

# Guide to IMMUNOPHARMACOLOGY Main Portal – Access Point to Immuno Data

The Guide to IMMUNOPHARMACOLOGY (GtoImmuPdb) is a Wellcome Trust-funded extension to the existing Guide to PHARMACOLOGY (GtoPdb). The development of GtoImmuPdb aims to provide improved data exchange between immunology and pharmacology expert communities, so to better support research and development of drugs targeted at modulating immune, inflammatory or infectious components of disease.

The underlying GtoPdb schema has been extended to incorporate new immune system specific data types (such as processes and cell types) and the GtoPdb website has been developed to surface this new data and incorporate it into the existing search and browse mechanisms. A new Guide to IMMUNOPHARMACOLOGY portal has been developed, which serves as a unique immunological access-point to the Guide to PHARMACOLOGY.

#### http://www.guidetoimmunopharmacology.org

The portal has its own unique branding (header bar, logo and colour scheme) to distinguish it, but retains many of the layout features from the main GtoPdb site. This consistency should help users already familiar with GtoPdb to orientate themselves with the new GtoImmuPdb.

Users can familiarise themselves with the existing GtoPdb site by reading its website tutorial:

http://www.guidetopharmacology.org/GuidetoPHARMACOLOGY\_Tutorial.pdf

The guide in this document gives an overview of the GtoImmuPdb portal, and illustrates the new additions to existing pages that have been developed for GtoImmuPdb.

Information on the new data incorporated into GtoImmuPdb is described in more detail in other documentation.

http://www.guidetoimmunopharmacology.org/immuno/immunoHelpPage.jsp#aboutDat a



# Guide to IMMUNOPHARMACOLOGY Main Portal – Access Point to Immuno Data

The GtoImmuPdb portal provides a unique access point to data of immunological relevance held in the database.



The main panels (highlighted by the dotted line) are fast routes into browsing the data by the main data-type categories:

- Processes
- Cell Types
- Disease
- Targets
- Ligands

These are explained in more detail later in the tutorial. Click on the category to jump to that section.





The site search in the top right can be used to search across all data. The predictive text feature provides suggestion. View tutorial on searching GtoImmuPdb. When searching from the Guide to IMMUNOPHARMACOLOGY results will be up-weighted based on their immuno relevance (see Help on Searching GtoImmuPdb)



## Guide to IMMUNOPHARMACOLOGY Process Associations to Targets

To view targets associated with immunological processes, select a process category from the 'Processes/pathways' panel on the GtoImmuPdb portal.

You can also select a category under the Processes menu item.



The list of targets is split by target class. The 'Jump to' links allow you to move fast to that section of the table.

The blue pull-down menu can be used to switch between different process categories

The table lists the target name (and family) and links to its detailed target page.

Gene Ontology annotations (GO) are displayed plus general curated immunopharmacology comments related to the target.

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lome About 🔻	Targets 🔻	Ligands 🔻	Processes 🔻	Cell Types 🔻	Diseases	Resources 🔻	Guide to PHARMACOLOGY	
Home Mome	no Processes	<ul> <li>B cell (activation)</li> </ul>						
Select Immuno F Cell (activation	rocess catego ))	o Processes -	B Cell (activatio	n) R   Ion Channels   NH	IRs   Enzymes	Catalytic Receptor	;   Transporters   Other Protein Targets	
9				GPCRs				
GtoPdb receptor name (family)	Process Association Comments		GO Associations			Immunopharmacology Comments		
CCR2 Chemokine eceptors)		<ul> <li>positive regu response (G</li> </ul>	positive regulation of T-helper 1 type immune response (GO:0002827) ISS			CCR2 is one of more than 20 distinct chemokine receptors expressed in human leukocytes. Chemokines primarily act to promote leukocyte chemotaxis to sites of inflammation. CCR2 is discussed in relation to immuno-oncology in [2]		
CCR6 Chemokine eceptors)		<ul> <li>isotype switc</li> </ul>	isotype switching to IgA isotypes (GO:0048290) ISS			is one of more than ssed in human leukoo nune cells including n	20 distinct chemokine receptors cytes. CCR6 is expressed on a variety nemory and regulatory T-cells [121,137]	
CXCR5 Chemokine eceptors)		B cell activat	ion (GO:0042113) IE	A	CXCF expre prome	R5 is one of more than ssed in human leukoo ote leukocyte chemota	20 distinct chemokine receptors rytes. Chemokines primarily act to axis to sites of inflammation.	
SPR183 (Class A Orphans)		<ul> <li>adaptive imm</li> <li>B cell activativative</li> <li>response (G</li> <li>mature B cell response (G</li> <li>positive regulative</li> </ul>	adaptive immune response (GO:0002250) ISS     B cell activation involved in immune     response (GO:0002312) IBA     mature B cell differentiation involved in immune     response (GO:0002313) ISS     positive regulation of B cell proliferation (GO:0030890) IDA			Gpr183-deficient mice show a reduction in the early antibody response to a T-dependent antigen. GPR183-deficient B cells fail to migrate to the outer follicle and instead stay in the follicle centre [115,177]		
				lon Channels				
	Process		GO Associations					



