

# CURATION GUIDE

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Further help and tips are available on the PI2 wiki  
[https://www.pathogenomics.ca/wiki/index.php/Curators\\_Group](https://www.pathogenomics.ca/wiki/index.php/Curators_Group)

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# Chapter 1: A Guide To The InnateDB Submission System

<http://www.innatedb.com/dashboard/>

## 1.1 Logging In

A user email address and password are required to access the submission system.



### System Login

Email

Password

First Page allows users to view & review submitted interactions:

list	details	1 - 20 of 9478 <a href="#">order</a> <a href="#">oldest</a>		
<a href="#">CIG-9908</a>	<a href="#">HDAC3::HIF1A</a>	HIF1A physically associates with HDAC3	PubMed ID 17273746	Misbah Naseer reviewed Mar 12
<a href="#">CIG-9907</a>	<a href="#">HDAC1::HIF1A</a>	HIF1A physically associates with HDAC1	PubMed ID 17273746	Misbah Naseer reviewed Mar 12
<a href="#">CIG-9906</a>	<a href="#">MDM2::HIF1A</a>	MDM2 physically associates with HIF1A	PubMed ID 17234751	Misbah Naseer reviewed Mar 12
<a href="#">CIG-9905</a>	<a href="#">MYC::ARD1A</a>	ARD1A physically associates with MYC gene	PubMed ID 18593917	Misbah Naseer reviewed Mar 12
<a href="#">CIG-9904</a>	<a href="#">MYC::CTNNB1</a>	CTNNB1 physically associates with MYC gene	PubMed ID 18593917	Misbah Naseer reviewed Mar 12
<a href="#">CIG-9903</a>	<a href="#">HIF1A::CTNNB1</a>	CTNNB1 physically associates with HIF1A	PubMed ID 18593917	Misbah Naseer reviewed Mar 12
<a href="#">CIG-9902</a>	<a href="#">HIF1A::ARD1A</a>	ARD1A physically associates with HIF1A	PubMed ID 18593917	Misbah Naseer reviewed Mar 12
<a href="#">CIG-9901</a>	<a href="#">MAP4K4::BIRC2</a>	MAP4K4 (NIK) physically associates with BIRC2 (cIAP1)	PubMed ID 20184394	Melissa Yau reviewed Mar 12
<a href="#">CIG-9900</a>	<a href="#">ARNT::HIF3A</a>	ARNT physically associates with HIF3A	PubMed ID 16126907	Misbah Naseer reviewed Mar 12
<a href="#">CIG-9899</a>	<a href="#">HIF1A::HIF3A</a>	HIF1A physically associates with HIF3A	PubMed ID 16126907	Misbah Naseer reviewed Mar 12
<a href="#">CIG-9898</a>	<a href="#">AIM2::AIM2</a>	AIM2 physically associates with itself	PubMed ID 15582594	Ana Sribnaia reviewed Mar 12
<a href="#">CIG-9897</a>	<a href="#">HIF1A::PGK1::ARNT</a>	A complex of HIF1A and ARNT transcriptionally regulates PGK1 gene	PubMed ID 16126907	Misbah Naseer reviewed Mar 12

## 1.2 Searching Interactions

The submission system allows users to search single or multiple criteria at a time. Searchable fields include:

- PubMed ID
- Interaction Name
- Interaction Type
- Participant Molecule
- Interaction Detection Method
- Evidence Comments
- Submission Status
- Submitter

To add multiple search criteria, click the “+” icon. The user can search for interactions matching **all** criteria or **any** of the criteria selected. To take out a search criteria, click on the “-” icon.

Interactions [add interaction](#)

Match **all** of the following rules:

(1)	PubMed ID	is		-	+
(2)	Interaction Name	contains		-	+
(3)	Interaction Type	is	OBO term	-	+
(4)	Participant Molecule	is	<a href="#">select...</a>	-	+
(5)	Interaction Detection Method	is	<a href="#">select...</a>	-	+
(6)	Evidence Comments	contains		-	+
(7)	Submission Status	is	pending	-	+
(8)	Submitter	is	<a href="#">select...</a>	-	+

[Reset](#) [Search](#)

Click the “Search” button after entering the search criteria. For example, if participant molecule= IRAK1, the following search results are shown:

Interactions [add interaction](#)

Match the following rule:

(1)	Participant Molecule	is	IRAK1	-	+
-----	----------------------	----	-------	---	---

[Reset](#) [Search](#)

Curated Interaction Public Interaction

list	details	1 - 20 of 86 <a href="#">older</a> <a href="#">oldest</a>			
<a href="#">CIG-9320</a>	<a href="#">IRAK1::VASP</a>	IRKA1 physically associates with VASP	PubMed ID 20044140	Ana Sribnala	reviewed Mar 07
<a href="#">CIG-9128</a>	<a href="#">IRAK1::Ptpn6</a>	IRAK1 physically associates with Ptpn6 (Shp-1)	PubMed ID 18391954	Misbah Naseer	reviewed Mar 07
<a href="#">CIG-8738</a>	<a href="#">PEL13::IRAK1</a>	IRAK1 phosphorylates PEL13	PubMed ID 17997719	Misbah Naseer	reviewed Nov 04
<a href="#">CIG-8737</a>	<a href="#">PEL11::IRAK1</a>	IRAK1 phosphorylates PEL1	PubMed ID 17997719	Misbah Naseer	reviewed Nov 04
<a href="#">CIG-8736</a>	<a href="#">IKBK1::IRAK1</a>	IKBK1 physically associates with polyubiquitinated IRAK1	PubMed ID 17997719	Misbah Naseer	reviewed Mar 07
<a href="#">CIG-8692</a>	<a href="#">TRAF6::IRAK1</a>	TRAF6 physically associates with IRAK1	PubMed ID 19716405	Misbah Naseer	reviewed Mar 07
<a href="#">CIG-8691</a>	<a href="#">TOLLIP::IRAK1</a>	TOLLIP physically associates with IRAK1	PubMed ID 19716405	Misbah Naseer	reviewed Mar 07
<a href="#">CIG-8690</a>	<a href="#">RCAN1::IRAK1</a>	RCAN1 (DSCR1) physically associates with IRAK1	PubMed ID 19716405	Misbah Naseer	reviewed Mar 07
<a href="#">CIG-8744</a>	<a href="#">PEL13::IRAK1</a>	PEL13 physically interacts with IRAK1	PubMed ID 19081057	Giselle Ring	reviewed Mar 07
<a href="#">CIG-8743</a>	<a href="#">PEL12::IRAK1</a>	PEL12 physically interacts with IRAK1	PubMed ID 19081057	Giselle Ring	reviewed Mar 07
<a href="#">CIG-8742</a>	<a href="#">Pel1::IRAK1</a>	Pel1 physically interacts with IRAK1	PubMed ID 19081057	Giselle Ring	reviewed Mar 07
<a href="#">CIG-4834</a>	<a href="#">hsa-mir-146b::IRAK1</a>	MIRN146B MicroRNA inhibits IRAK1 mRNA translation through its 3' UTR	PubMed ID 16885212	Misbah Naseer	reviewed Mar 07

Results are categorized into:

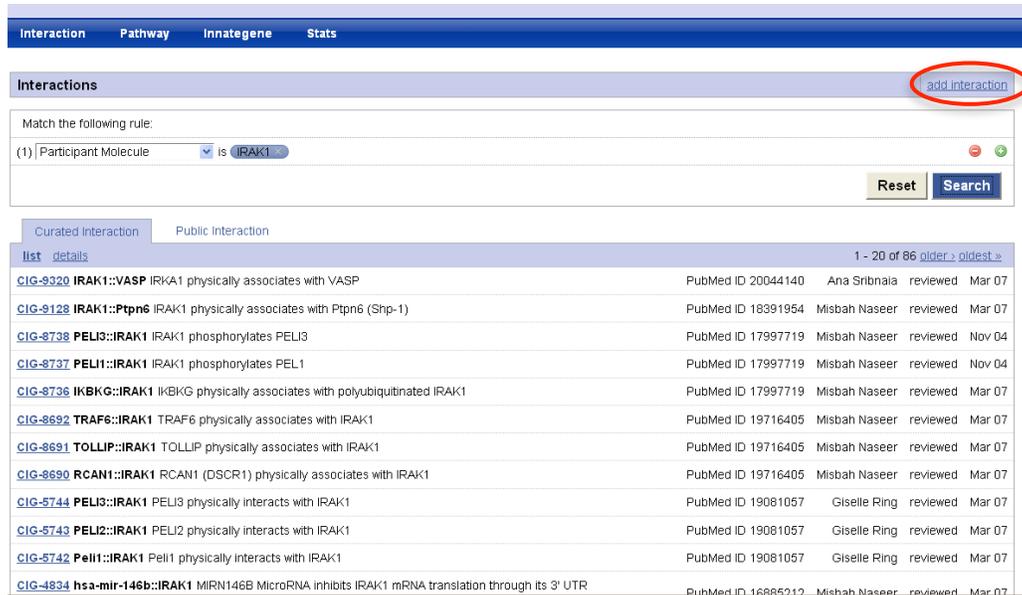
- “**Curated interactions**” which refer to interactions manually curated by the InnateDB team
- “**Public Interactions**” which refer to all interactions displayed on the main public site ([www.innatedb.com](http://www.innatedb.com))

The screenshot shows the InnateDB Interactions search results page. The search filter is set to 'Participant Molecule' is 'IRAK1'. Below the search bar, there are two tabs: 'Curated Interaction' and 'Public Interaction', both of which are circled in red. The main content area displays a list of interactions, including details like CIG ID, interaction type, and PubMed ID.

Interaction	Participant Molecule	Interaction Type	PubMed ID	Reviewer	Status	Date
<a href="#">CIG-9320</a>	IRAK1::VASP	IRAK1 physically associates with VASP	20044140	Ana Sribnaia	reviewed	Mar 07
<a href="#">CIG-9128</a>	IRAK1::Ptpn6	IRAK1 physically associates with Ptpn6 (Shp-1)	18391954	Misbah Naseer	reviewed	Mar 07
<a href="#">CIG-8738</a>	PEL13::IRAK1	IRAK1 phosphorylates PEL13	17997719	Misbah Naseer	reviewed	Nov 04
<a href="#">CIG-8737</a>	PEL11::IRAK1	IRAK1 phosphorylates PEL1	17997719	Misbah Naseer	reviewed	Nov 04
<a href="#">CIG-8736</a>	IKBK1::IRAK1	IKBK1 physically associates with polyubiquitinated IRAK1	17997719	Misbah Naseer	reviewed	Mar 07
<a href="#">CIG-8692</a>	TRAF6::IRAK1	TRAF6 physically associates with IRAK1	19716405	Misbah Naseer	reviewed	Mar 07
<a href="#">CIG-8691</a>	TOLLIP::IRAK1	TOLLIP physically associates with IRAK1	19716405	Misbah Naseer	reviewed	Mar 07
<a href="#">CIG-8690</a>	RCAN1::IRAK1	RCAN1 (DSCR1) physically associates with IRAK1	19716405	Misbah Naseer	reviewed	Mar 07
<a href="#">CIG-5744</a>	PEL13::IRAK1	PEL13 physically interacts with IRAK1	19081057	Giselle Ring	reviewed	Mar 07
<a href="#">CIG-5743</a>	PEL12::IRAK1	PEL12 physically interacts with IRAK1	19081057	Giselle Ring	reviewed	Mar 07
<a href="#">CIG-5742</a>	Pel11::IRAK1	Pel11 physically interacts with IRAK1	19081057	Giselle Ring	reviewed	Mar 07
<a href="#">CIG-4834</a>	hsa-mir-146b::IRAK1	MIRN146B MicroRNA inhibits IRAK1 mRNA translation through its 3' UTR	16885212	Misbah Naseer	reviewed	Mar 07

### 1.3 Adding a New Interaction

Click “Add Interaction” in the top right-hand corner of page to begin submitting a new interaction.



The screenshot shows the PSI-MI web interface. At the top, there are tabs for 'Interaction', 'Pathway', 'Innategene', and 'Stats'. Below this is the 'Interactions' section, which includes a search bar with a dropdown menu set to '(1) Participant Molecule' and a search input field containing 'IRAK1'. A red circle highlights the 'addInteraction' button in the top right corner. Below the search bar, there are two tabs: 'Curated interaction' and 'Public interaction'. The 'Public interaction' tab is active, showing a list of interactions. The table has columns for ID, description, PubMed ID, reviewer, and date. The first few rows are:

ID	Description	PubMed ID	Reviewer	Date
CIG-9320	IRAK1::VASP IRAK1 physically associates with VASP	20044140	Ana Sribnala	reviewed Mar 07
CIG-9128	IRAK1::Ptpn6 IRAK1 physically associates with Ptpn6 (Shp-1)	18391954	Misbah Naseer	reviewed Mar 07
CIG-8738	PEL3::IRAK1 IRAK1 phosphorylates PEL3	17997719	Misbah Naseer	reviewed Nov 04
CIG-8737	PEL1::IRAK1 IRAK1 phosphorylates PEL1	17997719	Misbah Naseer	reviewed Nov 04
CIG-8736	IKBKG::IRAK1 IKBKG physically associates with polyubiquitinated IRAK1	17997719	Misbah Naseer	reviewed Mar 07
CIG-8692	TRAF6::IRAK1 TRAF6 physically associates with IRAK1	19716405	Misbah Naseer	reviewed Mar 07
CIG-8691	TOLLIP::IRAK1 TOLLIP physically associates with IRAK1	19716405	Misbah Naseer	reviewed Mar 07
CIG-8690	RCAN1::IRAK1 RCAN1 (DSCR1) physically associates with IRAK1	19716405	Misbah Naseer	reviewed Mar 07
CIG-5744	PEL3::IRAK1 PEL3 physically interacts with IRAK1	19081057	Giselle Ring	reviewed Mar 07
CIG-5743	PEL2::IRAK1 PEL2 physically interacts with IRAK1	19081057	Giselle Ring	reviewed Mar 07
CIG-5742	Pel1::IRAK1 Pel1 physically interacts with IRAK1	19081057	Giselle Ring	reviewed Mar 07
CIG-4834	hsa-mir-146b::IRAK1 MIRN146B MicroRNA inhibits IRAK1 mRNA translation through its 3' UTR	16885212	Misbah Naseer	reviewed Mar 07

The submission page is broken into 3 main sections – Interaction, Participant & Evidence.

