# Brucellosis Ontology (IDOBRU) and Vaccine Ontology (VO), two IDO and infectious disease related ontologies

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# Outline

- **IDOBRU and its applications**
- **VO and its applications**

# IDOBRU: Brucellosis Ontology

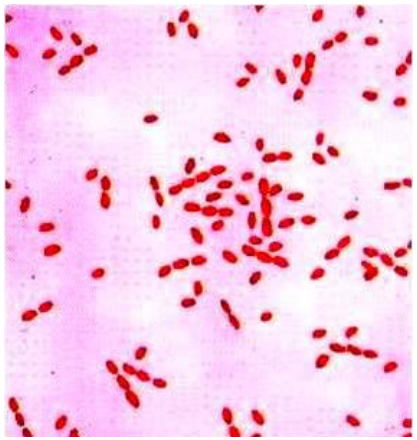
- An ontology in the domain of Brucella and brucellosis
- Aligned with the IDO-core.
- Wide coverage: host infection, transmission, symptoms, virulence factors, pathogenesis, diagnosis, vaccines, and treatments. Note: Brucella vaccines are imported from Vaccine Ontology (VO)

**References:**

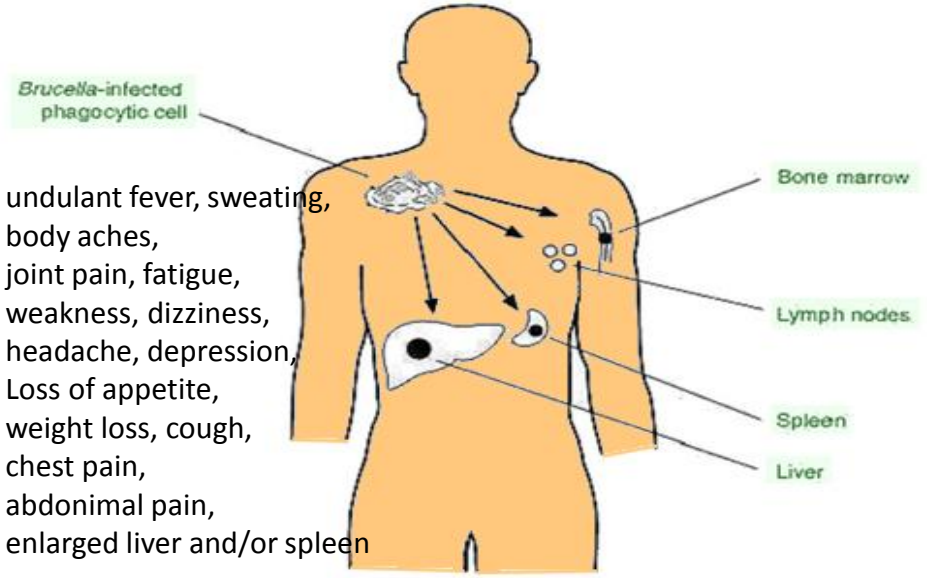

- Lin Y, Xiang Z, and He Y. Ontology-based representation and analysis of host-Brucella interactions. J Biomed Semantics. 2015, 6:37. DOI: 10.1186/s13326-015-0036-y. PMID: 26445639. PMCID: PMC4594885.
- Lin Y, Xiang Z, He Y. Brucellosis Ontology (IDOBRU) as an extension of the Infectious Disease Ontology. J Biomed Semantics. 2011 Oct 31;2(1):9. PMID: 22041276
- Lin Y, Xiang Z, and He Y. Ontology-based representation and analysis of host-Brucella interactions. J Biomed Semantics. 2015, 6:37. PMID: 26445639.

# Brucellosis and *Brucella*

- Brucellosis is a zoonotic infectious disease
- Pathogen: facultative intracellular Gram-negative bacteria *Brucella spp*
- Human brucellosis: 500,000 new cases annually

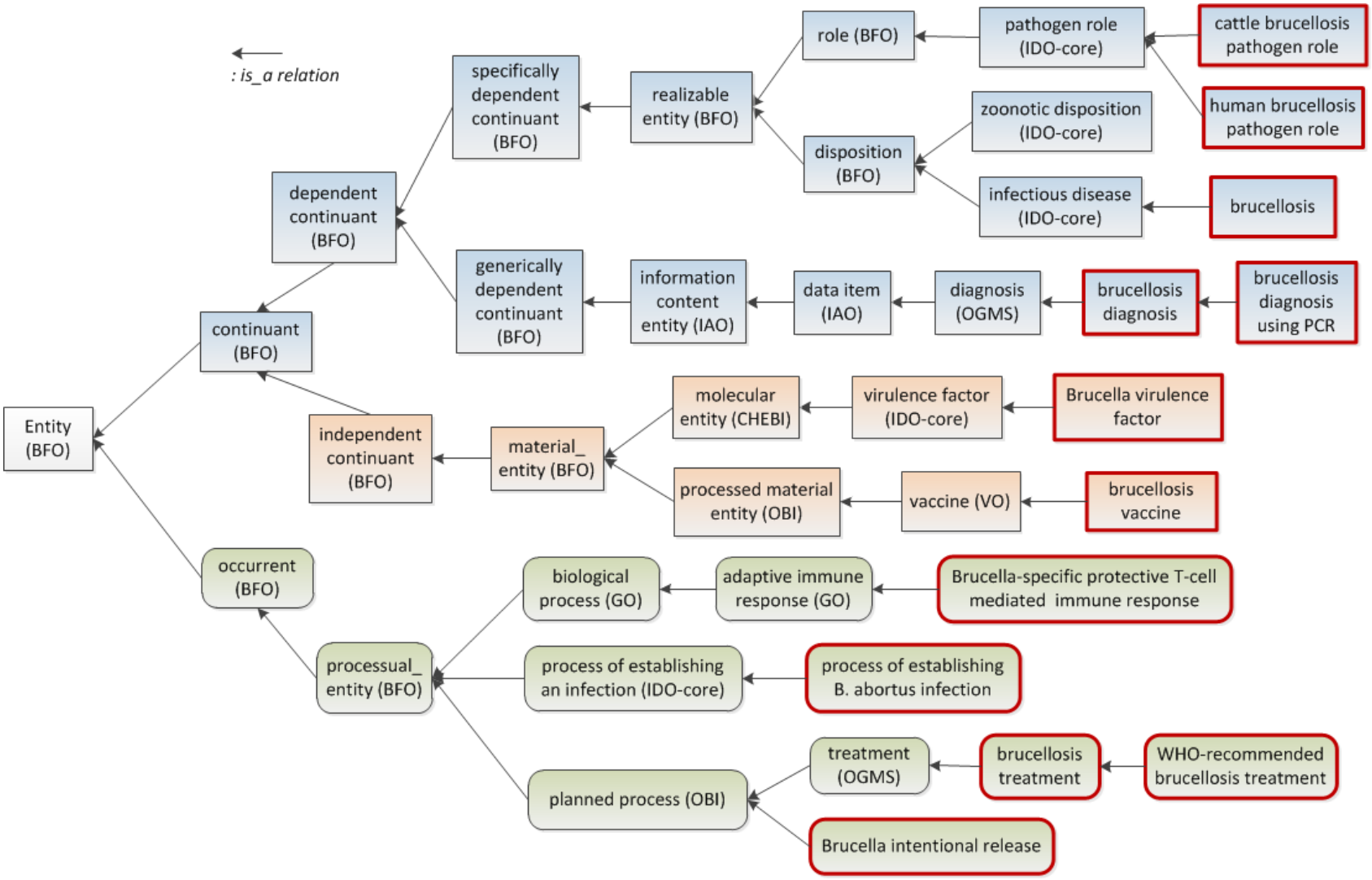


- Symptoms of human brucellosis is a systematic manifestation
- Human vaccine is not available



