

# Cross-Product Development of the Cell Ontology

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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
- 1<sup>st</sup> 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

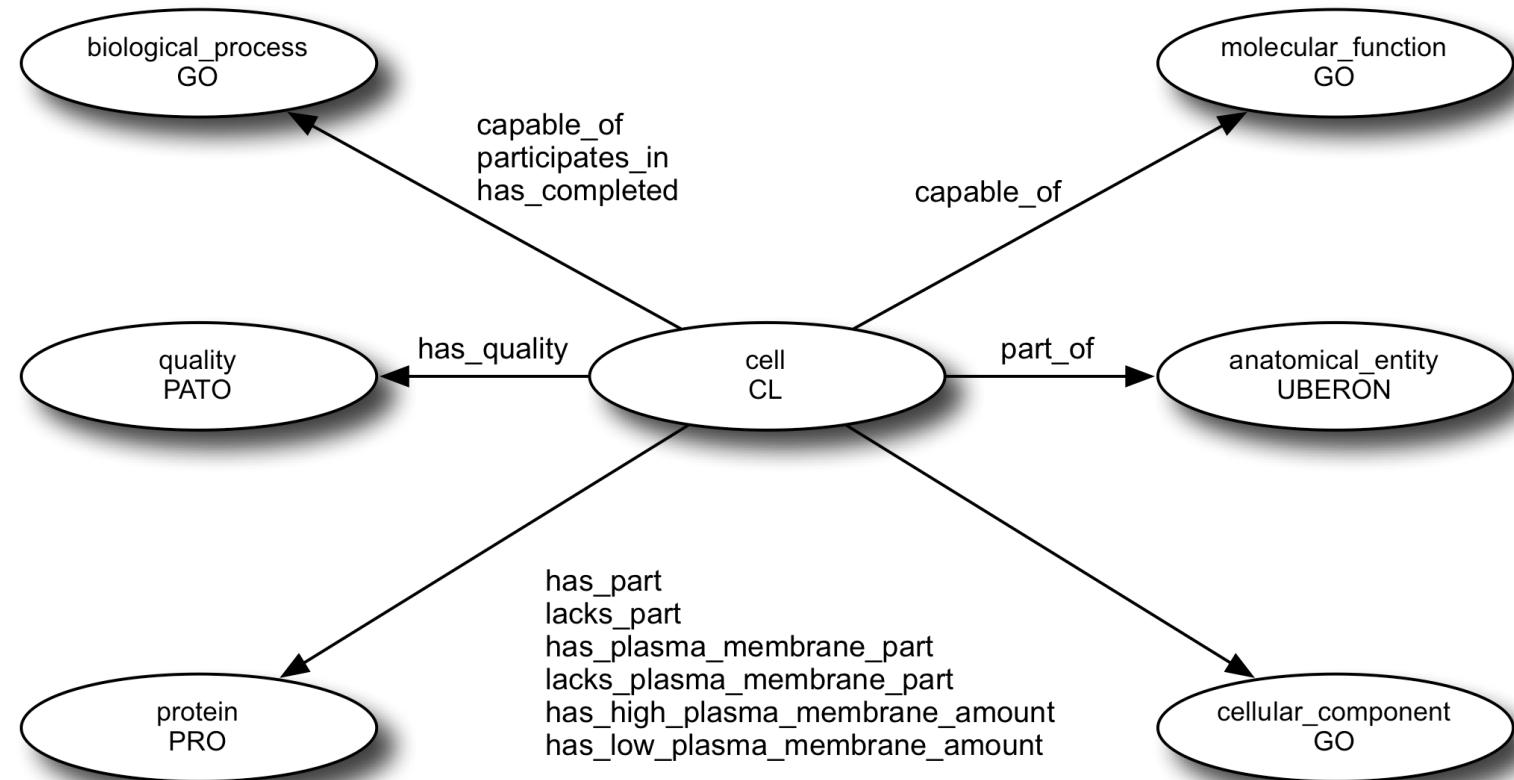
Textual definition:

"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
```

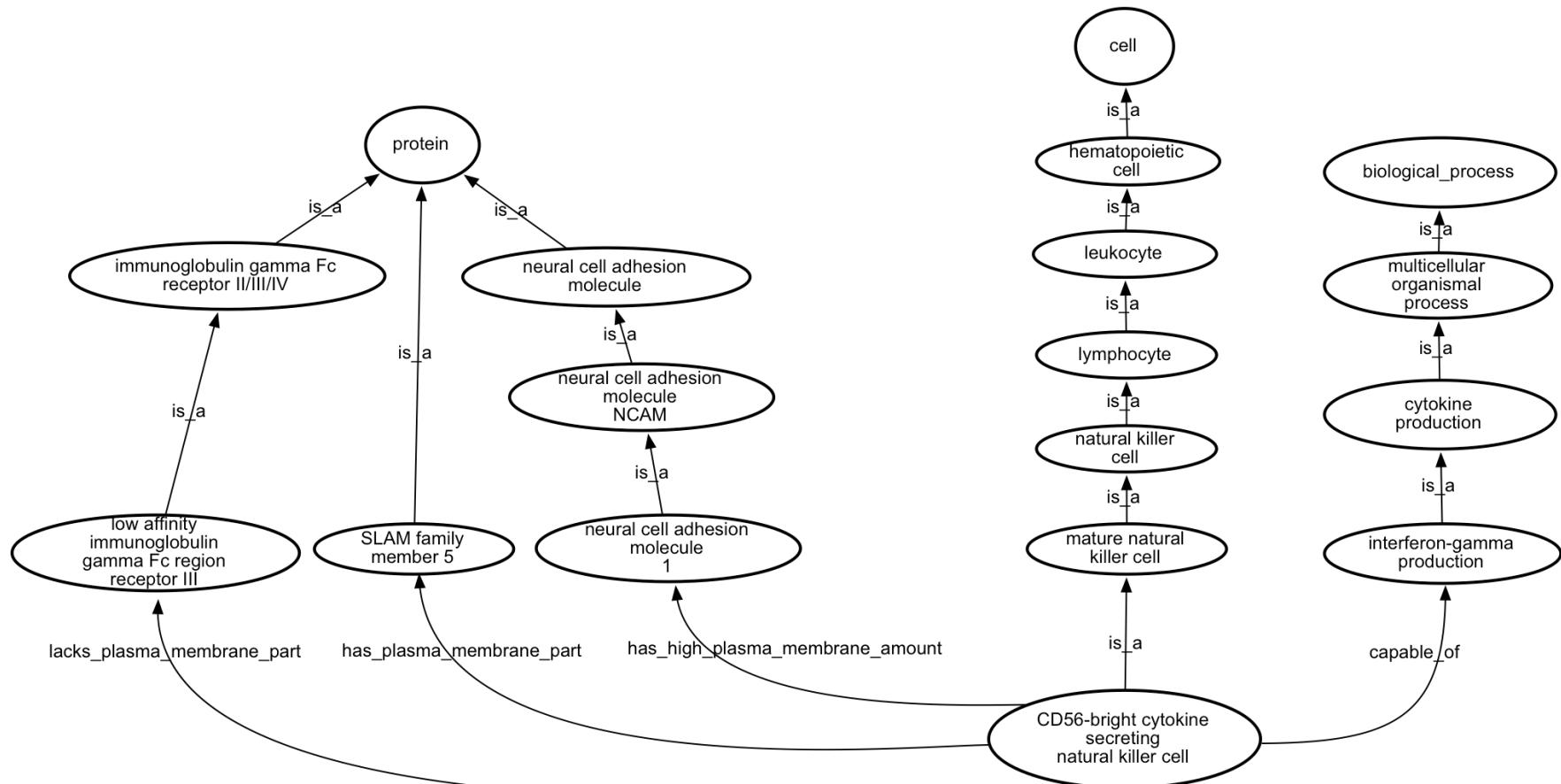
# Ontologies Utilized for Cross-Products



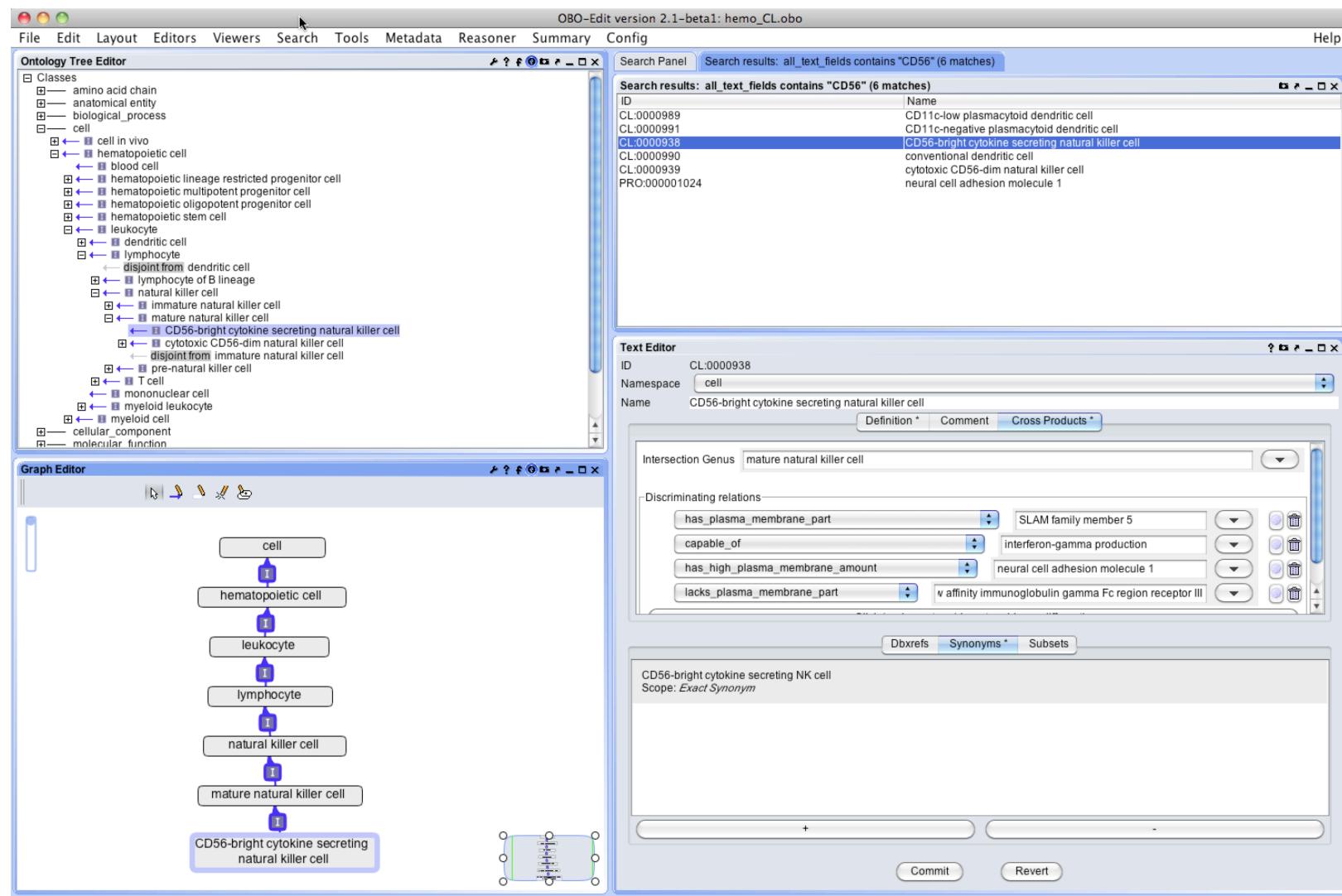