THE PSI-MI Controlled Vocabulary (CV) is a hierarchical ontology of terms used to describe molecular interactions.

It can be browsed here <http://www.ebi.ac.uk/ontology-lookup/browse.do?ontName=MI>

If a required term does not exist in the CV - it can be requested here [http://sourceforge.net/tracker/?atid=511101&group\\_id=65472&func=browse](http://sourceforge.net/tracker/?atid=511101&group_id=65472&func=browse)

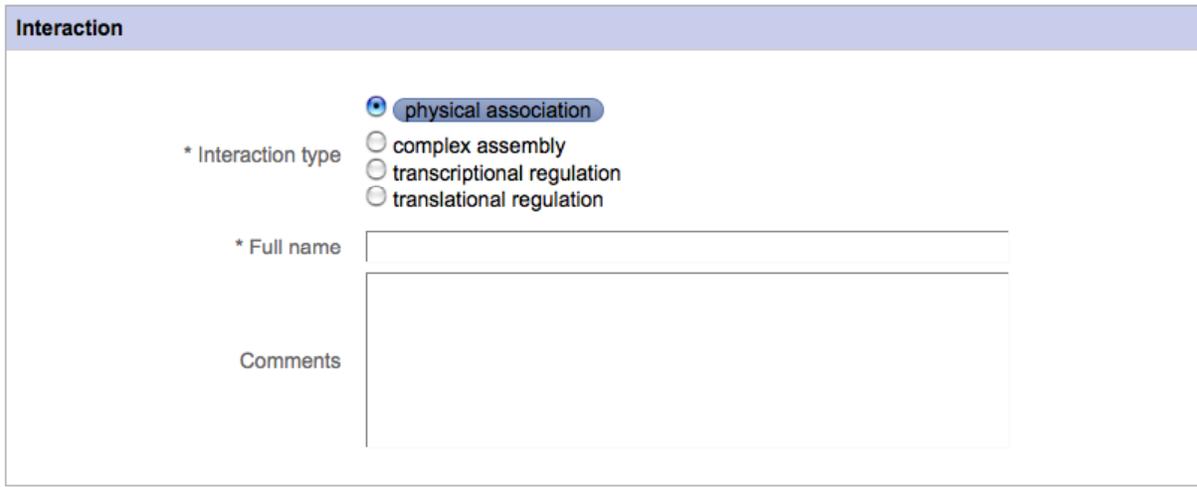
The PSI MI format is a data exchange format for molecular interactions.

Details of the XML Schema etc can be found here <http://www.psidev.info/index.php?q=node/60>

A PSI 2.5 XML validator can be found here <http://www.ebi.ac.uk/intact/validator/start.xhtml>

## 1.3.1 Interaction

### 1.3.1.1 Interaction type



The screenshot shows a form titled "Interaction". It contains the following fields:

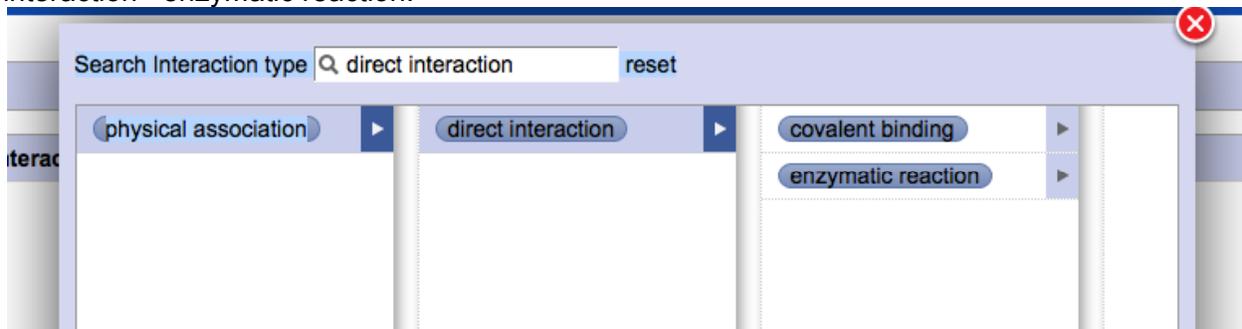
- \* Interaction type:** A group of radio buttons with the following options:
  - physical association
  - complex assembly
  - transcriptional regulation
  - translational regulation
- \* Full name:** A text input field.
- Comments:** A larger text area for additional notes.

Select the appropriate interaction type from the list.

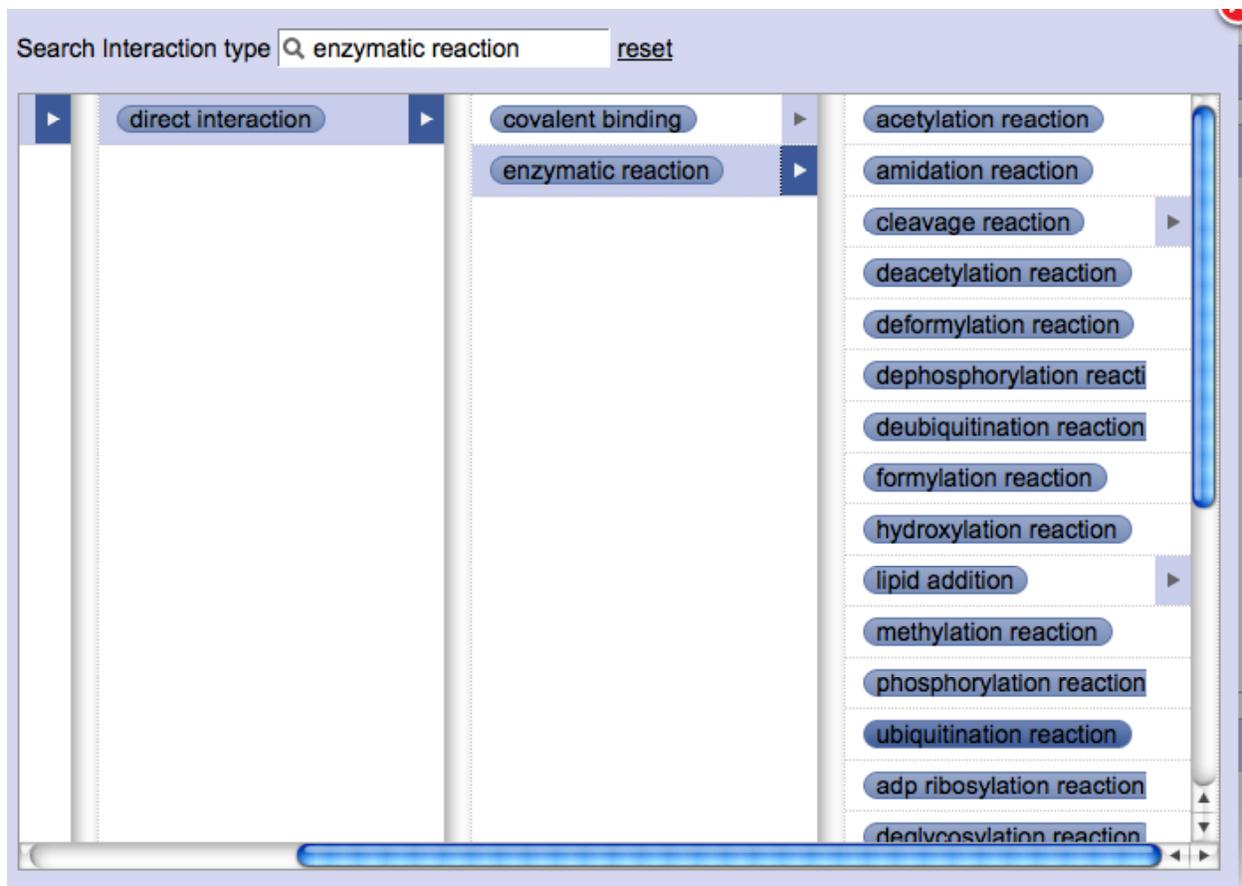
**“Physical Association”** is the most general term used to describe an interaction and should only be used when no other information is available (This is frequently the case).

“Direct Interaction” is the term used to describe an experiment in which the number of interactors equals 2 **highly purified** molecules and the interaction occurs in vitro, such that no host proteins may interfere.

For **biochemical reactions**, such as *phosphorylation*, *ubiquitination*, *cleavage* etc, click: “Physical Association”. A search window will pop-up. The user may either manually enter the term in the search box or click on the arrow beside physical association and expand to direct interaction >enzymatic reaction.



From the list of enzymatic reactions, select the appropriate term for the interaction.



Commonly used enzymatic reactions are:

- cleavage reaction
- phosphorylation reaction
- dephosphorylation reaction
- ubiquitination reaction

**“Complex Assembly”** This should no longer be used as it is not a valid PSI MI term. Use Physical Association instead.

**“Transcriptional Regulation”** – remember we only describe direct, experimentally validated interactions in InnateDB. Experiments where a gene up/down regulates another gene should not be entered unless a direct interaction has been confirmed i.e. a Transcription Factor is shown to bind the promoter region of gene (via CHIP or EMSA) and up/down regulation is observed in an assay e.g. luciferase assay. When both physical interaction and gene regulation are experimentally proven, select “transcriptional regulation” as interaction type. The physical interaction evidence is described in the evidence section for the interaction with the transcriptional regulation assay is described in the comments. If no up/down regulation observed then the interaction type is just “Physical Association”.

**“Translational Regulation”** – rarely used. See “Transcriptional Regulation”. Example interaction of RNA x with gene y leads to increased/decreased translation of protein. Examples of this are very rare.

### 1.3.1.2 Full name

Provide one sentence describing the interaction between the interactors and any specific conditions applying to the interaction. The format of the sentence should agree with the interaction type selected e.g. IRAK4 phosphorylates IRAK1; TLR4 physically associates with LY96; ITCH autoubiquitinates itself in the presence of UBE2L3; IL1 stimulation leads to the complex formation of IRAK1, TRAF6 and MAP3K3. Use HGNC (HUGO Gene Nomenclature Committee) symbols for human participants (UPPER CASE) and Mouse Genome Informatics (MGI) symbols (Title case) for mouse participants.

### 1.3.1.3 Comments

If information applicable to **all** possible evidences is available, record it in the comments field e.g. a common name for a complex etc. Usually this can be left blank.

## 1.3.2 Participant

**Participant** 2

---

**Participant 1**

\* Molecule type

\* Species

\* Molecule

\* Biological role

---

**Participant 2**

\* Molecule type

\* Species

\* Molecule

\* Biological role

If there are > 2 participants in an interaction click “add new participant”. This can be done as many times as required.

### 1.3.2.1 Molecule Type

Select the correct molecule type of the participant from the list (Protein, DNA, RNA). The default selection is Protein. Different participants may have different molecule types e.g. a protein (e.g. transcription factor) may interact with a gene.

Note: the ability to describe interactions between a complex and another molecule type will be added later in InnateDB development.

### 1.3.2.2 Species (Human & Mouse Only!)

Select the species of the participant from the list provided. InnateDB only includes interactions involving human/mouse molecules. The different participants may be of different species e.g. an experiment that shows a human protein interacts with a mouse protein. If no information about

species can be gathered from the paper and references, contact the author of the paper to ensure the species.

### 1.3.2.3 Molecule

Click “select” button. Enter the symbol for the participant in the text field and hit the ENTER key. Note: Often genes are more commonly known by another name (synonym) so you will need to watch out for this and ensure you are entering the correct name. If a synonym is entered (e.g. MEKK3), the search will provide HGNC symbol for gene(s) with the entered synonym (e.g. MAP3K3).