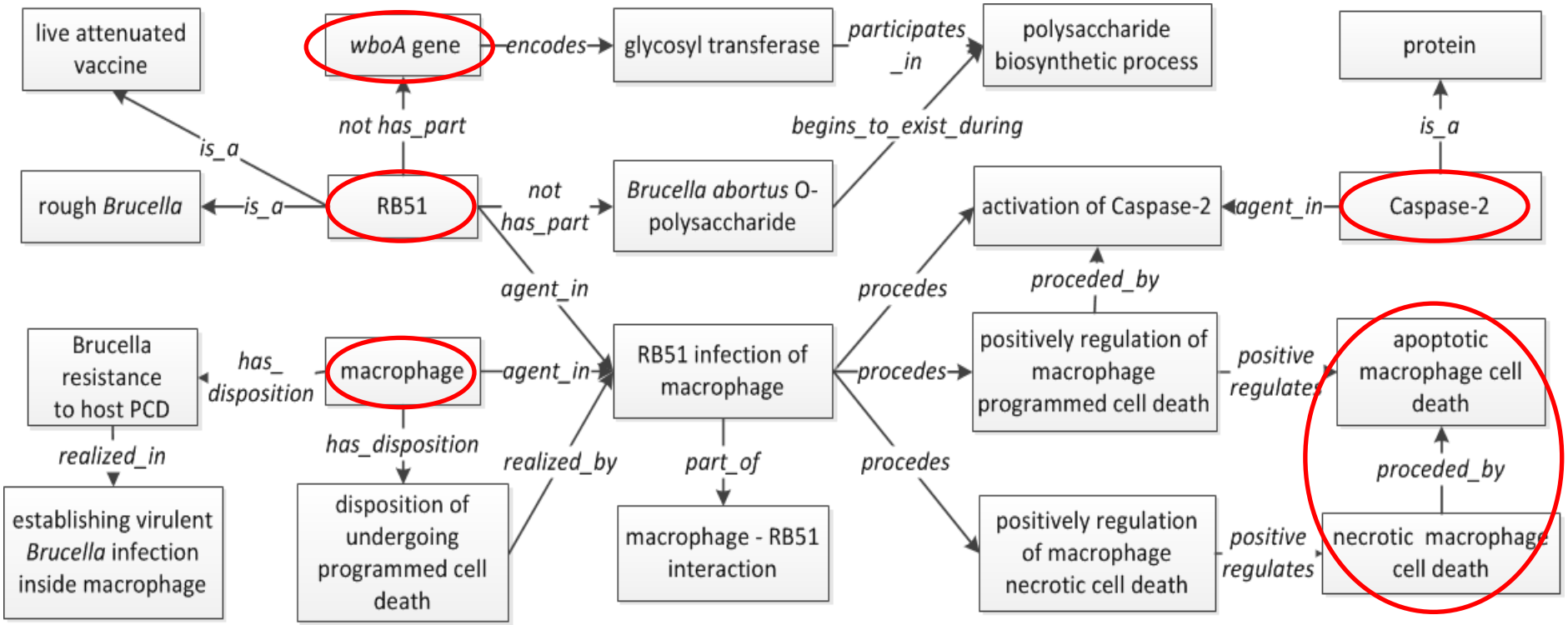

undulant fever, sweating,
body aches,
joint pain, fatigue,
weakness, dizziness,
headache, depression,
Loss of appetite,
weight loss, cough,
chest pain,
abdonimal pain,
enlarged liver and/or spleen
….

