is too broad. Narrow down your search by combining it with other medical terms (ex: 1 etiology, prognosis, incidence, etc.).

Submit

askMEDLINE [[Back to Home Page](#)]

Your question: *What is the therapy for cutaneous melanoma?*

If this search strategy does not meet your requirements, you may use **PICO** or **Ask** another question. You may also use **<BabelMeSH>**, if you want to search in Arabic, French, German, Italian, Japanese, Portuguese, Russian or Spanish.

34304 results:

- 1. Clonal neoantigens elicit T cell immunoreactivity and sensitivity to immune checkpoint blockade. McGranahan N; Furness AJ; Rosenthal R; Ramskov S; Lyngaa R; Saini SK; Jamal-Hanjani M; Wilson GA; Birnbak NJ; Hiley CT; Watkins TB; Shafi S; Murugaesu N; Mitter R; Akarca AU; Linares J; Marafioti T; Henry JY; Van Allen EM; Miao D; Schilling B; Schadendorf D; Garraway LA; Makarov V; Rizvi NA; Snyder A; Hellmann MD; Merghoub T; Wolchok JD; Shukla SA; Wu CJ; Peggs KS; Chan TA; Hadrup SR; Quezada SA; Swanton C Science; 2016 Mar; 351(6280):1463-9. PubMed ID: 26940869 [[TBL](#)] [[Abstract](#)] [[Full Text](#)] [[Related](#)]

<http://askmedline.nlm.nih.gov/ask/ask.php>



Enter what you want to **calculate** or **know about**:

Which genes are mutated in melanoma patients?



Examples Random

<http://www.wolframalpha.com/>



Assuming any type of malignant melanoma of the skin | Use [malignant melanoma of the ear and external auditory canal](#) or [more](#) instead

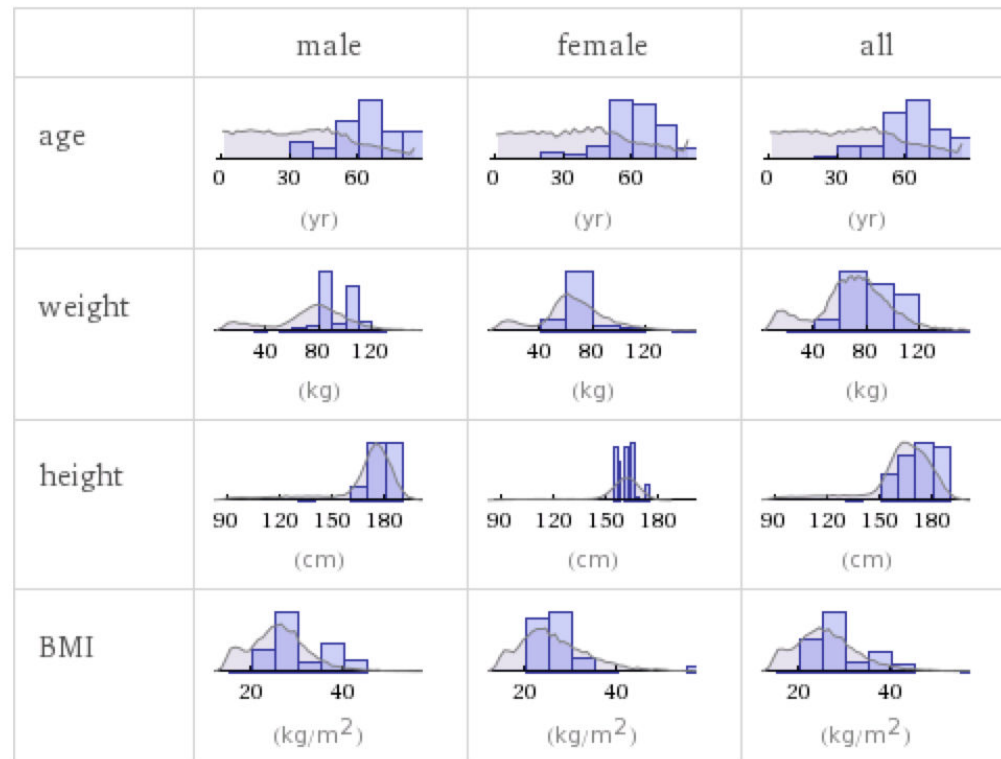
Input interpretation:

malignant melanoma of the skin characteristics of patients

Result:

