

Cross-Product Development of the Cell Ontology

Alexander Diehl
Mouse Genome Informatics
The Jackson Laboratory

Skeletal Anatomy Jamboree
April 9, 2010

The Cell Ontology

- An OBO-Foundry candidate ontology for in vivo cell types
- Initially developed by Jonathan Bard, Seung Rhee, and Michael Ashburner *Genome Biology*, 6:R21 (2005)
- Currently relies on *is_a* and *develops_from* relationships, with extensive multiple inheritance
- The Cell Ontology = Cell Type Ontology, “CL”

Cell Ontology and GO

- Alexander Diehl and Chris Mungall are leading a project to revise the Cell Ontology
- Goal: Increase CL's utility as a source for cell type-specific GO terms and in co-annotation with GO terms
- Funded by a two-year ARRA Competitive Revision to the main GO Consortium grant; funding began on September 30, 2009
- One full time curator reporting to Alexander Diehl and a part-time software engineer

Increasing the Utility of the CL

- Rebuild ontology via logical definitions based on cross-products
- Extend the content of the CL
 - developmental cells, neuronal cells
- Enrich the GO
- 1st project is developing the hematopoietic cell type terms into a full logical-definition/cross product format

Logical Definitions/Cross-Products

- Define an ontology term logically through necessary and sufficient conditions, which are specified through the relation of a genus term to specific differentia terms in the same or different ontologies.

Kupffer cell

Textual definition:

"A tissue-resident macrophage of the reticuloendothelial system found on the luminal surface of the hepatic sinusoids.

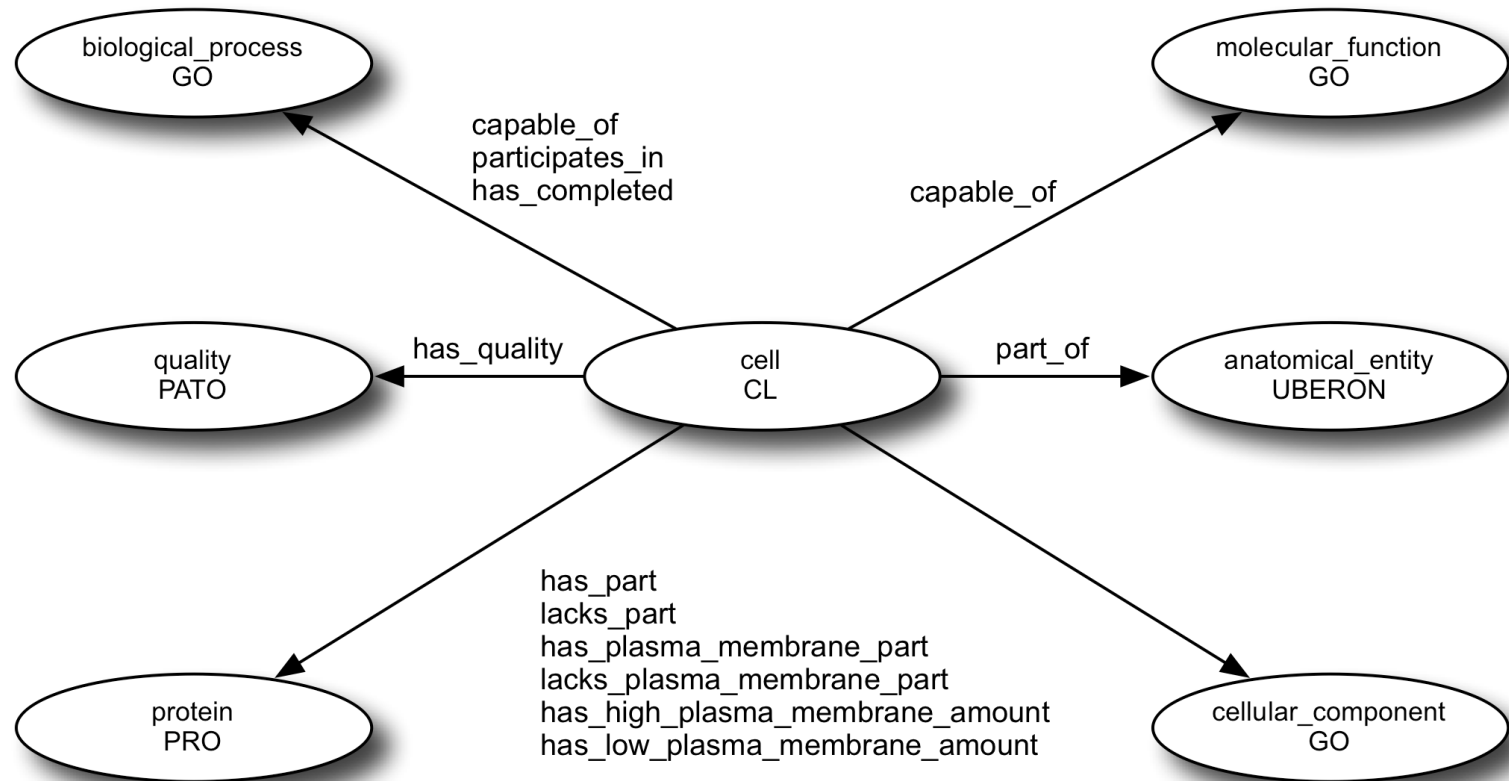
Logical definition:

