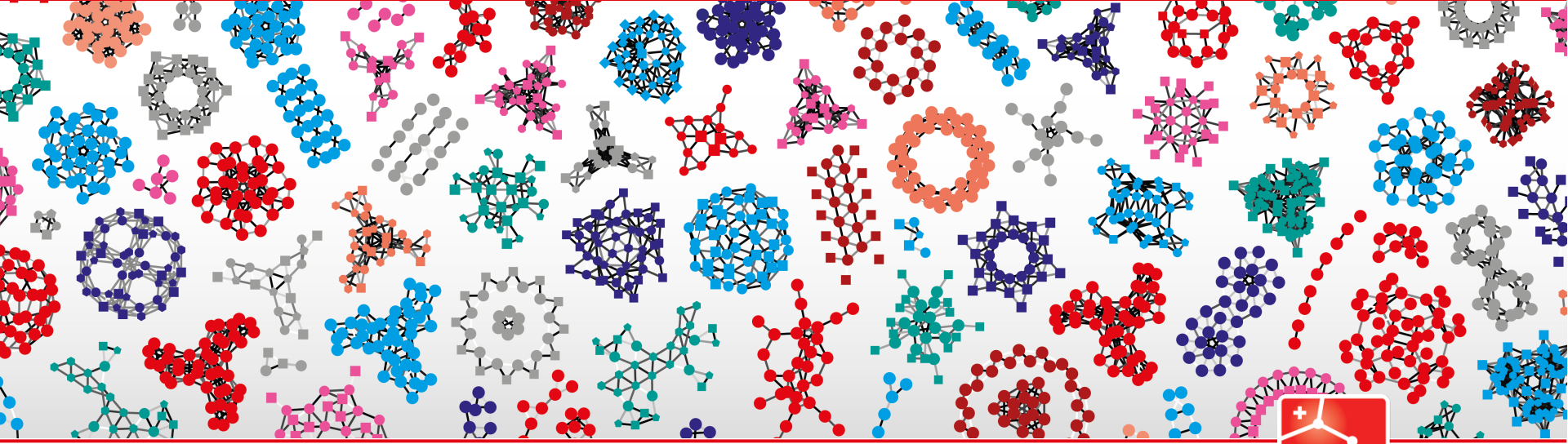


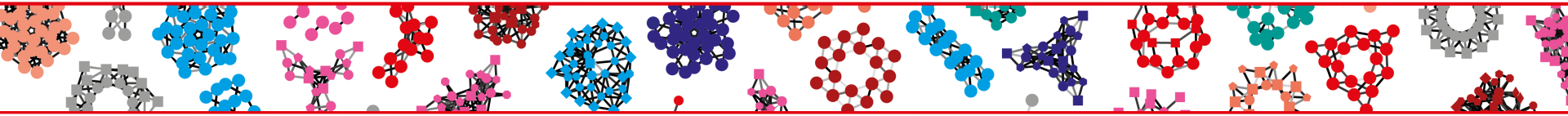
Swiss Institute of Bioinformatics

SPARQLing Rhea

Anne Morgat, Swiss-Prot group

elixir SWITZERLAND | swissprot | Rhea

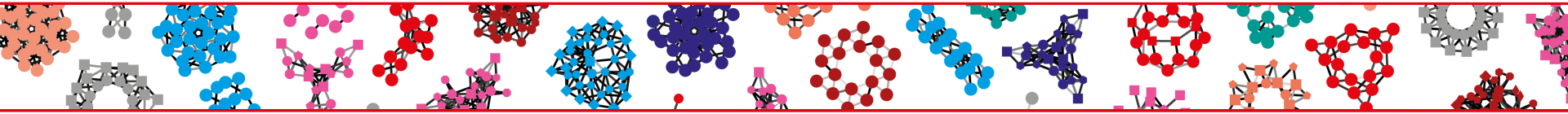
www.sib.swiss



Accompanying Jupyter notebook:

https://github.com/sib-swiss/sparql-training/tree/master/rhea/SWAT4HCLS_2019

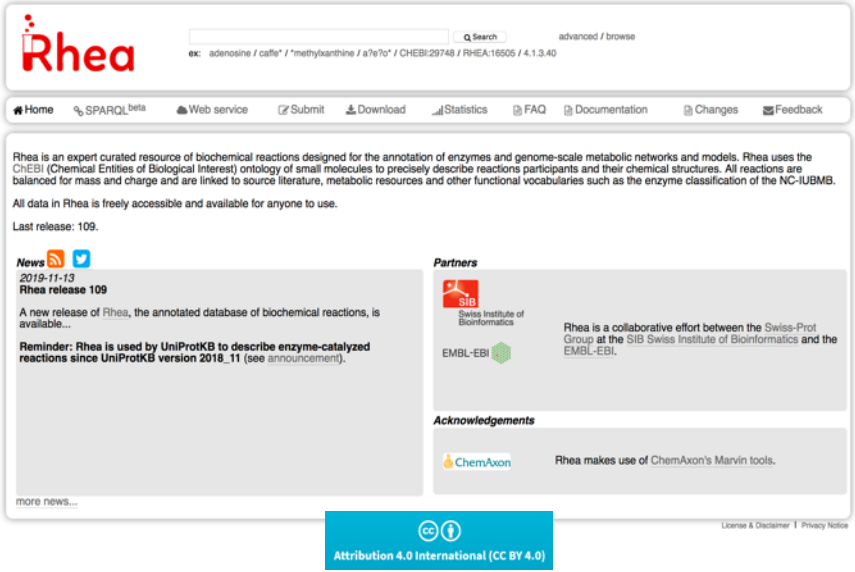
Overview



Rhea, a biochemical reactions knowledgebase

Rhea is an **expert curated knowledgebase of chemical and transport reactions of biological interest** that can be used for enzyme annotation, genome-scale metabolic modeling and omics-related analysis

- **12,290 biochemical reactions**
- **10,795 compounds**
- **14,082** curated **literature references**
- **covers all organisms**
- Used by **UniProtKB**, **ChEBI, SwissLipids, EBI Enzyme Portal, MetaboLights, MetaNetX,...** *and soon by GO (Gene Ontology)*



https://www.rhea-db.org

Rhea reactions: balanced – non redundant

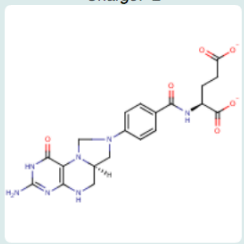
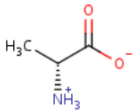
RHEA:10064 (APPROVED)

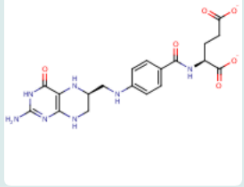
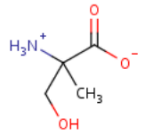
(6R)-5,10-methylene-5,6,7,8-tetrahydrofolate + D-alanine + H2O = (6S)-5,6,7,8-tetrahydrofolate + 2-methylserine

Last modified: 2017-10-18. **Chemically balanced:** yes.

(6*R*)-5,10-methylene-5,6,7,8-tetrahydrofolate + **D-alanine** + **H_2O** = **(6*S*)-5,6,7,8-tetrahydrofolate** + **2-methylserine**

(6*R*)-5,10-methylene-5,6,7,8-tetrahydrofolate	D-alanine	H_2O	(6*S*)-5,6,7,8-tetrahydrofolate	2-methylserine
CHEBI:15636	CHEBI:57416	CHEBI:15377	CHEBI:57453	CHEBI:58275
Formula: C20H21N7O6	*Formula:* C3H7NO2	*Formula:* H2O	*Formula:* C19H21N7O6	*Formula:* C4H9NO3
Charge: -2	*Charge:* 0	*Charge:* 0	*Charge:* -2	*Charge:* 0

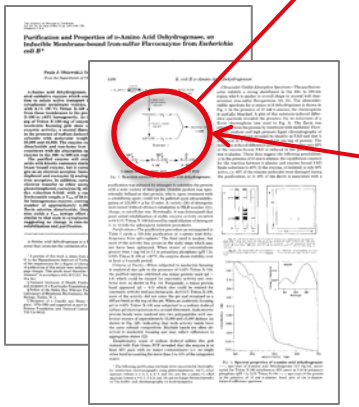



formula: $C_{23}\ H_{30}\ N_8\ O_9$, charge: -2

formula: $C_{23}\ H_{30}\ N_8\ O_9$, charge: -2

Rhea curation: describing chemical reactions using ChEBI

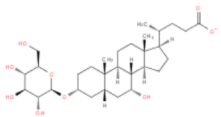
5,10-methylenetetrahydrofolate + D-alanine + H_2O = tetrahydrofolate + 2-methylserine



Rhea curators

www.ebi.ac.uk/chebi

CHEBI:142610 - chenodeoxycholate-3-*O*-β-D-glucoside(1−)



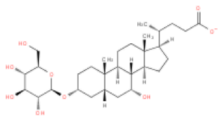
ChEBI Name	**chenodeoxycholate-3-*O*-β-D-glucoside(1−)**
ChEBI ID	**CHEBI:142610**
ChEBI ASCII Name	chenodeoxycholate-3-O-beta-D-glucoside(1-)
Definition	A β-D-glucoside resulting from the formal condensation of the 1*R*-hydroxy group of β-D-glucose with the 3*R*-hydroxy group of chenodeoxycholate.
Stars	⭐⭐⭐ This entity has been manually annotated by the ChEBI Team.
Submitter	Lucila Aimo
Supplier Information	No supplier information found for this compound.
Download	Molfile XML SDF

- Find compounds which contain this structure
- Find compounds which resemble this structure
- Take structure to the Advanced Search

Formula	C30H49O9
Net Charge	-1
Average Mass	553.706
Monoisotopic Mass	553.33821
InChI	InChI=1S/C30H50O9/c1-15(4-7-23(33)34)18-5-6-19-24-20(9-11-30(18,19)3)29(2)10-8-17(12-16(29)13-21(24)32)38-28-27(37)26(36)25(35)22(14-31)39-28/h15-22,24-28,31-32,35-37H,4-14H2,1-3H3,(H,33,34)/p-1/t15-,16+,17-,18-,19+,20+,21-,22-,24+,25-,26+,27-,28-,29+,30-/m1/s1
InChIKey	QRLIJDGVRXVHQD-UVMPBBQUSA-M
SMILES	C1[C@@]2([C@]3(CC[C@]4([C@]([C@@]3([C@@H](C[C@@]2(C[C@@H](C1)O[C@H]5[C@@H]([C@H]([C@@H]([C@H](O5)CO)O)O)O)[H])O)[H])(CC[C@@]4([C@@H](CCC([O-])=O)C)[H])[H])C)[H])C

CHEBI:142610 - chenodeoxycholate-3-*O*-β-D-glucoside(1−)

Main | ChEBI Ontology | Automatic Xrefs | Reactions | Pathways | Models



ChEBI Name	**chenodeoxycholate-3-*O*-β-D-glucoside(1−)**
ChEBI ID	**CHEBI:142610**
ChEBI ASCII Name	chenodeoxycholate-3-O-beta-D-glucoside(1-)
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Stars	⭐⭐⭐ This entity has been manually annotated by the ChEBI Team.
Submitter	Lucila Aimo
Supplier Information	No supplier information found for this compound.
Download	Molfile XML SDF

- Find compounds which contain this structure
- Find compounds which resemble this structure
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Formula	C30H49O9
Net Charge	-1
Average Mass	553.706
Monoisotopic Mass	553.33821
InChI	InChI=1S/C30H50O9/c1-15(4-7-23(33)34)18-5-6-19-24-20(9-11-30(18,19)3)29(2)10-8-17(12-16(29)13-21(24)32)38-28-27(37)26(36)25(35)22(14-31)39-28/h15-22,24-28,31-32,35-37H,4-14H2,1-3H3,(H,33,34)/p-1/t15-,16+,17-,18-,19+,20+,21-,22-,24+,25-,26+,27-,28-,29+,30-/m1/s1
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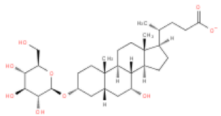
SMILES	C1[C@@]2([C@]3(CC[C@]4([C@]([C@@]3([C@@H](C[C@@]2(C[C@@H](C1)O[C@H]5[C@@H]([C@H]([C@@H]([C@H](O5)CO)O)O)O)[H])O)[H])(CC[C@@]4([C@@H](CCC([O-])=O)C)[H])[H])C)[H])C

ChEBI:142610 - relationships

CHEBI:142610 - chenodeoxycholate-3-*O*-β-D-glucoside(1−)

Main | ChEBI Ontology | Automatic Xrefs | Reactions | Pathways | Models



ChEBI Name	**chenodeoxycholate-3-*O*-β-D-glucoside(1−)**
ChEBI ID	**CHEBI:142610**
ChEBI ASCII Name	chenodeoxycholate-3-O-beta-D-glucoside(1-)
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Stars	⭐⭐⭐ This entity has been manually annotated by the ChEBI Team.
Submitter	Lucila Aimo
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- Find compounds which resemble this structure
- Take structure to the Advanced Search

Formula	C30H49O9
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Monoisotopic Mass	553.33821
InChI	InChI=1S/C30H50O9/c1-15(4-7-23(33)34)18-5-6-19-24-20(9-11-30(18,19)3)29(2)10-8-17(12-16(29)13-21(24)32)38-28-27(37)26(36)25(35)22(14-31)39-28/h15-22,24-28,31-32,35-37H,4-14H2,1-3H3,(H,33,34)/p-1/t15-,16+,17-,18-,19+,20+,21-,22-,24+,25-,26+,27-,28-,29+,30-/m1/s1
InChIKey	QRLIJDGVRXVHQD-UVMPBBQUSA-M
SMILES	C1[C@@]2([C@]3(CC[C@]4([C@]([C@@]3([C@@H](C[C@@]2(C[C@@H](C1)O[C@H]5[C@@H]([C@H]([C@@H]([C@H](O5)CO)O)O)O)[H])O)[H])(CC[C@@]4([C@@H](CCC([O-])=O)C)[H])[H])C)[H])C

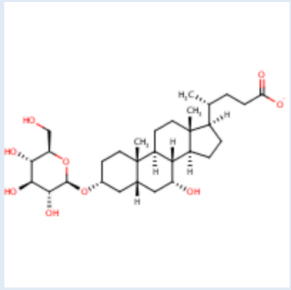
CHEBI:142610 - chenodeoxycholate-3-*O*-β-D-glucoside(1−)

Main | ChEBI Ontology | Automatic Xrefs | **Reactions** | Pathways | Models

select reaction: beta-D-glucosyl-(1->3)-O-chenodeoxycholate + H(2)O = chenodeoxycholate + D-glucose

RHEA:58340

beta-D-glucosyl-(1->3)-O-chenodeoxycholate
CHEBI:142610
Formula: C30H49O9
Charge: -1

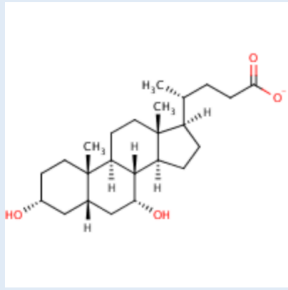


+

H2O
CHEBI:15377
Formula: H2O
Charge: 0

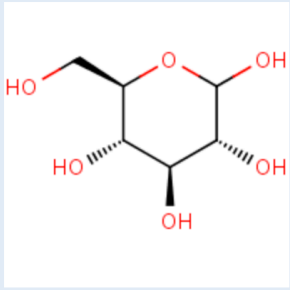
=

chenodeoxycholate
CHEBI:36234
Formula: C24H39O4
Charge: -1



+

D-glucose
CHEBI:4167
Formula: C6H12O6
Charge: 0



CHEBI:142610 - chenodeoxycholate-3-*O*-β-D-glucoside(1−)

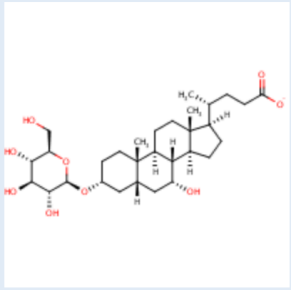
Main | ChEBI Ontology | Automatic Xrefs | **Reactions** | Pathways | Models

select reaction:

- ✓ beta-D-glucosyl-(1->3)-O-chenodeoxycholate + H(2)O = chenodeoxycholate + D-glucose
- chenodeoxycholate + dolichyl beta-D-glucosyl phosphate = beta-D-glucosyl-(1->3)-O-chenodeoxycholate + dolichyl phosphate + H(+)
- chenodeoxycholate + octyl beta-D-glucose = beta-D-glucosyl-(1->3)-O-chenodeoxycholate + octan-1-ol

RHEA:583

beta-D-glucosyl-(1->3)-O-chenodeoxycholate
CHEBI:142610
Formula: C30H49O9
Charge: -1

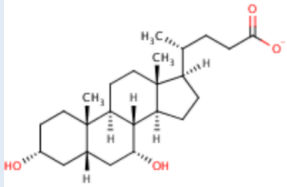


+

H2O
CHEBI:15377
Formula: H2O
Charge: 0

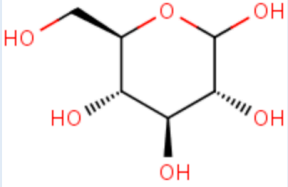
=

chenodeoxycholate
CHEBI:36234
Formula: C24H39O4
Charge: -1



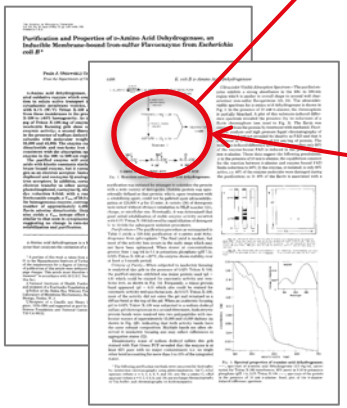
+

D-glucose
CHEBI:4167
Formula: C6H12O6
Charge: 0



Rhea curation: choice of reaction participants

5,10-methylenetetrahydrofolate + D-alanine + H_2O = tetrahydrofolate + 2-methylserine