# IDOBUR major hierarchy

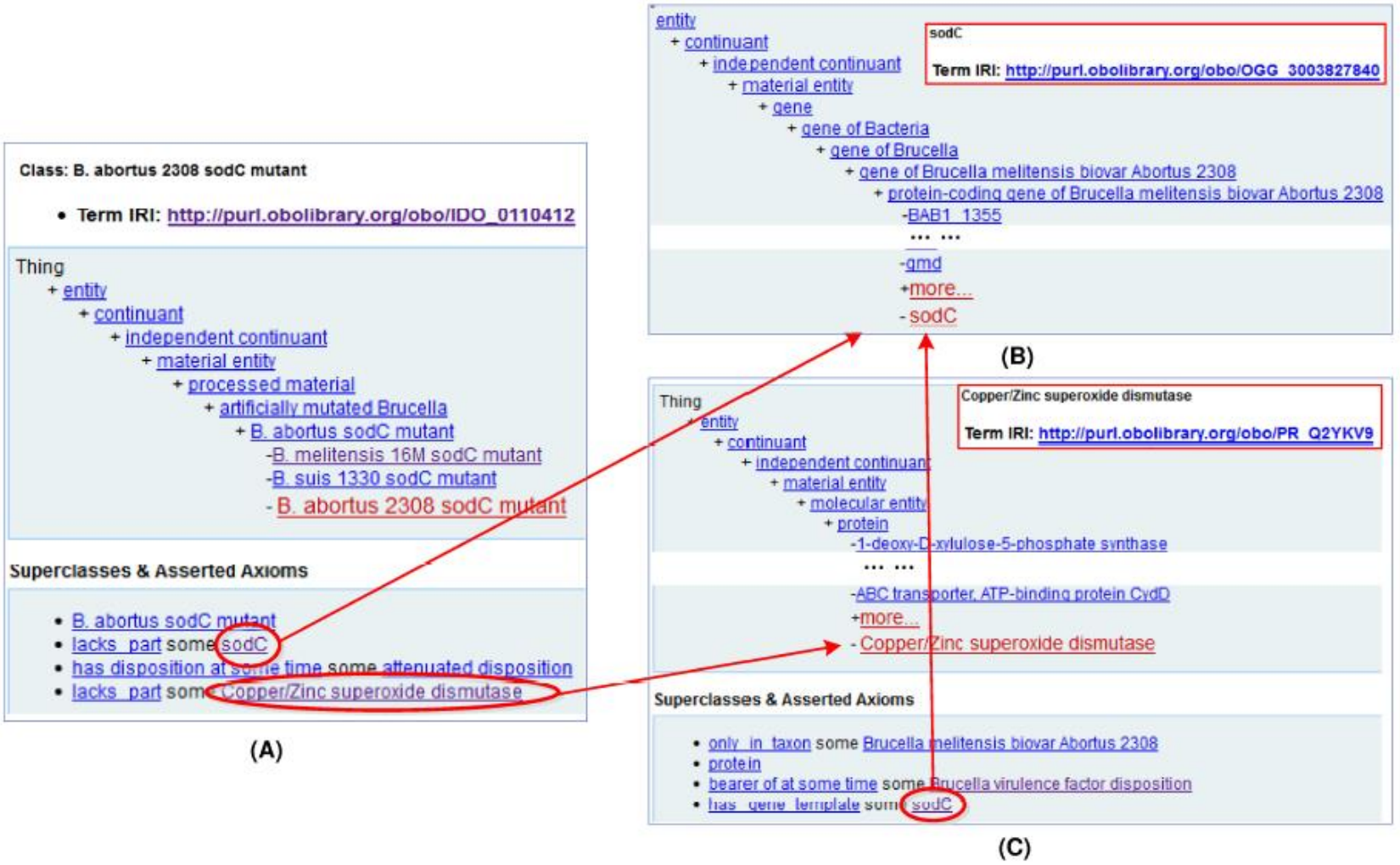


# Ontological representation of RB51-induced macrophage cell death

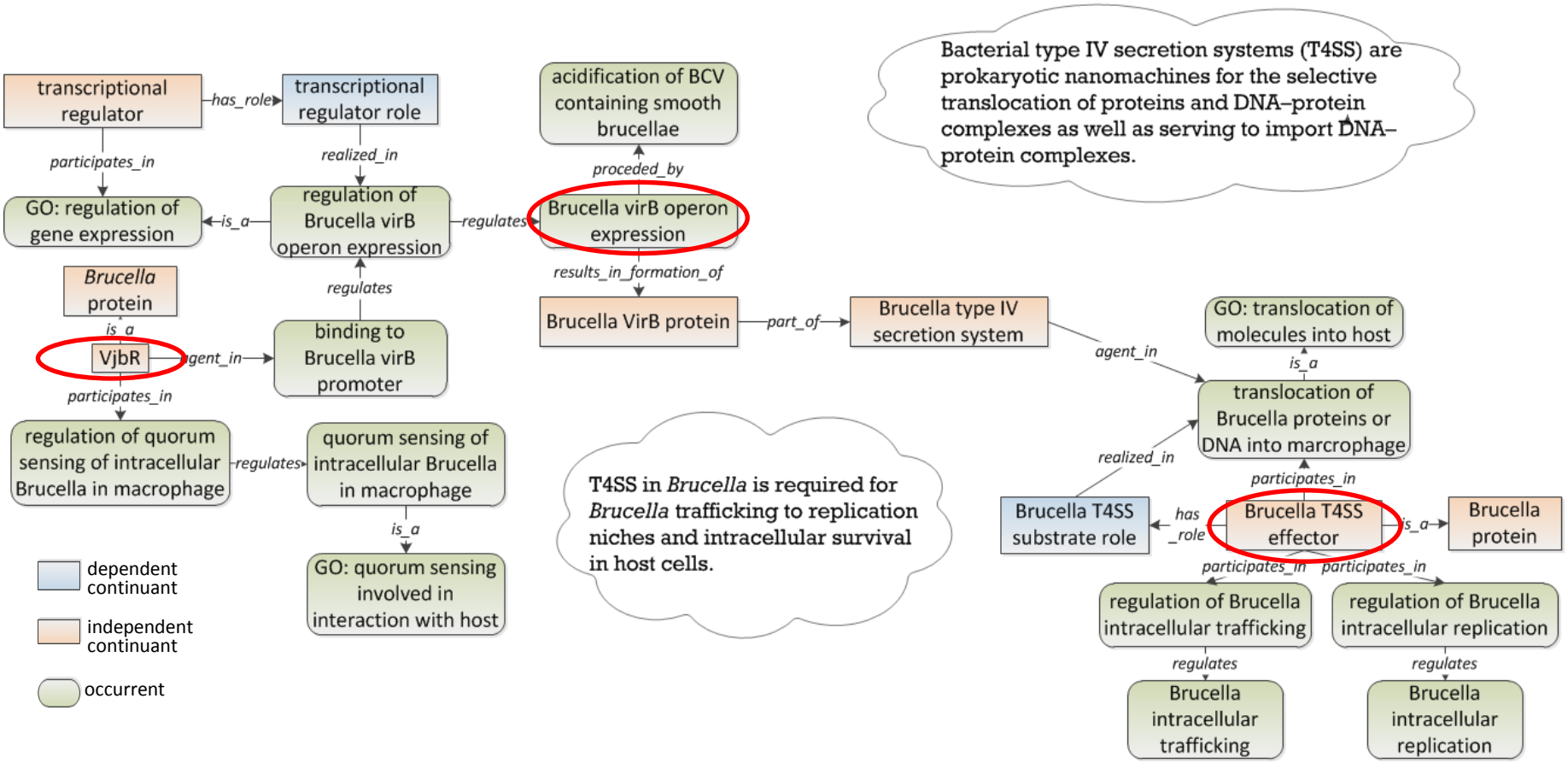
Live attenuated *B. abortus* vaccine RB51 (*wboA* gene mutant) induces macrophage cell death through activation of caspase-2



# How IDOBRU represents a *Brucella* mutant lacking virulence gene: *sodC*



# IDOBRU representing *Brucella* Type IV Secretion System (T4SS)




VjbR: binds to virB promoter → regulates virB operon expression → translocate T4SS effectors into macrophages …

# Query IDOBRU using SPARQL

- SPARQL: a query language to query ontology

Identify 432 virulence factors stored in IDOBRU

-- Prefixes -- | -- Template -- | -- Statement Help -- | Example 1, Example 2, Example 3, Examp

```
prefix rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
prefix owl: <http://www.w3.org/2002/07/owl#>
PREFIX obo: <http://purl.obolibrary.org/obo/>
SELECT (count(distinct ?n) as ?count)
from <http://purl.obolibrary.org/obo/merged/IDOBRU>
WHERE
{
?n rdfs:subClassOf ?n1  .
?n rdfs:subClassOf obo:PR_000000001 .
?n1 owl:onProperty obo:BFO_0000053 ; owl:someValuesFrom obo:IDO_0100116 .
}
```

Output format: Table | Max Rows: 10

Run Query | Reset

Result | Raw Request/Permalinks | Raw Response

| count |
|---|
| 432 |

Find 11 biological processes involving Brucella virulence factors

-- Prefixes -- | -- Template -- | -- Statement Help -- | Example 1, Example 2, Example 3, Example 4, Example 5, Ex

```
prefix rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#>
prefix owl: <http://www.w3.org/2002/07/owl#>
SELECT distinct ?p ?label
from <http://purl.obolibrary.org/obo/merged/IDOBRU>
WHERE
{
?n rdfs:subClassOf ?n1 .
?n1 owl:onProperty <http://purl.obolibrary.org/obo/IDO_0101168>; owl:someValuesFrom ?p.
?p rdfs:label ?label .
}
```