is_a: CL:0000864 ! tissue-resident macrophage

intersection_of: CL:0000864 ! tissue-resident macrophage

intersection_of: part_of UBERON:0001281 ! hepatic sinusoid

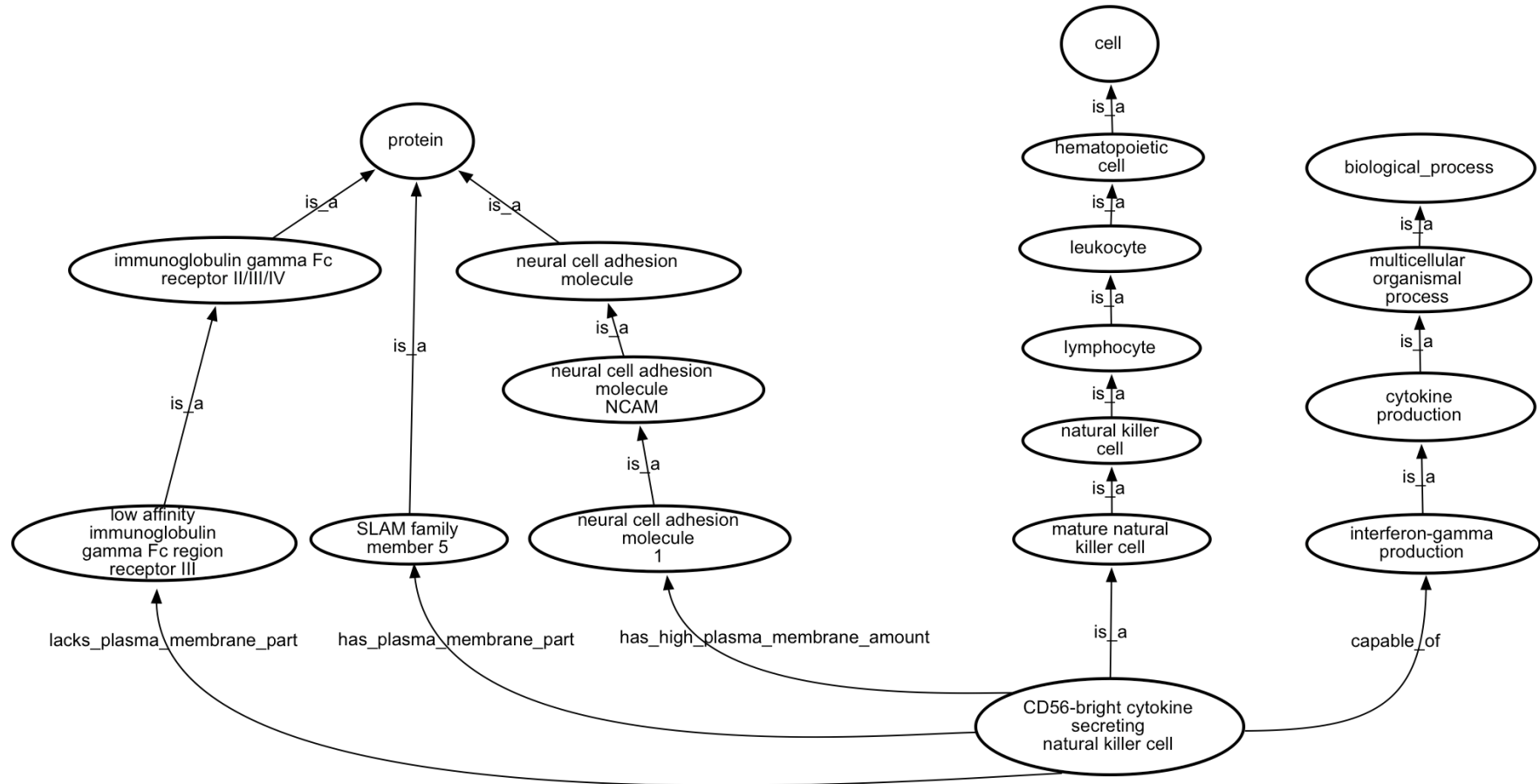
Ontologies Utilized for Cross-Products



CD56-bright cytokine secreting natural killer cell

- [Term]
- id: CL:0000938
- name: CD56-bright cytokine secreting natural killer cell
- namespace: cell
- def: "Mature NK cell that has the phenotype CD56-bright, CD16-negative, and CD84-positive with the function to secrete interferon-gamma but is not cytotoxic." [GOC :tfm, XX:PAM-ADD]
- synonym: "CD56-bright cytokine secreting NK cell" EXACT []
- is_a: CL:0000824 ! mature natural killer cell
- intersection_of: CL:0000824 ! mature natural killer cell
- intersection_of: capable_of GO:0032609 ! interferon-gamma production
- intersection_of: has_high_plasma_membrane_amount PRO:000001024 ! neural cell adhesion molecule 1
- intersection_of: has_plasma_membrane_part PRO:000001319 ! SLAM family member 5
- intersection_of: lacks_plasma_membrane_part PRO:000001483 ! low affinity immunoglobulin gamma Fc region receptor III
- disjoint_from: CL:0000939 ! cytotoxic CD56-dim natural killer cell

CD56-bright cytokine secreting natural killer cell



CD56-bright cytokine secreting natural killer cell

OBO-Edit version 2.1-beta1: hemo_CL.obo

File Edit Layout Editors Viewers Search Tools Metadata Reasoner Summary Config Help

Ontology Tree Editor

- Classes
 - amino acid chain
 - anatomical entity
 - biological_process
 - cell
 - cell in vivo
 - hematopoietic cell
 - blood cell
 - hematopoietic lineage restricted progenitor cell
 - hematopoietic multipotent progenitor cell
 - hematopoietic oligopotent progenitor cell