Rhea curators

D-alanine

D-alaninate CHEBI:32435

CHEBI:32436 D-alaninium

ChEBI

D-alanine CHEBI:15570

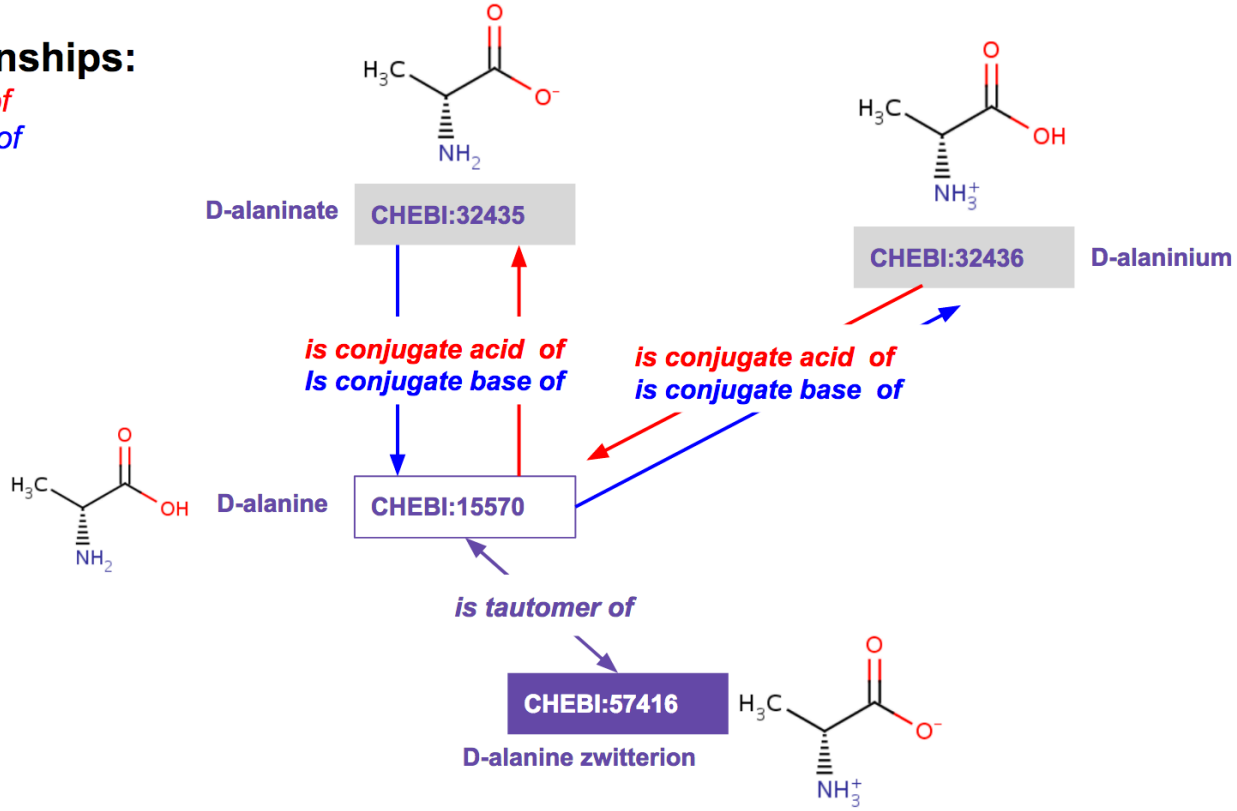
CHEBI:57416

D-alanine zwitterion

Different chemical species for the same compound

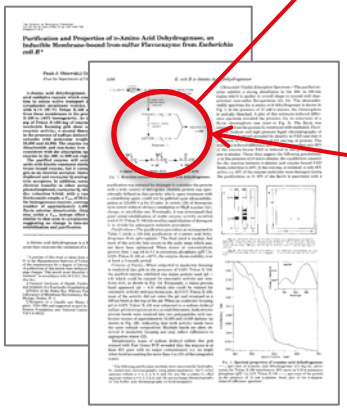
ChEBI relationships:

Is conjugate acid of
Is conjugate base of
Is tautomer of

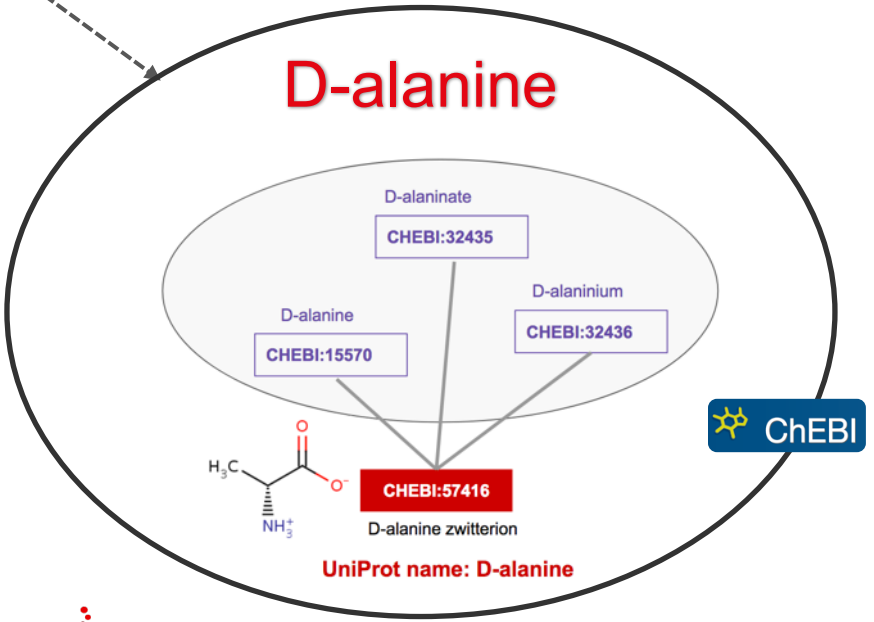


Rhea curation: choice of reaction participants

5,10-methylenetetrahydrofolate + D-alanine + H_2O = tetrahydrofolate + 2-methylserine



Rhea curators

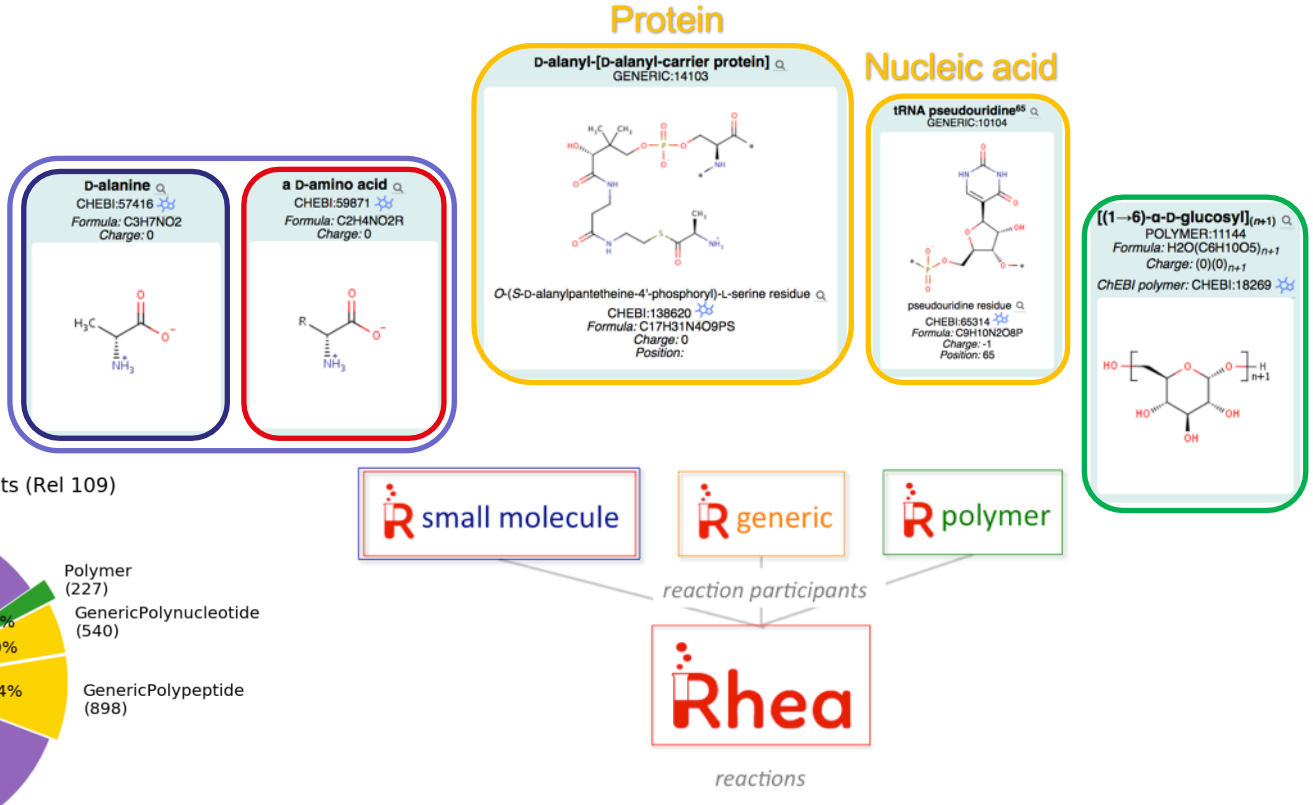


Rhea & MetaCyc: same convention
KEGG: different convention
→ Reconciliation issues (MetaNetX/MNXref)

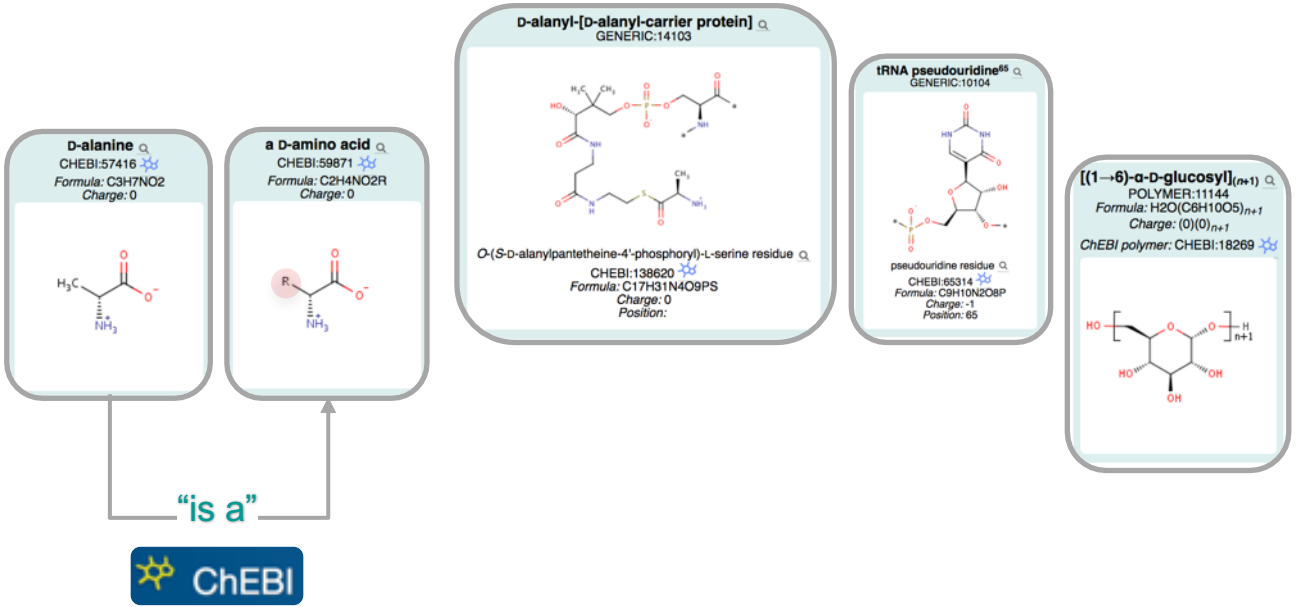
Rhea Major microspecies at pH 7.3

ChemAxon

Rhea reaction participants



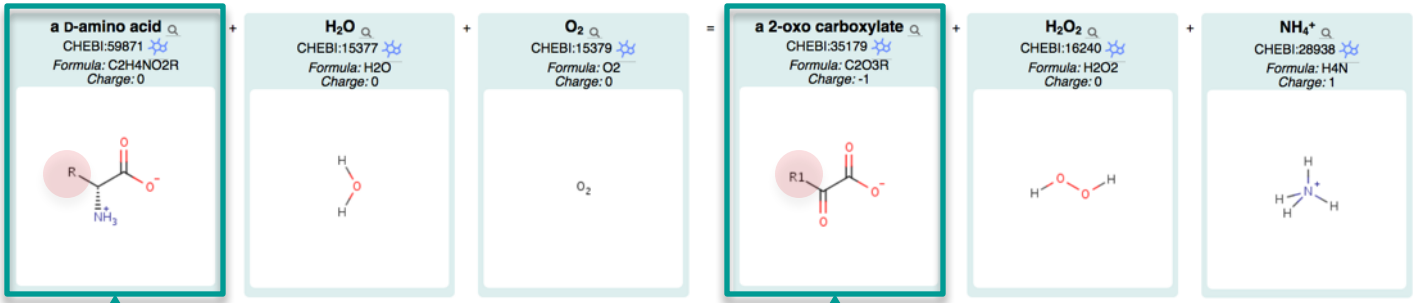
Rhea reactions hierarchical classification (exploit ChEBI ontology)



RHEA:21816 (APPROVED)

a D-amino acid + H2O + O2 = a 2-oxo carboxylate + H2O2 + NH4(+)

Last modified: 2017-07-11. **Chemically balanced:** yes.



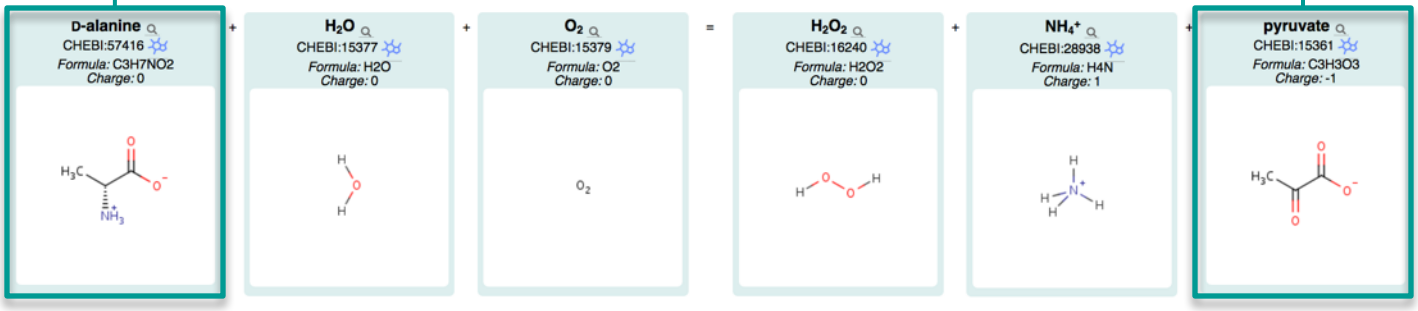
"is a" ChEBI

"is a" ChEBI

RHEA:22688 (APPROVED)

D-alanine + H2O + O2 = H2O2 + NH4(+) + pyruvate

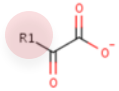
Last modified: 2017-11-08. **Chemically balanced:** yes.



RHEA:21816 (APPROVED)

a D-amino acid + H2O + O2 = a 2-oxo carboxylate + H2O2 + NH4(+)

Last modified: 2017-07-11. **Chemically balanced:** yes.

a D-amino acid	+	H_2O	+	O_2	=	a 2-oxo carboxylate	+	H_2O_2	+	NH_4^+
CHEBI:59871		CHEBI:15377		CHEBI:15379		CHEBI:35179		CHEBI:16240		CHEBI:28938
Formula: C2H4NO2R *Charge:* 0		*Formula:* H2O *Charge:* 0		*Formula:* O2 *Charge:* 0		*Formula:* C2O3R *Charge:* -1		*Formula:* H2O2 *Charge:* 0		*Formula:* H4N *Charge:* 1
										

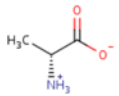
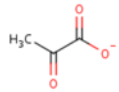
Rhea

"is a" reaction relationship

RHEA:22688 (APPROVED)

D-alanine + H2O + O2 = H2O2 + NH4(+) + pyruvate

Last modified: 2017-11-08. **Chemically balanced:** yes.

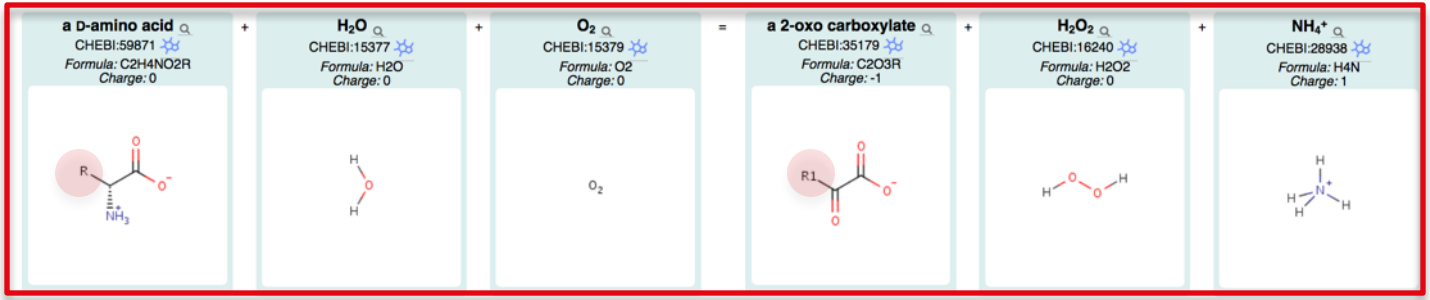
D-alanine	+	H_2O	+	O_2	=	H_2O_2	+	NH_4^+	+	pyruvate
CHEBI:57416		CHEBI:15377		CHEBI:15379		CHEBI:16240		CHEBI:28938		CHEBI:15361
Formula: C3H7NO2 *Charge:* 0		*Formula:* H2O *Charge:* 0		*Formula:* O2 *Charge:* 0		*Formula:* H2O2 *Charge:* 0		*Formula:* H4N *Charge:* 1		*Formula:* C3H3O3 *Charge:* -1
										

< 20% Rhea reactions are classified
(expert curation, on-going process)

RHEA:21816 (APPROVED)

a D-amino acid + H2O + O2 = a 2-oxo carboxylate + H2O2 + NH4(+)

Last modified: 2017-07-11. **Chemically balanced:** yes.