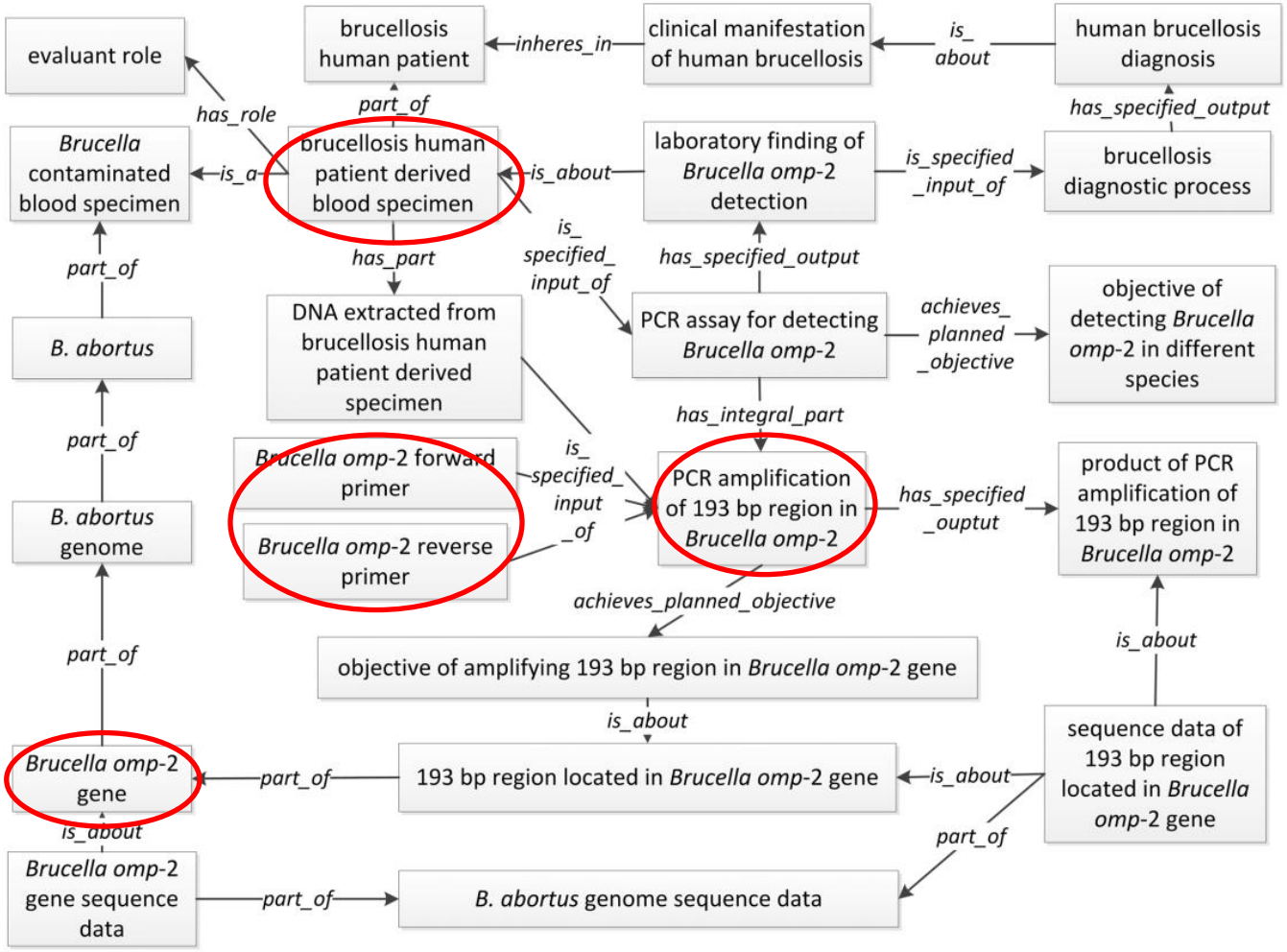
Output format: Table | Max Rows: 20

Run Query | Reset

Result | Raw Request/Permalinks | Raw Response

| p | label |
|---|---|
| http://purl.obolibrary.org/obo/IDO_0101178 | 'Brucella intracellular replication' |
| http://purl.obolibrary.org/obo/IDO_0100895 | Brucella intracellular survival |
| http://purl.obolibrary.org/obo/IDO_0101170 | Brucella entry into host cell |
| http://purl.obolibrary.org/obo/IDO_0100865 | smooth Brucella resistance to oxidative stress inside BCV |
| http://purl.obolibrary.org/obo/IDO_0100612 | Brucella intracellular replication in macrophage |
| http://purl.obolibrary.org/obo/IDO_0100927 | Brucella intracellular growth |
| http://purl.obolibrary.org/obo/IDO_0100613 | Brucella intracellular survival in macrophage |
| http://purl.obolibrary.org/obo/IDO_0101174 | Brucella intracellular survival in mouse |
| http://purl.obolibrary.org/obo/IDO_0100907 | Brucella intracellular replication in Hela cell |
| http://purl.obolibrary.org/obo/IDO_0100610 | Brucella entry into macrophage |
| http://purl.obolibrary.org/obo/IDO_0100983 | Brucella intracellular trafficking |

# IDOBRU ontological representation of *Brucella* diagnosis by *omp-2* PCR




This PCR assay uses human blood specimen and amplifies a region of 193 bp from *Brucella omp-2* gene.

# Summary and Discussion

IDOBRU serves as a knowledge base of brucellosis etiology, pathogenesis, diagnosis, prevention, treatment.

It is a new way of extending IDO …

# Vaccine Ontology (VO)

- VO: A biomedical ontology in the domain of vaccine and vaccination
- An OBO Foundry library ontology
- Follow OBO Foundry principles
- Utilize the Basic Formal Ontology (BFO) as its upper level ontology.
- A collaborative effect:
  - University of Michigan
  - IDO: Infectious Disease Ontology
  - OBI: Ontology for Biomedical Investigations (OBI)
  - GO: Gene Ontology
  - Many ontology developers: Barry Smith, Lindsay Cowell, Alexander Diehl, Richard H. Scheuermann, Bjoern Peters, …