# CD56-bright cytokine secreting natural killer cell

- [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

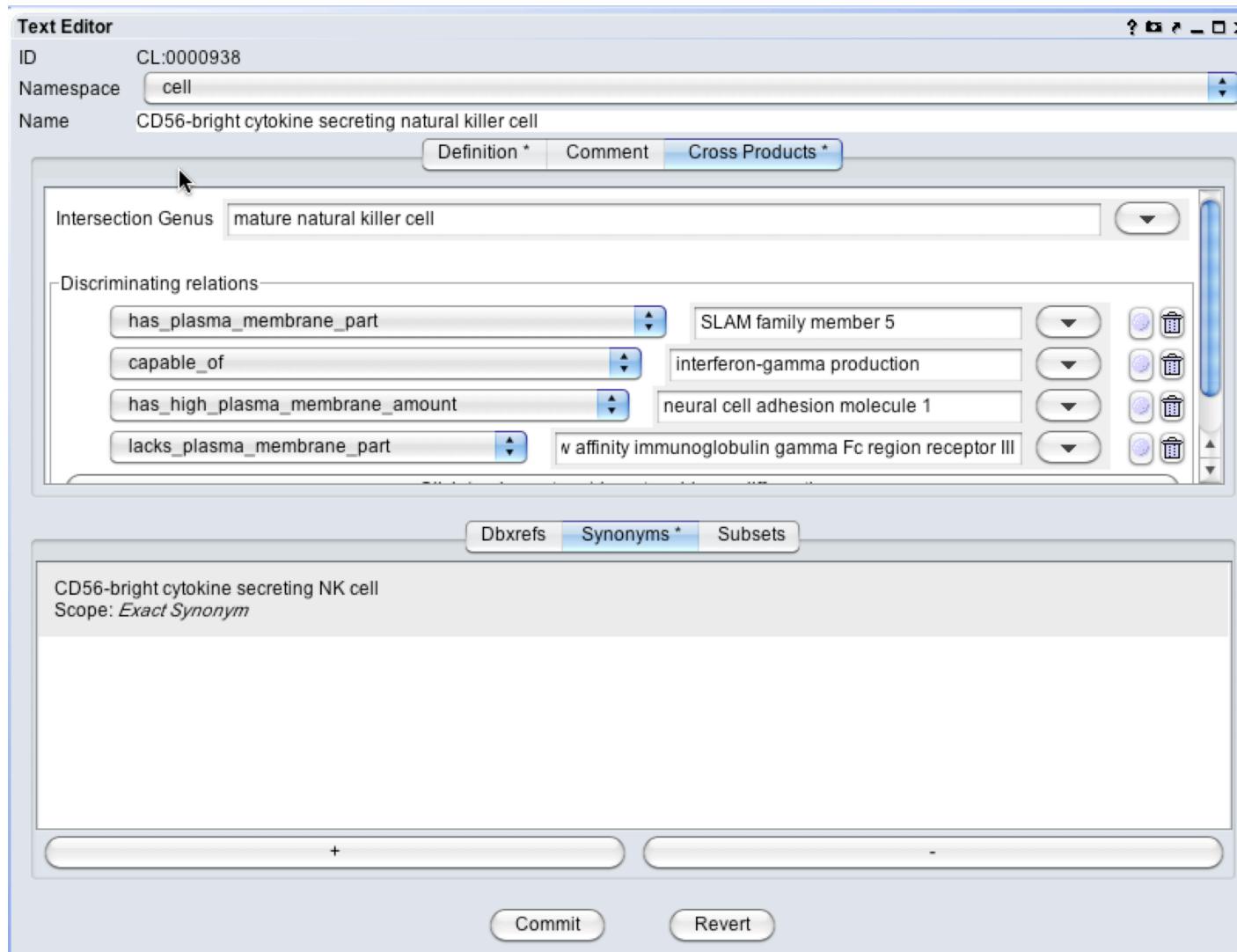
# CD56-bright cytokine secreting natural killer cell



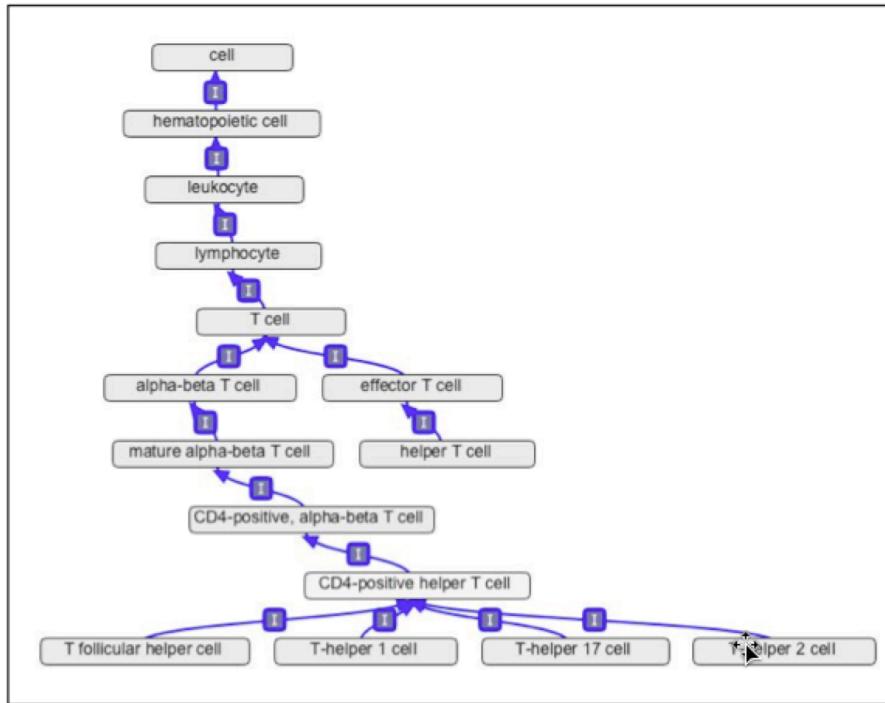