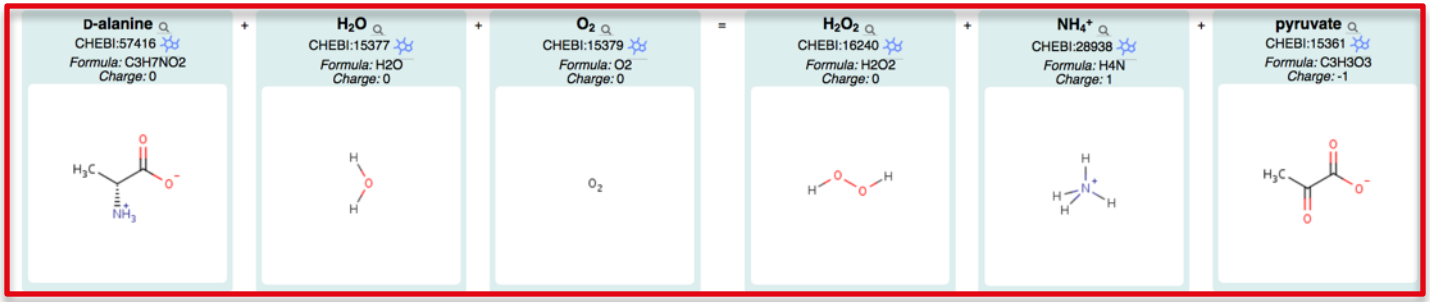
EC 1.4.3.**3** (*D-amino-acid oxidase*)

Rhea
"is a" reaction relationship

RHEA:22688 (APPROVED)

D-alanine + H2O + O2 = H2O2 + NH4(+) + pyruvate

Last modified: 2017-11-08. **Chemically balanced:** yes.



EC 1.4.3.**19** (alternate reaction of *glycine oxidase*)

Rhea reactions and enzyme catalysts

- Enzyme nomenclature (EC numbers)

- UniProt enzymes

Enzyme classification and EC numbers

- **EC 1 Oxidoreductases**
  - EC 1.1 Acting on the CH-OH group of donors
    - EC 1.1.1 With NAD+ or NADP+ as acceptor
      - EC 1.1.1.2 alcohol dehydrogenase (NADP+)

        an alcohol + NADP+ = an aldehyde + NADPH + H+

      - ...
      - EC 1.1.1.19 glucuronate reductase

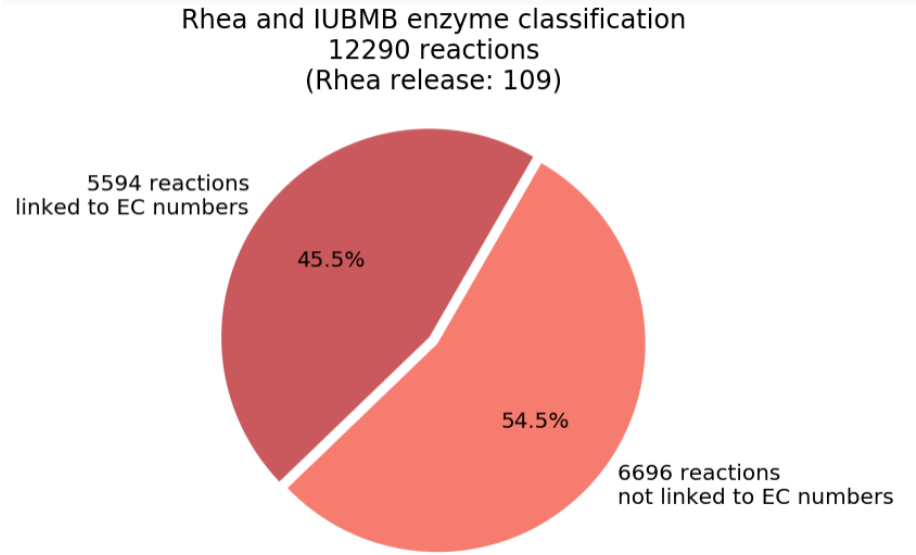
        L-gulonate + NADP+ = D-glucuronate + NADPH + H+

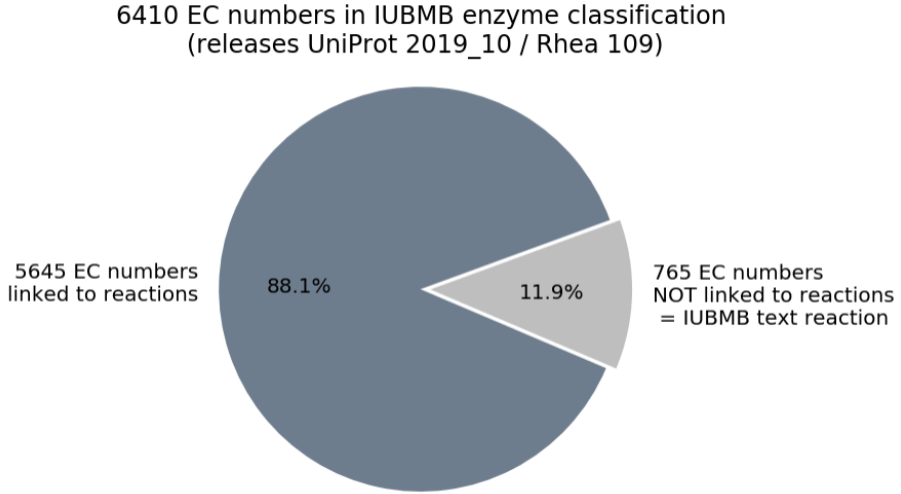
is a

missing deeper levels

- **EC 2 Transferases**
- **EC 3 Hydrolases**
- **EC 4 Lyases**
- **EC 5 Isomerases**
- **EC 6 Ligases**
- **EC 7 Translocases**

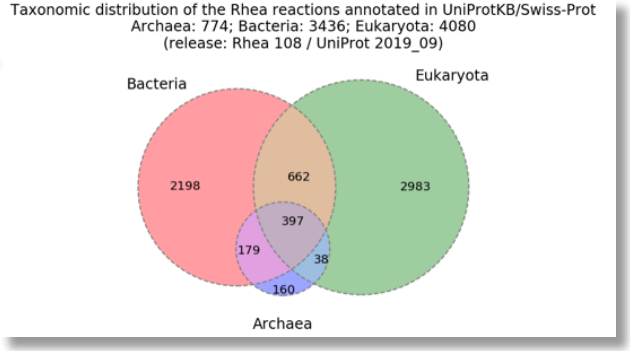
Rhea and Enzyme classification





Rhea is used in UniProt since December 2018

Rhea reactions used in UniProtKB/Swiss-Prot	6’629 / 12’290 (54.1%)
UniProtKB/Swiss-Prot proteins annotated with Rhea reactions	217’207 (38.7%)
UniProtKB/TrEMBL proteins automatically annotated with Rhea reactions	17’141’552 (9.4%)



OXFORD ACADEMIC

Bioinformatics

ACCEPTED MANUSCRIPT

Enzyme annotation in UniProtKB using Rhea

Anne Morgat ✉, Thierry Lombardot, Elisabeth Coudert, Kristian Axelsen, Teresa Batista Neto, Sebastien Gehant, Parit Bansal, Jerven Bolleman, Elisabeth Gasteiger, Edouard de Castro ... Show more

Bioinformatics, btz817, https://doi.org/10.1093/bioinformatics/btz817

Published: 05 November 2019 **Article history** ▾

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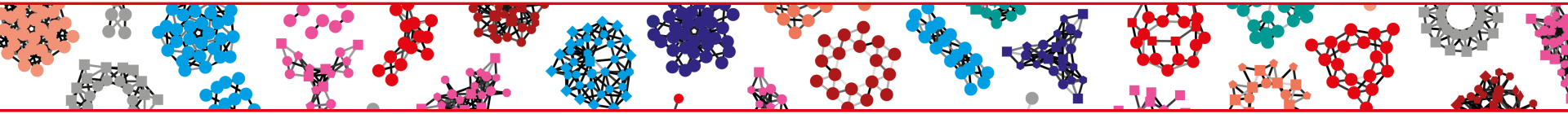
Abstract

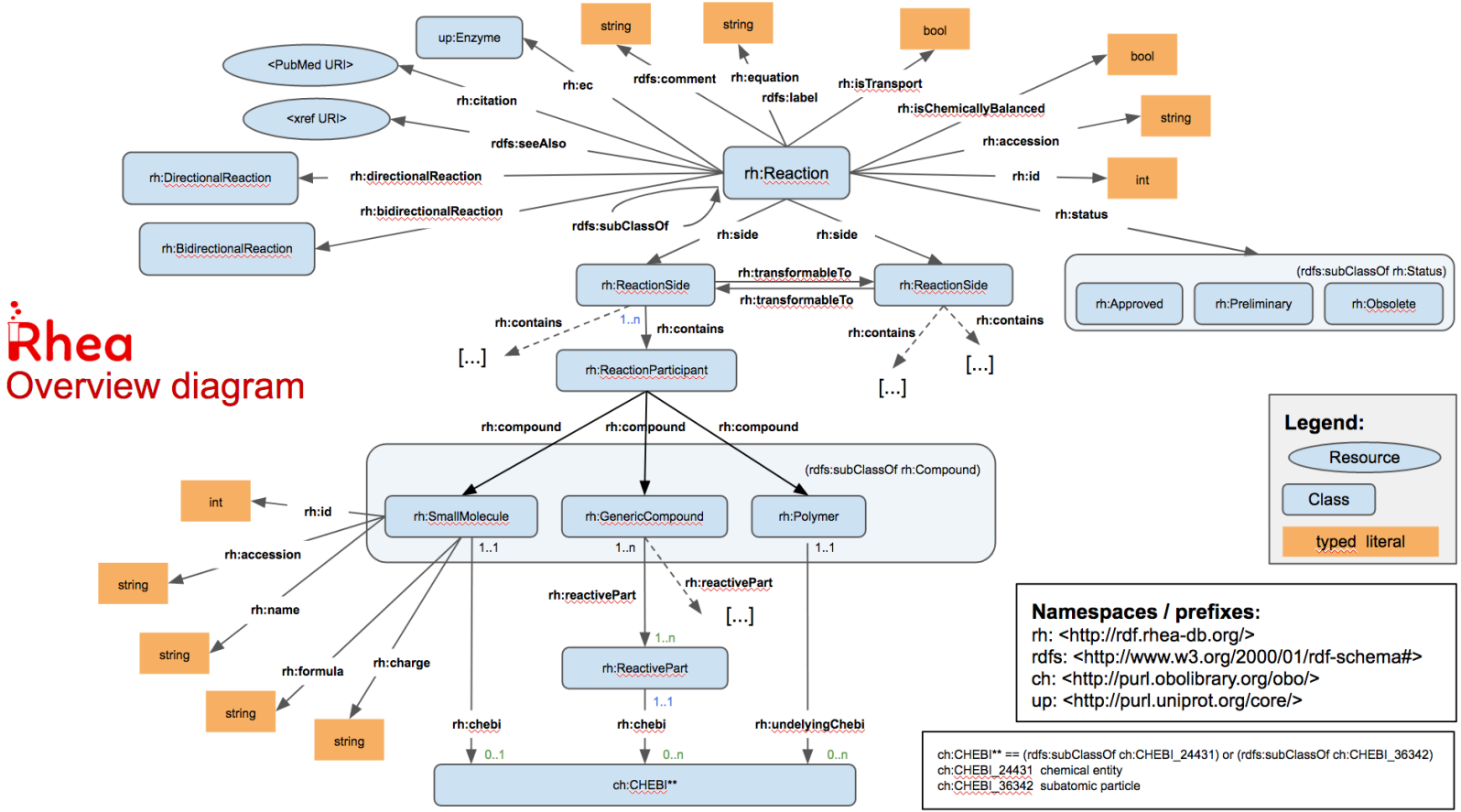
Motivation

To provide high quality computationally tractable enzyme annotation in UniProtKB using Rhea, a comprehensive expert-curated knowledgebase of biochemical reactions which describes reaction participants using the ChEBI (Chemical Entities of Biological Interest) ontology.

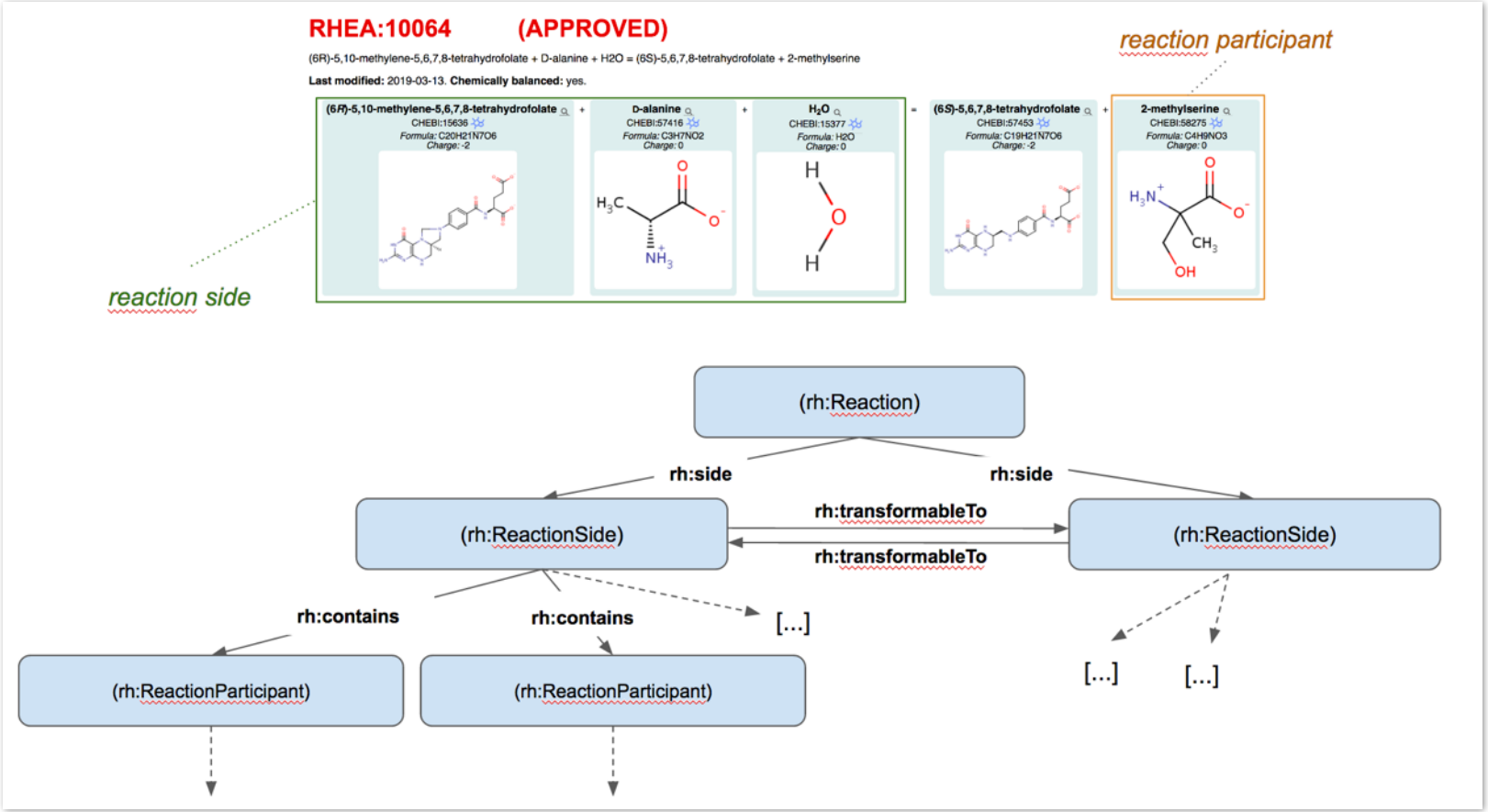
Overview



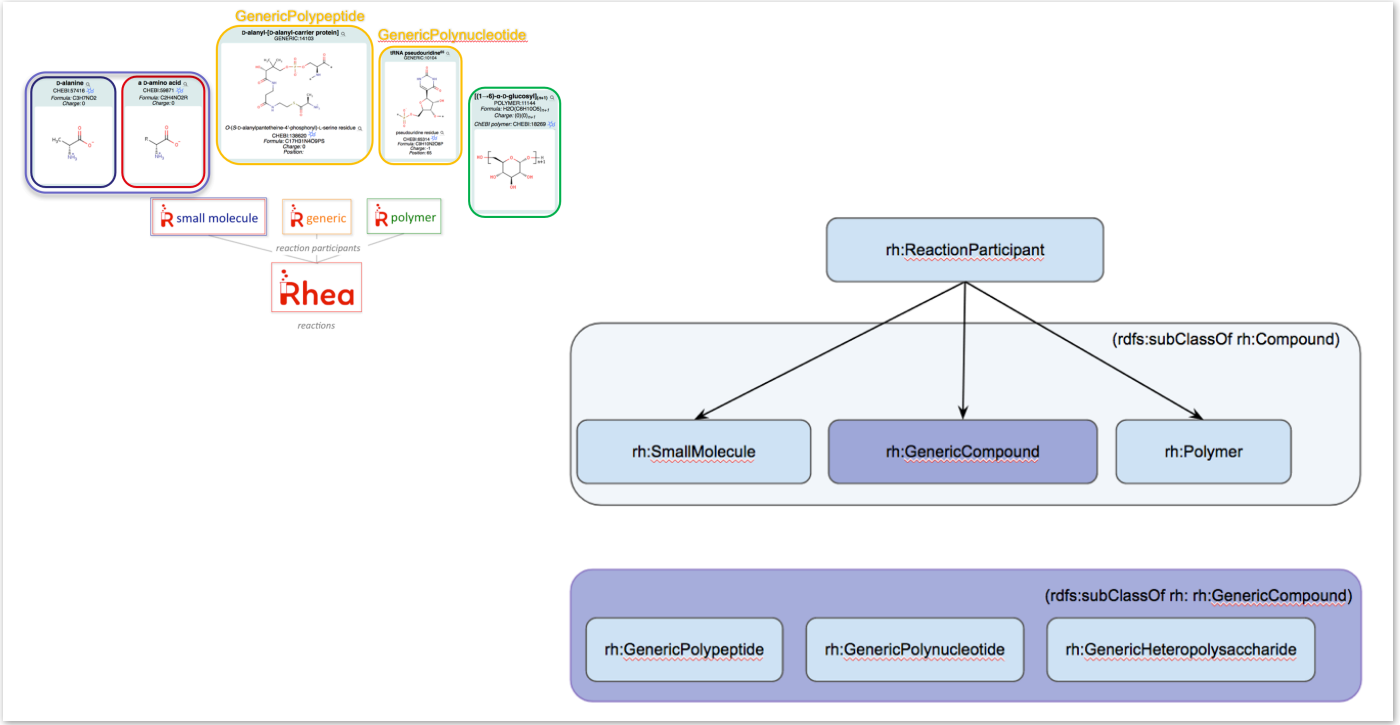
Data model (https://www.rhea-db.org/**rhea_rdf_documentation.pdf**)