VaccineOntology http://www.violinet.org/vaccineontology

# VO Statistics

VO reuses terms from other 34 ontologies

Now 6541

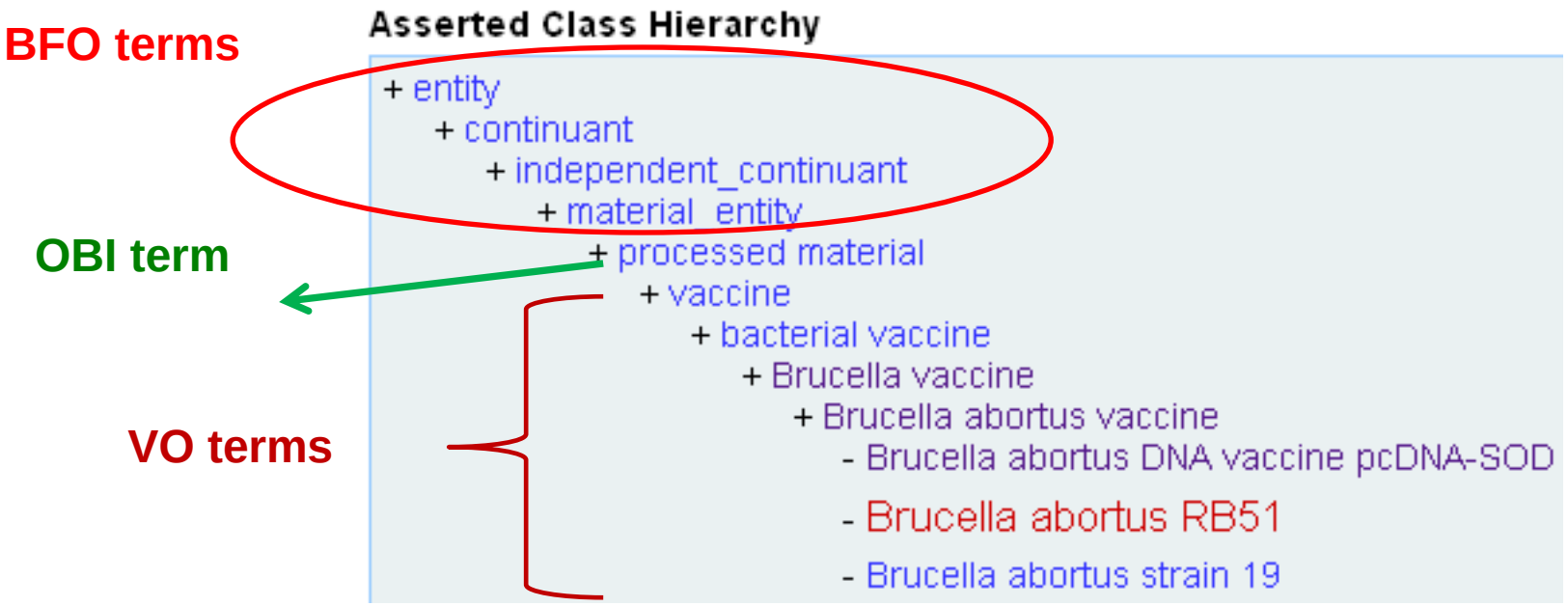
How to do it?
- Use OntoFox, a popular ontology development tool

How to align all ontologies?
- By BFO

| Index | Ontology Prefix | Class | ObjectProperty | DatatypeProperty | AnnotationProperty | Instance | Total |
|---|---|---|---|---|---|---|---|
| 1 | BFO | 35 | 38 | 0 | 2 | 0 | 75 |
| 2 | CARO | 3 | 0 | 0 | 0 | 0 | 3 |
| 3 | CHEBI | 26 | 0 | 0 | 0 | 0 | 26 |
| 4 | CL | 1 | 0 | 0 | 0 | 0 | 1 |
| 5 | CLO | 1 | 0 | 0 | 0 | 0 | 1 |
| 6 | DOID | 19 | 0 | 0 | 0 | 0 | 19 |
| 7 | EFO | 1 | 0 | 0 | 0 | 0 | 1 |
| 8 | FMA | 2 | 0 | 0 | 0 | 0 | 2 |
| 9 | GO | 12 | 0 | 0 | 0 | 0 | 12 |
| 10 | IAO | 54 | 9 | 4 | 16 | 18 | 101 |
| 11 | IDO | 2 | 0 | 0 | 0 | 0 | 2 |
| 12 | NCBITaxon | 457 | 0 | 0 | 0 | 0 | 457 |
| 13 | OAE | 4 | 0 | 0 | 0 | 0 | 4 |
| 14 | OBCS | 245 | 3 | 0 | 1 | 1 | 250 |
| 15 | OBI | 419 | 10 | 2 | 5 | 4 | 440 |
| 16 | OGG | 25 | 2 | 0 | 8 | 0 | 35 |
| 17 | OGMS | 3 | 0 | 0 | 0 | 0 | 3 |
| 18 | PATO | 24 | 0 | 0 | 0 | 0 | 24 |
| 19 | PR | 1 | 0 | 0 | 0 | 0 | 1 |
| 20 | PRO | 2 | 0 | 0 | 0 | 0 | 2 |
| 21 | RO | 0 | 30 | 0 | 2 | 1 | 33 |
| 22 | SO | 5 | 0 | 0 | 0 | 0 | 5 |
| 23 | STATO | 50 | 0 | 0 | 0 | 0 | 50 |
| 24 | UBERON | 8 | 0 | 0 | 0 | 0 | 8 |
| 25 | UO | 6 | 0 | 0 | 0 | 0 | 6 |
| 26 | VO | 4,815 | 31 | 0 | 1 | 74 | 4,921 |
| 27 | external_byhand.owl | 0 | 0 | 0 | 5 | 0 | 5 |
| 28 | ncbitaxon | 0 | 0 | 0 | 1 | 0 | 1 |
| 29 | oboInOwl | 5 | 1 | 0 | 15 | 0 | 21 |
| 30 | owl | 1 | 0 | 0 | 2 | 0 | 3 |
| 31 | protege | 0 | 0 | 0 | 1 | 0 | 1 |
| 32 | rdf-schema | 0 | 0 | 0 | 4 | 0 | 4 |
| 33 | ro.owl | 0 | 2 | 0 | 0 | 0 | 2 |
| 34 | NoPrefix | 0 | 4 | 0 | 17 | 1 | 22 |
| Total | - | 6,226 | 130 | 6 | 80 | 99 | 6,541 |

http://www.ontobee.org/ontostat/VO

# How VO defines a vaccine?




**Superclasses & Asserted Axioms**

- Brucella abortus vaccine
- has_part some (Brucella abortus lipopolysaccharide and (lacks_part some Brucella O-polysaccharide))

VO includes >1000 vaccines for >20 host species against >150 pathogens or diseases

# Define and differ ‘vaccination’ and ‘vaccine immunization’ in VO

**Equivalents**

- (realizes some (material to be added role and (role_of some vaccine))) and (realizes some (target of material addition role and (role_of some anatomical entity or organism)))

**Asserted Class Hierarchy**

+ entity
  + occurrent
    + processual_entity
      + process
        + planned process
          + processing material
            + adding a material entity into a target
              + administering substance in vivo
                + vaccination

**Class Hierarchy**

Thing
+ entity
  + occurrent
    + process
      + immunization
        + active immunization
          - induction of adaptive immune response to antigen
          - modification of adaptive immune response to antigen
          - natural active immunization
          + vaccine immunization
            - bacterial vaccine immunization
            - cancer vaccine immunization
            - viral vaccine immunization
            - parasite vaccine immunization

**Superclasses & Asserted Axioms**

- active immunization
- has_specified_input some vaccine
- achieves_planned_objective some immunization objective
- realizes some (vaccine host role and (inheres_in some organism))

- Both are processes
- **Vaccination:** administrating vaccine to inside host
- **Immunization:** priming or modifying adaptive immune response to an antigen.
- Some vaccination may not result in immunization

# VO-supported immunology data integration

- Transfer VIOLIN vaccine data to VO directly.
- Use VO to integrate different VIOLIN components.
- The VO IDs more like primary keys in VIOLIN relational database.
- VIOLIN links its data contents to VO data
- VO contents provide ports to integrate with other existing data resources such as GO

# VO supports VIOLIN vaccine data integration and sharing

VIOLIN: Largest vaccine research database and analysis system


http://www.violinet.org

VIOLIN: >3200 vaccines for 200 pathogens diseases (e.g., cancer).