[More](#)

[Primary diagnosis at visit](#) ▼





Text mining at CNIO



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Keywords **Compounds** Cytochromes Markers Tox. Endpoints Genes

Troglitazone **Search**

What are you searching?

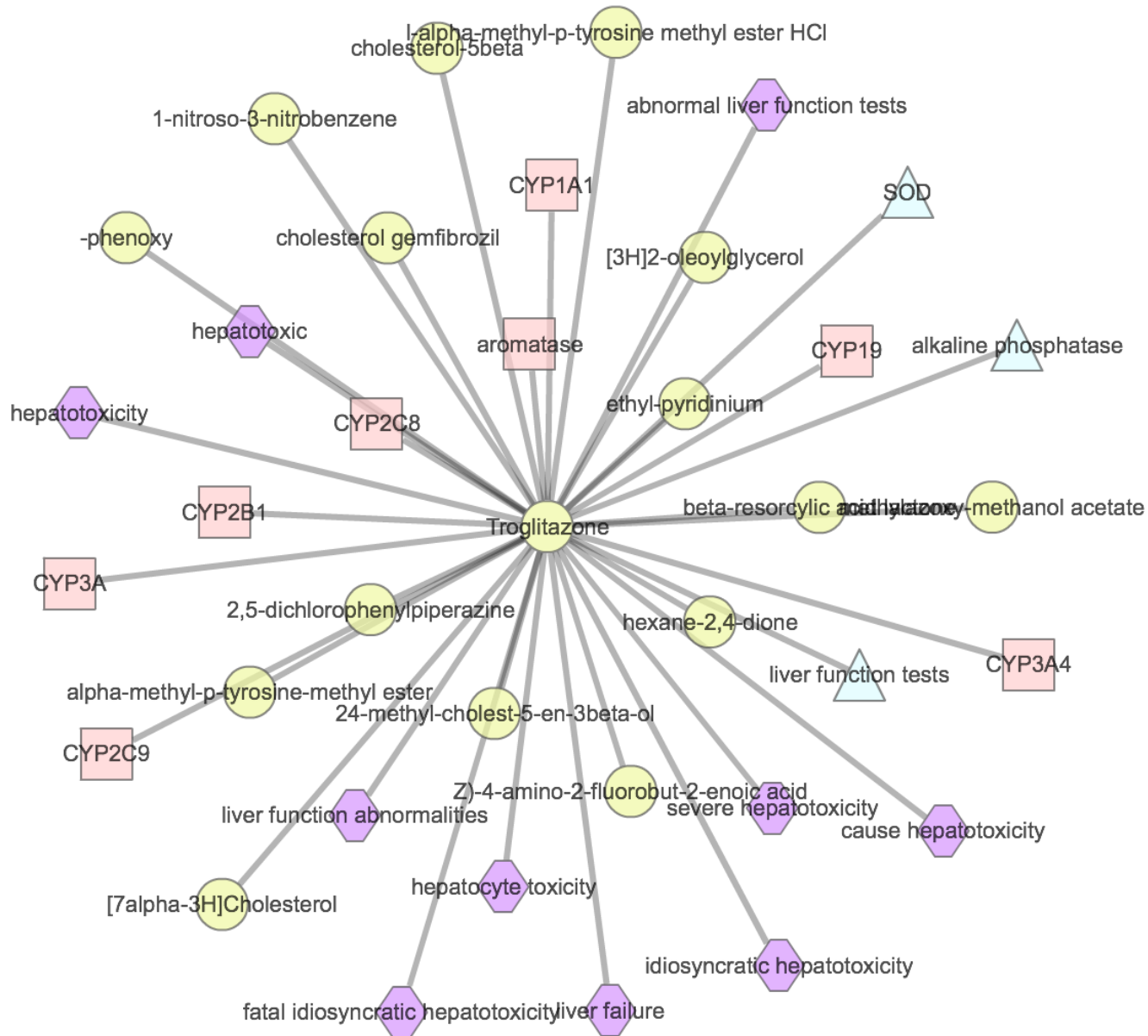
- Name
- Chemical identifiers
- SMILES
- InChI
- Any (Free search)
- With CYPs
- With Markers
- Term relations