# CD56-bright cytokine secreting natural killer cell



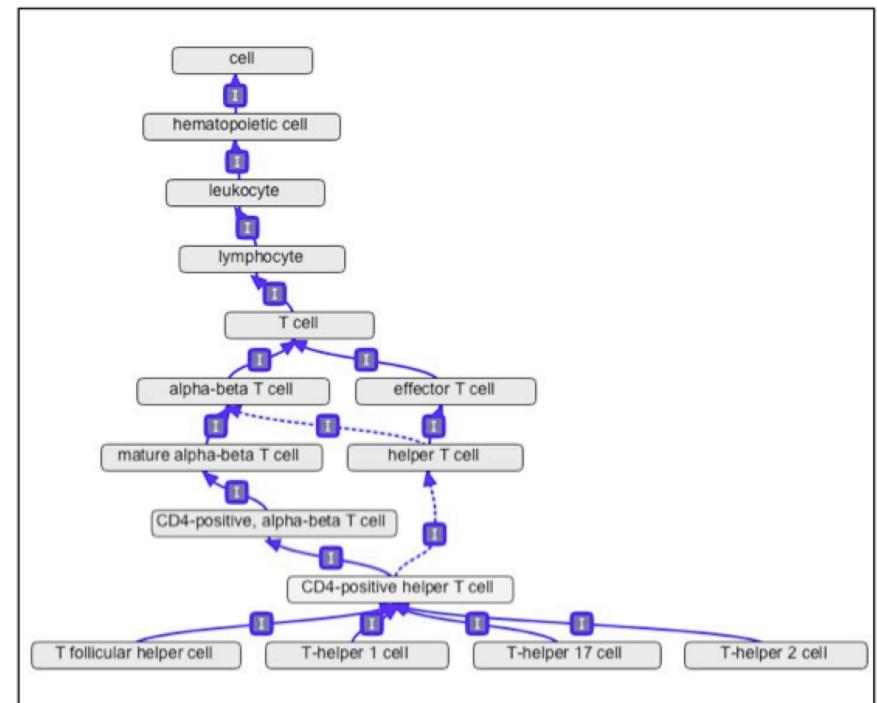
# CD56-bright cytokine secreting natural killer cell



# 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

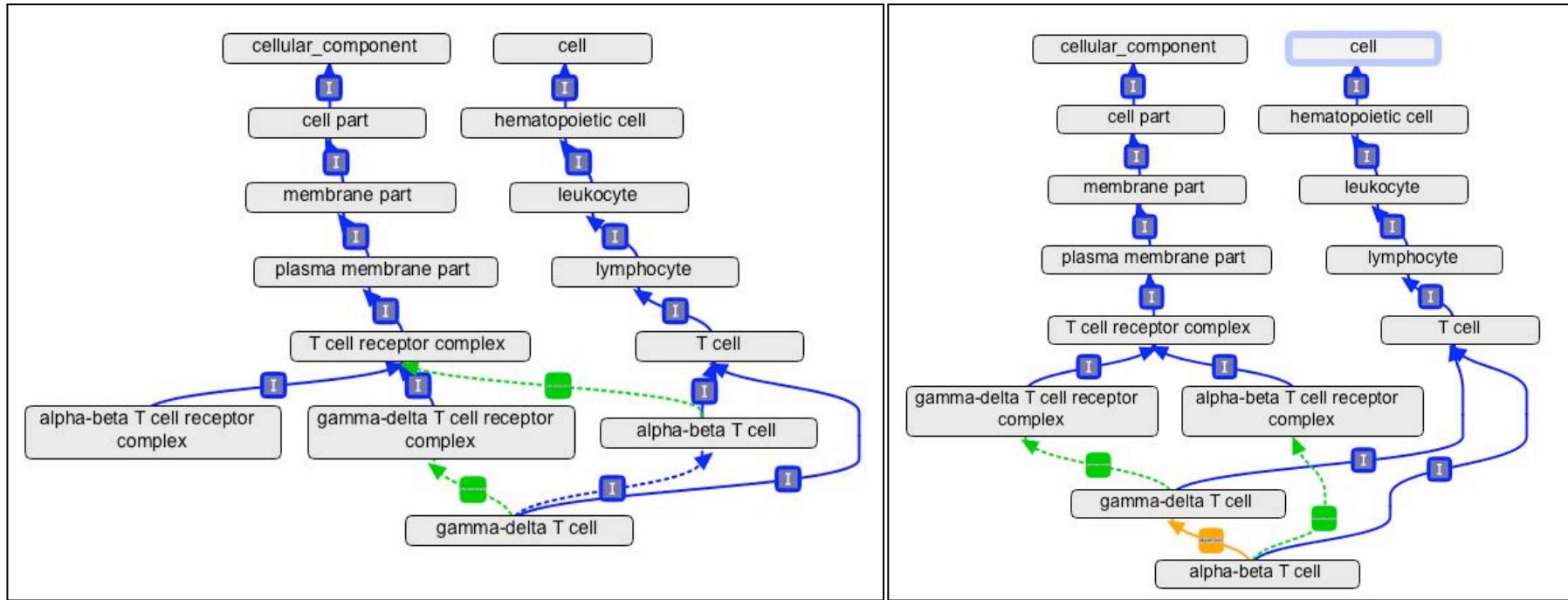