 - hematopoietic stem cell
 - leukocyte
 - dendritic cell
 - lymphocyte
 - disjoint from dendritic cell
 - lymphocyte of B lineage
 - natural killer cell
 - immature natural killer cell
 - mature natural killer cell
 - CD56-bright cytokine secreting natural killer cell
 - cytotoxic CD56-dim natural killer cell
 - disjoint from immature natural killer cell
 - pre-natural killer cell
 - T cell
 - mononuclear cell
 - myeloid leukocyte
 - myeloid cell
 - cellular_component
 - molecular_function

Graph Editor

```
graph TD
    cell --> hematopoietic_cell[hematopoietic cell]
    hematopoietic_cell --> leukocyte
    leukocyte --> lymphocyte
    lymphocyte --> natural_killer_cell[natural killer cell]
    natural_killer_cell --> mature_natural_killer_cell[mature natural killer cell]
    mature_natural_killer_cell --> CD56_bright_cell[CD56-bright cytokine secreting natural killer cell]
```

Search Panel Search results: all_text_fields contains "CD56" (6 matches)

ID	Name
CL:0000989	CD11c-low plasmacytoid dendritic cell
CL:0000991	CD11c-negative plasmacytoid dendritic cell
CL:0000938	CD56-bright cytokine secreting natural killer cell
CL:0000990	conventional dendritic cell
CL:0000939	cytotoxic CD56-dim natural killer cell
PRO:00001024	neural cell adhesion molecule 1

Text Editor

ID: CL:0000938
Namespace: cell
Name: CD56-bright cytokine secreting natural killer cell

Definition * Comment Cross Products *

Intersection Genus: mature natural killer cell

Discriminating relations:

- has_plasma_membrane_part: SLAM family member 5
- capable_of: interferon-gamma production
- has_high_plasma_membrane_amount: neural cell adhesion molecule 1
- lacks_plasma_membrane_part: v affinity immunoglobulin gamma Fc region receptor III