Source:

- All
- Pubmed
- Fulltext
- NDA
- EPAR
- Abstracts

<http://limtox.bioinfo.cnio.es/>

Text mining





See Compound info: Troglitazone ([Download mol file](#))

name: [Troglitazone](#)

chemIdPlus: 097322877

chebi: [CHEBI:9753](#)

cas Registry Number: [97322-87-7](#)

inChi: [InChI=1/C24H27NO5S/c1-13-14\(2\)21-18\(15\(3\)20\(13\)26\)9-10-24\(4,30-21\)12-29-17-7-5-16\(6-8-17\)11-19-22\(27\)25-23\(28\)31-19/h5-8,19,26H,9-12H2,1-4H3,\(H,25,27,28\)](#)

drugBank: [DB00197](#)

keggCompound: [D00395](#)

keggDrug: [D00395](#)

mesh: [C057693](#)

nrDblds: 9

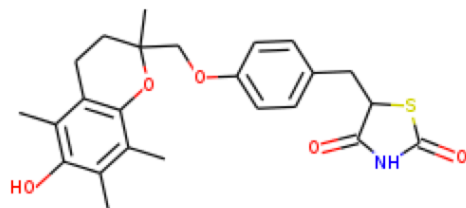
smile:

```
Cc1c(C)c2OC(C)(COc3ccc(CC4SC(=O)NC4=O)cc3)CCc2c(C)c1O
```

[Search SMILE in ChemSpider](#)

Alliases

Troglitazone, CS-045, Noscalt, Prelay, Rezulin, troglitazone, Troglitazone maleate, Troglitazone sulfate, troglitazone, troglitazone sulfate, troglitazone sulphate, troglitazone,



Text mining




Entity mentions are highlighted as follows: **What you searched**, **Compounds**, **Cytochromes**, **Markers**, **Terms**, **Species**. Curated evidences are indicated by: ✓

Source	SVM	Conf.	Pattern	Term	Rule	Nephro	Cardio	Sentence	Curation
PubMed	11.15	1.095	-	1	3	0.7	0.72	Drug-induced idiosyncratic hepatotoxicity prevention strategy developed after the Troglitazone case	<input checked="" type="checkbox"/> <input type="checkbox"/> 3
PubMed	10.04	2.159	-	2	3	0.37	-0.78	Troglitazone induced an idiosyncratic hepatocellular injury-type hepatotoxicity in humans	<input checked="" type="checkbox"/> <input type="checkbox"/> 1
PubMed	9.99	1.209	-	1	2.5	0.47	-0.76	If hepatotoxicity is associated with this effect then hepatotoxicity is not limited to Troglitazone	<input checked="" type="checkbox"/> <input type="checkbox"/> 2
PubMed	9.35	0.935	-	2	3	-1.08	-0.97	Hepatocarcinogenic susceptibility of rasH2 mice to Troglitazone in a two- stage hepatocarcinogenesis model	<input checked="" type="checkbox"/> <input type="checkbox"/> None
PubMed	9.3	1.136	-	1	2.5	0.45	-0.77	Alternatively if hepatotoxicity is limited to troglitazone other mechanisms are responsible for its reported hepatotoxicity	<input checked="" type="checkbox"/> <input type="checkbox"/> None

<http://limtox.bioinfo.cnio.es/>



 **MelanomaMine** [Home](#) [Feedback](#) [Contact](#) [Help](#)
[login](#) | [Register](#)

Search Keyword Genes Mutations Chemicals Diseases Mutated Proteins Other Cancer

Endolysosomal **Search**

What are you searching?