**Protein kinase C-associated kinase can activate NFkappaB in both a kinase-dependent and a kinase-independent manner.**

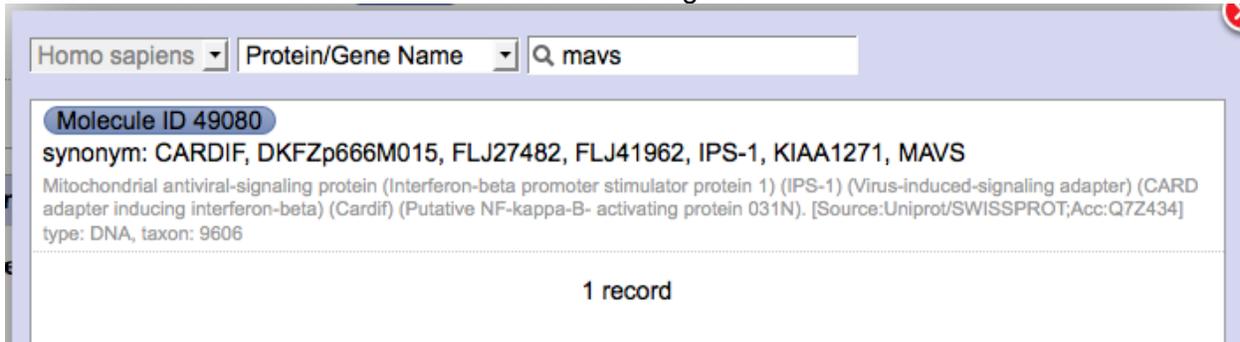
[Moran ST](#), [Haider K](#), [Ow Y](#), [Milton P](#), [Chen L](#), [Pillai S](#).

Massachusetts General Hospital Cancer Center, Harvard Medical School, Building 149, 13th Street, Charlestown, MA 02129, USA.

Protein kinase C-associated kinase (PKK, also known as RIP4/DIK) activates NFkappaB when overexpressed in cell lines and is required for keratinocyte differentiation in vivo. However, very little is understood about the factors upstream of PKK or how PKK activates NFkappaB. Here we show that certain catalytically inactive mutants of PKK can activate NFkappaB, although to a lesser degree than wild type PKK. The deletion of specific domains of wild type PKK diminishes the ability of this enzyme to activate NFkappaB; the same deletions made on a catalytically inactive PKK background completely ablate NFkappaB activation. PKK may be phosphorylated by two specific mitogen-activated protein kinase kinase kinases, MEKK2 and MEKK3, and this interaction may in part be mediated through a critical activation loop residue, Thr184. Catalytically inactive PKK mutants that block phorbol ester-induced NFkappaB activation do not interfere with, but unexpectedly enhance, the activation of NFkappaB by these two mitogen-activated protein kinase kinase kinases. Taken together, these data indicate that PKK may function in both a kinase-dependent as well as a kinase-independent manner to activate NFkappaB.

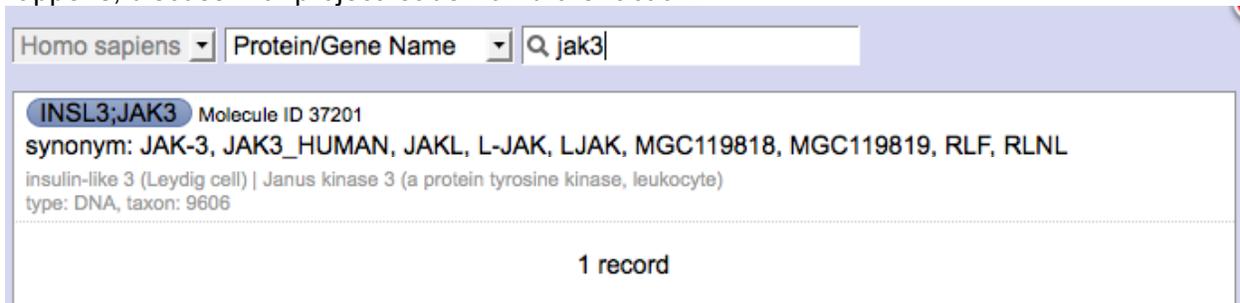
The screenshot shows a search interface with a dropdown menu set to 'Homo sapiens' and a search box containing 'mekk3'. Below the search box, a single record is displayed for 'MAP3K3' (Molecule ID 63432). The record includes the synonym 'MAP3K3, MEKK3' and the full name 'mitogen-activated protein kinase kinase kinase 3'. The record type is 'DNA' and the taxon is '9606'. At the bottom of the record, it indicates '1 record'.

**Special case 1:** If a HGNC symbol has not been assigned to a gene, search the gene and select the InnateDB molecule ID associated with the gene.



The screenshot shows the InnateDB search interface. At the top, there is a dropdown menu set to 'Homo sapiens', a 'Protein/Gene Name' dropdown, and a search box containing 'mavs'. Below the search bar, the results are displayed in a light blue box. The first result is highlighted with a blue background and contains the following information: 'Molecule ID 49080', 'synonym: CARDIF, DKFZp666M015, FLJ27482, FLJ41962, IPS-1, KIAA1271, MAVS', 'Mitochondrial antiviral-signaling protein (Interferon-beta promoter stimulator protein 1) (IPS-1) (Virus-induced-signaling adapter) (CARD adapter inducing interferon-beta) (Cardif) (Putative NF-kappa-B- activating protein 031N). [Source:Uniprot/SWISSPROT;Acc:Q7Z434]', and 'type: DNA, taxon: 9606'. At the bottom of the results box, it says '1 record'.

**Special case 2:** Sometimes 2 HGNC IDs are assigned to the same InnateDB gene. If this happens, discuss with project leader for further action.



The screenshot shows the InnateDB search interface. At the top, there is a dropdown menu set to 'Homo sapiens', a 'Protein/Gene Name' dropdown, and a search box containing 'jak3'. Below the search bar, the results are displayed in a light blue box. The first result is highlighted with a blue background and contains the following information: 'INSL3;JAK3 Molecule ID 37201', 'synonym: JAK-3, JAK3\_HUMAN, JAKL, L-JAK, LJAK, MGC119818, MGC119819, RLF, RLNL', 'insulin-like 3 (Leydig cell) | Janus kinase 3 (a protein tyrosine kinase, leukocyte)', and 'type: DNA, taxon: 9606'. At the bottom of the results box, it says '1 record'.

**Special case 3:** Since 2009, ENSEMBL has included nine haplotypic regions, mainly in the MHC region of chromosome 6 in its gene database. Consequently, searches for a gene may generate several results with identical HGNC IDs but different InnateDB molecule IDs.

If this happens, search the gene on the main site ([www.innatedb.com](http://www.innatedb.com)). Note the InnateDB molecule ID of the gene which is located on Chromosome 6 (not the MHC regions). Use this molecule ID for submitting interactions for the gene.

interaction type  
 transcriptional regulation  
 translational regulation

Homo sapiens Protein/Gene Name Q TUBB

RP11-631M21.2 Molecule ID 43552  
 synonym: FLJ40100, TUBB8  
 Tubulin beta-8 chain [Source:UniProtKB/Swiss-Prot;Acc:G3ZCM7]  
 type: DNA, taxon: 9606

**TUBB** Molecule ID 76778  
 synonym: M40, MGC117247, MGC16435, OK/SW-cl.56, TUBB1, TUBB5  
 tubulin, beta  
 type: DNA, taxon: 9606

**TUBB** Molecule ID 126212  
 Tubulin beta chain (Tubulin beta-5 chain) [Source:UniProtKB/Swiss-Prot;Acc:P07437]  
 type: DNA, taxon: 9606

**TUBB** Molecule ID 299022  
 Tubulin beta chain (Tubulin beta-5 chain) [Source:UniProtKB/Swiss-Prot;Acc:P07437]  
 type: DNA, taxon: 9606

**TUBB** Molecule ID 299260  
 Tubulin beta chain (Tubulin beta-5 chain) [Source:UniProtKB/Swiss-Prot;Acc:P07437]  
 type: DNA, taxon: 9606

**TUBB** Molecule ID 299290  
 Tubulin beta chain (Tubulin beta-5 chain) [Source:UniProtKB/Swiss-Prot;Acc:P07437]  
 type: DNA, taxon: 9606

**TUBB** Molecule ID 299374  
 Tubulin beta chain (Tubulin beta-5 chain) [Source:UniProtKB/Swiss-Prot;Acc:P07437]  
 type: DNA, taxon: 9606

+ add new participant

InnateDB  
 A Knowledge Resource For Innate Immunity Interactions & Pathways

Home About Search Data Analysis Browse Download Resources Statistics Contact Help

Display Options (Show/Hide)

Sorted by: Gene symbol ascending then by Organism ascending Sort

Download MS Excel TAB CSV Show Orthologs

Viewing genes 1 to 10 of 10 hits matching query ( Name 'tubb' )

Page(s): 1

InnateDB ID	Ensembl Gene ID	Organism	Chromosome	Gene symbol	Gene name	Interactions	
IDBG-299439	ENSG00000235067	Homo sapiens	HSCHR6_MHC_DBB	TUBB	Tubulin beta chain (Tubulin beta-5 chain)		Gene Details
IDBG-299374	ENSG00000227739	Homo sapiens	HSCHR6_MHC_CDX	TUBB	Tubulin beta chain (Tubulin beta-5 chain)		Gene Details
<b>IDBG-76778</b>	ENSG00000196230	Homo sapiens	<b>6</b>	<b>TUBB</b>	tubulin, beta	21	Gene Details
IDBG-126212	ENSG00000183311	Homo sapiens	HSCHR6_MHC_QBL	TUBB	Tubulin beta chain (Tubulin beta-5 chain)	32	Gene Details
IDBG-299260	ENSG00000229684	Homo sapiens	HSCHR6_MHC_MCF	TUBB	Tubulin beta chain (Tubulin beta-5 chain)		Gene Details
IDBG-299290	ENSG00000232421	Homo sapiens	HSCHR6_MHC_SSTO	TUBB	Tubulin beta chain (Tubulin beta-5 chain)		Gene Details
IDBG-299480	ENSG00000232575	Homo sapiens	HSCHR6_MHC_MANN	TUBB	Tubulin beta chain (Tubulin beta-5 chain)		Gene Details
IDBG-57522	ENSG00000137267	Homo sapiens	6	TUBB2A	tubulin, beta 2A	36	Gene Details
IDBG-299022	ENSG00000224156	Homo sapiens	HSCHR6_MHC_APD	TUBB	Tubulin beta chain (Tubulin beta-5 chain)		Gene Details
IDBG-193657	ENSMUSG00000062591	Mus musculus	17	Tubb4	tubulin, beta 4		Gene Details

InnateDB is being developed jointly by the Brinkman Laboratory, Simon Fraser University and the Hancock Laboratory, University of British Columbia, Vancouver, British Columbia, Canada and the Lynn

### 1.3.2.4 Biological Role

Select an appropriate term for the biological role for the interactor in context of the interaction e.g. *unspecified* for physical interactions, *enzyme and enzyme target* for phosphorylation, ubiquitination, dephosphorylation etc.

Search Biological role

- unspecified role
- enzyme
- enzyme target
- self
- inhibitor
- cofactor
- stimulator
- putative self
- donor
- acceptor

### 1.3.3 Evidence

**Evidence**

1

\* Reference type  PubMed ID  Book  Website

\* PubMed ID

Interaction detection method

[add additional method](#)

Host system  In Vitro  In Vivo  Ex Vivo  unspecified

Host organism

Cell status  Primary  Cell-line  unspecified

Participants

Cell line

Cell type

Tissue type

Subcellular localization

Comments

[add new evidence](#)

Multiple evidences are possible for an interaction; either from the same PubMed ID where different experiments prove the same interaction or where two or more papers describe evidence of an interaction. Click “+ add new evidence” to add additional evidence either with the same PubMed ID or with a different one.

**Evidence**

1

**Evidence 1**

\* Reference type  PubMed ID

\* PubMed ID

Interaction detection method

[add additional method](#)

Host system  In Vitro  In Vivo  Ex Vivo  unspecified

Host organism

Cell status  Primary  Cell-line  unspecified

Cell line

Cell type

Tissue type

Subcellular localization

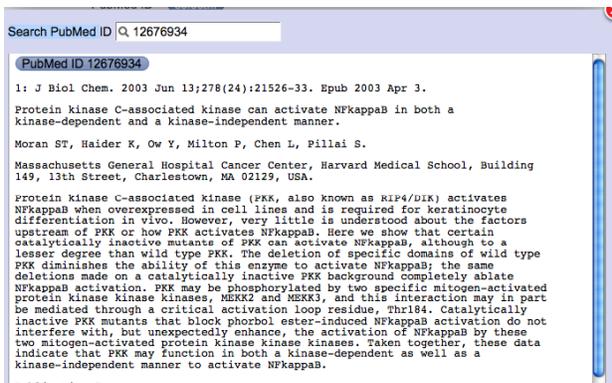
Comments

Participant	Participant identification method	Experimental role	Accession number
(1)	<input type="button" value="select..."/>	<input type="button" value="unspecified role"/>	<input type="text"/>
(2)	<input type="button" value="select..."/>	<input type="button" value="unspecified role"/>	<input type="text"/>

[add new evidence](#)

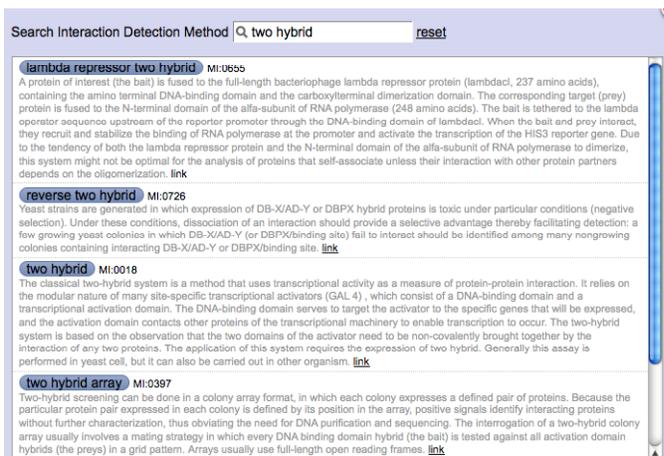
#### 1.3.3.1 PubMed ID

Enter the PubMed ID (PMID) for the publication in which the interaction and its evidence is described. The search box will display the abstract for the entered PMID. Ensure that the correct paper is retrieved.