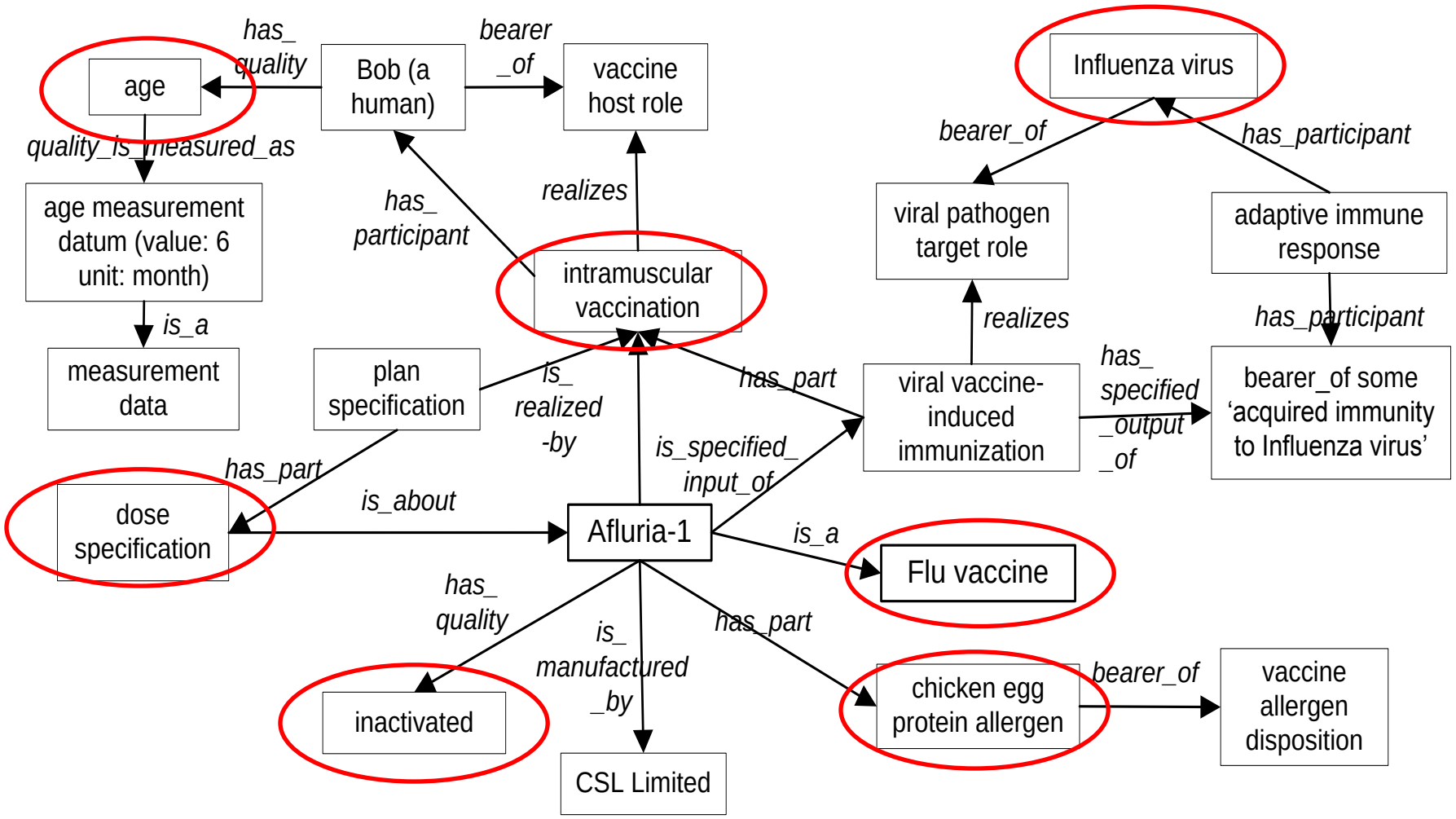
Tools: vaccine literature mining and vaccine design, …

VO for data sharing and integration

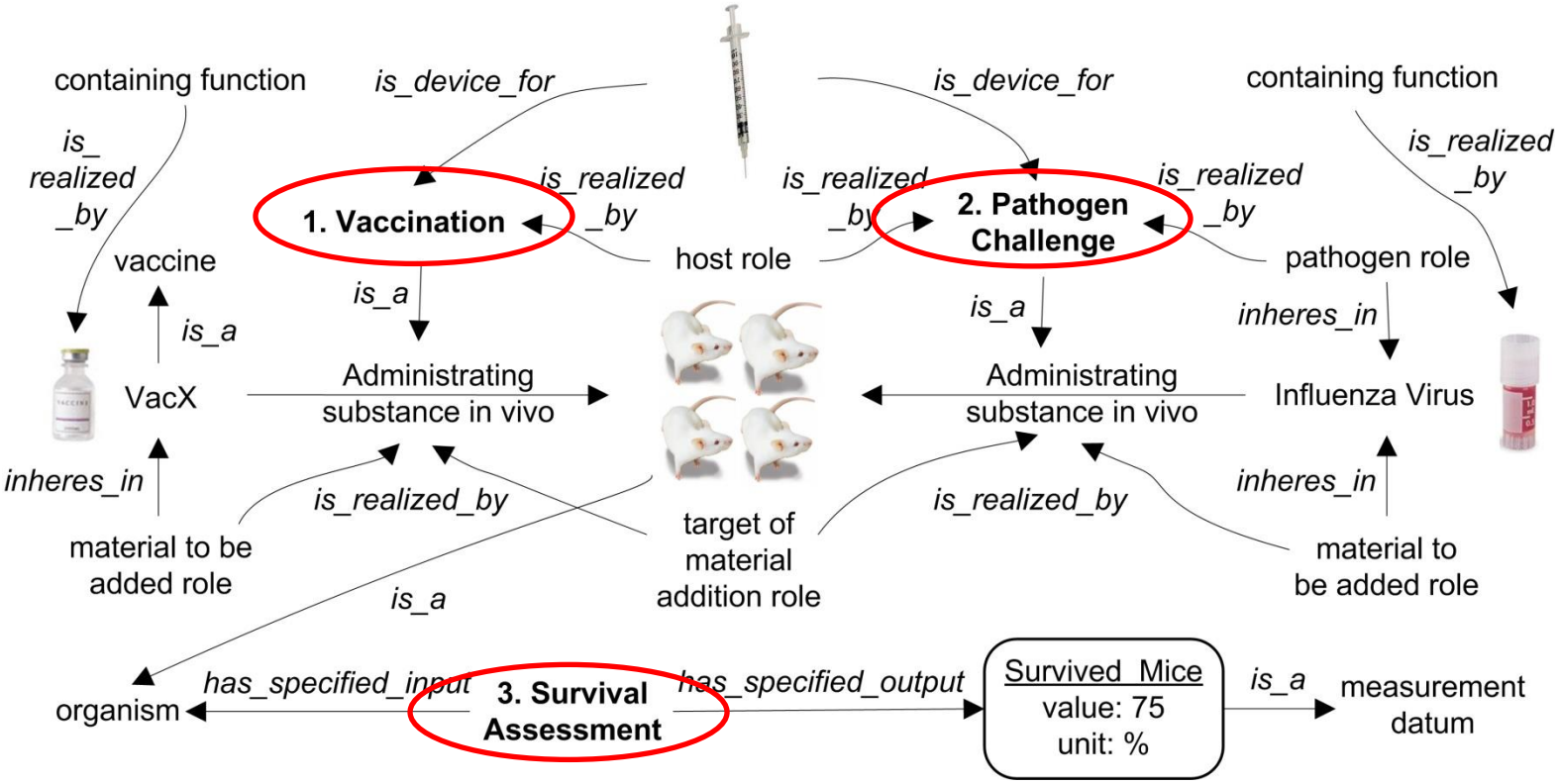
**Reference:** He Y, Racz R, Sayers S, Lin Y, Todd T, Hur J, Li X, et al. Updates on the web-based VIOLIN vaccine database and analysis system. Nucleic Acids Research. 2014. 42 (D1): D1124-D1132.