# Guide to IMMUNOPHARMACOLOGY Cell Type Associations to Targets

To view targets associated with immunological cell types, select a cell type category from the 'Cell Types' panel on the GtoImmuPdb portal.

You can also select a category under the Cell Types menu item.



The list of targets is split by target class. The 'Jump to' links allow you to move fast to that section of the table.

The blue pull-down menu can be used to switch between different cell type categories

The table lists the target name (and family) and links to its detailed target page.

Cell Ontology annotations are displayed plus general curated immunopharmacology comments related to the target.





#### Guide to IMMUNOPHARMACOLOGY Disease List

Disease association data is via the Disease List page. These are accessed by selecting the link from the Disease panel on the portal or via the Disease menu item.

	MMUNOPHARMACOL	Search Da	
Home About Targets Ligands F	Processes  Cell Types  Diseases Resources  Guide to PH	IARMACO	LOGY
	2V disease list		
All Diseases Immuno Disease			
Immunologically relevant diseases A B C	described in GtoPdb. CDEFGHIJKLMNOPRSTUVW	4	ŀ
Disease name	Synonyms	Targets	Ligano
Α			Back to t
Activated PI3K delta syndrome	APDS/PASLI   Immunodeficiency 14   p110 delta activating mutation causing senescent T cells, lymphadenopathy, and immunodeficiency	1	3
Acute lymphocytic leukemia (ALL)	Acute lymphoblastic leukemia	3	2
Acute myeloid leukemia	Acute myelogenous leukemia	6	5
Adult T-cell leukemia	Adult T-cell leukemia/lymphoma   ATLL	0	1
Allergic conjunctivitis		0	8
Allergic rhinitis 3	atopic rhinitis   hay fever   Non-seasonal allergic rhinitis   Perenial allergic rhinitis   pollenosis   seasonal allergic rhinitis	0	13
Allergic urticaria	hives	0	9
Alopecia areata	circumscribed alopecia	0	2
Anaphylactic shock	hypersensitivity reaction disease	0	1
Anaplastic large cell lymphoma		0	1
Ankylosing spondylitis	Bekhterev syndrome   Marie-Strumpell disease	0	14
Aspirin exacerbated respiratory diseases		1	1
Asthma		6	77
Atopic dermatitis		2	15
Autoimmune lymphoproliferative syndrome; ALPS		1	1
Autoimmune thrombocytopenic purpura	idiopathic thrombocytopenic purpura   Immune thrombocytopenia   Immune thrombocytopenic purpura   ITP   primary immune thrombocytopenia   primary thrombocytopenic purpura	0	4

The page is organised with a tab to switch (1) between the disease categories.

Diseases are listed alphabetically (2). The disease name is listed in the first column (3). This links through to more detailed information on the Disease Summary page.

Synonyms are shown in the third column.

The final two columns (4) indicated how many targets and ligands have an association to that disease.



#### Guide to IMMUNOPHARMACOLOGY Disease Summary Page

Disease summary pages show an overview of the disease at the top. This can include counts of associated targets and ligands, disease descriptions, synonyms and links to external database where we have mapped our disease to.