### 1.3.3.2 Interaction Detection Method

This is the experimental method used to detect the interaction, usually the basis for evidence of an interaction. Interaction detection method terms are controlled PSI MI (<http://www.ebi.ac.uk/ontology-lookup/browse.do?ontName=MI>) terms for Molecular Interactions. These terms are searchable by typing a term (or part of a term) into the box and hitting the ENTER key. Once search terms are entered, a selection of controlled vocabulary terms appear in a drop down menu, select the interaction term which best fits the experiment performed.



Alternatively, different PSI MI terms listed in the search menu can be expanded until the appropriate term is found.

Search Interaction Detection Method  [reset](#)

biophysical	cosedimentation	deacetylase assay
protein complementation	cross-linking study	protein kinase assay
genetic interference	chromatography technology	phosphatase assay
post transcriptional interference	affinity technology	protease assay
biochemical	enzymatic study	methyltransferase assay
imaging techniques	footprinting	polymerase assay
	comigration in gel electrophoresis	phosphotransfer assay
		demethylase assay
		nucleoside triphosphatase assay
		acetylation assay
		ribonuclease assay

Following are some PSI MI terms used for common detection methods:

- *coimmunoprecipitation/ anti-tag coimmunoprecipitation*: coimmunoprecipitation
- *protease assay*: cleavage reactions
- *enzymatic study*: luciferase assay, ubiquitination/conjugation assay
- *protein kinase assay/ in-gel kinase assay*: phosphorylation reaction
- *phosphatase assay*: dephosphorylation reaction
- *pull down*: *GST pull down assay*

### 1.3.3.6 Host System and Host Organism

Host system  In Vitro  In Vivo  Ex Vivo  unspecified

Host organism

#### Host System:

**In Vitro** – experiments performed in a cell-free system; also used for experiments involving immortalized and commercially sold cell lines.

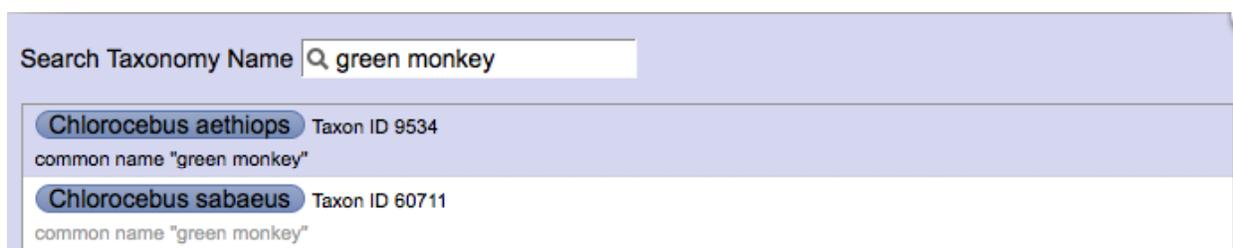
**In Vivo** – experiments performed in an organism or with cells extracted from an organism which have not been subject to any treatment.

**Ex Vivo** – experiments performed on cells extracted from a living organism that have been subjected to some form of treatment e.g. TNF, LPS stimulation, also cells derived/cultured from living cells e.g. monocytes cultured from PBMCs.

**Unspecified** – Experiments performed in a foreign system such as yeast two hybrid experiment.

### **Host Organism:**

The host system is the species where the interaction was shown to take place. This is NOT to be confused with the species of the participant molecules (human and mouse only). For example yeast two-hybrid would be “yeast” and HEK293 cells would be “human”. This is a searchable field with controlled vocabulary (NCBI Taxonomy homepage: <http://www.ncbi.nlm.nih.gov/Taxonomy/>), thus the host system species must be selected from the drop menu of controlled vocabulary which appears in the search box. Any species can be added here e.g. African green monkey, yeast. Sometimes there are several possible options for a common name – make sure you choose the correct species based on the scientific name.



The image shows a screenshot of the NCBI Taxonomy search interface. At the top, there is a search bar with the text "Search Taxonomy Name" and a search box containing "green monkey". Below the search bar, two results are displayed. The first result is "Chlorocebus aethiops" with Taxon ID 9534 and a common name of "green monkey". The second result is "Chlorocebus sabaesus" with Taxon ID 60711 and a common name of "green monkey".

### **1.3.3.7 Cell Status**

**Primary** - Cells were taken directly from a living organism, which is not immortalized. Cells may be cultured following isolation e.g. monocytes derived from peripheral blood mononuclear cells (PBMCs), bone-marrow derived macrophages

**Cell-line** - Cells which are grown under controlled conditions e.g. HeLa.

**Unspecified** - when primary cells or cell line were not used or not indicated in the experiment.

### **1.3.3.8 Cell Line**

Enter the name of the cell line in which the interaction was found to occur. Where possible use the ATCC cell line names found at <http://www.atcc.org/>. Other details such as what cell type, tissue and species a cell line is derived from can also be looked up here. See [https://www.pathogenomics.ca/wiki/index.php/Curators\\_Group](https://www.pathogenomics.ca/wiki/index.php/Curators_Group) for cell line details that have already been looked up and for information about standards used to classify a cell line not listed on the page.

**Example:** Caco 2: cell type: epithelial cell; Tissue type: colorectal adenocarcinoma cell line; *Homo sapiens*

### **1.3.3.9 Cell Type**

Enter the distinct morphological or functional form of cell e.g. macrophage, epithelial etc. Cell line names should not be entered here. The cell type of a cell line should be entered. Cell type terms are OBO controlled terms and can be searched similarly to interaction detection method.

### 1.3.3.10 Tissue Type

The tissue in which the cells were derived from e.g. lung, heart, brain etc. Tissue terms are OBO controlled terms and can be searched similarly to interaction detection method.

#### Example

To determine the cell type, tissue type and species of the cell line, search the ATCC cultures to find most of the cell line descriptions.

For example if a paper mentions SW480 cells:

**ATCC**  
The Global Bioresource Center™

**Search Catalog**  
Cell Lines and Hybridomas  
SW480 Go

About | Cultures and Products | Science | Standards | Deposit Services | Custom Services | Product Use Policy

Home

**Highlights** ▶  
Available Now... - ATCC® Primary Cell Solutions™: a new product line designed to...  
ATCC Achieves ISO Guide 34 Accreditation -ATCC was

**Cell Biology**

**ATCC® Number:** CCL-228™ [Order this Item](#) **Price:** \$244.00

**Designations:** SW480 [SW-480] **Depositors:** A Leibovitz

**Biosafety Level:** 1 **Shipped:** frozen

**Medium & Serum:** [See Propagation](#) **Growth Properties:** adherent

**Organism:** Homo sapiens (human) **Morphology:** epithelial

**Source:** **Organ:** colon **Tumor Stage:** Dukes' type B **Diseases:** colorectal adenocarcinoma

**Cellular Products:** carcinoembryonic antigen (CEA) 0.7 ng/10 exp6 cells/10 days; keratin; transforming growth factor beta

**Permits/Forms:** In addition to the [MTA](#) mentioned above, other [ATCC and/or regulatory permits](#) may be required for the transfer of this ATCC material. Anyone purchasing ATCC material is ultimately responsible for obtaining the permits. Please [click here](#) for information regarding the specific requirements for shipment to your location.

**Applications:** transfection host(technology from amaxa) [Related Cell Culture Products](#)

Hence, the following information will be entered:

Cell line: SW480

Cell type: epithelial cell

Tissue type: colorectal adenocarcinoma cell line

### 1.3.3.11 Subcellular localization

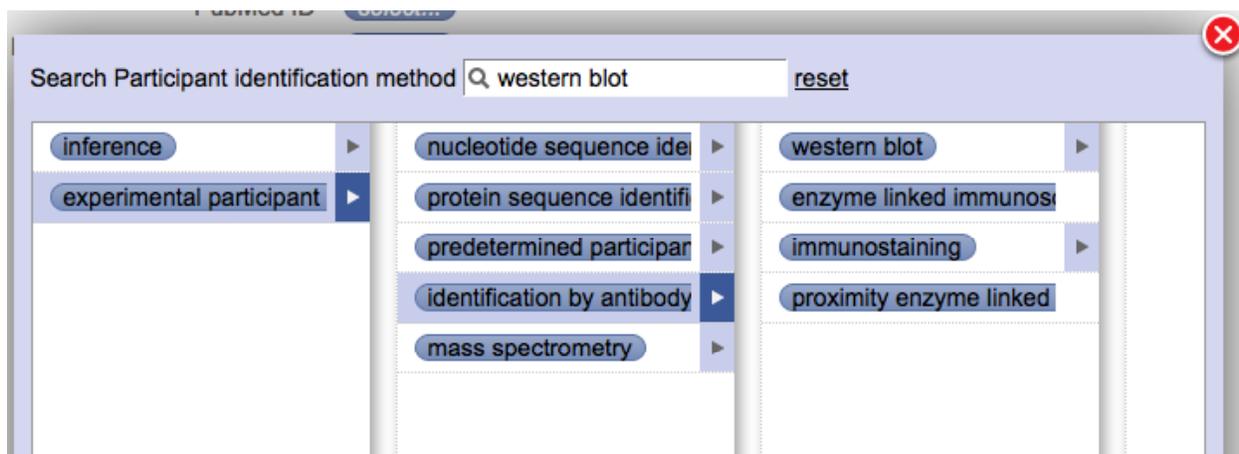
If specified, this is where the location within the cell in which the **interaction** is observed and NOT the subcellular localization of where a protein is normally located. When inputting subcellular localization, only controlled terms are allowed and thus this is a searchable field. Once search terms are entered, a selection of controlled vocabulary terms appear in the search window, select the term which best fits the subcellular localization. Alternatively, the given list in the search box can be expanded to the appropriate term.

Search Subcellular Localization  [reset](#)

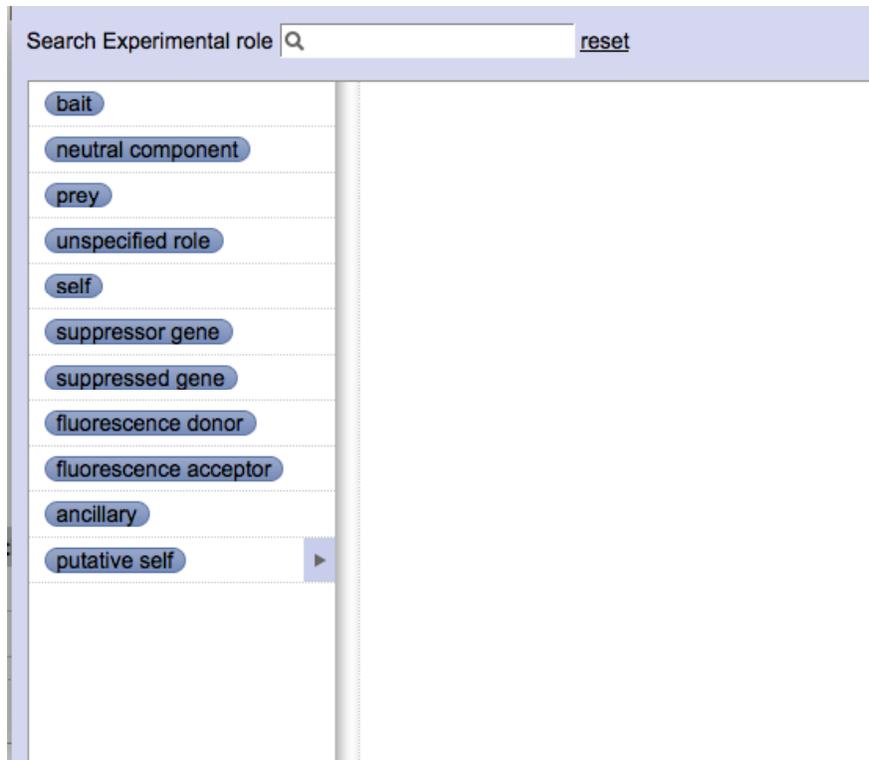
<a href="#">cilium</a>	<a href="#">nuclear envelope</a>	<a href="#">nuclear inner membrane</a>
<a href="#">cytoplasm</a>	<a href="#">nuclear lumen</a>	<a href="#">nuclear outer membrane</a>
<a href="#">cytoplasmic vesicle</a>	<a href="#">nuclear lamina</a>	
<a href="#">cytoskeleton</a>	<a href="#">nuclear matrix</a>	
<a href="#">endoplasmic reticulum</a>	<a href="#">nuclear membrane</a>	
<a href="#">extracellular region</a>	<a href="#">nuclear pore</a>	
<a href="#">golgi apparatus</a>	<a href="#">nucleolus</a>	
<a href="#">membrane</a>	<a href="#">nucleoplasm</a>	
<a href="#">mitochondrion</a>		
<a href="#">nucleus</a>		
<a href="#">secreted protein</a>		

### 1.3.3.12 Participant Identification Method and Experimental Role

The method used to identify or determine the participant in the interaction detection experiment is entered in this field. The participant identification method is usually found in the Materials and Methods sections of papers describing interactions and there may more than one used. If more than one method is used, add the one which is more specific in identifying the participant.