# VO integrates different vaccine data

## Example: Afluria Influenza Vaccine



# VO-based integration of vaccine protection assay data

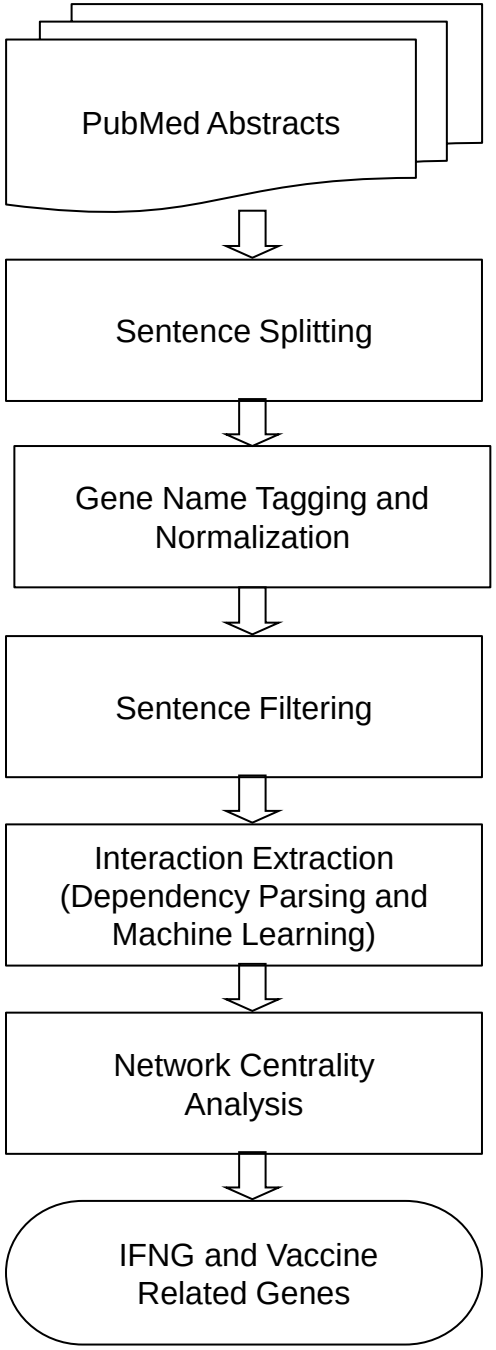



This model was also used for *Brucella* vaccine data meta-analysis

**Reference: Brinkman et al.** (2007). **Modeling biomedical experimental processes with OBI.** ***Journal of Biomedical Semantics*. 2010, 1(Suppl 1):S7. PMID: 20626927.**

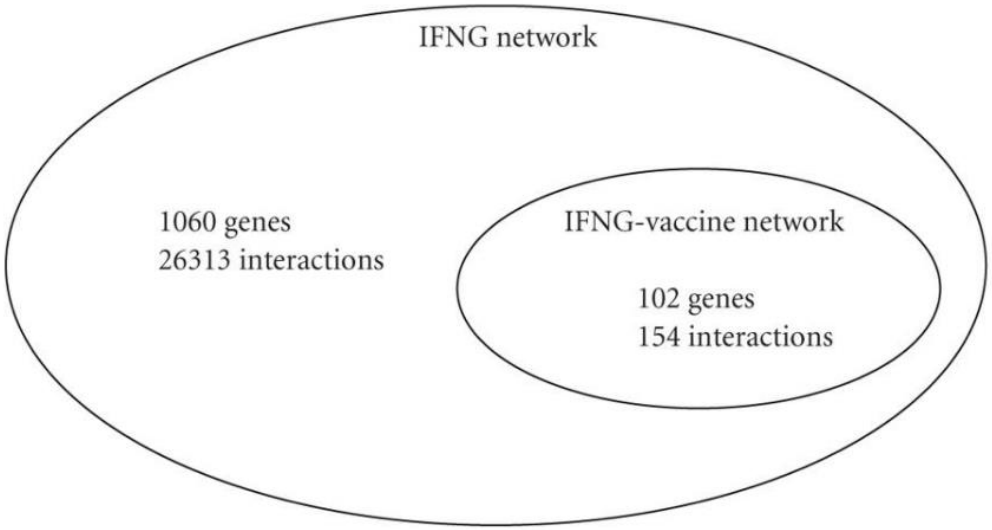
# VO-based literature mining of IFN-γ gene interaction network

- Interferon-gamma (IFN-γ; Gene symbol: IFNG): Regulates immune responses critical for vaccine protection.
- Search “Interferon-gamma OR IFNG” in PubMed: 69816 hits (~2 years ago) → 5/2/2012:73696 hits.
- Question: How can we identify the generic IFNG interaction network and a specific IFNG and vaccine-mediated sub-network using all PubMed publications?