Dbxrefs Synonyms * Subsets

CD56-bright cytokine secreting NK cell
Scope: Exact Synonym

Commit Revert

CD56-bright cytokine secreting natural killer cell

Text Editor

ID CL:0000938

Namespace cell

Name CD56-bright cytokine secreting natural killer cell

Definition * Comment Cross Products *

Intersection Genus mature natural killer cell

Discriminating relations

has_plasma_membrane_part	SLAM family member 5
capable_of	interferon-gamma production
has_high_plasma_membrane_amount	neural cell adhesion molecule 1
lacks_plasma_membrane_part	v affinity immunoglobulin gamma Fc region receptor III

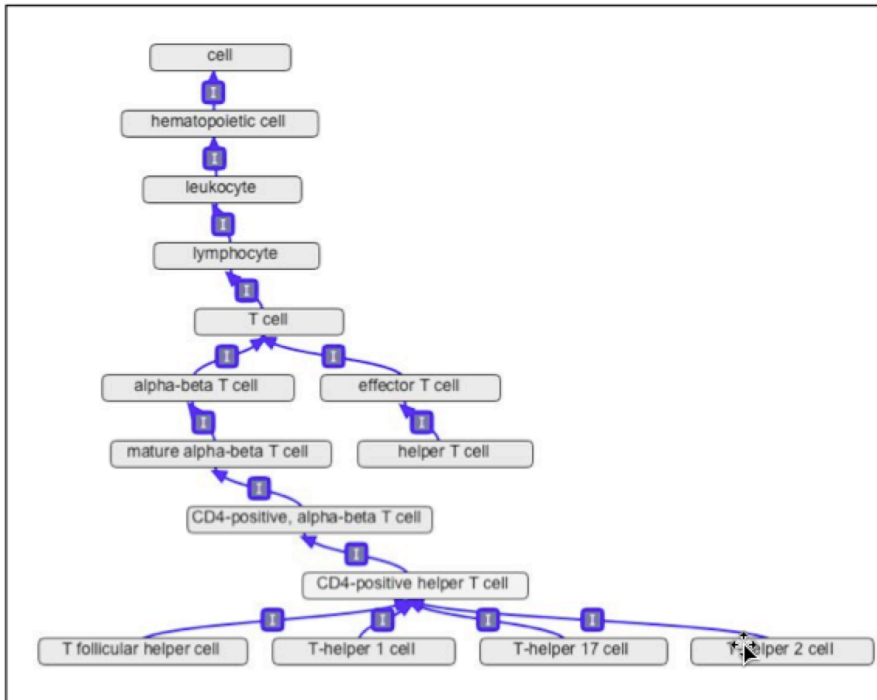
Dbxrefs Synonyms * Subsets

CD56-bright cytokine secreting NK cell
Scope: *Exact Synonym*

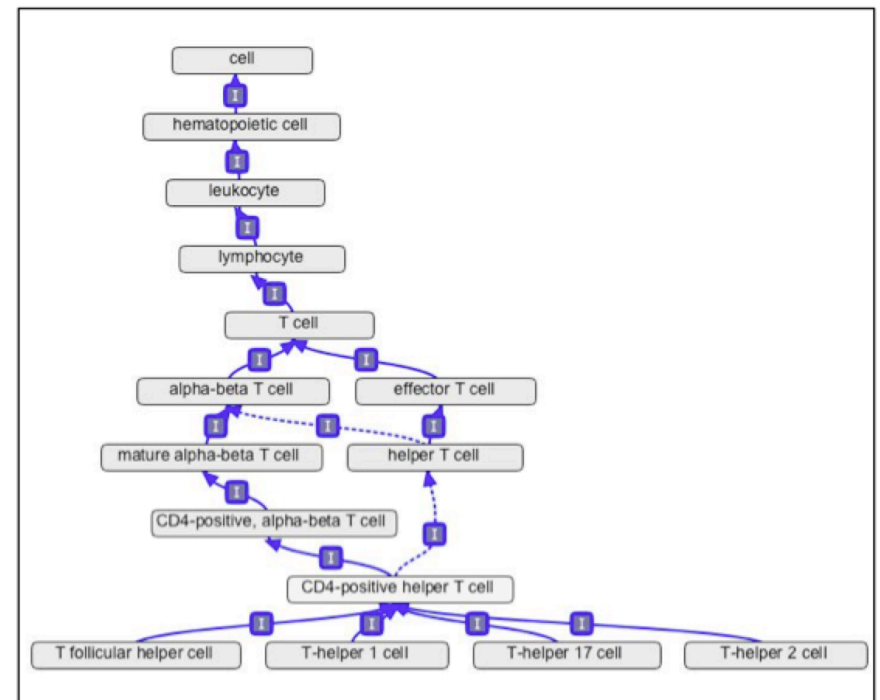
+ -

Commit Revert

Benefits of Logical Definitions/Cross-Products



Pre-reasoning



Post-reasoning

Benefits of Logical Definitions/Cross-Products

[Term]

id: CL:0000912

name: helper T cell

namespace: cell

def: "A effector T cell that provides help in the form of secreted cytokines to other immune cells." [GOC:add, GOC:tfm]