**Experimental Role** explains the role of each interaction participant in the experiment demonstrating the interaction.



**bait** – The participant was used as a “bait” to find the other participant(s). For example, in a GST pulldown experiment, the GST fusion protein is the bait since it is used to detect other interacting proteins. This is usually the stationary/immobilized participant.

**prey** – The participant that interacts with the bait; the interactor that is detected because of its interaction with the bait.

**ancillary** – This is the participant(s) in a complex which links other components of a complex together.

**neutral component** – An interaction participant that has a neutral role in the interaction; for example in a non-screening yeast two hybrid, neither component is the bait or prey, but instead come together to demonstrate an interaction.

**suppressor gene** – The gene which suppresses another gene.

**suppressed gene** – The gene which is suppressed by a suppressor gene.

**fluorescence donor** – In experiments where fluorescence energy transfer is used (such as in FRET), this is the participant which is the source of fluorescence energy.

**fluorescence acceptor** – In experiments where fluorescence energy transfer is used (such as in FRET), this is the participant which receives fluorescence energy from the fluorescence donor.

**fluorescence acceptor donor pair** – Comprised of a fluorescence acceptor and donor.

**self** – When there is only one participant i.e. an interaction with itself (dimer formation, auto-phosphorylation).

**unspecified role** – Used when the role of the participant is unknown. This option is rarely used.

In general, there are many methods which may be used in an article to detect the participant in the interaction, however here are some common ones:

<b>Interaction Detection Method</b>	<b>Expt. Role</b>	<b>Participant Identification Method</b>
Yeast two hybrid	<ul style="list-style-type: none"> <li>• <b>Bait</b></li> <li>• <b>Prey</b></li> </ul>	Plasmid verified by nucleotide sequencing  Positive clones verified by nucleotide sequencing
Coimmunoprecipitation	<ul style="list-style-type: none"> <li>• <b>Bait</b></li> <li>• <b>Prey</b></li> </ul>	<ul style="list-style-type: none"> <li>- Western blot (mono/polyclonal if specified) or</li> <li>- Plasmid was verified by nucleotide sequencing</li> </ul> Western blot (mono/polyclonal if specified)
Anti Tag Coimmunoprecipitation	<ul style="list-style-type: none"> <li>• <b>Bait</b></li> <li>• <b>Prey</b></li> </ul>	Western blot (mono/polyclonal if specified) or tag western blot  <ul style="list-style-type: none"> <li>- Anti tag western blot or</li> <li>- Western blot (mono/polyclonal if specified)</li> </ul>
Pull down  Chromatin Immunopercipitation Assays  Electrophoretic Mobility Shift Assay	<ul style="list-style-type: none"> <li>• <b>Bait</b></li> <li>• <b>Prey</b></li> <li>• <b>Neutral Component</b></li> <li>• <b>Neutral Component</b></li> <li>• <b>Neutral Component</b></li> <li>• <b>Neutral Component</b></li> </ul>	Predetermined participant  <ul style="list-style-type: none"> <li>- Western blot (mono/polyclonal if specified) or</li> <li>- Autoradiography if used in vitro translated 35S-labelled protein</li> <li>- Primer specific PCR (gene)</li> </ul> <ul style="list-style-type: none"> <li>- Identification by antibody (protein)</li> </ul> <ul style="list-style-type: none"> <li>- Autoradiography (gene)</li> <li>- Identification by antibody (protein)</li> </ul>

### 1.3.3.13 Accession Number

A unique identifier given to a biological polymer sequence (DNA, protein) when it is submitted to a sequence database. If an accession number for a participant(s) is given in the paper please record it as it can be used to identify the exact variant of a gene or protein used in the experiment. Many different identifiers could be named in articles; the more common identifiers are GenBank, Swiss-Prot, RefSeq and are usually found in material and methods section.

**\*\*TIP: It is best to verify the accession number by going to NCBI to make sure that it is the protein you are interested in and it also verifies the species of the protein.**

*et al.*, 1993) and in combination with other hemopoietins increases the frequency of erythroid, myeloid and lymphoid progenitor cells. The signalling pathways that define Kit-dependent survival responses versus those that support proliferation are presently unknown. Steel factor-dependent induction of Socs1, however, may function to modulate Kit signals that mediate cell survival and thus co-ordinate the processes of self-renewal and lineage commitment in hematopoiesis.

#### Materials and methods

##### *Cells and culture conditions*

Bone marrow-derived mast cells were cultured as outlined (Reith *et al.*, 1990) and were grown in OPTI-modified Eagle's medium (MEM), 10% fetal bovine serum (FBS) and 0.5% of conditioned media from V62 II-2 cells containing IL-3 (Kocumura and Malabar, 1989).

The same procedure was used for the yeast two-hybrid screen of Socs1. The full-length Socs1 cDNA was inserted into the pBTM116 vector which contained a constitutively active form of the Src tyrosine kinase cloned into the *PvuII* site of pBTM116. Colonies expressing a VP-16 fusion protein that interact with the Socs1 bait in a phosphotyrosine-independent manner were cured of the pBTM116-Src-Socs1 plasmid and mated with AMR70 containing pBTM116-Socs1 plasmid.

##### *Isolation of full-length Socs1 cDNA*

A  $\lambda$  phage library ( $\lambda$ ZAPII vector, Stratagene) containing cDNAs obtained by oligo(dT) priming of mRNAs expressed in EML-C1 cells was screened using clone #99 as a probe. After the second round of screening, phagemids (pBluescript SK plasmids) were obtained from the positive phages and sequenced. Two independent cDNA clones (pSK-Socs1) were sequenced. Both clones started at the same nucleotide but had a different poly(A) tail. The sequence of pSK-Socs1 has been deposited in the DDBJ/EMBL/GenBank database (accession No. AF120490).

##### *Northern blot analysis*

### 1.3.3.14 Comments

Any additional comments or clarification about the experiment can be entered here. Special conditions or treatments in the experiment must be specified. For common additional information, the format for entry into comments is:

Tags: \_\_\_\_\_; Treatment: \_\_\_\_\_; interacting domain: \_\_\_\_\_; [any other information.]

#### **Example Comments:**

- The interaction was only present in absence of serum stimulation or very low in serum stimulated cells. Also cells treated with 200 ng/ml EGF for 10 min found to inhibit the interaction.
- Tags: CFLAR (Casper) - Flag, NFKB1 (p105) - HA;
- NFKB1 (p50) is 35S labeled
- Interaction strengthened after IL-1 beta stimulation whereas interaction between IRAK2 and AKT1 weakened after stimulation; When LY294002, inhibitor of Akt1 phosphorylation was added simultaneously with IL-1 beta treatment, interaction with IRAK2 was restored while interaction with IL1R1 weakened.

## Preview and Submit

After all information has been entered, select preview to view the record and confirm the accuracy prior to submission. If interaction is not ready to be submitted, select 'Save Draft'. All information of the submission page will be saved for later access.

Participant	Participant identification method	Experimental role	Accession number
(1)	<a href="#">experimental participant identification</a> ✕	<a href="#">unspecified role</a>	<input type="text"/>
(2)	<a href="#">select...</a>	<a href="#">unspecified role</a>	<input type="text"/>

[+ add new evidence](#)

[Discard](#)
[Save Draft](#)
[Preview »](#)

If changes are needed, select “previous” and make the desired changes. If no changes need to be made to the submission, click “commit”.

**Evidence** 1

**Evidence 1**

InnateDB ID

Cross-reference

Submission status

Reference type **pmid**

PubMed ID **12676934**

Interaction detection method **coimmunoprecipitation**

Host system **invitro**

Host organism **9606**

Cell status **cell line**

Cell line **hela**

Cell type **epithelial cell**

Tissue type **cervical cancer cell line**

Subcellular localization

Comments

Participant	Participant identification method	Experimental role	Accession number
(1) 90782	western blot	bait	
(2) 28022	western blot	prey	

[« Previous](#)
[Commit »](#)

Accepted

Curated Interaction Group has been created as [CIG-4737](#).

To create a new interaction, click [New Submission]

To create a new interaction with last submission data, click [Copy Submission]

[New Submission](#)[Copy Submission](#)

You have now successfully submitted a new interaction. In order to submit another interaction, you can select:

**New submission:** a blank submission page will open OR

**Copy submission:** a submission page with data from your previous submission will open. This option is usually used for similar interactions in the same paper.

## 1.4 Editing an Interaction

An interaction in InnateDB may need to be edited due to misspelled words or further details may be needed to be added in the comment section after discussion among the curators. More importantly, an interaction may need to be edited due to incorrect species or missing information in uploaded interactions from other databases (MINT, BIND, etc) which were not manually curated by our own team.

### 1.4.1 Editing a Curated Interaction

Search the desired interaction using the search criteria (see section 1.2). Click on the interaction from “**Curated Interaction**” Tab (make sure it is not the “Public Interaction” Tab). Click on “Edit” button and the make the appropriate changes. Click on “Preview” to review the interaction.

InnateDB  
A Knowledge Resource For Innate Immunity Interactions & Pathways

Logged in as meyau@interchange.ubc.ca  
[account](#) | [logout](#)

Interaction Stats

Interactions » Curated Interaction Group CIG-4754 [edit](#) [reject](#)

Interaction	
Short name	ILK:CASP9
Full name	ILK physically associates with CASP9
Interaction type	physical association
Comments	

Participant <span>2</span>	
Participant 1	
Molecule type	protein
Species	9606
Molecule	29381
Biological role	unspecified role

Click on “Commit” to when changes have been verified.

Cell line	h160
Cell type	
Tissue type	promyelocytic leukemia cell
Subcellular localization	
Comments	ILK recruits CASP9 4 hr. after irradiation in suspension cultures. Reciprocal coimmunoprecipitation was also performed. Treatment: irradiation with 0 Gy and 10 Gy

Participant	Participant identification method	Experimental role	Accession number
(1) 29381	western blot	bait	
(2) 90895	western blot	prey	

« Previous **Commit** »

## 1.4.2 Editing a Public Interaction

Search the desired interaction using the search criteria (see section). Click on the interaction from Public Interaction Tab. Click on “Curate” button and the make the appropriate changes. Click on “Preview” to review the interaction.

*A Knowledge Resource For Innate Immunity Interactions & Pathways*

Interaction Pathway Innatogene Stats

Interactions » **Public Interaction Group IDBG-76625** curate delete

**Interaction**

Short name: WDR62:WDR62  
 Full name: WDR62 interacts with WDR62  
 Interaction type: physical association  
 Comments:

**Participant** 2

**Participant 1**

Molecule type: protein  
 Species: 9606  
 Molecule: 46287  
 Biological role: unspecified role

**Participant 2**

Molecule type: protein  
 Species: 9606  
 Molecule: 46287  
 Biological role: unspecified role

**Evidence** 2

If more than one public interaction belongs to the interaction group, you will need to click on the specific interaction you are referring to.

Interactions » Public Interaction Group IDBG-76625 » Delete

Select a group member:

You cannot directly delete the whole group. Please select one of the following members to delete:

- [Public Interaction IDB-5181](#)
- [Public Interaction IDB-80406](#)

Make the appropriate changes to the interaction and click on “Preview”.

The preview page will display the following warning:

“Once committed, this public interaction IDB-XXXXX **will be deleted** from the public interaction database and no longer be searchable. Your submission will be submitted as a new curated interaction and published after the next import cycle.”

Click on the check box to confirm the deletion of the published interaction.

I understand, please delete IDB-XXXXX & add as new curated interaction.

Comments

Participant	Participant identification method	Experimental role	Accession number
(1) 46287	bait		Q43379
(2) 46287		prey	Q43379

**Warning!**

Once committed, this public interaction IDB-5181 **will be deleted** from the public interaction database and no longer be searchable. Your submission will be submitted as a new curated interaction and published after the next import cycle.

I understand, please delete IDB-5181 & add as new curated interaction.

« Previous
Commit »

Click on “Commit” to successfully delete the published interaction and submitted a new curated interaction.