	Home About * Targets * Ligands * Processes * Cell Ty	Search Database OPHARMACOLOGY pes  Diseases Resources Guide to PHARMACOLOGY				
	► Home ► Diseases ► Psoriasis					
	Psoriasis  Disease ID: 801 Name: Psoriasis Associated with: 4 targets 2 immuno-relevant targets 56 immuno-relevant ligands  Description					
	A long-term autoimmune disease characterized by patches of red, itchy, and scaly skin. F pustular, and erythrodermic, with plaque psoriasis being the most common type. Database Links Disease Ontology: DOID:8893	ive types of psoriasis are recognised: plaque (psoriasis vulgari), guttate, inverse,				
1		<u>Target section</u> Displays any pathophysiology or mutatior				
CD2		data curated against the target.				
Comments:	CD2 is the molecular target of alefacept, a drug that was approved f	Lists an ligands that are associated with				
Ligand interactions:	Ligand	the disease that interact with the target				
	alefacept	Approved drug for plaque psonasis (no longer authorised for use in some countries).				
CD6						
Comments:	CD6 is the molecular target of itolizumab, a drug approved for the tre	atment of chronic plaque psoriasis.				
Ligand interactions:	Ligand	Comments				
	itolizumab 🖾 🔘					
		Ligands section				
Ligands		Lists associated ligands				
0		Icons indicate is approved drug				
Key to terms and sym	ubols Click ligand name to view	Expandable comments section show,				
	Ligand	curator, clinical use and bio-activity				
AbGn-168H		comments				
ACTH						
adalimumab						
alefacept						
Glinical Use: This dru discontinued in the US Bioactivity Commen assessed by measurin inhibition of induced T	is approved on g ion praque psonasis (no longer authorised for ig was approved for the treatment of inflammation in moderate to sever S.   View clinical data ts: The Miller <i>et al.</i> (1993) article does not provide a calculated IC <sub>50</sub> va ing rosetting of Jurkat/human red blood cells (with an approximate IC <sub>50</sub> ( cell proliferation (with LFA3TIP inhibition at approximately 86%) [38].	lue for LFA3TIP's inhibition of the CD2/LFA-3 interaction [38]. The inhibition is of 1-5µg/ml of protein from graphical data in Figure 3a), or by measuring View biological activity				



# Guide to IMMUNOPHARMACOLOGY Browsing Targets in GtolmmuPdb

Users can browse for different targets by selecting one of the main target classes on the Targets panel.



IUPHAR Guide to



# Guide to IMMUNOPHARMACOLOGY Target Families Page



# Guide to IMMUNOPHARMACOLOGY Target Family Page

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=	, ∖⊧	Guio	de to	ΙΜΜ	JNOP	PHAP	RMAC		_OGY
Home	About 🔻	Targets 🔻	Ligands 🔻	Processes 🔻	Cell Types 🔻	Diseases	Resources 🔻	Guide to	PHARMACOLOGY
Home	e 🕨 Targets	G protein-co	oupled receptors	Adenosine rece	eptors				
				Adenc	sine recer	otors			
	Lipiona atba	ruise stated all date	to on this page refe	r to the human protein	o. Cons information is a	vouidad far huma	n (Llo), mourse (Mm) er	d rat (Da)	
	Unless othe	erwise stated all dat	ta on this page rele	r to the numan protein	s. Gene information is p	novided for huma	n (Hs), mouse (Min) ar	u rai (Rii).	
				GtoImmuPo	db view: ON Toggl	e GtolmmuPdl	View Expand a	II sections	Collapse all sections
Overvie	w								
?	« Hide							Мо	re detailed introduction GO
Recepto ?	ors Targets o	of relevance to	immunopharm	acology are high	lighted in blue				
	A <sub>1</sub> rec	ceptor Show sum	mary »						More detailed page GO
	A <sub>2A</sub> r	eceptor Show su	immary »	2				3	More detailed page 💿
		eceptor Show su eceptor Show su	immary »	2				3	More detailed page 💿
	A <sub>2A</sub> r A <sub>2B</sub> r A <sub>3</sub> re	eceptor Show su eceptor Show su ceptor Show sun	immary »	2				3	More detailed page <b>6</b> 0 More detailed page <b>6</b> 0 More detailed page <b>6</b> 0
Comme	A <sub>2A</sub> r A <sub>2B</sub> r A <sub>3</sub> re	eceptor Show su eceptor Show su ceptor Show sum	immary » immary » immary »	2				3	More detailed page More detailed page More detailed page
Comme ?	A <sub>2A</sub> r A <sub>2B</sub> r A <sub>3</sub> rec	eceptor Show su eceptor Show su ceptor Show sun	immary »	2				3	More detailed page More detailed page More detailed page More detailed page
Comme ? Further	A2A T A2B T A3 red nts Show »	eceptor Show su eceptor Show su ceptor Show sum	immary »	2				3	More detailed page 30