synonym: "helper T lymphocyte" EXACT

synonym: "helper T-cell" EXACT

synonym: "helper T-lymphocyte" EXACT

synonym: "T-helper cell" EXACT

is_a: CL:0000911 ! effector T cell

intersection_of: CL:0000911 ! effector T cell

intersection_of: capable_of GO:0002369 ! T cell cytokine production

intersection_of: has_plasma_membrane_part GO:0042105 ! alpha-beta T cell receptor complex

[Term]

id: CL:0000492

name: CD4-positive helper T cell

namespace: cell

def: "A CD4-positive, alpha-beta T cell that cooperates with other lymphocytes via direct contact or cytokine release to initiate a variety of immune functions." [GOC:add, GOC:tfm, ISBN: 0781735149, MESH:A.11.118.637.555.567.569.200.40]

synonym: "CD4-positive helper T lymphocyte" EXACT

synonym: "CD4-positive helper T-cell" EXACT

synonym: "CD4-positive helper T-lymphocyte" EXACT

synonym: "CD4-positive T-helper cell" EXACT

xref: FMA:70572

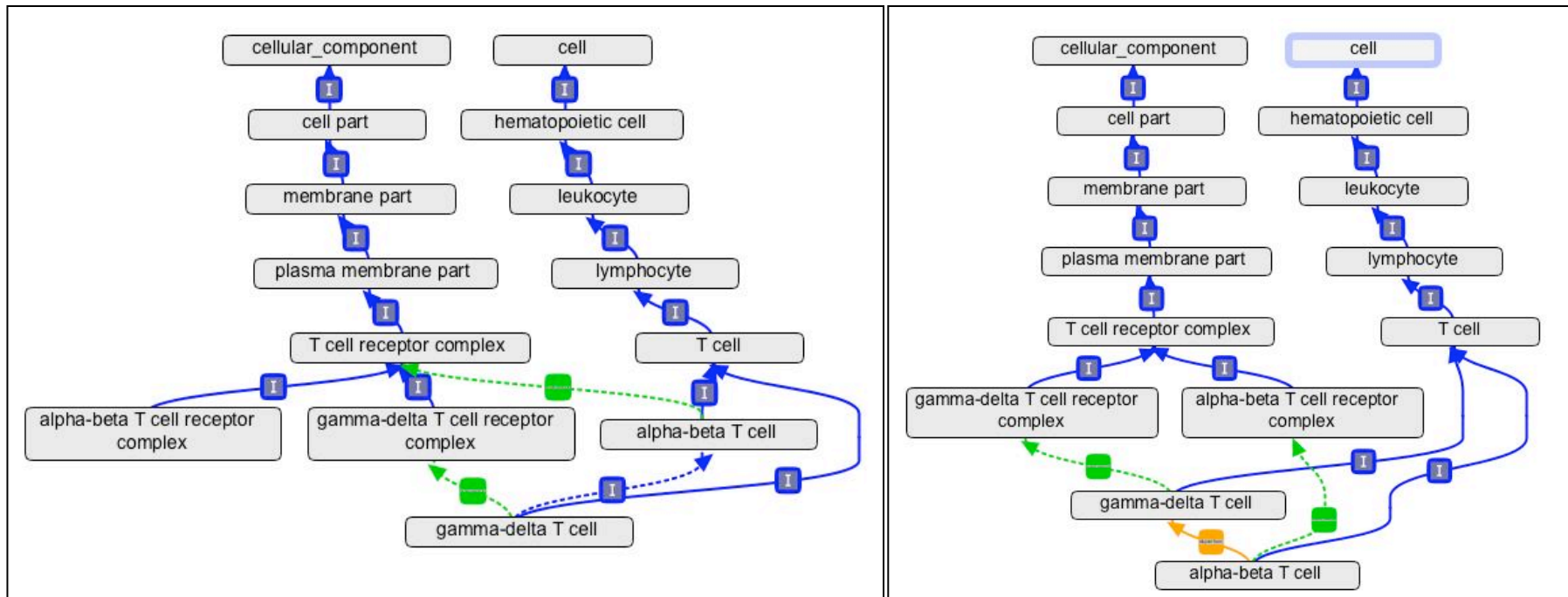
is_a: CL:0000624 ! CD4-positive, alpha-beta T cell