is\_a: CL:0000624 ! CD4-positive, alpha-beta T cell

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

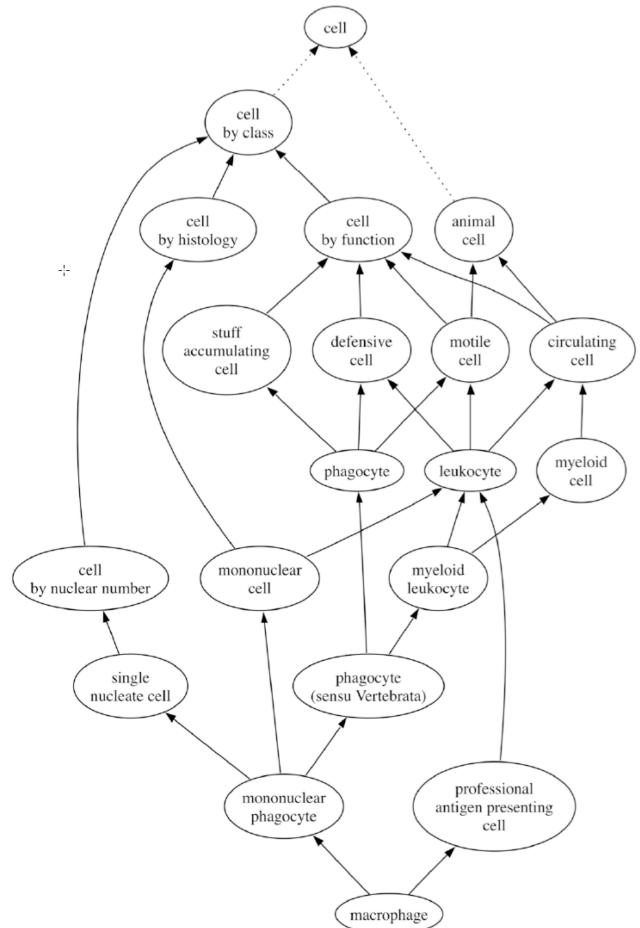
# Benefits of Logical Definitions/Cross-Products



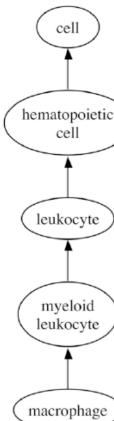