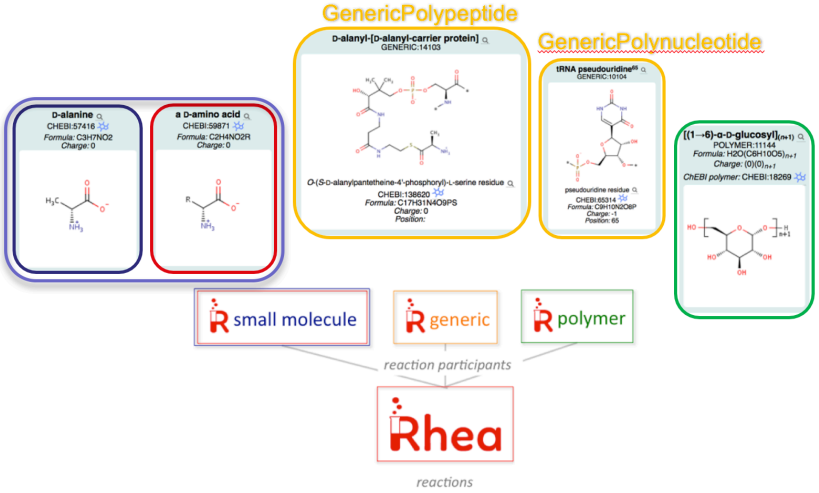
Reactions, sides and participants

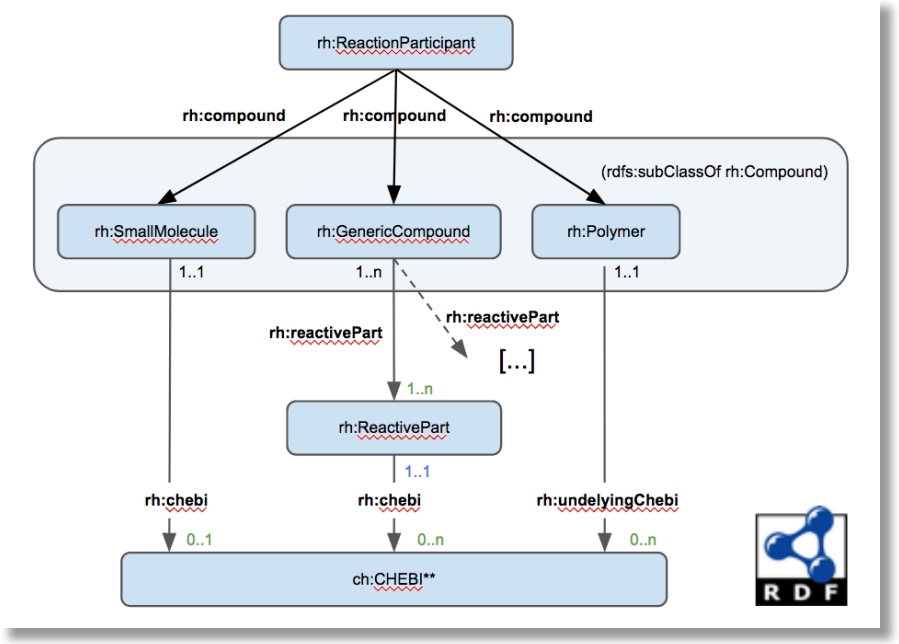


Reactions participants: rh:Compound classes

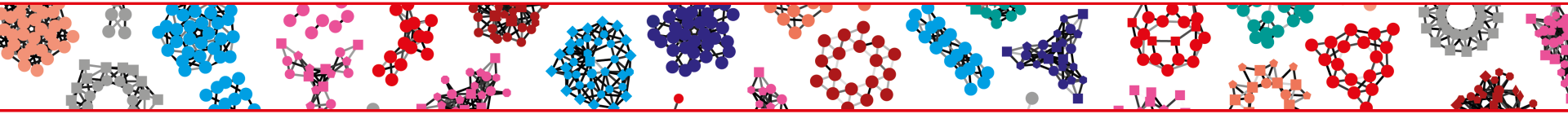


Reactions participants: links to ChEBI





Overview



01 What is Rhea?

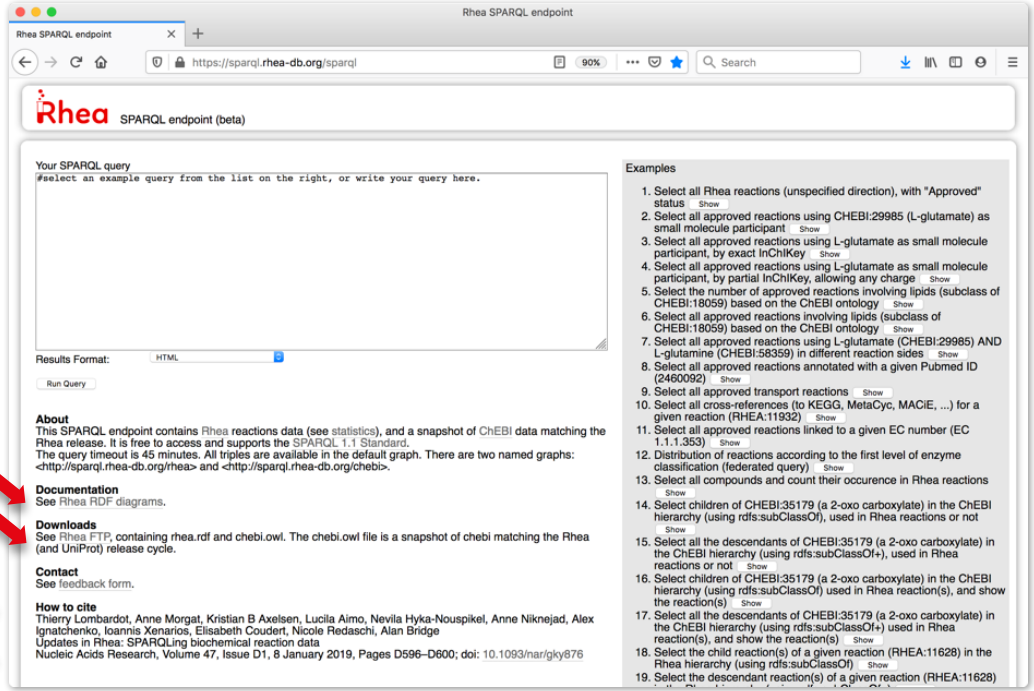
02 Data model

03 SPARQLing Rhea

04 Summary

Rhea SPARQL endpoint: rhea.rdf + chebi.owl

https://sparql.rhea-db.org/sparql



D596–D600 *Nucleic Acids Research, 2019, Vol. 47, Database issue* *Published online 1 October 2018*
doi: 10.1093/nar/gky876

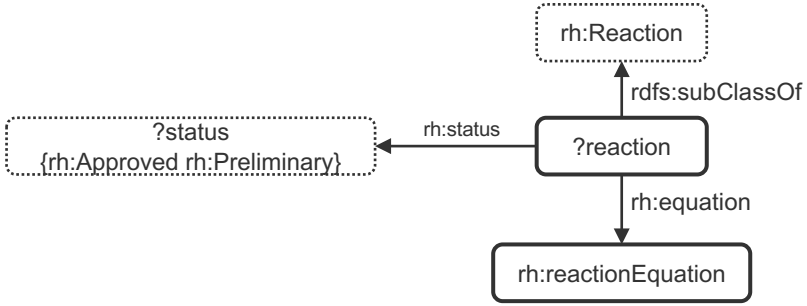
Updates in Rhea: SPARQLing biochemical reaction data

Thierry Lombardot[1,†], Anne Morgat[1,†], Kristian B. Axelsen[1], Lucila Aimo[1], Nevila Hyka-Nouspikel[1], Anne Niknejad[2], Alex Ignatchenko[3], Ioannis Xenarios[4,5], Elisabeth Coudert[1], Nicole Redaschi[1] and Alan Bridge[1,*]

[1]Swiss-Prot Group, SIB Swiss Institute of Bioinformatics, CMU, 1 rue Michel-Servet, CH-1211 Geneva 4, Switzerland, [2]Vital-IT Group, SIB Swiss Institute of Bioinformatics, Quartier Sorge, Bâtiment Génopode, CH-1015 Lausanne, Switzerland, [3]European Molecular Biology Laboratory, European Bioinformatics Institute (EMBL-EBI), Wellcome Trust Genome Campus, Hinxton, Cambridge CB10 1SD, UK, [4]Department of Biochemistry, University of Geneva, CH-1211 Geneva, Switzerland and [5]Center for Integrative Genomics, University of Lausanne, CH-1015 Lausanne, Switzerland

Received August 13, 2018; Editorial Decision September 11, 2018; Accepted September 27, 2018

Q1: Retrieve **all** Rhea reactions (approved or preliminary) and display their chemical equation




```
#endpoint: https://sparql.rhea-db.org/sparql

PREFIX rh:<http://rdf.rhea-db.org/>
SELECT ?reaction ?reactionEquation
WHERE {
  ?reaction rdfs:subClassOf rh:Reaction .
  ?reaction rh:status ?status .
  VALUES ?status {rh:Approved rh:Preliminary}
  ?reaction rh:equation ?reactionEquation .
}
ORDER BY ?reaction
```

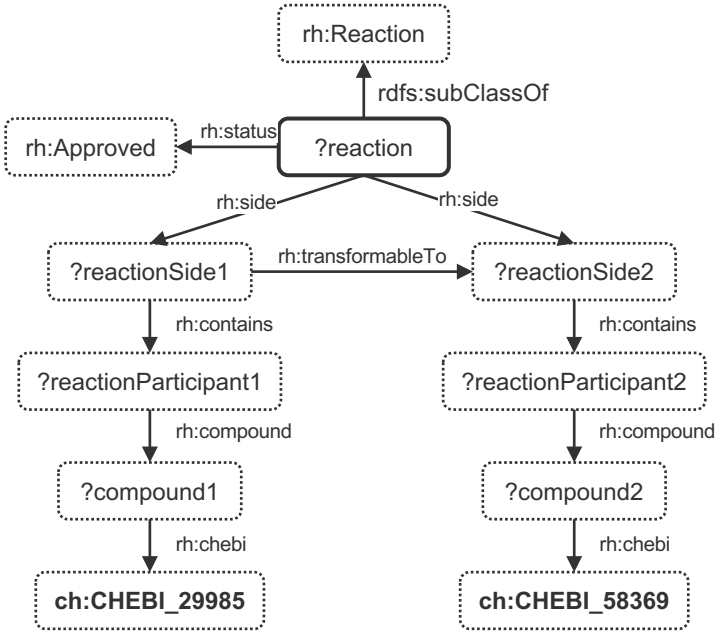
reaction	reactionEquation
http://rdf.rhea-db.org/10000	"H2O + pentanamide = NH4(+) + pentanoate"
http://rdf.rhea-db.org/10004	"benzyl isothiocyanate = benzyl thiocyanate"
http://rdf.rhea-db.org/10008	"[protein]-dithiol + a hydroperoxide = [protein]-disulfide + an alcohol + H2O"
http://rdf.rhea-db.org/10012	"(R)-6-hydroxynicotine + H2O + O2 = 6-hydroxypseudooxynicotine + H2O2"
http://rdf.rhea-db.org/10016	"H2O + O-sinapoylcholine = choline + H(+) + trans-sinapate"
http://rdf.rhea-db.org/10020	"H2O + L-saccharopine + NADP(+) = (S)-2-amino-6-oxohexanoate + H(+) + L-glutamate + NADPH"
http://rdf.rhea-db.org/10024	"L-lysyl-[histone] + S-adenosyl-L-methionine = H(+) + N(6)-methyl-L-lysyl-[histone] + S-adenosyl-L-homocysteine"
http://rdf.rhea-db.org/10028	"D-glutamate + H2O + O2 = 2-oxoglutarate + H2O2 + NH4(+)"
http://rdf.rhea-db.org/10032	"[protein]-C-terminal-L-glutamine + H2O = [protein]-C-terminal-L-glutamate + NH4(+)"
http://rdf.rhea-db.org/10036	"4-hydroxy-3-methoxy-benzenemethanol + O2 = 4-hydroxy-3-methoxybenzaldehyde + H2O2"

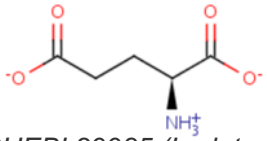
[…]

Chemical search (data from chebi.owl)

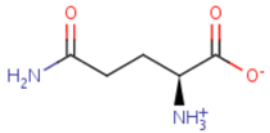
- Identifiers (**ChEBI IDs**, cross-references IDs) *[query Q2]*
- Names and synonyms
- **ChEBI ontology ('is a', 'has role' relationships)** *[query Q3]*
- **Structural search**
  - Formula, SMILES, InChi, **InChiKey** *[query Q4]*
  - ***Substructure search (IDSM/Sachem)*** *[query Q20]*

Q2: Retrieve all approved reactions using L-glutamate (CHEBI:29985) AND L-glutamine (CHEBI:58359) in opposite reaction sides





CHEBI:29985 (L-glutamate)

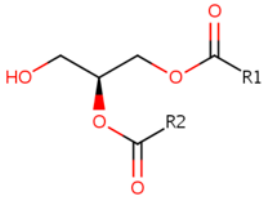


CHEBI:58359 (L-glutamine)

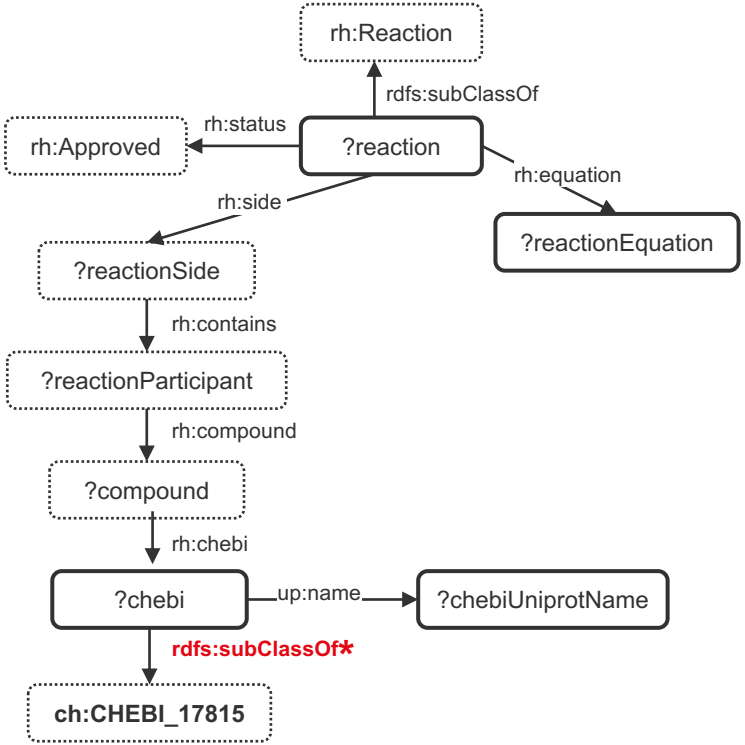
```
#endpoint:https://sparql.rhea-db.org/sparql

PREFIX rh:<http://rdf.rhea-db.org/>
PREFIX ch:<http://purl.obolibrary.org/obo/>

SELECT ?reaction
WHERE {
  ?reaction rdfs:subClassOf rh:Reaction .
  ?reaction rh:status rh:Approved .

  ?reaction rh:side ?reactionSide1 .
  ?reactionSide1 rh:contains ?participant1 .
  ?participant1 rh:compound ?compound1 .
  ?compound1 rh:chebi ch:CHEBI_29985 .

  ?reaction rh:side ?reactionSide2 .
  ?reactionSide2 rh:contains ?participant2 .
  ?participant2 rh:compound ?compound2 .
  ?compound2 rh:chebi ch:CHEBI_58359 .

  ?reactionSide1 rh:transformableTo ?reactionSide2 .
}
```

reaction
http://rdf.rhea-db.org/21732
http://rdf.rhea-db.org/23256
http://rdf.rhea-db.org/24384
http://rdf.rhea-db.org/24793
http://rdf.rhea-db.org/25512
http://rdf.rhea-db.org/26289
http://rdf.rhea-db.org/26426
http://rdf.rhea-db.org/31507
http://rdf.rhea-db.org/34547
http://rdf.rhea-db.org/34551
http://rdf.rhea-db.org/11672
http://rdf.rhea-db.org/11680
http://rdf.rhea-db.org/12128
http://rdf.rhea-db.org/12228
http://rdf.rhea-db.org/12544
http://rdf.rhea-db.org/13237
http://rdf.rhea-db.org/13753
http://rdf.rhea-db.org/14513
http://rdf.rhea-db.org/14905
http://rdf.rhea-db.org/16169
http://rdf.rhea-db.org/17129
http://rdf.rhea-db.org/17521
http://rdf.rhea-db.org/18633
http://rdf.rhea-db.org/15501
http://rdf.rhea-db.org/15889
http://rdf.rhea-db.org/52896
http://rdf.rhea-db.org/54084
http://rdf.rhea-db.org/57928

Q3: Select all approved reactions with **CHEBI:17815 (a 1,2-diacyl-sn-glycerol)** or one of its descendant.