intersection_of: CL:0000624 ! CD4-positive, alpha-beta T cell

intersection_of: capable_of GO:0002369 ! T cell cytokine production

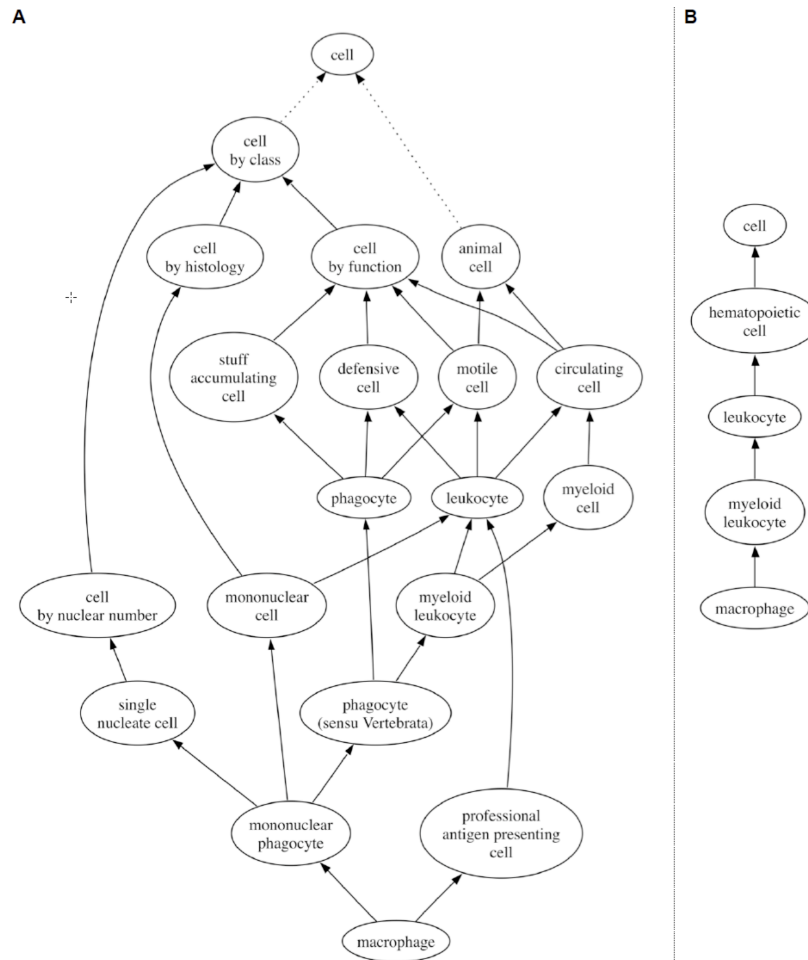
relationship: develops_from CL:0000896 ! activated CD4-positive, alpha-beta T cell