- Free-text Search
- With Genes/Protein
- With Protein Mutations
- With SNPs
- With DNA Mutations
- With Chemicals
- With Drugs
- With Diseases
- With Mutated Proteins

<http://melanomamine.bioinfo.cnio.es/>



Search Keyword Genes **Mutations** Chemicals Diseases Mutated Proteins Other Cancer

V599E **Search**

DNA/Protein mutations

DNA
 Protein

What are you searching?

Substitutions
 Insertions
 Deletions
 INDELS
 Frameshifts
 SNPs
 All

Search Normalized Protein Mutations

Wild-Type:


Position:

Mutant:

Search

<http://melanomamine.bioinfo.cnio.es/>



Pubmed Link	Title	Abstract
 7.64	<p>A tumor-infiltrating lymphocyte from a melanoma metastasis with decreased expression of melanoma differentiation antigens recognizes MAGE-12 <i>class='diseases_highlight' data-tooltip='sticky1'></i></p> <hr/> <p>Genes: MAGE-12 [5], gp100 [3], IFN-alpha [1], PMel17 [1], MAGE-1, 2, 3, 4a, and 6 [1], IFN-gamma [1], Diseases: tumor [7], melanoma [7], allogeneic melanoma [1], melanoma metastasis [1], A tumor [1], Species: patient [1], human [1], MutatedProteins: 187 D-->A [2], Chemicals: amino acid [1], Mutations: 187 D-->A [2]</p>	<p>Twenty separate tumor infiltrating lymphocyte (TIL) bulk cultures and a tumor cell line were originated simultaneously from a fine needle aspiration biopsy of a metastasis in a patient with melanoma (F001) previously immunized with the HLA-A*0201-associated gp100:209-217(210 M) peptide. None of the TIL recognized gp100. However, 12 recognized autologous (F001-MEL) and allogeneic melanoma cells expressing the HLA haplotype A*0201, B*0702, Cw*0702. Further characterization of F001-MEL demonstrated loss of gp100/PMel17, severely decreased expression of other melanoma differentiation Ags and retained expression of tumor-specific Ags. Transfection of HLA class I alleles into B*0702/Cw*0702-negative melanoma cell lines identified HLA-Cw*0702 as the restriction element for F001-TIL. A cDNA library from F001-MEL was used to transfect IFN-alpha-stimulated 293 human embryonal kidney (293-HEK) cells expressing HLA-Cw*0702. A 100-gene pool was identified that induced recognition of 293-HEK cells by F001-TIL. Subsequent cloning of the pool identified a cDNA sequence homologous, except for one amino acid (aa 187 D-->A), to MAGE-12. Among 25 peptide sequences from MAGE-12 with the HLA-Cw*0702 binding motif, MAGE-12:170-178 (VRIGHLYIL) induced IFN-gamma release by F001-TIL when pulsed on F001-EBV-B cells at concentrations as low as 10 pg/ml. Peptide sequences from MAGE-1, 2, 3, 4a, and 6 aligned to MAGE-12:170-178 were not recognized by F001-TIL. In summary a TIL recognizing a MAGE protein was developed from an HLA-A*0201 expressing tumor with strongly reduced expression of melanoma differentiation Ags. Persisting tumor-specific Ag expression maintained tumor immune competence suggesting that tumor-specific Ags/melanoma differentiation Ags may complement each other in the context of melanoma Ag-specific vaccination.</p>

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