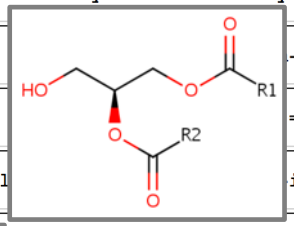
CHEBI:17815
(a 1,2-diacyl-sn-glycerol)




```
#endpoint:https://sparql.rhea-db.org/sparql

PREFIX up:<http://purl.uniprot.org/core/>

SELECT distinct ?chebi ?chebiUniprotName
                ?reaction ?reactionEquation
WHERE {
  ?reaction rdfs:subClassOf rh:Reaction .
  ?reaction rh:status rh:Approved .
  ?reaction rh:equation ?reactionEquation .
  ?reaction rh:side ?reactionSide .
  ?reactionSide rh:contains ?participant .
  ?participant rh:compound ?compound .
  ?compound rh:chebi ?chebi .
  ?chebi rdfs:subClassOf* ch:CHEBI_17815 .
  ?chebi up:name ?chebiUniprotName .
}
```

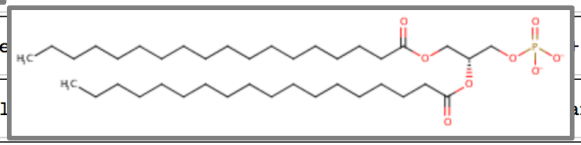
Q3: Select all approved reactions with **CHEBI:17815 (a 1,2-diacyl-sn-glycerol)** or one of its descendant.

reaction	reactionEquation
http://rdf.rhea-db.org/10272	"a 1,2-diacyl-sn-glycerol + ATP = a 1,2-diacyl-sn-glycero-3-phosphate + ADP + H(+)"
http://rdf.rhea-db.org/10604	"a 1,2-diacyl-sn-glycero-3-phosphocholine + H2O = a 1,2-diacyl-sn-glycerol + H(+) + phosphocholine"
http://rdf.rhea-db.org/10868	"a 1,2-diacyl-sn-glycerol + an acyl-CoA = a triacyl-sn-glycerol + CoA"
http://rdf.rhea-db.org/13301	"a 1,2-diacyl-sn-glycerol -glycerol + a sterol ester"
http://rdf.rhea-db.org/14057	"a 1,2-diacyl-sn-glycerol = a monoacylglycerophospholipid + a triacyl-sn-glycerol"
http://rdf.rhea-db.org/14333	"a 6-(alpha-D-glucosaminyl inositol = 6-(alpha-D-glucosaminyl)-1D-myo-inositol 1,2-cyclic phosphate + a 1,2-diacyl-sn-glycerol"
http://rdf.rhea-db.org/14945	"a 1,2-diacyl-sn-glycerol + UDP-alpha-D-galactose = a 1,2-diacyl-3-O-(beta-D-galactosyl)-sn-glycerol + H(+) + UDP"



[...]

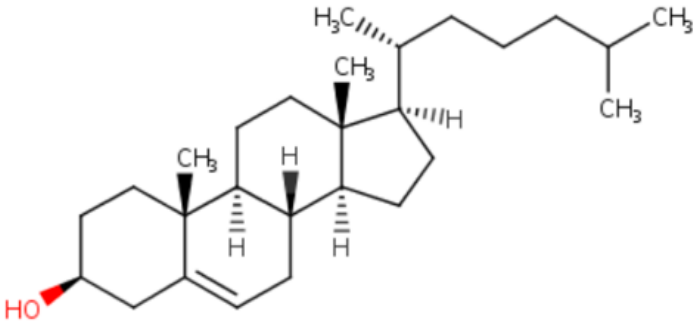
http://rdf.rhea-db.org/33335	"1,2-dioctadecanoyl-sn-glycero-3-phosphate + H2O = 1,2-dioctadecanoyl-sn-glycerol + phosphate"
http://rdf.rhea-db.org/36179	"1-O-alkyl-2-acyl-sn-glycerol + CDP-choline - CMP + H(+)"
http://rdf.rhea-db.org/36187	"1-O-alkyl-2-acyl-sn-glycerol + CDP-ethanol anolamine + CMP + H(+)"
http://rdf.rhea-db.org/36207	"1-O-(1Z-alkenyl)-sn-glycero-3-phosphate + an acyl-CoA = 1-O-(1Z-alkenyl)-2-acyl-sn-glycero-3-phosphate + CoA"



[...]

Chemical structure search

CHEBI:16113
(cholesterol)



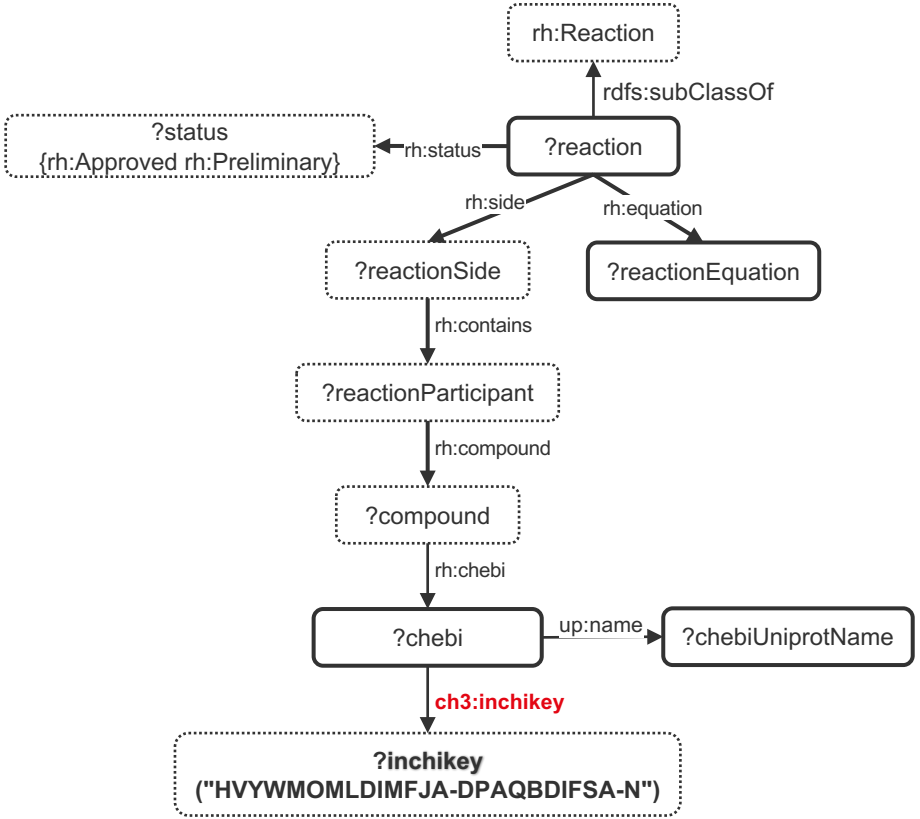
Formula: C27H46O

SMILES
C1[C@@]2([C@]3(CC[C@]4([C@]([C@@]3(CC=C2C[C@H](C1)O)[H])(CC[C@@]4([C@H](C)CCCC(C)C)[H])[H])C)[H])C

InChI
InChI=1S/C27H46O/c1-18(2)7-6-8-19(3)23-11-12-24-22-10-9-20-17-21(28)13-15-26(20,4)25(22)14-16-27(23,24)5/h9,18-19,21-25,28H,6-8,10-17H2,1-5H3/t19-,21+,22+,23-,24+,25+,26+,27-/m1/s1

InChIKey
HVYWMOMLDIMFJA-DPAQBDIFSA-N

Q4: Retrieve Rhea reactions that involve cholesterol using its **InChiKey**




```
#endpoint:https://sparql.rhea-db.org/sparql

PREFIX rh:<http://rdf.rhea-db.org/>
PREFIX ch:<http://purl.obolibrary.org/obo/>
PREFIX ch3:<http://purl.obolibrary.org/obo/chebi/>
PREFIX up:<http://purl.uniprot.org/core/>

SELECT distinct ?chebi ?chebiUniprotName
            ?reaction ?reactionEquation
WHERE {
  ?reaction rdfs:subClassOf rh:Reaction .
  ?reaction rh:status ?status .
  VALUES (?status) {(rh:Approved) (rh:Preliminary)}
  ?reaction rh:equation ?reactionEquation .
  ?reaction rh:side ?reactionSide .
  ?reactionSide rh:contains ?participant .
  ?participant rh:compound ?compound .
  ?compound rh:chebi ?chebi .
  ?chebi up:name ?chebiUniprotName .
  ?chebi ch3:inchikey ?inchikey .
  VALUES (?inchikey) {("HVYWMOMLDIMFJA-DPAQBDIFSA-N")}
}
ORDER BY ?reaction
```

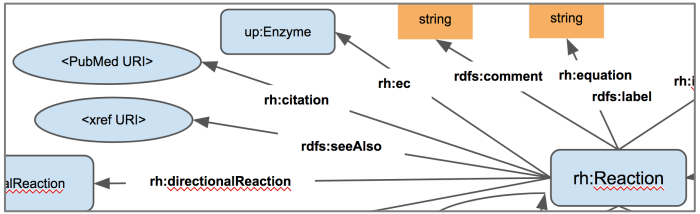
Q4: Retrieve Rhea reactions that involve cholesterol using its **InChiKey**

chebi	chebiUniprotName	reaction	reactionEquation
http://purl.obolibrary.org/obo/CHEBI_16113	"cholesterol"	http://rdf.rhea-db.org/11956	"cholesteryl-beta-D-glucoside + H2O = cholesterol + D-glucose"
http://purl.obolibrary.org/obo/CHEBI_16113	"cholesterol"	http://rdf.rhea-db.org/17729	"an acyl-CoA + cholesterol = a cholesterol ester + CoA"
http://purl.obolibrary.org/obo/CHEBI_16113	"cholesterol"	http://rdf.rhea-db.org/21104	"AH2 + cholesterol + O2 = 25-hydroxycholesterol + A + H2O"
http://purl.obolibrary.org/obo/CHEBI_16113	"cholesterol"	http://rdf.rhea-db.org/21328	"cholesterol + O2 = cholest-4-en-3-one + H2O2"
http://purl.obolibrary.org/obo/CHEBI_16113	"cholesterol"	http://rdf.rhea-db.org/21812	"cholesterol + O2 + reduced [NADPH--hemoprotein reductase] = 7alpha-hydroxycholesterol + H(+) + H2O + oxidized [NADPH--hemoprotein reductase]"
http://purl.obolibrary.org/obo/CHEBI_16113	"cholesterol"	http://rdf.rhea-db.org/22716	"cholesterol + O2 + reduced [NADPH--hemoprotein reductase] = (24S)-hydroxycholesterol + H(+) + H2O + oxidized [NADPH--hemoprotein reductase]"
http://purl.obolibrary.org/obo/CHEBI_16113	"cholesterol"	http://rdf.rhea-db.org/23984	"cholesterol + NADP(+) = cholesta-5,7-dien-3beta-ol + H(+) + NADPH"
http://purl.obolibrary.org/obo/CHEBI_16113	"cholesterol"	http://rdf.rhea-db.org/32183	"cholesterol + O2 = cholest-5-en-3-one + H2O2"
http://purl.obolibrary.org/obo/CHEBI_16113	"cholesterol"	http://rdf.rhea-db.org/33875	"cholesteryl (9Z-octadecenoate) + H2O = (9Z)-octadecenoate + cholesterol + H(+)"
http://purl.obolibrary.org/obo/CHEBI_16113	"cholesterol"	http://rdf.rhea-db.org/34087	"a 1,2-diacyl-sn-glycero-3-phosphocholine + cholesterol = a 1-acyl-sn-glycero-3-phosphocholine + a cholesterol ester"

[…]

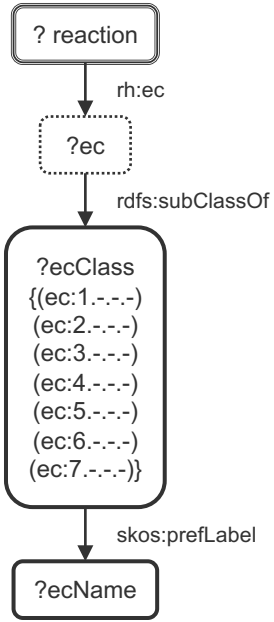
Enzyme search

- Enzyme nomenclature (EC numbers)



- UniProt enzymes

Q5: Distribution of Rhea reactions based on the first level of IUBMB enzyme classification



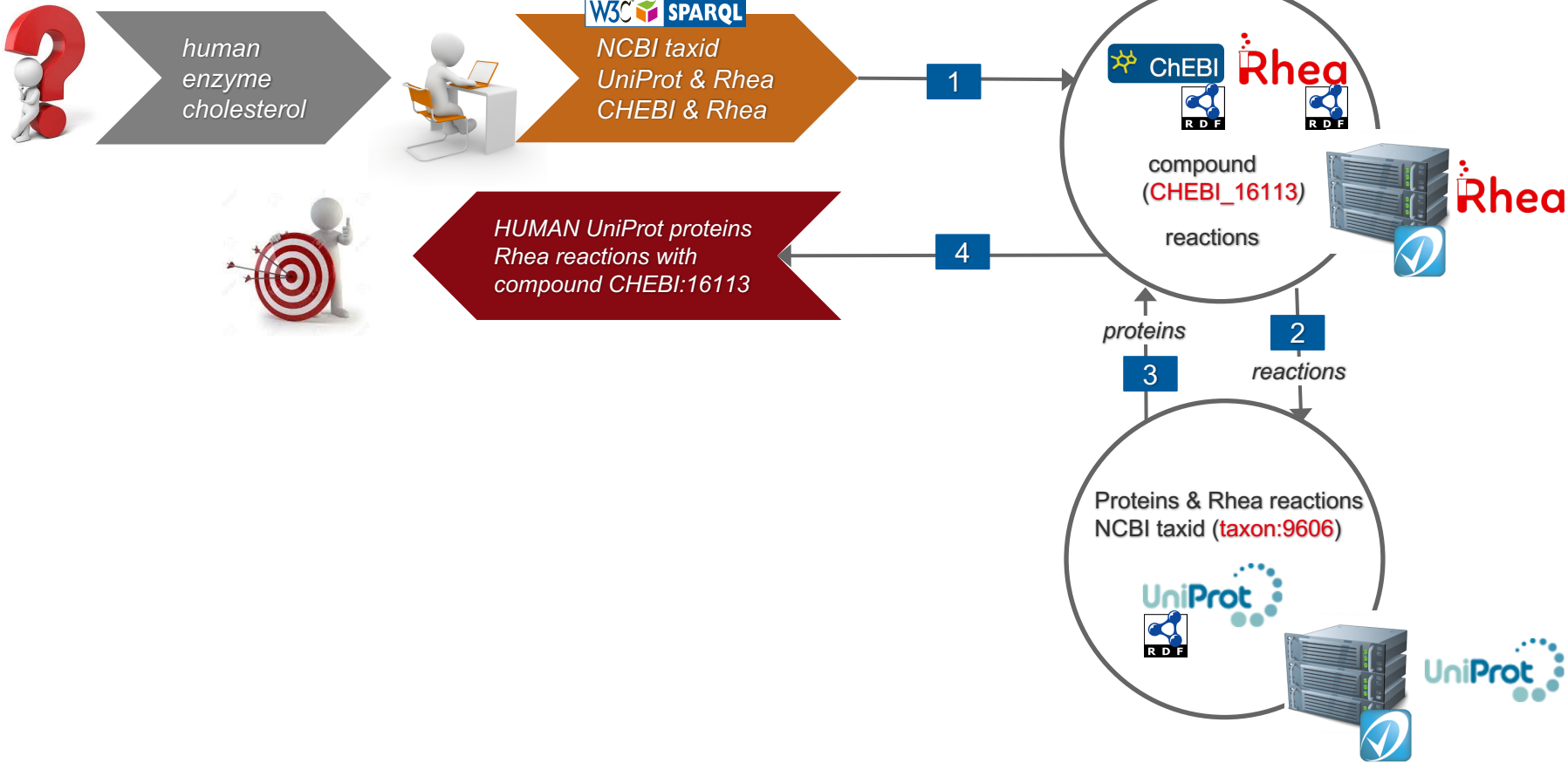

```
#endpoint:https://sparql.rhea-db.org/sparql

PREFIX rh:<http://rdf.rhea-db.org/>
PREFIX ec:<http://purl.uniprot.org/enzyme/>
PREFIX rdfs:<http://www.w3.org/2000/01/rdf-schema#>
PREFIX skos:<http://www.w3.org/2004/02/skos/core#>

SELECT ?ecClass
       ?ecClassName
       (count(?reaction) as ?reactionCount)
WHERE
{
 SERVICE <http://sparql.uniprot.org/sparql> {
   ?ec rdfs:subClassOf ?ecClass .
   ?ecClass skos:prefLabel ?ecClassName .
   VALUES (?ecClass) { (ec:1.-.-.-) (ec:2.-.-.-)(ec:3.-.-.-)
                       (ec:4.-.-.-)(ec:5.-.-.-) (ec:6.-.-.-)
                       (ec:7.-.-.-) }
 }
 ?reaction rh:ec ?ec .
}
ORDER BY ?ecClass
```

ecClass	ecClassName	reactionCount
http://purl.uniprot.org/enzyme/1.-.-.-	Oxidoreductases	2445
http://purl.uniprot.org/enzyme/2.-.-.-	Transferases	2218
http://purl.uniprot.org/enzyme/3.-.-.-	Hydrolases	909
http://purl.uniprot.org/enzyme/4.-.-.-	Lyases	760
http://purl.uniprot.org/enzyme/5.-.-.-	Isomerases	322
http://purl.uniprot.org/enzyme/6.-.-.-	Ligases	224
http://purl.uniprot.org/enzyme/7.-.-.-	Translocases	76