Benefits of Logical Definitions/Cross-Products

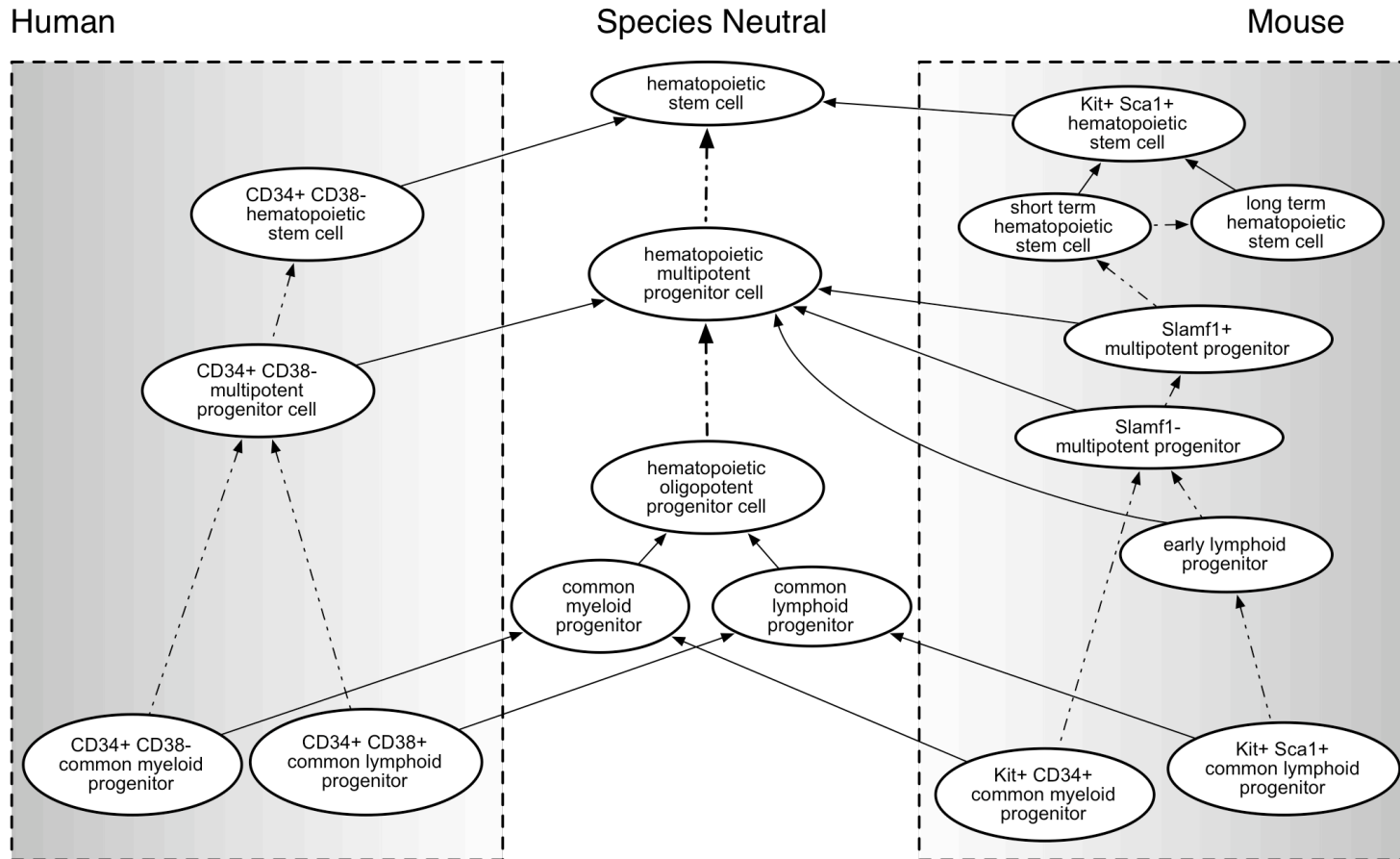


Reasoner shows error and allows for correction of logical definitions

Removal of Multiple Inheritance



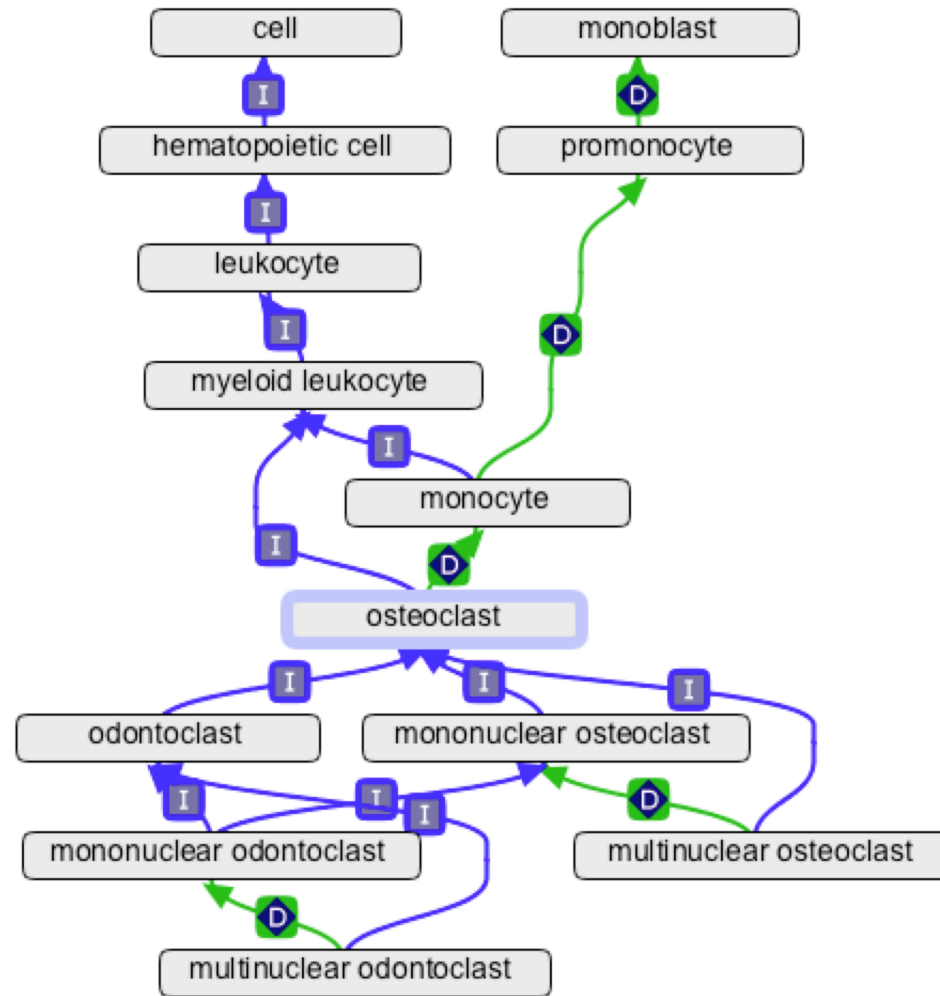
New Developmental Cell Types



Bone and Related Cell Types in CL

- osteocyte
- osteoblast
- osteoclast
- mononuclear osteoclast
- multinuclear osteoclast
- osteoprogenitor cell
- odontoblast
- odontocyte
- cementoblast
- cementocyte
- odontoclast
- mononuclear odontoclast
- multinuclear odontoblast
- chondroblast
- chondrocyte
- periarticular chondrocyte
- hypertrophic chondrocyte
- columnar chondrocyte

Bone and related Cell Types in CL



Summary of Progress

- 340 hematopoietic cell type terms now have cross product definitions
- 22 new developmental cell types added
- Reasoners in OBO-edit used to infer new relationships and flags inconsistencies in logic
- 20+ new terms requested for the GO
 - needed for cross product definitions
- Collaborations initiated with ImmPort, NIF & INCF (neurons), Virtual Library of Cell Images

Future Directions