- 1. The family page also has a toggle to switch between GtoImmuPdb and GtoPdb
- 2. When switch on, target flagged as having immunological relevance are highlighted
- 3. Clicking the 'More detailed page' link moves to the detailed view for that target



Transduction Mechanisms ==

Physiological Consequences of Altering Gene Expression

Clinically-Relevant Mutations and Pathophysiology

Phenotypes, Alleles and Disease Models

Tissue Distribution Expression Datasets

Functional Assays Physiological Functions

General Comments

References

Contributors How to cite this page 1. The detailed view also has a toggle, and informs the user if the displayed target has been curated in GtoImmuPdb.

2. With the GtoImmuPdb view switched on, sections of immunological relevance are highlighted within the 'Contents' section – alerting the user to them. Clicking those jumps down to those sections..

3. When selected toggle on, target families that contain target flagged in the database as being of immunological relevance

IUPHAR Guide to



#### Guide to IMMUNOPHARMACOLOGY Target Detailed View Page Immunopharmacology Data Sections

#### Immunopharmacology Comments

CD80 (B7-1) is expressed on dendritic cells and activated B cells and monocytes. It is required to provide a costimulatory signal necessary for T cell activation and survival. CD80 works in concert with CD86 to prime T cells. CD80 binds CD28 and CTLA-4 on T cells. It is the interaction with CTLA-4 that is targeted by the approved immunosuppresive drugs abatacept and belatacept.

The immunopharmacology comments are rich, curator comments specific to the target about its relevance to immunopharmacology. Usually these will refers the targets involvement with different processes, cell types and disease.

Cell Type Associations	
Immuno Cell Type: Cell Ontology Term:	Macrophages & monocytes macrophage (CL:0000235) monocyte (CL:0000576)
Immuno Cell Type:	Dendritic cells
Cell Ontology Term:	dendritic cell (CL:0000451)
Immuno Cell Type:	B cells
Cell Ontology Term:	B cell (CL:0000236)

Cell type associations shows one sub-section per top-level cell type category. Associations with specific Cell Ontology terms are shown along with curator comments and references.

Immuno Process Associations			
Immuno Process: GO Annotations:	Inflammation Associated to 3 GO:0045627	1 GO processes positive regulation of T-helper 1 cell differentiation	NAS
Immuno Process:	T cell (activatio	yn)	
GO Annotations:	Associated to 4	4 GO processes	TAR
	GO:0031295 GO:0042110	T cell activation	IAS
	GO:0045627	positive regulation of T-helper 1 cell differentiation	NAS
	•	click arrow to show/hide IEA associations	

Process associations shows one sub-section per top-level process category. Associations with specific Gene Ontology terms (and evidence codes) are shown along with curator comments and references.

Immuno Disease Association	S
Disease Name:	Rheumatoid arthritis
Disease Synonyms:	no synonynms
Comment:	CD80 is a primary target of the ligand abatacept, which is clinically approved for the treatment of rheumatoid arthritis.
Disease X-refs:	Disease Ontology: DOID:7148
	OMIM: 180300
References:	3
Disease Name:	Allograft rejection
Disease Synonyms:	no synonynms
Comment:	CD80 is a primary target of the approved anti-rejection drug belatacept.