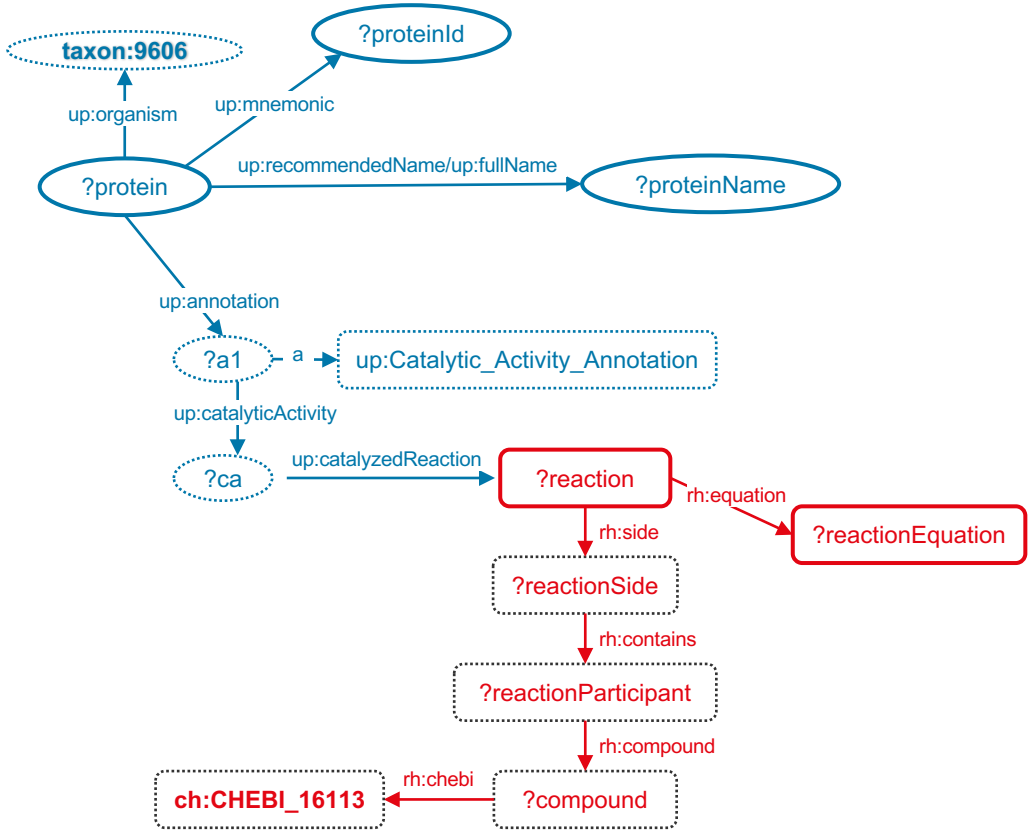
Query: retrieve human enzyme metabolizing cholesterol and their reactions

human
enzyme
cholesterol

Query: retrieve human enzyme metabolizing cholesterol and their reactions



Q6: Retrieve human enzyme metabolizing cholesterol and their reactions




```
#endpoint:https://sparql.rhea-db.org/sparql
PREFIX rdfs: <http://www.w3.org/2000/01/rdf-schema#>
PREFIX up: <http://purl.uniprot.org/core/>
PREFIX taxon:<http://purl.uniprot.org/taxonomy/>
PREFIX rh: <http://rdf.rhea-db.org/>
PREFIX ch:<http://purl.obolibrary.org/obo/>
SELECT DISTINCT ?protein  ?proteinId ?proteinName
                ?reaction ?reactionEquation
WHERE {
 ?reaction rdfs:subClassOf rh:Reaction .
 ?reaction rh:side ?reactionSide .
 ?reactionSide rh:contains ?participant .
 ?participant rh:compound ?compound .
 # cholesterol (CHEBI:16113)
 ?compound rh:chebi ch:CHEBI_16113 .
 ?reaction rh:equation ?reactionEquation .
 SERVICE <https://sparql.uniprot.org/sparql/> {
  ?protein up:mnemonic ?proteinId .
  ?protein up:recommendedName ?rn .
  ?rn up:fullName ?proteinName .
  # HUMAN proteins (taxid=9606)
  ?protein up:organism taxon:9606 .
  ?protein up:annotation ?a1 .
  ?a1 a up:Catalytic_Activity_Annotation .
  ?a1 up:catalyticActivity ?ca .
  ?ca up:catalyzedReaction ?reaction .
 }
}
```

Q6: Retrieve human enzyme metabolizing cholesterol and their reactions

protein	proteinId	proteinName	reaction	reactionEquation
http://purl.uniprot.org/uniprot/Q9UBM7	"DHCR7_HUMAN"	"7-dehydrocholesterol reductase"	http://rdf.rhea-db.org/23984	"cholesterol + NADP(+) = cholesta-5,7-dien-3beta-ol + H(+) + NADPH"
http://purl.uniprot.org/uniprot/P45844	"ABCG1_HUMAN"	"ATP-binding cassette sub-family G member 1"	http://rdf.rhea-db.org/39051	"ATP + cholesterol(in) + H2O = ADP + cholesterol(out) + H(+) + phosphate"
http://purl.uniprot.org/uniprot/Q9H222	"ABCG5_HUMAN"	"ATP-binding cassette sub-family G member 5"	http://rdf.rhea-db.org/39051	"ATP + cholesterol(in) + H2O = ADP + cholesterol(out) + H(+) + phosphate"
http://purl.uniprot.org/uniprot/Q9H221	"ABCG8_HUMAN"	"ATP-binding cassette sub-family G member 8"	http://rdf.rhea-db.org/39051	"ATP + cholesterol(in) + H2O = ADP + cholesterol(out) + H(+) + phosphate"
http://purl.uniprot.org/uniprot/P19835	"CEL_HUMAN"	"Bile salt-activated lipase"	http://rdf.rhea-db.org/33875	"cholesteryl (9Z-octadecenoate) + H2O = (9Z)-octadecenoate + cholesterol + H(+)"
http://purl.uniprot.org/uniprot/Q9Y6A2	"CP46A_HUMAN"	"Cholesterol 24-hydroxylase"	http://rdf.rhea-db.org/22716	"cholesterol + O2 + reduced [NADPH--hemoprotein reductase] = (24S)-hydroxycholesterol + H(+) +
http://purl.uniprot.org/uniprot/O95992	"CH25H_HUMAN"	"Cholesterol 25-hydroxylase"	http://rdf.rhea-db.org/21104	"AH2 + cholesterol + O2 = 25-hydroxycholesterol + A + H2O"
http://purl.uniprot.org/uniprot/O95992	"CH25H_HUMAN"	"Cholesterol 25-hydroxylase"	http://rdf.rhea-db.org/46132	"cholesterol + H(+) + NADPH + O2 = 25-hydroxycholesterol + H2O + NADP(+)"
http://purl.uniprot.org/uniprot/P05108	"CP11A_HUMAN"	"Cholesterol side-chain cleavage enzyme, mitochondrial"	http://rdf.rhea-db.org/34335	"cholesterol + 2 H(+) + O2 + 2 reduced [adrenodoxin] = 22R-hydroxycholesterol + H2O + 2 oxidiz
http://purl.uniprot.org/uniprot/P05108	"CP11A_HUMAN"	"Cholesterol side-chain cleavage enzyme, mitochondrial"	http://rdf.rhea-db.org/35739	"cholesterol + 6 H(+) + 3 O2 + 6 reduced [adrenodoxin] = 4-methylpentanal + 4 H2O + 6 oxidized

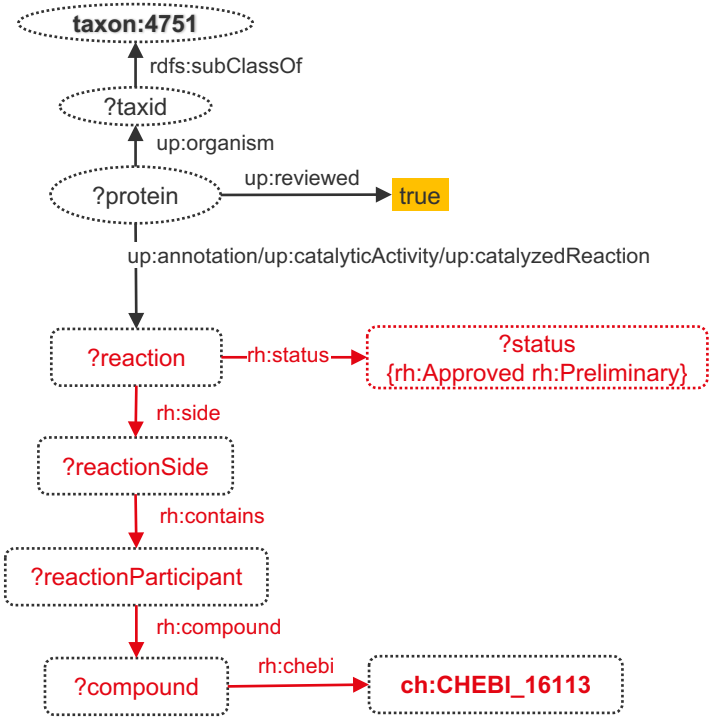
[...]

SPARQL query forms

Query form	
SELECT	Returns all, or a subset of, the variables bound in a query pattern match.
ASK	Returns a boolean indicating whether a query pattern matches or not.
CONSTRUCT	Returns an RDF graph constructed by substituting variables in a set of triple templates.
DESCRIBE	Returns an RDF graph that describes the resources found.

(from https://www.w3.org/TR/rdf-sparql-query/#QueryForms)

Q7: Ask if there are *fungal* UniProtKB/Swiss-Prot protein(s) metabolizing cholesterol (for QC)

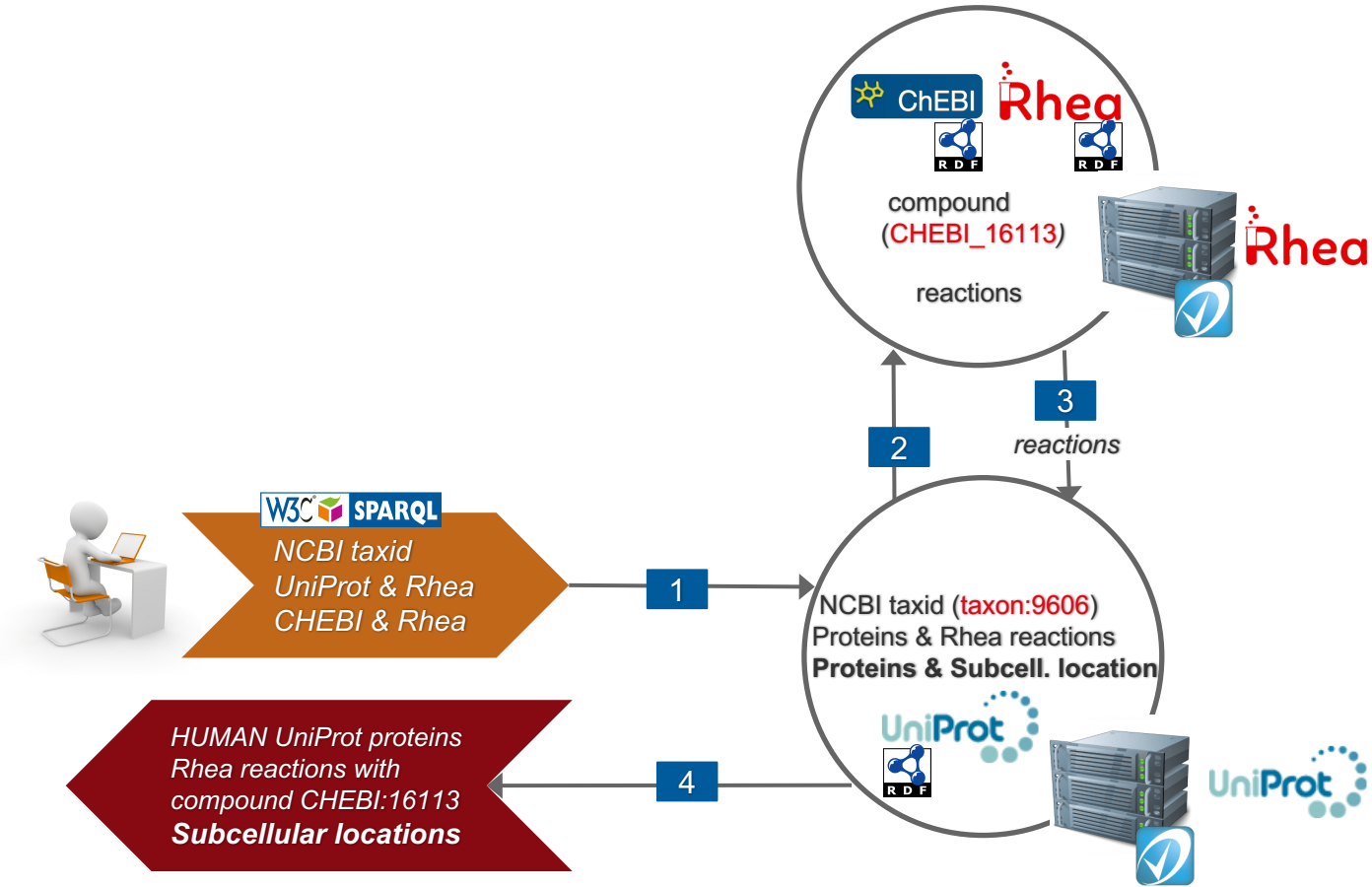



```
#endpoint: https://sparql.uniprot.org/sparql/

PREFIX up:<http://purl.uniprot.org/core/>
PREFIX rh:<http://rdf.rhea-db.org/>
PREFIX taxon:<http://purl.uniprot.org/taxonomy/>
PREFIX ch:<http://purl.obolibrary.org/obo/>
ASK {
 SERVICE <https://sparql.rhea-db.org/sparql> {
  ?reaction rh:status ?status .
  VALUES (?status) {(rh:Approved) (rh:Preliminary)}
  ?reaction rh:side ?reactionSide .
  ?reactionSide rh:contains ?participant .
  ?participant rh:compound ?compound .
  # cholesterol: CHEBI:16113
  ?compound rh:chebi ch:CHEBI_16113 .
 }
 ?protein up:annotation/up:catalyticActivity/up:catalyzedReaction ?reaction .
 # Fungi (taxon:4751),  kingdom
 ?protein up:organism ?taxid .
 ?taxid rdfs:subClassOf taxon:4751 .
 ?protein up:reviewed true .
}
```

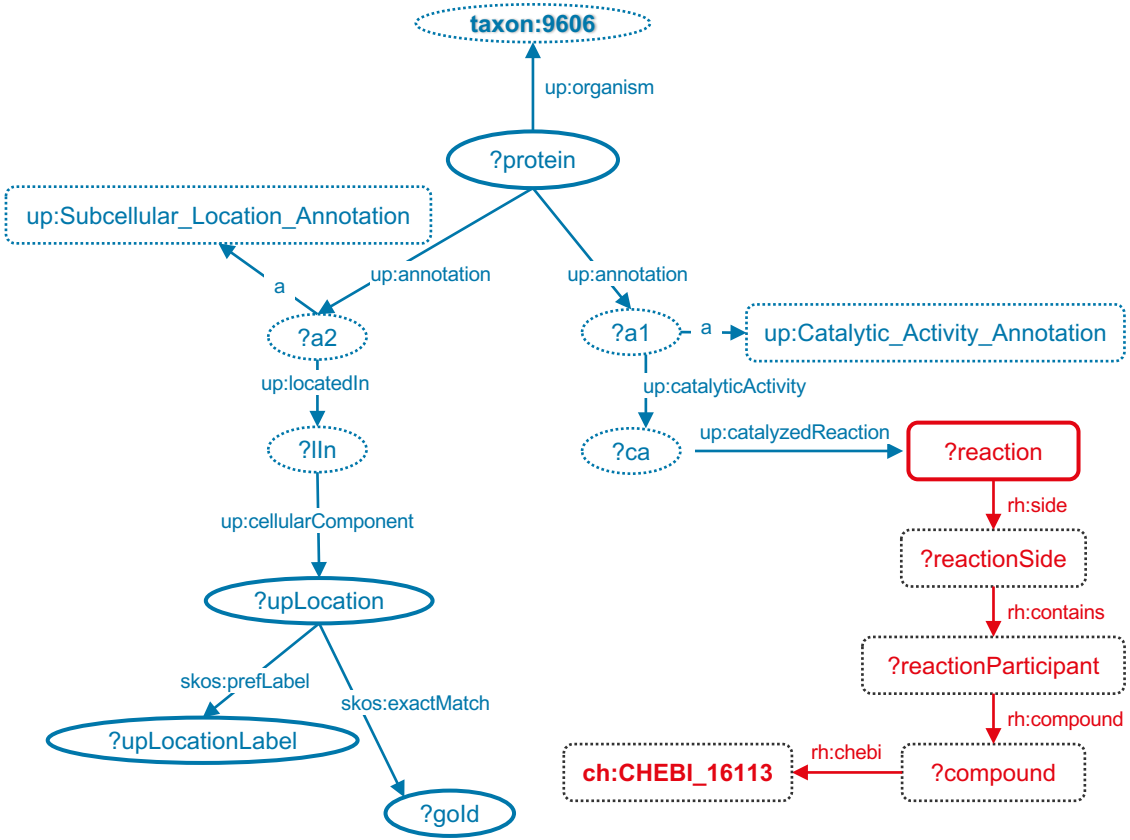
Expected: *false*

Answer (2019_10): *true* → to-do: fix errors

Query: where are the human enzymes metabolizing cholesterol **located in the cell?**



Q8: Where are the human enzymes metabolizing cholesterol **located in the cell**?




```
#endpoint: https://sparql.uniprot.org/sparql/
PREFIX rdfs:<http://www.w3.org/2000/01/rdf-schema#>
PREFIX rh:<http://rdf.rhea-db.org/>
PREFIX ch:<http://purl.obolibrary.org/obo/>
PREFIX up:<http://purl.uniprot.org/core/>
PREFIX taxon:http://purl.uniprot.org/taxonomy/
PREFIX skos:<http://www.w3.org/2004/02/skos/core#>
SELECT distinct ?protein ?reaction
                ?upLocation ?upLocationLabel ?goId
WHERE {
 SERVICE <https://sparql.rhea-db.org/sparql> {
  ?reaction rdfs:subClassOf rh:Reaction .
  ?reaction rh:equation ?reactionEquation .
  ?reaction rh:side ?reactionSide .
  ?reactionSide rh:contains ?participant .
  ?participant rh:compound ?compound .
  ?compound rh:chebi ch:CHEBI_16113 .
 }
 # Human proteins (taxid=9606)
 ?protein up:organism taxon:9606 .
 # Rhea catalayzed reactions
 ?protein up:annotation ?a1 .
 ?a1 a up:Catalytic_Activity_Annotation .
 ?a1 up:catalyticActivity ?ca .
 ?ca up:catalyzedReaction ?reaction .
 # UniProt cellular components
 ?protein up:annotation ?a2 .
 ?a2  a  up:Subcellular_Location_Annotation .
 ?a2 up:locatedIn ?IIn .
 ?IIn up:cellularComponent ?upLocation .
 ?upLocation skos:prefLabel ?upLocationLabel  .
 ?upLocation skos:exactMatch ?goId .
}
```

Q8: Where are the human enzymes metabolizing cholesterol **located in the cell**?