- Restructure upper level ontology of the CL
 - hosting workshop on May 18-19, 2010 at JAX
- Greatly extend neuronal cell-types
 - collaborating with the Neuroscience Information Framework (Neurolex)
 - host a 2nd workshop in 2011 with Neuroscientists
- Applying CL to the GO
 - ensure that all cell types referenced by the GO are present in the CL
 - enhance curator's tools to specify the cell type in which a gene product is active

Acknowledgments

Participants in NIAID Cell Ontology Workshop

Martin Zand

R.E.W Hancock

Terry Meehan

Bjoen Peters

Elizabeth Gold

Jeremy Seto

Elena Naumova

Bali Pulendran

Alex Sette

Alison Yao

Ashley Xia

Alexander Diehl

Lindsay Cowell

Jingming Ma

Christopher Mungall

Christopher Cavnor

Thomas Kepler

Penelope Morel

Anastasia Nijnik

Richard Scheuermann

Alison Deckhut

Lynda Chiodetti

Timothy Gondre-Lewis

Anna Maria Masci

The Jackson Laboratory

Judith Blake

Morgan Hightshoe

Wade Valleau

The Protein Ontology

Cecilia N. Arighi

The Gene Ontology Consortium

Funding

NIAID

NHGRI HG000330 (MGD)

NHGRI HG002273 (GO)

NHGRI HG002273-09Z (CL)