Reasoner shows error and allows for correction of logical definitions

# Removal of Multiple Inheritance

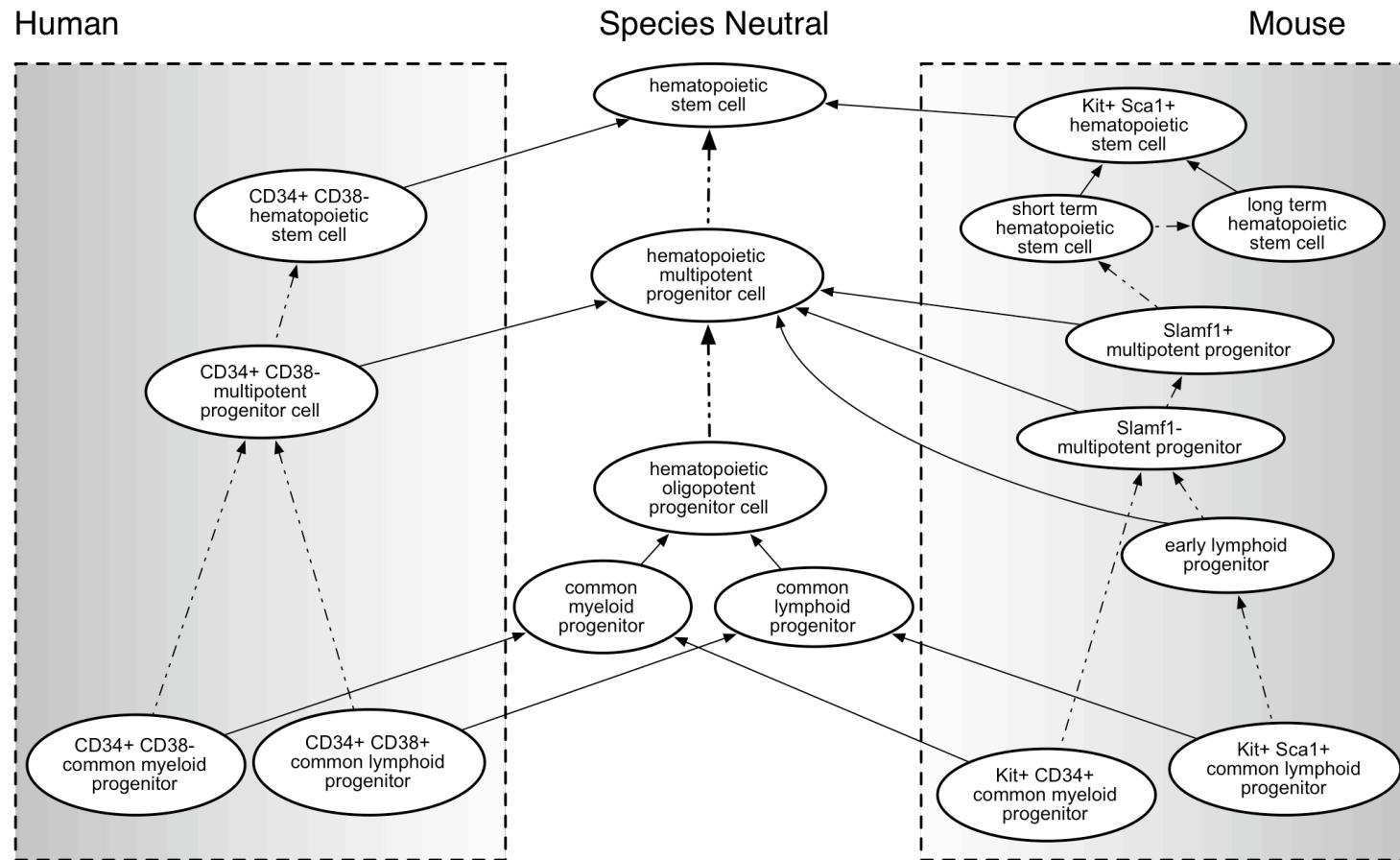
A



B



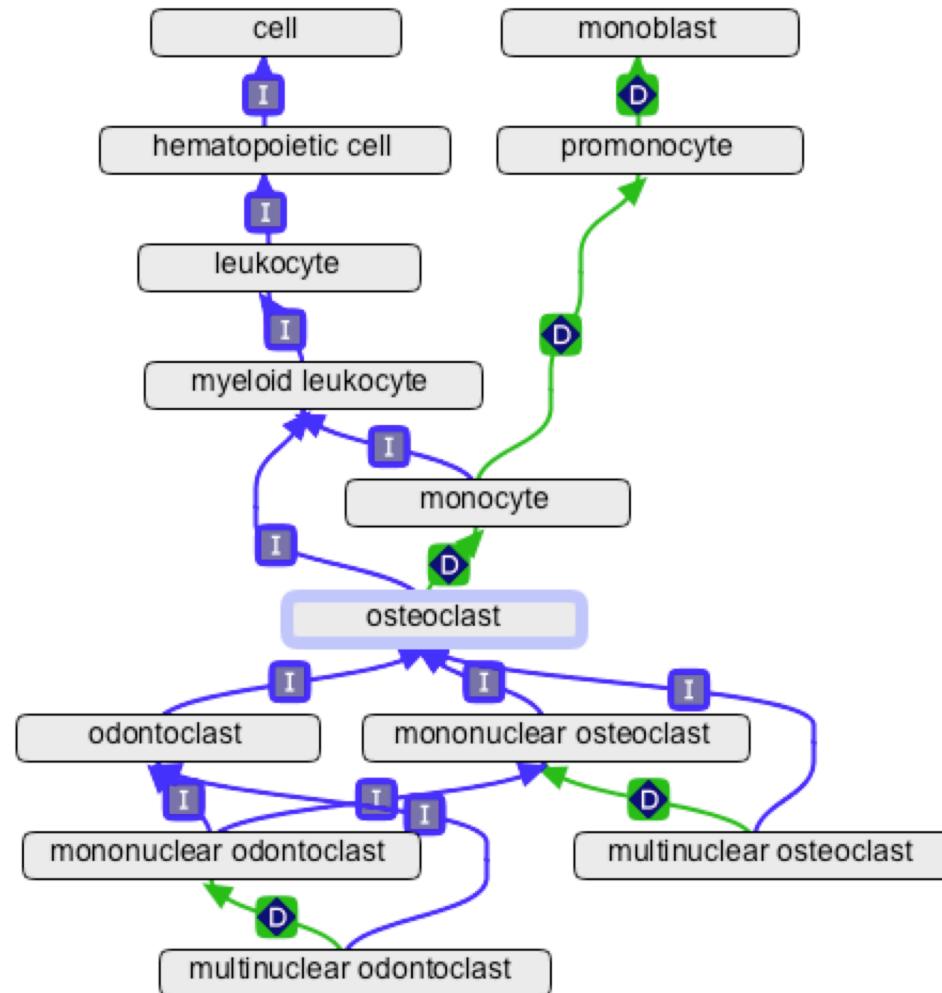
# New Developmental Cell Types



# 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 2<sup>nd</sup> 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	Lindsay Cowell
R.E.W Hancock	Jingming Ma
Terry Meehan	Christopher Mungall
Bjoen Peters	Christopher Cavnor
Elizabeth Gold	Thomas Kepler
Jeremy Seto	Penelope Morel
Elena Naumova	Anastasia Nijnik
Bali Pulendran	Richard Scheuermann
Alex Sette	Alison Deckhut
Alison Yao	Lynda Chiodetti
Ashley Xia	Timothy Gondre-Lewis
Alexander Diehl	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)