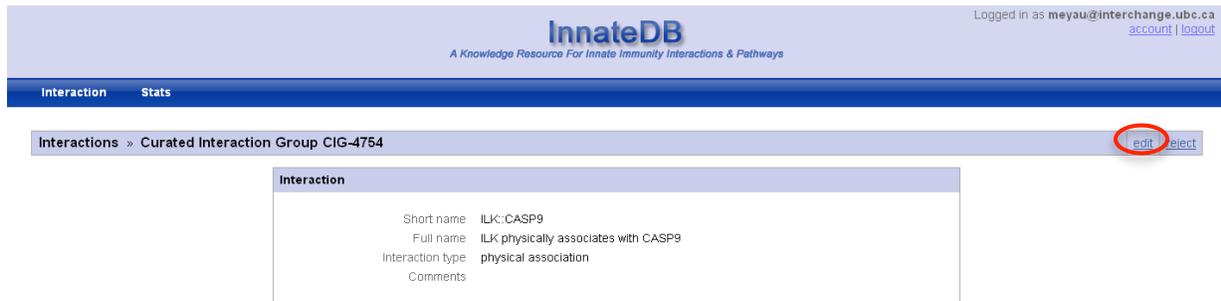
## 1.5 Deleting an interaction

Deleting an interaction results when published interactions uploaded into InnateDB:

- used an interaction detection method which our curation team has decided is insufficient direct evidence to support an interaction (e.g. interaction detection method using confocal microscopy),
- when the public interaction is not found in the paper when manually curated,
- when the interaction involves other species other than human or mouse.

## 1.5.1 Deleting a Curated interaction

Search the desired interaction using the search criteria (see 1.2 in this chapter). Click on the interaction from the Curated Interaction Tab. Click on “Reject”. If more than one interaction belongs to the interaction group, you will need to click on the specific interaction you are referring to.



The screenshot shows the InnateDB website header with the logo and navigation tabs for 'Interaction' and 'Stats'. The user is logged in as 'meyau@interchange.ubc.ca'. The main content area shows a breadcrumb trail: 'Interactions > Curated Interaction Group CIG-4754'. A red circle highlights the 'edit reject' button. Below this is a table with the following data:

Interaction	
Short name	ILK:CASP9
Full name	ILK physically associates with CASP9
Interaction type	physical association
Comments	

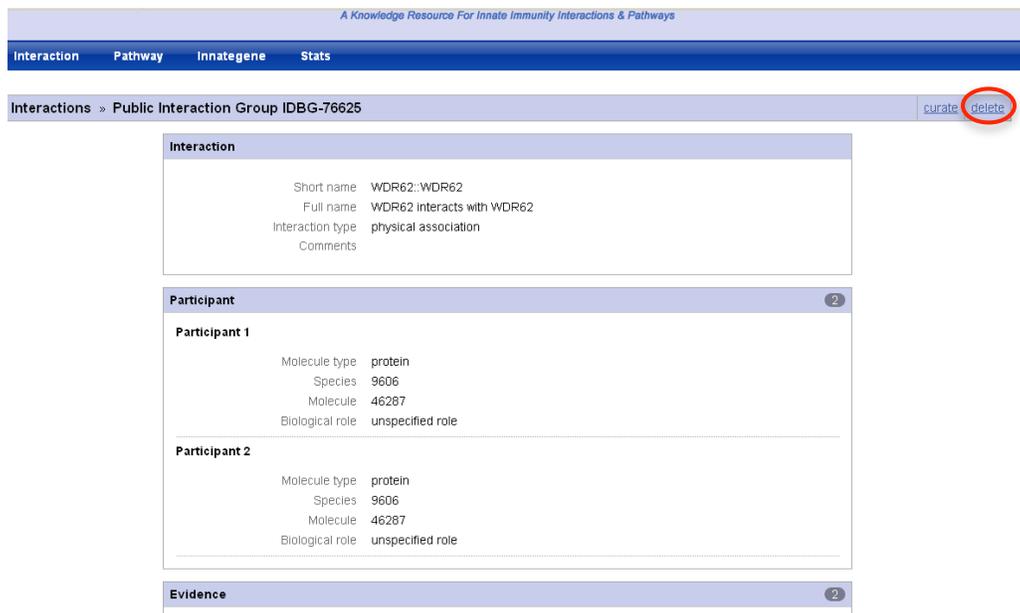
Confirm the rejection by clicking on the “Reject” button.



The screenshot shows a confirmation dialog for rejecting a specific interaction. The breadcrumb trail is 'Interactions > Curated Interaction Group CIG-4756 > Curated Interaction CI-6393 > Reject'. The dialog title is 'Reject CI-6393?' and the text below reads 'Birc2::Birc3 Birc2 physically associates with Birc3'. At the bottom, there are two buttons: 'Don't reject' and 'Reject'.

## 1.5.2 Deleting a Public interaction

Search the desired interaction using the search criteria (see 1.2 in this chapter). Click on the interaction from the Public Interaction Tab. Click on “Delete”. If more than one interaction belongs to the interaction group, you will need to click on the specific interaction you are referring to.



The screenshot shows the InnateDB website header with the logo and navigation tabs for 'Interaction', 'Pathway', 'Innategene', and 'Stats'. The user is logged in as 'meyau@interchange.ubc.ca'. The main content area shows a breadcrumb trail: 'Interactions > Public Interaction Group IDBG-76625'. A red circle highlights the 'curate delete' button. Below this is a table with the following data:

Interaction	
Short name	WDR62:WDR62
Full name	WDR62 interacts with WDR62
Interaction type	physical association
Comments	

Below the interaction table is a 'Participant' section with two participants:

Participant 1	
Molecule type	protein
Species	9606
Molecule	46287
Biological role	unspecified role

Participant 2 has the same details as Participant 1.

Confirm the rejection by clicking on the “Delete” button.

## 1.6 Annotating Innate Immune Genes

Aside from annotating innate immunity interactions and pathways, the InnateDB curation team has also established a project to annotate genes that have a role in the innate immune response. This has been initiated in response to the fact that Gene Ontology annotation of the innate immune response is quite limited in the numbers of genes which have been identified and in response to the fact that many users have been eager to have a defined list of innate immune genes. For innate immune gene annotation, curators employ a new tool in the InnateDB curation system to associate relevant genes with publications which provide evidence for that gene having a role in innate immunity. Along with the link to the relevant publication(s), the curators provide a one-line summary of the role similar to Entrez GeneRIFs. Such genes are also automatically associated with the Gene Ontology term "innate immune response" in InnateDB, which provides a more comprehensive list of these genes for use in the InnateDB Gene Ontology over-representation analysis tool. To date, Nearly 1000 genes have been annotated to some extent (as this is an on-going process). It should be noted that it is not the intention of InnateDB to comprehensively annotate all the roles of a given gene, but rather to provide a brief indication if a gene has a role in innate immunity.

The **Innategene** function on the main page is used to record immune genes and their function in innate immunity as described in specific scientific publications. This information can also be extracted from review articles, however the experimentally defined role of the gene/protein is preferred. This information is displayed on the gene card on the main site, under the section “InnateDB annotation.”

Innategenes are annotated as a part of the curation process (i.e. not restricted to innategene/curation emails) and should be captured whenever possible. The gene annotated should be the primary focus of the article, and its function should be apparent from the abstract body.

Innategene annotations should be one or two sentences, and should begin with the gene name and describe the function only as it relates to innate immunity. For example, classic innate immune receptors, such as the TLRs, may play a role in neural development, but those annotations are irrelevant to InnateDB and should not be entered.

Human and murine orthologs should be annotated together, provided that the genecard of the corresponding genes cross-references each other under the “Orthologs” section. If the gene function is only demonstrated in one species, the ortholog should be tagged with “(Demonstrated in mouse/human)”. Gene nomenclature is standardized to HGNC/MGI for human and mouse, respectively. The annotation text should adhere to Canadian English spelling (e.g. “signalling”, “defence”).

The innategene annotations are compiled in a word document on a weekly basis using the template outlined below, and reviewed internally before submitting to InnateDB.

Gene Symbol	Gene (Author)	Species	Publication	Description
TLR2		<i>Homo sapiens</i>	<a href="#">21698237</a>	TLR2 is required for rapid inflammasome activation in response to infection by cytosolic bacterial pathogens such as <i>Francisella novicida</i> . (Demonstrated in mouse)
Tlr2	TLR2	<i>Mus musculus</i>	<a href="#">21698237</a>	Tlr2 is required for rapid inflammasome activation in response to infection by cytosolic bacterial pathogens such as <i>Francisella novicida</i> .

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## InnateDB

A Knowledge Resource For Innate Immunity Interactions & Pathways

Interaction   Pathway   **Innategene**   Stats

Interactions [add interaction](#)

🔍 click here to search

Curated Interaction   Public Interaction

[list](#) [details](#) 1 - 20 of 9488 [older](#) > [oldest](#) >

<a href="#">CIG-9908</a>	<b>HDAC3::HIF1A</b>	HIF1A physically associates with HDAC3	PubMed ID 17273746	Misbah Naseer	reviewed	Mar 12
<a href="#">CIG-9907</a>	<b>HDAC1::HIF1A</b>	HIF1A physically associates with HDAC1	PubMed ID 17273746	Misbah Naseer	reviewed	Mar 12
<a href="#">CIG-9906</a>	<b>MDM2::HIF1A</b>	MDM2 physically associates with HIF1A	PubMed ID 17234751	Misbah Naseer	reviewed	Mar 12
<a href="#">CIG-9905</a>	<b>MYC::ARD1A</b>	ARD1A physically associates with MYC gene	PubMed ID 18593917	Misbah Naseer	reviewed	Mar 12
<a href="#">CIG-9904</a>	<b>MYC::CTNNB1</b>	CTNNB1 physically associates with MYC gene	PubMed ID 18593917	Misbah Naseer	reviewed	Mar 12
<a href="#">CIG-9903</a>	<b>HIF1A::CTNNB1</b>	CTNNB1 physically associates with HIF1A	PubMed ID 18593917	Misbah Naseer	reviewed	Mar 12
<a href="#">CIG-9902</a>	<b>HIF1A::ARD1A</b>	ARD1A physically associates with HIF1A	PubMed ID 18593917	Misbah Naseer	reviewed	Mar 12
<a href="#">CIG-9901</a>	<b>MAP4K4::BIRC2</b>	MAP4K4 (NIK) physically associates with BIRC2 (cIAP1)	PubMed ID 20184394	Melissa Yau	reviewed	Mar 12
<a href="#">CIG-9900</a>	<b>ARNT::HIF3A</b>	ARNT physically associates with HIF3A	PubMed ID 16126907	Misbah Naseer	reviewed	Mar 12
<a href="#">CIG-9899</a>	<b>HIF1A::HIF3A</b>	HIF1A physically associates with HIF3A	PubMed ID 16126907	Misbah Naseer	reviewed	Mar 12
<a href="#">CIG-9898</a>	<b>AIM2::AIM2</b>	AIM2 physically associates with itself	PubMed ID 15582594	Ana Sribnaia	reviewed	Mar 12
<a href="#">CIG-9897</a>	<b>HIF1A::PGK1::ARNT</b>	A complex of HIF1A and ARNT transcriptionally regulates PGK1 gene	PubMed ID 16126907	Misbah Naseer	reviewed	Mar 12

### 1.6.1 Adding annotation for a gene

Click **Innategene** in the top right-hand corner of page to begin submitting a new annotation.

The main Innate Genes page displays the most recently annotated genes. Click **Add** icon on the main page.

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## InnateDB

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Interaction   Pathway   Innatogene   Stats

### Innate Genes

Add
Edit
Delete
Reset

Gene ID	Gene Symbol	Species	Descriptions	Created on
<a href="#">130586</a>	Cd209a	10090	Has a role in the regulation of inflammation in a model of experimental colitis and	2010-03-11 10:43:10
<a href="#">103863</a>	AIM2	9606	Recognizes cytosolic dsDNA and forms a caspase-1-activating inflammasome wit	2010-03-11 09:55:02
<a href="#">21100</a>	HMGB1	9606	Functions as universal sentinel for nucleic-acid-mediated innate immune respons	2010-03-11 09:37:15
<a href="#">6462</a>	SPON2	9606	SPON2 expression is upregulated during intestinal inflammation and may induce	2010-03-11 09:33:15
<a href="#">62191</a>	IL31	9606	Antimicrobial Peptides Human (beta)-Defensins and Cathelicidin LL-37 Induce th	2010-03-11 09:31:25
<a href="#">32341</a>	CAMP	9606	Activates human mast cells and is degraded by mast cell tryptase ; Vitamin D3 in	2010-03-11 09:28:58
<a href="#">18750</a>	IDO1	9606	Induction of IDO-1 by Immunostimulatory DNA limits severity of experimental coliti	2010-03-11 09:19:18
<a href="#">97033</a>	TNFAIP3	9606	Restricts TLR signals by restricting ubiquitination of TRAF6; Accomplishes deubi	2010-03-11 09:08:12
<a href="#">83441</a>	INPP5D	9606	Absence of SHIP-1 results in constitutive phosphorylation of tank-binding kinase	2010-03-11 08:51:53
<a href="#">8115</a>	RAC1	9606	LTA-induced MAPKs activation is mediated through the TLR-2/MyD88/PI3K/Rac	2010-03-11 08:44:49

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Displaying 1 to 10 of 468 items

On the **New Innate Genes** page, enter the gene symbol in InnateDB Gene ID field. Select the desired gene as per section 1.3.2.3.

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[ac](#)

## InnateDB

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Interaction   Pathway   Innatogene   Stats

Innate Genes » [New Innate Genes](#)

**Innate Genes Basic Information**

InnateDB Gene ID: select...