Each sub-section gives details of the association between the target and a disease. It lists disease synonyms and curator comments. External links to other disease resources are provided.



# Guide to IMMUNOPHARMACOLOGY Ligand List Pages

Users can browse for different ligands by selecting one of the ligand categories on the Ligands panel.

Ligand categories can also be selected under the Ligands menu item.



The ligand list page is organised by category – which can be selected by the tabs at the top of the page **(1)**.

Ligands are listed alphabetically, and link to their summary pages **(2)**. Any ligands tagged in the database as being immuno relevance display the immnuo icon **(3)**.

All immuno tagged ligands are shown under the Immuno ligands tab.

A toggle button allows switching between the GtoImmuPdb and GtoPdb views **(4)**.

UPHAR Guide t	o IMM	UN	
Home About 🔻 Targets 🔻 Ligands	<ul> <li>Processes</li> </ul>	- Cel	I Types  Diseases Resources  Guide to PHARMACOLOGY
Home Ligands			
The IUPHAR Guide to IMMUNOPHARMA	COLOGY ligand	list	
Approved Syn organic Metabolite Nat i	product Endogeno	ous pentid	e Other pentide Inorganic Antibody Labelled Immuno AntiMal
A Ligand name	B C D E F G H I	JKLN	INOPQRSTUVWXYZ
A <b>Z</b>	3		Back to t
852A	¥	9025	
A286982	¥	6592	A 286982, A-286982
A438079	Ŵ	4118	A 438079, A-438079
abatacept	ā 🕅	6891	BMS-188667, CTLA4-IgG4m, Orencia®, RG-1046, RG-2077
abediterol	¥	9326	LAS-100977
AbGn-168H	ý	10013	AbGn-168, neihulizumab
ABT-737	S 🕅	8320	ABT 737, ABT737, compound 2 [PMID 17256834]
AC430	¥	9177	AC-430
acalabrutinib	ð 🕅	8912	ACP-196, Calquence®, Example 6 [US20140155385 A1]
Ac-SDKP	¥	10060	goralatide, seraspenide
ACT-389949	¥	9511	
ACTH {Sp: Human}	Đ 🕅	3633	Acthar®, adrenocorticotropic hormone (1-39), corticotropin
acumapimod	¥	9203	BCT 197, BCT-197, BCT197, compound A [WO2013139809]
	e 🅅	4860	D2E7, FKB327, Humira®
adalimumab			
adalimumab adavivint	¥	9620	SM0-4690, SM04690



# Guide to IMMUNOPHARMACOLOGY Ligand Summary Pages

The ligands summary pages contains detailed information about the ligand. In GtoImmuPdb.

بر بر ا	ιι G	JPHAR uide to	IMM	UN	OPł	HAF	RMA		Gearch Database
Home	About 🔻 Targe	ts 🔻 Ligands 🔻	Processes	Cell T	īypes 🔻 l	Diseases	Resources 🔻	Guide to PH	ARMACOLOGY
► Hom	ne 🕨 Ligands 🕨 aca	alabrutinib							
acalab	rutinib								
0	Ligand id: 8912								
	Neme: acalabrut	inih							
	Name: acaiabrui	מוחו							
Structu	ire and Physico-cl	hemical Propertie	S						
2D Stru	cture 🕜				Calculated F	Physico-che	mical Properties	0	
					Hydrogen bo	nd acceptor	5		9
		S-N CEC-			Hydrogen bo	ond donors			2
		H			Rotatable bo	nds			6
	N				Topological p	olar surface	area		118.51
	т ч				Molecular weight			465.19	
					XLogP				3.58
		NH			No. Lipinski's	s rules broke	n		0
					Molecular pr	operties gene	rated using the CDK		
Summary	Biological activity	Clinical data Re	eferences Struct	ure Imm	unopharmacc	ology 1	_	_	_
Immunop	pharmacology Comme	nts							
Pharmac malignan	ological inhibition of BTH t B cells overexpressing	K prevents the activatio BTK.	n of B cells and BTK	-mediated a	activation of do	wnstream si	irvival pathways. 1	This leads to inhibit	ion of the growth
Immunop	oharmacology Disease								
	Disease	X-R	efs			Com	ment		References
Rheumat	oid arthritis	Disease Ontology: OMIM: 180300	DOID:7148	Phase 2 cli	nical trial in RA	completed	(NCT02387762)		
B-cell chr Ieukemia	onic lymphocytic	OMIM: 151400 Orphanet: ORPHA	67038	Phase 3 cli	nical candidate	e for CLL.			
	ell lymphoma	Disease Ontology:	DOID:0050746	Approved d	Irug for MCL pa	atients who I	nave received at le	east one prior	4