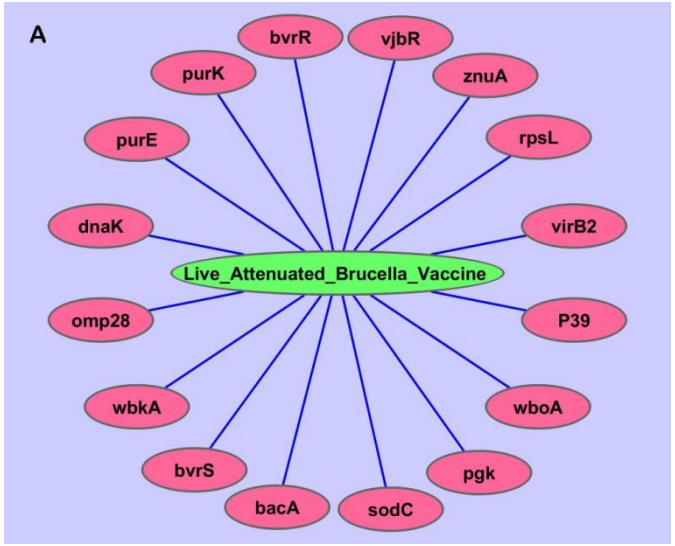


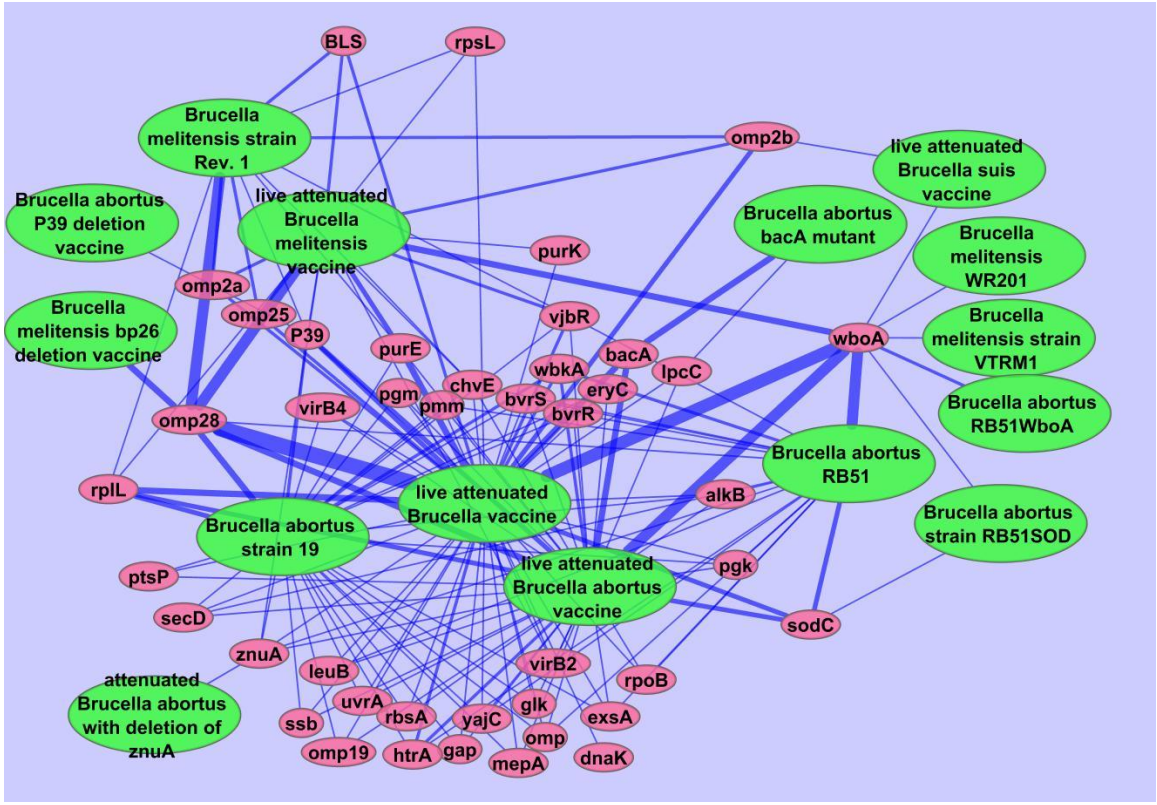
# VO supports literature mining

- VO classifies vaccines, e.g., live attenuated vaccines
- VO supports literature mining of vaccine-mediated gene interaction networks
- Predicts new vaccine candidates and gene interaction mechanisms



# VO-based literature mining identifed more genes interacting with “live attenuated *Brucella* vaccine”



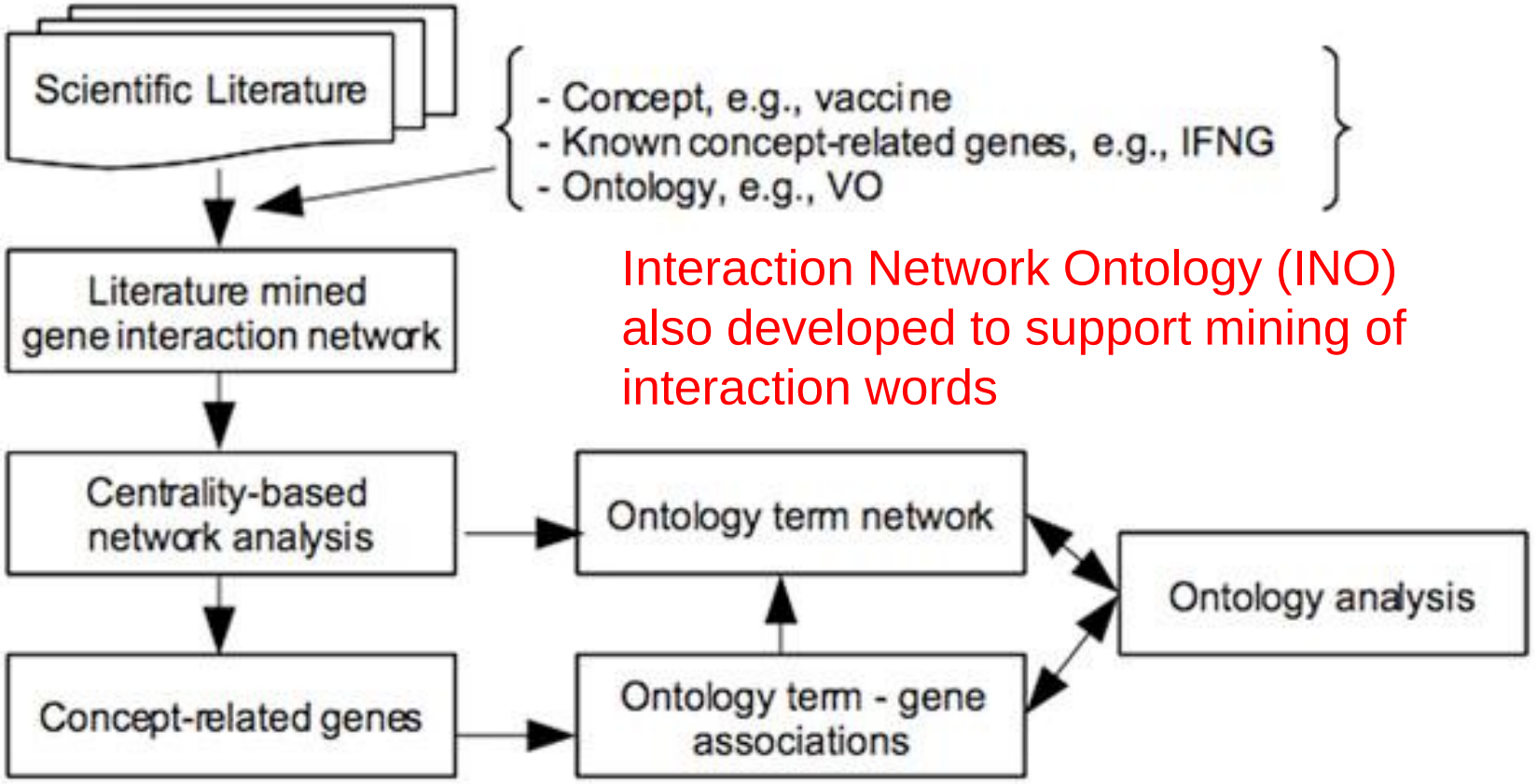




**PubMed**

**VO-SciMiner**

# CONDL Strategy:

## Centrality and Ontology-based Network Discovery using Literature data



# VO is also used to support he development of other ontologies

- Ontology of Adverse Events (OAE)
- Ontology of Vaccine Adverse Events (OVAE)
- Vaccination Informed Consent Ontology (VICO)

**VO has also been used as the ontology model for developing Ontoanimal tools (e.g., OntoFox, Ontorat) in He lab.**

# Discussion

# What's next?

# Acknowledgements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