Gene Symbol:

Species:

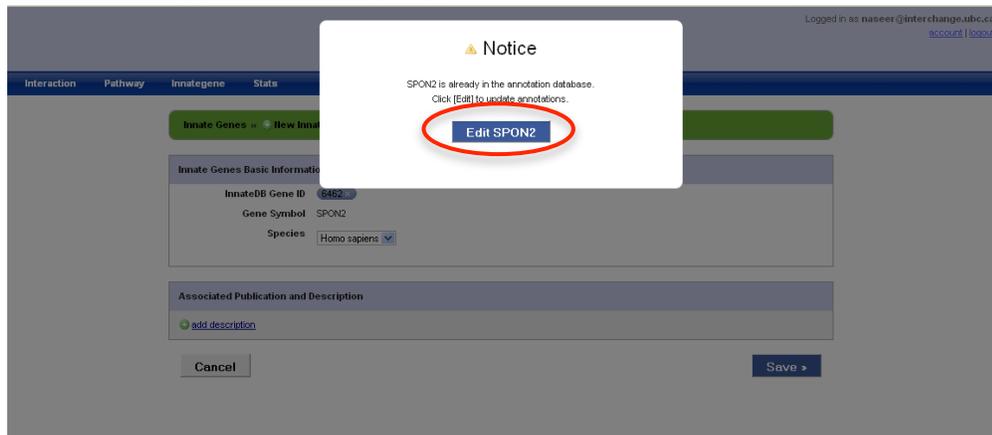
**Associated Publication and Description**

add description

InnateDB is being developed jointly by the Brinkman Laboratory, Simon Fraser University and the Hancock Laboratory, University of British Columbia, Vancouver, British Columbia, Canada and the Lynn Laboratory, Teagasc Animal Bioscience Department, Ireland.

Funding is provided by Genome Canada through the Pathogenomics of Innate Immunity (PI2) project, and the Foundation for the National Institutes of Health through the Grand Challenges in Global Health initiative.

**Note:** When looking up a gene ID, a pop-up screen may appear notifying the user of an existing annotation for the gene. Click **EDIT [GENE SYMBOL]** button to continue.



Click **add description** to enter a new annotation.

Enter the PMID of the source journal article in the **Pubmed ID** field. In the **Description** field, enter a one-sentence description of the gene in relation to its function in innate immunity. This information can usually be derived from the conclusion statement of the abstract of the source journal article.

After entering the required information, click **Save** button. The information will be updated instantly on the gene card on [www.innatedb.com](http://www.innatedb.com).



## 1.6.2 Editing/Deleting an annotation

Click on the magnifying glass icon in the bottom right-hand corner to search for all annotations of the gene entered in InnateDB.

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Interaction Pathway Innategene Stats

**Innate Genes**

Gene ID	Gene Symbol	Species	Descriptions	Created on
<a href="#">130586</a>	Cd209a	10090	Has a role in the regulation of inflammation in a model of experimental colitis and	2010-03-11 10:43:10
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<a href="#">97033</a>	TNFAIP3	9606	Restricts TLR signals by restricting ubiquitination of TRAF6, Accomplishes deubi	2010-03-11 09:08:12
<a href="#">83441</a>	INPP5D	9606	Absence of SHIP-1 results in constitutive phosphorylation of tank-binding kinase	2010-03-11 08:51:53
<a href="#">8115</a>	RAC1	9606	LTA-induced MAPKs activation is mediated through the TLR-2/MyD88/PI3K/Rac	2010-03-11 08:44:49

Enter the HGNC symbol for the gene and hit the **ENTER** key.

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Interaction Pathway Innategene Stats

**Innate Genes**

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If the gene has been annotated previously, the search results page will show the entry for the desired gene.

Highlight the row displaying the gene by clicking it and click **Edit** icon.

**InnateDB**  
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**Interaction Pathway Innategene Stats**

**Innate Genes**

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[Edit](#)
[Delete](#)
[Reset](#)

Gene ID	Gene Symbol	Species	Descriptions	Created on
90782	IRAK1	9606	Upregulates IL1 and binds to TRAF6 in TLR4 pathway, IRAK1 binds to the NFkB	2010-01-04 09:27:04

Quick Search

Page 1 of 1
 
 Displaying 1 to 1 of 1 items

All annotations for the selected gene will be displayed. To delete an annotation, click **remove**. To edit the text of an annotation, make the required changes on the page. Once all changes have been made, click **Save** button at the bottom of the screen.

[remove](#)

**PubMed ID** 20044140

**Description**

Functionally associates with [PKCepsilon](#) and [VASP](#) in the regulation of macrophage migration

[remove](#)

[add description](#)

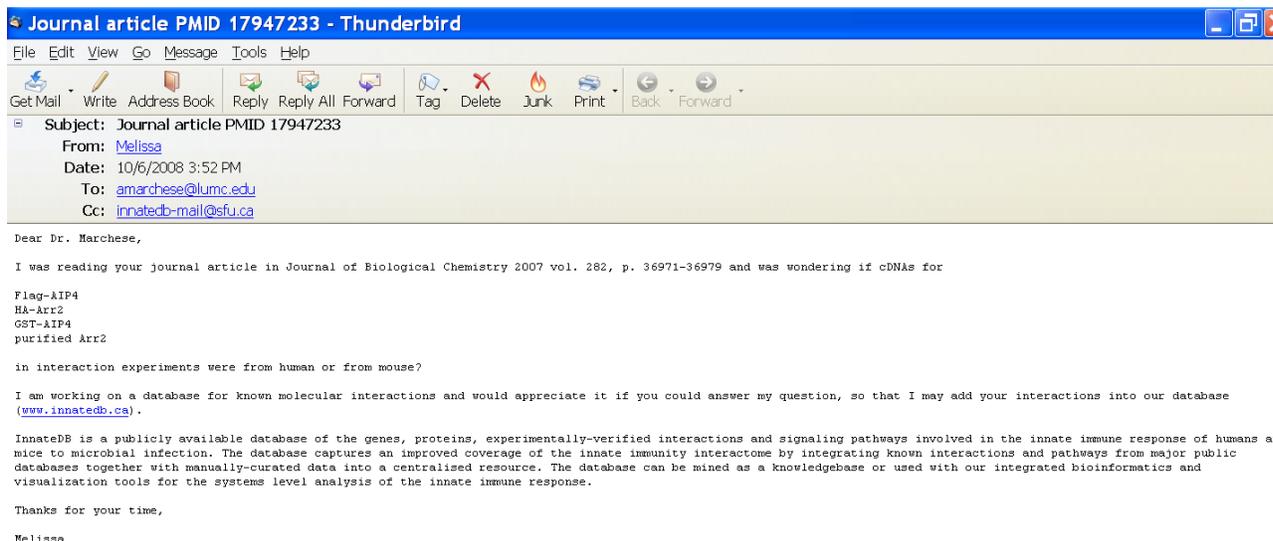
## Chapter 2: Curation Related Issues

### 2.1 *Confirming Species*

If species are not specified in the scientific article, the following steps can be taken:

- 1) If there is an article referring to the plasmid in the Material and Methods section, look up the species from this article.
- 2) Contact the corresponding author in the article for species confirmation. Note: remember to copy the email to [innatedb-mail@sfu.ca](mailto:innatedb-mail@sfu.ca)

For Example:



### 2.2 *Recording Subcellular Localization for a Gene*

If the Subcellular Localization is specified for a gene in a paper, check the gene card on InnateDB to see if the subcellular localization has been recorded. If not, then record the InnateDB gene ID and the Gene ontology term referring to the subcellular localization in an excel sheet, which will be sent to the InnateDB database developer.

The gene ontology term can be looked up at the following link:  
<http://www.ebi.ac.uk/ontology-lookup/>

## 2.3 Using Pathogenomics Wiki Site

The Pathogenomics Wiki Site can be accessed at [https://www.pathogenomics.ca/wiki/index.php/Main\\_Page](https://www.pathogenomics.ca/wiki/index.php/Main_Page). This site enables the curators to:

- Guidelines for submitting interactions
- Track curation progress (requested and curated genes)
- Record innate immune genes and their function

### 2.3.1 Guidelines for submitting interactions

[https://www.pathogenomics.ca/wiki/index.php/Curators\\_Group](https://www.pathogenomics.ca/wiki/index.php/Curators_Group)

To ensure consistency among curators, general rules have been outlined for submitting interactions.

Curators Group - PI2 Wiki - Mozilla Firefox

File Edit View History Bookmarks Tools Help

https://www.pathogenomics.ca/wiki/index.php/Curators\_Group

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The Pathogenomics of Innate Immunity

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## Curators Group

[edit]

### Submission System

#### PARTICIPANTS

- Proteins with no HUGO symbol: search the innatDB id for the **gene** encoding your protein of interest and enter it the "name" field.
- Biological Role:
  - Specifies the role of the protein in the particular interaction e.g. kinase-phospho donor, phosphorylated protein --phospho acceptor
  - Ubiquitination: Ubiquitinating molecule: Enzyme, Ubiquitinated molecule: Enzyme Target
  - Dephosphorylation: Dephosphorylating molecule: Enzyme, Dephosphorylated molecule: Enzyme Target
  - FRET (Fluorescent resonance energy transfer: CFP tag-protein: Fluorescence donor; YFP tag-protein: Fluorescence acceptor
  - Transcriptional regulation: title: transcriptionally downregulates/upregulates; biological role of the protein: transcription factor; interaction detection method: enzymatic study and mention the type of assay used to detect the upregulation or downregulation of the promoter of interest in comments

#### EVIDENCE

*Experimental type:*

- In order to add more than one experimental method from the same paper, add two separate evidences with same PMIDs.
- ELISA, in-gel kinase assay, Yeast two hybrid: No cell line, cell type, tissue defined. Usually "neutral component", except when doing a Y2H screen in which there is an obvious bait.
- GST pulldowns: (A) in-vitro translated proteins (at least one GST fusion protein), pulled down on glutathione-agarose beads; this type of pulldown does not have a cell type. (B) GST fusion protein transfected into the cell, and cell lysate is run on glutathione-agarose beads; this type of pulldown has a cell type (C) GST fusion protein also has a tag: if protein is pulled out using glutathione-agarose (or similar), this is called a GST pulldown; if GST fusion protein was pulled out using an anti-tag antibody, this is a co-immunoprecipitation.
- ALWAYS select anti-tag Co-IP for experiments with one or more tagged protein(s), specifying the tags in comments is optional.

*Experimental Role*

Select one of the following for each participant:

- bait
- prey
- neutral component e.g. kinase assays, ubiquitination assays, x-ray crystallography, Y2H in which no bait is used (i.e. binding domain of Protein 1 with Activating domain of other)
- unspecified role

navigation

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- Community portal
- Current events
- Recent changes
- Random page
- Help
- Donations

search

Go Search

toolbox

- What links here
- Related changes
- Upload file
- Special pages
- Printable version

To save time and ensure consistency, tissue type, cell type and species have been recorded for curated cell lines. If a cell line is not listed, add it to the page by following the example in section 1.3.3.10 in 1.3: Adding an interaction.

## 2.3.2 Track Curation Progress

[https://www.pathogenomics.ca/wiki/index.php/List\\_of\\_Genes\\_-\\_Curated\\_and\\_Requests](https://www.pathogenomics.ca/wiki/index.php/List_of_Genes_-_Curated_and_Requests)

This page is used to record systematically curated genes with the number of interactions in human and mouse. And genes requested by the lab or project manager are also documented.

List of Genes - Curated and Requests - PI2 Wiki - Mozilla Firefox

File Edit View History Bookmarks Tools Help

https://www.pathogenomics.ca/wiki/index.php/List\_of\_Genes\_-\_Curated\_and\_Requests

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## List of Genes - Curated and Requests

**CURATED GENES**

- AKT2 by Jaimmie & Aaron (18 human, 1 mouse, total 19)
- AZ12 (NAP1) by Melissa (8 human)
- BIRC4 Aug 2007 by Melissa and Raymond (70 human, 4 mouse, total: 74)
- CAMP by Ray
- CCL20 by Ray
- BTK by Misbah (25 human, 9 mouse, total: 34)
- CARD6 by Misbah (5 human, 1 mouse, total: 6)
- CARD9 by Misbah (6 human)
- CD14 by Jaimmie (2 human, 0 mouse, total: 2)
- CDH1 by Melissa (46 human, 20 mouse, total: 66)
- CENTB1 (ACAP1) by Misbah: (11 human, 1 mouse, total: 12)
- CHUK (IKK alpha) by Misbah (60 human, 7 mouse, total: 67)
- COP56 (CSN6) by Misbah (8 h)
- CTNNB1 by Melissa (118 human, 40 mouse, total: 158)
- DDX58 by Jaimmie (9 human, 0 mouse, total: 9)
- DHX58 (LSP2) by Melissa (5 human)
- DEDD by Melissa (6 human, 2 mouse, total: 8)
- DUSP16 (MLK7) by Misbah and Alex (8 human, 1 mouse, total: 9)
- ECSIT by Misbah (1 human)
- EPC1 by Misbah (9 human, 2 mouse, total: 11)
- ERBB2IP (ERBIN) by Misbah (48 human, 5 mouse, total: 53)
- FADD by Melissa (23 human, 1 mouse, total: 24)
- GAPDH by Misbah (9 human, 3 mouse, total: 12)
- GSR by Ray
- HRAS September 2007 by Melissa and Raymond (50 human, 6 mouse, total: 56)
- IFIH1 by Jaimmie (2 human, 0 mouse, total: 2)
- IFIT1 by Ray
- IKBK1 by Misbah (69 human, 6 mouse, total: 75)
- IKBKE by Jaimmie (18 human, 0 mouse, total: 18)

## 2.3.3 Record immune genes and their function

[https://www.pathogenomics.ca/wiki/index.php/InnateDB\\_curators\\_list](https://www.pathogenomics.ca/wiki/index.php/InnateDB_curators_list)

This page was used previously to record immune genes and their function in specific scientific publications while curating. This is now replaced by the innategenes function in the submission system.