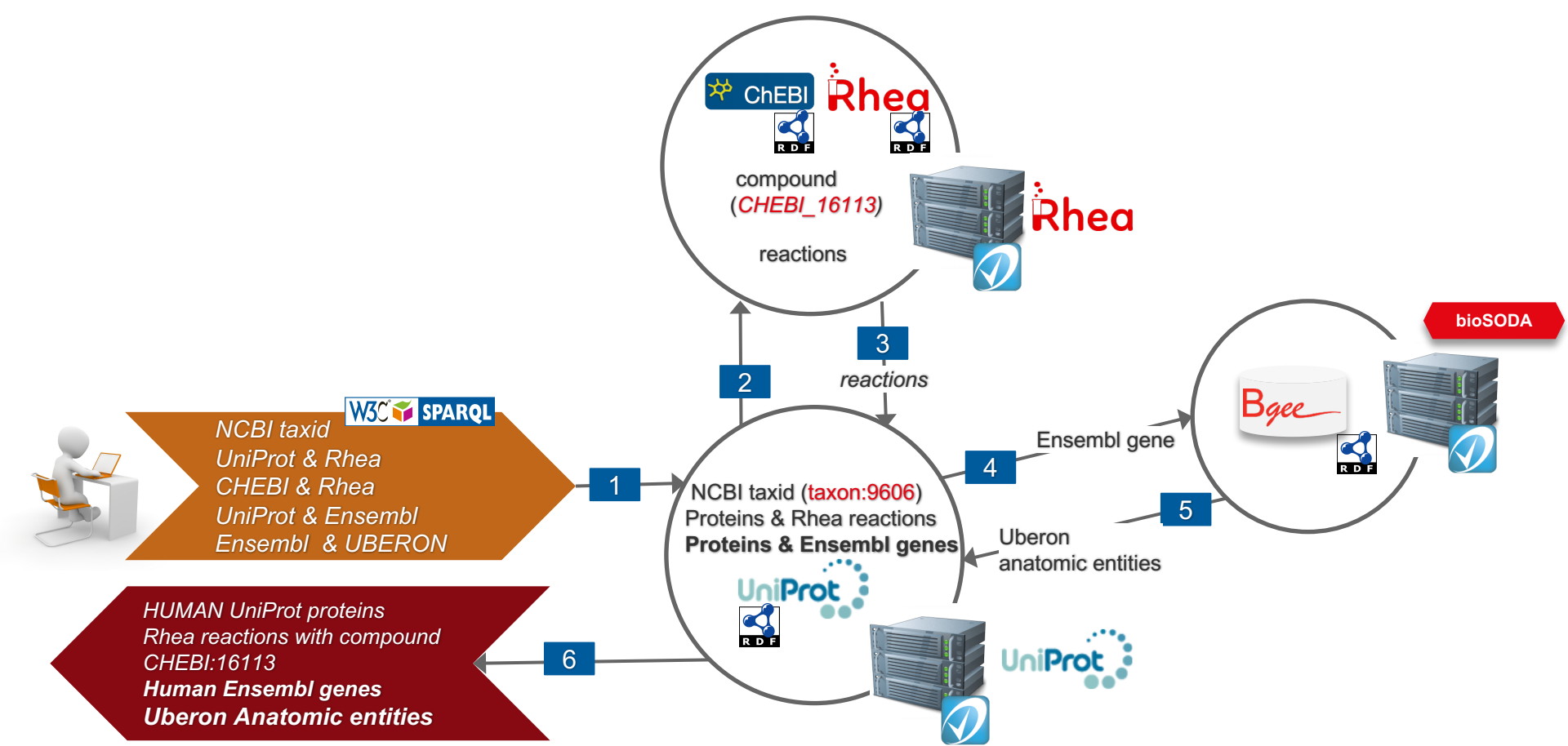
Results

Sparql XML | Sparql JSON | CSV | Show query | Share

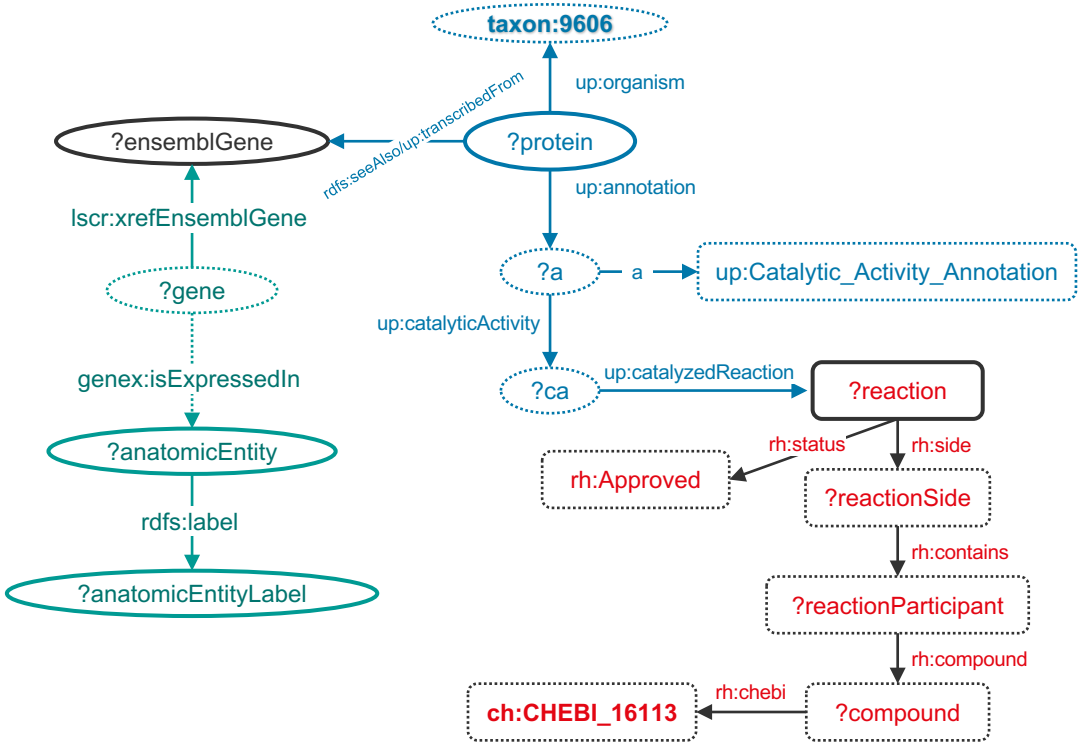
protein	proteinId	reaction	upLocation	upLocationLabel	gold
http://purl.uniprot.org/uniprot/O95477	"ABCA1_HUMAN"xsd:string	http://rdf.rhea-db.org/39051	http://purl.uniprot.org/locations/101	"Endosome"xsd:string	http://purl.obolibrary.org/obo/GO_0005768
http://purl.uniprot.org/uniprot/P45844	"ABCG1_HUMAN"xsd:string	http://rdf.rhea-db.org/39051	http://purl.uniprot.org/locations/134	"Golgi apparatus membrane"xsd:string	http://purl.obolibrary.org/obo/GO_0000139
http://purl.uniprot.org/uniprot/Q15392	"DHC24_HUMAN"xsd:string	http://rdf.rhea-db.org/36391	http://purl.uniprot.org/locations/134	"Golgi apparatus membrane"xsd:string	http://purl.obolibrary.org/obo/GO_0000139
http://purl.uniprot.org/uniprot/Q9HCG7	"GBA2_HUMAN"xsd:string	http://rdf.rhea-db.org/11956	http://purl.uniprot.org/locations/134	"Golgi apparatus membrane"xsd:string	http://purl.obolibrary.org/obo/GO_0000139
http://purl.uniprot.org/uniprot/Q9HCG7	"GBA2_HUMAN"xsd:string	http://rdf.rhea-db.org/58264	http://purl.uniprot.org/locations/134	"Golgi apparatus membrane"xsd:string	http://purl.obolibrary.org/obo/GO_0000139

[…]

Query: where are the human genes encoding enzymes metabolizing cholesterol **expressed**?



Q9: Where are the human genes encoding enzymes metabolizing cholesterol **expressed**?




```
#endpoint: https://sparql.uniprot.org/sparql/
PREFIX rdfs:<http://www.w3.org/2000/01/rdf-schema#>
PREFIX rh:<http://rdf.rhea-db.org/>
PREFIX ch:<http://purl.obolibrary.org/obo/>
PREFIX up:<http://purl.uniprot.org/core/>
PREFIX taxon:<http://purl.uniprot.org/taxonomy/>
PREFIX genex: <http://purl.org/genex#>
PREFIX lscr: <http://purl.org/lscr#>

SELECT distinct ?protein ?ensemblGene ?reaction
                ?anatomicEntityLabel ?anatomicEntity
WHERE {
 SERVICE <https://sparql.rhea-db.org/sparql> {
  ?reaction rdfs:subClassOf rh:Reaction .
  ?reaction rh:equation ?reactionEquation .
  ?reaction rh:side ?reactionSide .
  ?reactionSide rh:contains ?participant .
  ?participant rh:compound ?compound .
  ?compound rh:chebi ch:CHEBI_16113 .
 }

 ?protein up:organism taxon:9606 .
 ?protein up:annotation ?a .
 ?a a up:Catalytic_Activity_Annotation .
 ?a up:catalyticActivity ?ca .
 ?ca up:catalyzedReaction ?reaction .
 ?protein rdfs:seeAlso / up:transcribedFrom ?ensemblGene .

 SERVICE <http://biosoda.expasy.org/rdf4j-server/repositories/bgeelight> {
  ?gene genex:isExpressedIn ?anatomicEntity .
  ?gene lscr:xrefEnsemblGene ?ensemblGene .
  ?anatomicEntity rdfs:label ?anatomicEntityLabel .
 }
}
```

Q9: Where are the human genes encoding enzymes metabolizing cholesterol **expressed**?

UniProt

SPARQL Downloads Documentation/Help Contact

Results

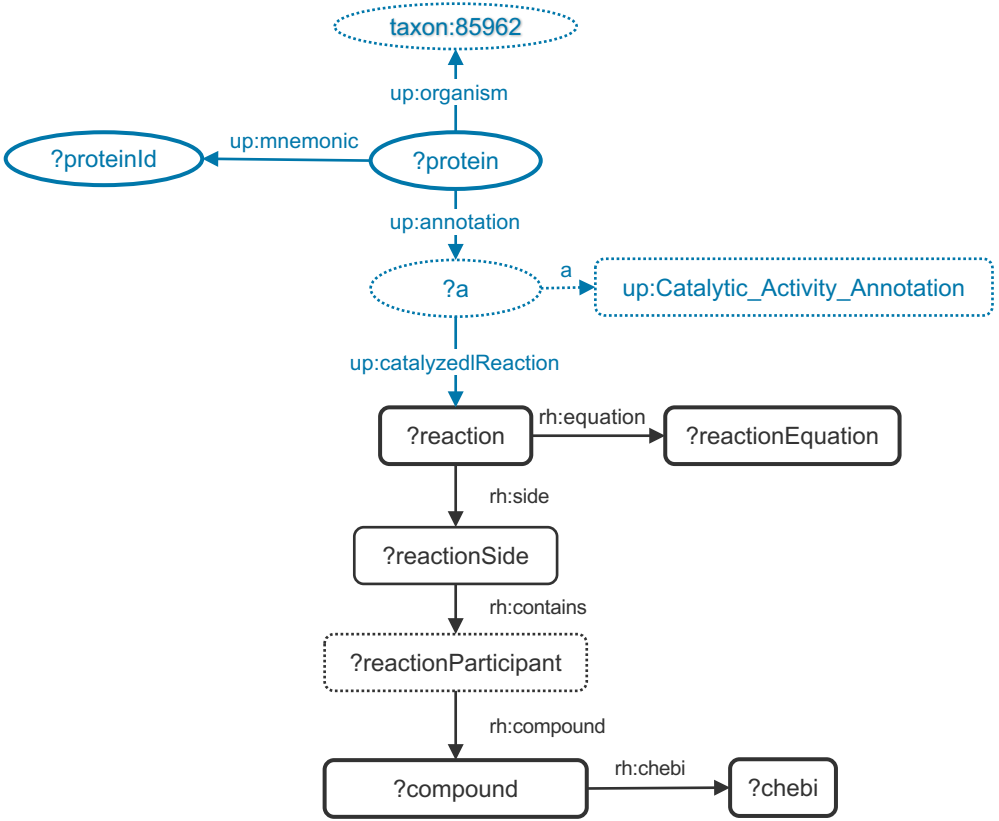
Sparql XML | Sparql JSON | CSV | Show query | Share

protein	ensemblGene	reaction	anatomicEntityLabel	anatomicEntity
uniprot:P08684	http://rdf.ebi.ac.uk/resource/ensembl/ENSG00000160868	rh:46140	"left testis"xsd:string	obo:UBERON_0004533
uniprot:P08684	http://rdf.ebi.ac.uk/resource/ensembl/ENSG00000160868	rh:46140	"pituitary gland"xsd:string	obo:UBERON_0000007
uniprot:P08684	http://rdf.ebi.ac.uk/resource/ensembl/ENSG00000160868	rh:46140	"anterior cingulate cortex"xsd:string	obo:UBERON_0009835
uniprot:P08684	http://rdf.ebi.ac.uk/resource/ensembl/ENSG00000160868	rh:46140	"ectocervix"xsd:string	obo:UBERON_0012249
uniprot:P08684	http://rdf.ebi.ac.uk/resource/ensembl/ENSG00000160868	rh:46140	"putamen"xsd:string	obo:UBERON_0001874
uniprot:P08684	http://rdf.ebi.ac.uk/resource/ensembl/ENSG00000160868	rh:46140	"right lung"xsd:string	obo:UBERON_0002167
uniprot:P08684	http://rdf.ebi.ac.uk/resource/ensembl/ENSG00000160868	rh:46140	"esophagogastric junction muscularis propria"xsd:string	obo:UBERON_0035841
uniprot:P08684	http://rdf.ebi.ac.uk/resource/ensembl/ENSG00000160868	rh:46140	"right ovary"xsd:string	obo:UBERON_0002118
uniprot:P08684	http://rdf.ebi.ac.uk/resource/ensembl/ENSG00000160868	rh:46140	"aorta"xsd:string	obo:UBERON_0000947
uniprot:P08684	http://rdf.ebi.ac.uk/resource/ensembl/ENSG00000160868	rh:46140	"minor salivary gland"xsd:string	obo:UBERON_0001830
uniprot:P08684	http://rdf.ebi.ac.uk/resource/ensembl/ENSG00000160868	rh:46140	"subcutaneous adipose tissue"xsd:string	obo:UBERON_0002190
uniprot:P08684	http://rdf.ebi.ac.uk/resource/ensembl/ENSG00000160868	rh:46140	"small intestine Peyer's patch"xsd:string	obo:UBERON_0003454
uniprot:P08684	http://rdf.ebi.ac.uk/resource/ensembl/ENSG00000160868	rh:46140	"blood"xsd:string	obo:UBERON_0000178

Explore/exploit the enormous richness of UniProt (Jerven)

- **Diseases**
- **3D structures (PDB)**
- **Homologs: orthoDB (Dima) and OMA (Tarcisio)**
- **Taxonomy / complete proteomes**
- **…**

Q10: Build the UniProt *H. pylori* proteome scale metabolic network




```
#endpoint: https://sparql.rhea-db.org/sparql

PREFIX rh:<http://rdf.rhea-db.org/>
PREFIX up:<http://purl.uniprot.org/core/>
PREFIX taxon:<http://purl.uniprot.org/taxonomy/>
SELECT  ?protein ?proteinId
        ?reaction ?reactionSide
        ?compound  ?chebi
        ?reactionEquation
WHERE {
 SERVICE <http://sparql.uniprot.org/sparql> {
  ?protein up:reviewed ?status .
  # Filter by NCBI taxid (H. pylori == 85962)
  ?protein up:organism taxon:85962 .
  ?protein up:mnemonic ?proteinId .
  # Rhea reactions catalyzed by UniProt proteins
  ?protein up:annotation ?a .
  ?a up:catalyticActivity ?ca .
  ?ca up:catalyzedReaction ?reaction .
 }
 ?reaction rh:equation ?reactionEquation .
 ?reaction rh:side ?reactionSide .
 ?reactionSide rh:contains ?participant .
 ?participant rh:compound ?compound .
 OPTIONAL {?compound rh:chebi ?chebi } .
}
```

