Guide to IMMUNOPHARMACOLOGY

Immuno Process Association Data

Author: Dr. Simon D. Harding

This document describes the immuno process association data that has been incorporated into the Guide to IMMUNOPHARMACOLOGY (GtoImmuPdb).

Defining GtoImmuPdb Process Categories

GtoImmuPdb has defined its own set of top-level immunological process categories against which targets in the database can be annotated and which form the basis of organising, navigating and searching for immunological processes and associations.

These categories are:
- **Barrier Integrity**
- **Inflammation (innate response)**
  - **including pattern recognition, macrophage activation, phagocytosis and granulopoesis**
- **Antigen Presentation**
- **T cell activation (adaptive)**
- **B cell activation (adaptive)**
- **Immune regulation**
- **Tissue Repair**
- **Immune System Development**
- **Cytokine Production & Signalling**
- **Chemotaxis & Migration**
- **Cellular Signalling**

We have associated sets of Gene Ontology (GO) terms with each of these categories. This enables us to auto-curate targets annotated to any of those terms (or their children) by GO into our top-level immunological categories.

The GO terms associated with our immunological categories are:

Barrier Integrity
- entry into host (GO:0044409)
- epithelial cell-cell adhesion (GO:0090136)

Inflammation (innate response)
- GO:0006954 inflammatory response
- GO:0002532 production of molecular mediator involved in inflammatory response
- GO:0050900 leukocyte migration
- GO:0050727 regulation of inflammatory response
- GO:0045087 innate immune response

- GO:0045088 regulation of innate immune response
- GO:0006909 phagocyotosis
- GO:0002366 leukocyte activation invloved in immune responses
- GO:0002369 leukocyte activation invloved in inflammatory responses
- GO:0050902 leukocyte adhesive activation
- GO:0002274 myeloid leukocyte activation
- GO:0002270 plasmacytoid dendritic cell activation
- GO:0038187 pattern recognition receptor activity

Antigen Presentation
- GO:0019882 antigen processing and presentation
- GO:0002404 antigen sampling in mucosal-associated lymphoid tissue
- GO:0006897 endocytosis (inc. phagocytosis)

T cell activation (adaptive)
- GO:0042110 T cell activation
- GO:0002456 T cell mediated immunity
- GO:0031295 T cell costimulation
- GO:0002250 adaptive immune respsonse
- GO:0002819 regulation of adaptive immune response
- GO:0070231 T cell apoptotic processes

B cell activation (adaptive)
- GO:0042113 B cell activation
- GO:0019724 B cell mediated immunity
- GO:0031296 B cell costimulation
- GO:0001783 B cell apoptotic processes
- GO:0048305 immunoglobin secretion
- GO:0002250 adatpive immune respsonse
- GO:0002819 regulation of adaptive immune response

Immune Regulation
- GO:0002682 regulation of immune system process
- GO:0050727 regulation of inflammatory response
- GO:0001776 leukocyte homeostasis
- GO:0002262 myeloid cell homeostasis

Tissue Repair
- GO:0042246 tissue regeneration
- GO:0090594 wound healing invloved in inflammatory response to wounding

Immune System Development
- GO:0002520 immune system development
- GO:0002200 somatic diversification of immune receptors

- GO:0002339 B cell selection
- GO:0045058 T cell selection
- GO:0002507 tolerance induction
- GO:0042386 hemocyte differentiation

Cytoline Production & Signalling
- GO:0034097 response to cytokine
- GO:0001816 cytokine production

Chemotaxis & Migration
- GO:0050900 leukocyte migration
- GO:0007159 leukocyte cell-cell adhesion
- GO:0032602 chemokine production
- GO:1990868 response to chemokine

Cellular Signalling
- GO:0002764 immune response-regulating signal transduction
- GO:0045321 leukocyte activation
- GO:0016567 protein ubiquitination
- GO:0035420 MAPK cascade involved in innate immune response

Obtaining GO data

GO data is obtain via an OBO file

http://purl.obolibrary.org/obo/go.obo

This file is then edited and exported using OBO-Edit (http://oboedit.org/) to restrict it to immuno-specific terms.

The output from OBO-Edit contains only terms that include or have as an ancestor in a specified set of GO terms that cover the GO terms used in the mappings to top-level categories (above)

Parsing OBO out to database

The edited OBO file is then parsed into the database and populates tables that contain the terms, IDs, definitions and is_a relationships. The is_a relationships are important as these are used by the website searches. This means a search on a parent term will not only search on that term specifically, but also on its children.

Java code parses the file are executes SQL to populate and update tables that contains object IDs (targets) and the GO IDs they are annotated with, along with the GO evidence code. This information is obtained from UniProt. An output file is obtained by directly accessing UniProt and collecting lists of targets, for Homo sapiens that are cross-referenced in GtoPdb (all executed within our Java code).

http://www.uniprot.org/uniprot/?query=organism%3A%22Homo+sapiens+%5B9606%5D%22&sort=score&format=txt

Auto-curating targets to top-level processes via GO

After populating the underlying GO process tables, including the table that store the target annotated to these terms, further Java code is used to auto-curate targets to the top-level process categories based on their GO annotations. This code either removes, updates or inserts associations based on the latest GO annotations and ontology.

In essence, this identifies if a target is annotated to a GO term that corresponds to any of the GO terms (or children of those terms) listed under each top-level category (see above **Defining GtoImmuPdb Process Categories**).

Updating GO evidence code

In addition we store the GO evidence code. This flag informs whether the association between a target and a top-level process category is based on GO annotations, GO annotation (with only IEA evidence), or not based on GO annotations at all.

This level of annotation is part of our effort to distinguish between targets associated to processes (via GO only) and those that our curatorial team have identified as being of immunological relevance. It also distinguishes associations from GO that only have IEA evidence (therefore not reviewed by GO curator).

A full list of the annotations of GtoP targets against immune process categories is detailed in the spreadsheet (**UniProt_GO_Annotation_in_GtoImmuPdb.xls**).