InnateDB curators list - PI2 Wiki - Mozilla Firefox

File Edit View History Bookmarks Tools Help

https://www.pathogenomics.ca/wiki/index.php/InnateDB\_curators\_list

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article discussion edit history move watch

## InnateDB curators list

Innate Immune Genes [edit]

**HUGO Symbol: function**

- ADIPOQ:** Adipose-specific protein adiponectin, member of pattern-recognition family of defense collagens, binds to C1Q and activates the classical pathway of complement; PMID 18179772
- ATG5:** ATG5-ATG12 conjugate associates with innate antiviral immune responses by its direct association with DDX58 and MAVS, which negatively regulates IFN production pathway by mediating autophagy PMID 17709747
- AXL:** Tyrosine protein kinase, acts with TYRO3 and MERTK as Pleiotropic Inhibitor of the Innate Immune Response in DCs; PMID 18083102
- AZ12(NAP1):** NAP1 participates in both the TLR3 and cytoplasmic RIG pathways in type I IFN induction, binding to MAVS and DDX58 and MDA5 PMID 17142768
- BCL10:** selectively regulates JNK2 kinase in T cell receptor signalling pathway, serves as JNK-interacting protein like scaffold to assemble MAPK9, MAP3K7 and MAP2K7. The latter two kinases are recruited by BCL10 to activate MAPK9; PMID 17189706
- BDKRB2:** The bradykinin B2 receptor in the early immune response against Listeria infection—potentiates the production of IL-12p70 in human monocyte-derived dendritic cells PMID 18810490
- BECN1:** key factor in autophagosome formation, binds Th4, Myd88 and Ticam1 in mouse. Selective TLR signaling via its adaptor proteins reduces the binding of Becn1 to Bcl-2 by recruiting Becn1 into the TLR-signaling complex leading to autophagy, PMID 18772134
- BIRC2:** regulates TNF alpha-mediated NFkappa B activation by binding to TNFR1; PMID 18697935; Tumour necrosis factor receptor 2 signaling induces selective BIRC2-dependent ASK1 ubiquitination and terminates mitogen-activated protein kinase signaling PMID 1720297
- BIRC3:** regulates TNF alpha-mediated NFkappa B activation by binding to TNFR1; PMID 18697935
- BIMX:** Tyrosine protein kinase, regulates TLR4 induced IL-6 in macrophages independent of MAPK14 (P38 alpha) and NFKB; PMID 18025155
- BTK:** Tyrosine protein kinase, downstream of B cell receptor regulating NFKB activation; PMID 12724322; negative regulator of Fas-mediated apoptosis PMID 9880544
- C1Q:** Recognition subunit of the classical complement C1 complex. PMID 15207504
- BECN1:** Protease that mediates activation of the C1 complex of classical complement. PMID 11445889
- C1S:** Associates with C1R and C1Q to form the first component (C1) of the classical complement pathway. C1S is the modular serine protease responsible for cleavage of C4 and C2, the protein substrates for C1. PMID 16177097
- C2:** Complement component 2 is part of the classical and lectin complement pathways. C2 molecule binds to C4B and is cleaved by C1S protease into C2A and C2B fragments. The resulting C4B2A complex

## 2.3.4 Curation Tips

### ***Papers should be read in full***

Articles sent out via innatene/curation emails should always be read to ensure all relevant interactions are being captured. Introductions and discussion sections may reference interactions or genes that are relevant for curation and innatene annotations, and it may be necessary to track those articles. [Note: Nature Immunology articles are performed as a part of InnateDB's contribution to IMEx, so those papers can be put on hold for curation until the full issue is released.]

### ***Innate Immunity Pubcrawler queries on a semi-weekly basis***

It is important that each curator set-up independent PubCrawler queries and perform dedicated searches at least once every two weeks on canonical innate immunity pathways, such as the TLR / NLR / RIG-I pathways, to ensure that InnateDB is up-to-date with current literature.

## Chapter 3: IMEx Curations by InnateDB

### ***3.1 The International Molecular Exchange Consortium***

InnateDB is an active member of the International Molecular Exchange Consortium ([IMEx](#)). This organization is dedicated to developing rules for capturing protein-protein interaction data, actively curating these interactions from the scientific literature and making them available through a common website.

### ***3.2 Curating for IMEx***

InnateDB have committed to curating every issue of [Nature Immunology](#) from Sep 2010 onwards using IMEx curation standards. Since IMEx curation requires more annotation detail than InnateDB is able to capture with the current submission system, InnateDB will submit the interactions via the [IntAct interaction database](#).

Curation is performed using a hierarchical method of PMID > Experiments > Interactions > Participant > Features, with annotations at each level. Upon submission, all interactions are thoroughly reviewed by an IntAct curator and any changes are made by the original InnateDB curator before it is accepted and released.

In addition to submitting to IntAct, all InnateDB acceptable interactions (i.e. interactions of relevance to innate immunity) and innatene annotations from Nat Immunol should be deposited into InnateDB.

This chapter will highlight the major differences between InnateDB and IMEx curation. Since interactions are submitted to and reviewed by IntAct, the official IntAct annotation rules should also be reviewed (see Useful Links).

### 3.2.1 PMID

#### **Publications are curated in full**

All protein-protein interactions described in the original body of the article as well as any supplementary material should be captured. As long as the protein(s) described can be mapped in [UniProt](#), which annotates all proteins from all species, it should be annotated.

#### **Email of corresponding author is captured**

Upon the acceptance of the submitted interactions, an email will be sent to the author notifying the release of the interaction data.

#### **Annotation details and Xrefs**

As much detail describing the interaction should be recorded in the annotation fields at the Experiment, Interaction and Participant level. Some of the commonly used ones are described in Table 1, the full list and official definitions can be found in the IntAct Annotation Rules. Xref should also be used at each level, especially if an accession code is referenced in the paper (e.g. [PDB](#) deposition).

Table 1. Commonly Used IntAct Annotation Fields

PMID	
External-curation	"Curated by: InnateDB - a knowledge resource for innate immunity"
Contact-comments	Info from author correspondence (e.g. species)
Experiment	
Caution	Possible errors in experiments or on specifications (e.g. a non-specific antibody was used for WB)
Exp-modifications	Departure from standard procedures (e.g. modified cell lines)
Library-used	For Y2H or phage display
Interaction	
3d-r-factor, 3d-resolution, 3d-structure	X-ray crystallography or NMR studies
Agonist / Antagonist	Treatments on the cell that induced or inhibited the interaction, respectively
Stimulation / Inhibition	Proteins or small compounds that facilitated or inhibited the interactions, respectively
Figure legend	Reference the figure or table supporting the interaction
Kinetics	Used in isothermal titration calorimetry (can also be captured under Parameter)
Parameters	Captures Kd, Kon, Koff in SPR studies
Resulting-ptm	Post-translational modifications for enzymatic reactions

### 3.2.2 Experiment(s)

#### **Redundant evidences are captured separately**

IMEx curation requires the meticulous documentation of all experimental evidence supporting an interaction within a single publication. With the exception of two-hybrids, all interaction should have an accompanying figure or table reference in the publication. Evidence may be merged only if the experimental conditions, the interaction and participant detection methods, as well as the participant features are identical. A reciprocal CoIP, for example, should be entered as two separate lines of evidence.

#### **In vitro is reserved for cell-free environments and extracellular interactions**

Unlike InnateDB, where *in vitro* is used for cell-free as well as cell culture studies.

### 3.2.3 Interaction(s)

#### ***Exclusion of nucleic acid::protein interactions***

IMEx does not accept DNA and RNA as interaction participants. These interactions should still be curated using standard InnateDB rules and deposited into InnateDB only.

#### ***Inclusion of colocalisation interactions***

These interactions are typically demonstrated via confocal or fluorescent microscopy experiments at the cellular level of resolution. Marker proteins (as specified in the paper) should not be entered as a participant. Colocalisation interactions should also be Xref to the appropriate cellular component via [GO](#).

#### ***Protein Complexes are annotated as n-ary “association” interactions***

In situations where one bait captures more than two preys (e.g. pull down, LC MS/MS), the participants are entered in a single “Association” interaction. “Physical Association” designations are normally reserved for binary interactions.

### 3.2.4 Participants

#### ***Participants are mapped to UniProt***

Participants are imported via their [UniProt](#) accession number, which designates protein and not genes. It allows the mapping to specific protein isoforms if the information is available. If the author does not specify the protein isoform used, the participants are mapped to the parent protein. In cases where a synthetic protein construct is used and is conserved across multiple species, curator may map the synthetic participant to the species matching that of its interactor(s).

#### ***Oligomer participants are imported once and assigned a stoichiometric value***

Proteins that oligomerize are imported as one participant with stoichiometric value of  $\geq 2$ . For example, A dimerizes and binds to B. Instead of entering A::A::B, it should be submitted as A::B with a stoichiometric ratio of 2:1.

#### ***Participant features annotates tags, binding region, mutations... etc.***

The full participant feature MI terminology tree can be found on OLS (MI:0116). Each participant feature is mapped to a region on the protein (e.g. amino acids 320-400, c-c, n-n, ?-?). All tags, radiolabel, or isotope labels should be captured, and if possible, mapped to a protein region.

Deletion experiments are distilled to the narrowest possible binding region and assigned as “required to bind”; where as if the interaction is shown with a partial protein, the region is denoted as “sufficient to bind”. If the region overlaps with an [InterPro](#) protein domain, it should be cross-referenced to the domain accession number.

Amino acid substitutions affecting the interaction are also captured using 3-letter codes of amino acids (e.g. Tyr34Ala) and assigned as increasing, decreasing or disrupting based on their influence.

## 3.3 Useful Links

### 3.3.1 IMEx

#### **IMEx Consortium**

<http://www.imexconsortium.org/>

This is the public website for the IMEx consortium where it lists the purpose of the consortium, the participating databases, and the journals that each of the database is responsible for. The official IMEx curation rules are also found here. It is a good idea to note which journals are being curated by other IMEx members to avoid duplication of curation efforts, especially for high-throughput interactome papers.

#### **IMExCentral**

<https://imexcentral.org/icentralbeta/>

IMExCentral is the semi-internal website that the IMEx member use to reserve PMIDs for curation, and it will return a unique IMEx accession number if that publication has not been curated by one of the IMEx members. In addition, it allows for the recommendation of papers from public users. The generation of IMEx ID is automatic through the IntAct editor so the curator should not have to manually reserve Nat Immunol articles.

#### **IMEx Interactions via PSQUIC**

<http://www.ebi.ac.uk/intact/imex/main.xhtml?query=&Search=Search>

This is the search engine for all of the IMEx interactions from all the participating databases.

### 3.3.2 IntAct

#### **IntAct Database**

<http://www.ebi.ac.uk/intact/main.xhtml>

The IntAct interaction database.

#### **IntAct Annotation Rules**

<http://www.ebi.ac.uk/~intact/site/doc/IntActAnnotationRules.pdf?conversationContext=2>

The complete IntAct annotation manual. Keep in mind that since these interactions are submitted to IntAct, they should adhere to the IntAct annotation rules, which may be more stringent than IMEx. For example, curators are expected to capture a negative interaction if it accompanies a positive interaction evidence; conversely, IMEx does not take negative interactions at all.

#### **Ontology Lookup Service (Molecular Interaction)**

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

Nomenclature for all IMEx interaction data annotations, including participant features (MI:0116), should adhere to OLS standards. This browser offers the official definition of each MI term.

### 3.3.3 Cross References

#### ***Nature Immunology***

<http://www.nature.com/ni/index.html>

Nature Immunology issues are published on a monthly basis, and was chosen by InnateDB for its focus on immunity research and the impact factor of the journal. Each issue will consist of approximately 8 original research articles for IMEx curation. Each article, including all supplementary materials, should be thoroughly read to ensure all interactions are being captured. InnateDB have curated Nature Immunology from Aug. 2010.

#### ***UniProtKB***

<http://www.uniprot.org/>

Instead of mapping to ENSEMBL genes like InnateDB, IntAct maps their participants to UniProtKB. UniProt/TrEMBL (★) automatically annotates proteins from all species, while UniProt/SwissProt (★) entries have been manually reviewed by a curator with high quality annotations and are non-redundant. Always try to use the reviewed entries if possible.

#### ***InterPro***

<http://www.ebi.ac.uk/interpro/>

InterPro annotates protein signatures or domains. Since each participant feature is mapped to a particular region on the protein, curators are expected to cross-reference InterPro accession number(s) if the region spans an InterPro annotated domain.

#### ***Gene Ontology***

<http://www.geneontology.org/>

Gene Ontology is cross-referenced in colocalisation interactions to specify the cellular component that the protein complex was found in.