1. Tagged ligands have an Immunopharmacology tab that contains immuno relevant data.

2. The immunopharmacology comments sections contains specific curators comments about the ligands relevance to immunopharmacology.

3. The immunopharmacology disease section shows all immune-related diseases the ligand is associated with, including curator comments and external references for the disease.





#### Guide to IMMUNOPHARMACOLOGY Searching GtolmmuPdb

Search mechanisms have been extended to incorporate all additional immunopharmacological data - this includes all process, cell type and disease terms, definitions and ontology IDs. Running searches on GtoImmuPdb will up-weight results of higher immunological relevance.

	Regulation of cytokine production	Search Database	
Search results		-	
			Page 1 of 23
Your search for regulation	of cytokine production returned 230 results		
_		Order results by: Match • Go	Download as a CSV: Download
Target: TLR4 (Toll-like recepto	r family)		
GO Process Term: regulation of GO Process Term: negative reg GO Process Term: positive reg GO Process Term: regulation of GO Process Term: positive reg GO Process Term: regulation of GO Process Term: regulation of GO Process Term: regulation of GO Process Term: regulation of GO Process Term: negative reg GO Process Term: negative reg	of cytokine production (5 annotations to shift terms) julation of cytokine production (5 annotations to child ter ulation of cytokine production (17 annotations to child ter of cytokine production involved in immune response (2 an of cytokine production involved in immune response ulation of cytokine production involved in immune response ulation of cytokine production involved in inflammatory re- of macrophage cytokine production (1 annotations to child ulation of myeloid leukocyte cytokine production (1 annotations to child the production (1 annotations to child ulation of myeloid leukocyte cytokine production involved of dendritic cell cytokine production (1 annotations to child of tumor necrosis factor superfamily cytokine production or ulation of tumor necrosis factor superfamily cytokine production or ulation of tumor necrosis factor superfamily cytokine production production or ulation of tumor necrosis factor superfamily cytokine production or production of tumor necrosis factor superfamily cytokine production or produ	rms) rms) nnotations to child terms) (1 annotations to child terms) nse (1 annotations to child terms) esponse (1 annotations to child terms) Id terms) d in immune response (1 annotations to child terms) Id terms) (3 annotations to child terms) oduction (1 annotations to child terms) duction (2 annotations to child terms)	,
Target: nucleotide binding of GO Process Term: regulation of GO Process Term: positive regu GO Process Term: regulation of GO Process Term: positive regu GO Process Term: positive regu GO Process Term: regulative regu GO Process Term: regulative regulation GO Process Term: regulation GO P	igomerization domain containing 2 (NOD-like receipt of cytokine production (9 annotations to child terms) ulation of cytokine production (same barrowards to chine eff of cytokine production involved in immune response ulation of cytokine production involved in immune response ulation of cytokine production involved in inflammatory re- of dendritic cell cytokine production involved in inflammatory to child ulation of cytokine production involved in inflammatory to dendritic cell cytokine production (1 annotations to child ulation of dendritic cell cytokine production (1 annotations to child ulation of dendritic cell cytokine production (1 annotations to child)	eptor family) ms) nnotations to child terms) (1 annotations to child terms) nse (1 annotations to child terms) esponse (1 annotations to child terms) d terms) as to child terms)	

Example search results for 'regulation of cytokine production' shows hits against targets under the GtoImmuPdb process category 'Cytokine production & signalling'.



Example search results for 'Granulocytes' shows hits against targets under the GtoImmuPdb cell type category 'Granulocytes'.