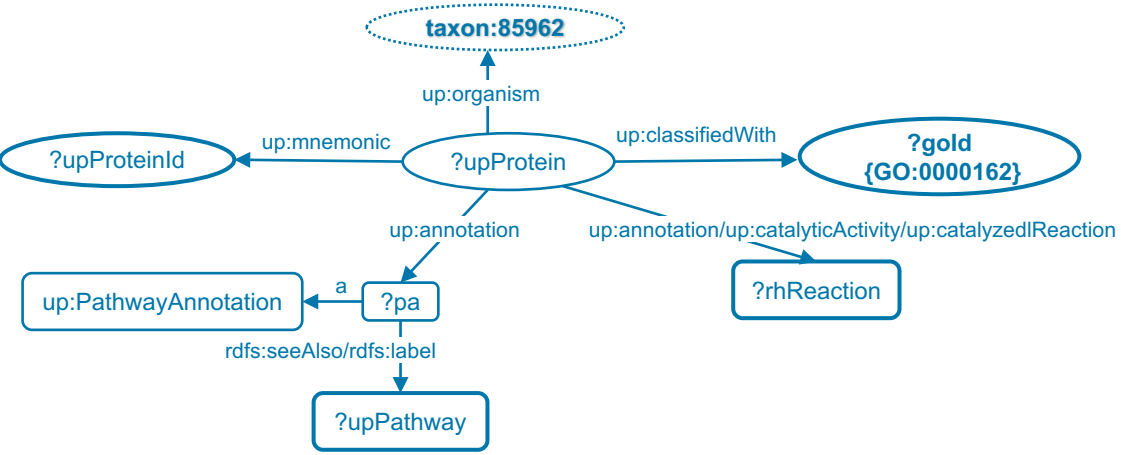
Q10: *H. pylori* metabolic network (UniProtKB/Swiss-Prot and Rhea-ChEBI)

protein	proteinId	reaction	reactionSide	compound	chebi	reactionEquation
http://purl.uniprot.org/uniprot/P56463	"DEOD_HELPY"	http://rdf.rhea-db.org/36431	http://rdf.rhea-db.org/36431_R	http://rdf.rhea-db.org/Compound_14976	http://purl.obolibrary.org/obo/CHEBI_26386	"a purine 2'-deoxy-D-ribonucleoside + phosphate = 2-deoxy-alpha-D-ribose 1-phosphate + a purine nucleobas
http://purl.uniprot.org/uniprot/P56463	"DEOD_HELPY"	http://rdf.rhea-db.org/36431	http://rdf.rhea-db.org/36431_L	http://rdf.rhea-db.org/Compound_15011	http://purl.obolibrary.org/obo/CHEBI_142361	"a purine 2'-deoxy-D-ribonucleoside + phosphate = 2-deoxy-alpha-D-ribose 1-phosphate + a purine nucleobas
http://purl.uniprot.org/uniprot/O26027	"MURE_HELPY"	http://rdf.rhea-db.org/23676	http://rdf.rhea-db.org/23676_R	http://rdf.rhea-db.org/Compound_10767	http://purl.obolibrary.org/obo/CHEBI_83905	"ATP + meso-2,6-diaminopimelate + UDP-N-acetyl-alpha-D-muramoyl-L-alanyl-D-glutamate = ADP + H(+) + phosp
http://purl.uniprot.org/uniprot/O25016	"KDSB_HELPY"	http://rdf.rhea-db.org/23448	http://rdf.rhea-db.org/23448_R	http://rdf.rhea-db.org/Compound_11525	http://purl.obolibrary.org/obo/CHEBI_85987	"3-deoxy-alpha-D-manno-oct-2-ulosonate + CTP = CMP-3-deoxy-beta-D-manno-octulosonate + diphosphate"
http://purl.uniprot.org/uniprot/O25611	"O25611_HELPY"	http://rdf.rhea-db.org/28066	http://rdf.rhea-db.org/28066_L	http://rdf.rhea-db.org/Compound_11525	http://purl.obolibrary.org/obo/CHEBI_85987	"CMP-3-deoxy-beta-D-manno-octulosonate + lipid IVA (E. coli) = alpha-Kdo-(2->6)-lipid IVA + CMP + H(+)"
http://purl.uniprot.org/uniprot/P56006	"SCOA_HELPY"	http://rdf.rhea-db.org/24564	http://rdf.rhea-db.org/24564_R	http://rdf.rhea-db.org/Compound_12177	http://purl.obolibrary.org/obo/CHEBI_90726	"a 3-oxo acid + succinyl-CoA = a 3-oxoacyl-CoA + succinate"
http://purl.uniprot.org/uniprot/P56007	"SCOB_HELPY"	http://rdf.rhea-db.org/24564	http://rdf.rhea-db.org/24564_R	http://rdf.rhea-db.org/Compound_12177	http://purl.obolibrary.org/obo/CHEBI_90726	"a 3-oxo acid + succinyl-CoA = a 3-oxoacyl-CoA + succinate"
http://purl.uniprot.org/uniprot/P56122	"AROC_HELPY"	http://rdf.rhea-db.org/21020	http://rdf.rhea-db.org/21020_L	http://rdf.rhea-db.org/Compound_1720	http://purl.obolibrary.org/obo/CHEBI_57701	"5-O-(1-carboxyvinyl)-3-phosphoshikimate = chorismate + phosphate"
http://purl.uniprot.org/uniprot/P56197	"AROA_HELPY"	http://rdf.rhea-db.org/21256	http://rdf.rhea-db.org/21256_R	http://rdf.rhea-db.org/Compound_1720	http://purl.obolibrary.org/obo/CHEBI_57701	"3-phosphoshikimate + phosphoenolpyruvate = 5-O-(1-carboxyvinyl)-3-phosphoshikimate + phosphate"
http://purl.uniprot.org/uniprot/O24865	"O24865_HELPY"	http://rdf.rhea-db.org/34099	http://rdf.rhea-db.org/34099_R	http://rdf.rhea-db.org/Compound_2551	http://purl.obolibrary.org/obo/CHEBI_57920	"carboxynorspermidine + H(+) = CO2 + norspermidine"

[…]

→ To compare with published GSMNs (MetaNetX, Marco)

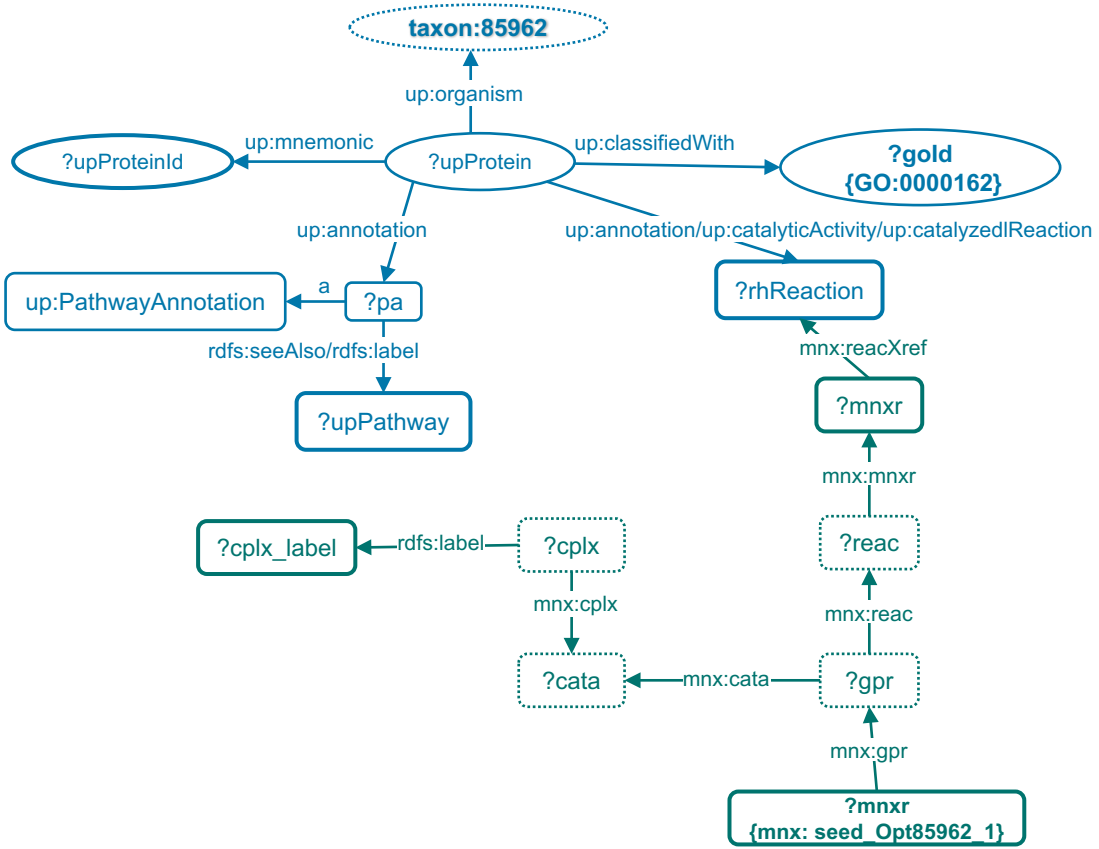
Q11: Explore *H. pylori* tryptophan biosynthesis pathway (GO:0000162)




```
#endpoint: https://sparql.uniprot.org/sparql/
PREFIX rdfs:<http://www.w3.org/2000/01/rdf-schema#>
PREFIX up:<http://purl.uniprot.org/core/>
PREFIX rh:<http://rdf.rhea-db.org/>
PREFIX taxon:<http://purl.uniprot.org/taxonomy/>
PREFIX ch:<http://purl.obolibrary.org/obo/>
PREFIX GO:<http://purl.obolibrary.org/obo/GO_>
SELECT distinct ?upProteinId ?gold ?rhReaction ?upPathway
WHERE{
 ?upProtein up:reviewed true .
 ?upProtein up:mnemonic  ?upProteinId .
 # HELPY proteins (taxid=85962)
 ?upProtein up:organism taxon:85962 .
 ?upProtein up:annotation/up:catalyticActivity/up:catalyzedReaction ?rhReaction .
 ?upProtein up:classifiedWith ?gold .
 VALUES ?gold {GO:0000162} # GO: tryptophan biosynthesis
 OPTIONAL {?upProtein up:annotation ?pa . # Pathway annotation
           ?pa a up:Pathway_Annotation .
           ?pa rdfs:seeAlso/rdfs:label ?upPathway . }
}
ORDER BY ?upPathway
```

upProteinId	gold	rhReaction	upPathway
"TRPE_HELPY"xsd:string	http://purl.obolibrary.org/obo/GO_0000162	http://rdf.rhea-db.org/21732	"Amino-acid biosynthesis; L-tryptophan biosynthesis; L-tryptophan from chorismate: step 1/5"xsd:string
"TRPG_HELPY"xsd:string	http://purl.obolibrary.org/obo/GO_0000162	http://rdf.rhea-db.org/21732	"Amino-acid biosynthesis; L-tryptophan biosynthesis; L-tryptophan from chorismate: step 1/5"xsd:string
"TRPD_HELPY"xsd:string	http://purl.obolibrary.org/obo/GO_0000162	http://rdf.rhea-db.org/11768	"Amino-acid biosynthesis; L-tryptophan biosynthesis; L-tryptophan from chorismate: step 2/5"xsd:string
"TRPC_HELPY"xsd:string	http://purl.obolibrary.org/obo/GO_0000162	http://rdf.rhea-db.org/23476	"Amino-acid biosynthesis; L-tryptophan biosynthesis; L-tryptophan from chorismate: step 3/5"xsd:string
"TRPC_HELPY"xsd:string	http://purl.obolibrary.org/obo/GO_0000162	http://rdf.rhea-db.org/21540	"Amino-acid biosynthesis; L-tryptophan biosynthesis; L-tryptophan from chorismate: step 3/5"xsd:string
"TRPC_HELPY"xsd:string	http://purl.obolibrary.org/obo/GO_0000162	http://rdf.rhea-db.org/23476	"Amino-acid biosynthesis; L-tryptophan biosynthesis; L-tryptophan from chorismate: step 4/5"xsd:string
"TRPC_HELPY"xsd:string	http://purl.obolibrary.org/obo/GO_0000162	http://rdf.rhea-db.org/21540	"Amino-acid biosynthesis; L-tryptophan biosynthesis; L-tryptophan from chorismate: step 4/5"xsd:string
"TRPA_HELPY"xsd:string	http://purl.obolibrary.org/obo/GO_0000162	http://rdf.rhea-db.org/10532	"Amino-acid biosynthesis; L-tryptophan biosynthesis; L-tryptophan from chorismate: step 5/5"xsd:string
"TRPB_HELPY"xsd:string	http://purl.obolibrary.org/obo/GO_0000162	http://rdf.rhea-db.org/10532	"Amino-acid biosynthesis; L-tryptophan biosynthesis; L-tryptophan from chorismate: step 5/5"xsd:string

Q12: H. pylori enzyme complexes for tryptophan biosynthesis pathway (MetaNetX: seed_Opt85962_1)




```
#endpoint: https://sparql.uniprot.org/sparql/
PREFIX rdfs:<http://www.w3.org/2000/01/rdf-schema#>
PREFIX up:<http://purl.uniprot.org/core/>
PREFIX rh:<http://rdf.rhea-db.org/>
PREFIX taxon:<http://purl.uniprot.org/taxonomy/>
PREFIX mnx:<https://rdf.metanetx.org/schema/>
PREFIX mnet:<https://rdf.metanetx.org/mnet/>
PREFIX GO:<http://purl.obolibrary.org/obo/GO_>

SELECT distinct ?upPathway ?upProteinId ?rhReaction
                ?mnxr ?cplx_label ?mnet
WHERE{
   ?upProtein up:reviewed true .
   ?upProtein up:mnemonic ?upProteinId .
   ?upProtein up:organism taxon:85962 .
   ?upProtein up:classifiedWith GO:0000162.
   ?upProtein up:annotation/up:catalyticActivity/up:catalyzedReaction ?rhReaction
.
   # Pathway annotation
   OPTIONAL {?upProtein up:annotation ?pa          .
          ?pa a up:Pathway_Annotation          ;
             rdfs:seeAlso/rdfs:label ?upPathway . }
   SERVICE <https://rdf.metanetx.org/sparql> {
      ?mnxr mnx:reacXref ?rhReaction .
      ?reac mnx:mnxr ?mnxr .
      ?gpr  mnx:reac ?reac .
      ?gpr  mnx:cata ?cata .
      ?cata mnx:cplx ?cplx .
      ?cplx rdfs:label ?cplx_label .
      ?mnet mnx:gpr ?gpr .
      VALUES ?mnet {mnet:seed_Opt85962_1}
   }
}
ORDER BY ?upPathway
```

Q12: H. pylori enzyme complexes for tryptophan biosynthesis pathway (MetaNetX: seed_Opt85962_1)

upPathway	upProteinId	rhReaction	mnxr	cplx_label	mnet
"Amino-acid biosynthesis; L-tryptophan biosynthesis; L-tryptophan from chorismate: step 1/5"xsd:string	"TRPE_HELPY"xsd:string	http://rdf.rhea-db.org/21732	https://rdf.metanetx.org/reac/MNXR95843	"bact:TRPE_HELPY+bact:TRPG_HELPY"xsd:string	https://rdf.metanetx.org/mnet/seed_Opt85962_1
"Amino-acid biosynthesis; L-tryptophan biosynthesis; L-tryptophan from chorismate: step 1/5"xsd:string	"TRPG_HELPY"xsd:string	http://rdf.rhea-db.org/21732	https://rdf.metanetx.org/reac/MNXR95843	"bact:TRPE_HELPY+bact:TRPG_HELPY"xsd:string	https://rdf.metanetx.org/mnet/seed_Opt85962_1
"Amino-acid biosynthesis; L-tryptophan biosynthesis; L-tryptophan from chorismate: step 2/5"xsd:string	"TRPD_HELPY"xsd:string	http://rdf.rhea-db.org/11768	https://rdf.metanetx.org/reac/MNXR95842	"bact:TRPD_HELPY"xsd:string	https://rdf.metanetx.org/mnet/seed_Opt85962_1
"Amino-acid biosynthesis; L-tryptophan biosynthesis; L-tryptophan from chorismate: step 3/5"xsd:string	"TRPC_HELPY"xsd:string	http://rdf.rhea-db.org/23476	https://rdf.metanetx.org/reac/MNXR100814	"bact:TRPC_HELPY"xsd:string	https://rdf.metanetx.org/mnet/seed_Opt85962_1
"Amino-acid biosynthesis; L-tryptophan biosynthesis; L-tryptophan from chorismate: step 3/5"xsd:string	"TRPC_HELPY"xsd:string	http://rdf.rhea-db.org/21540	https://rdf.metanetx.org/reac/MNXR103156	"bact:TRPC_HELPY"xsd:string	https://rdf.metanetx.org/mnet/seed_Opt85962_1
"Amino-acid biosynthesis; L-tryptophan biosynthesis; L-tryptophan from chorismate: step 4/5"xsd:string	"TRPC_HELPY"xsd:string	http://rdf.rhea-db.org/21540	https://rdf.metanetx.org/reac/MNXR103156	"bact:TRPC_HELPY"xsd:string	https://rdf.metanetx.org/mnet/seed_Opt85962_1
"Amino-acid biosynthesis; L-tryptophan biosynthesis; L-tryptophan from chorismate: step 4/5"xsd:string	"TRPC_HELPY"xsd:string	http://rdf.rhea-db.org/23476	https://rdf.metanetx.org/reac/MNXR100814	"bact:TRPC_HELPY"xsd:string	https://rdf.metanetx.org/mnet/seed_Opt85962_1
"Amino-acid biosynthesis; L-tryptophan biosynthesis; L-tryptophan from chorismate: step 5/5"xsd:string	"TRPB_HELPY"xsd:string	http://rdf.rhea-db.org/10532	https://rdf.metanetx.org/reac/MNXR104343	"bact:TRPA_HELPY+bact:TRPB_HELPY"xsd:string	https://rdf.metanetx.org/mnet/seed_Opt85962_1
"Amino-acid biosynthesis; L-tryptophan biosynthesis; L-tryptophan from chorismate: step 5/5"xsd:string	"TRPA_HELPY"xsd:string	http://rdf.rhea-db.org/10532	https://rdf.metanetx.org/reac/MNXR104343	"bact:TRPA_HELPY+bact:TRPB_HELPY"xsd:string	https://rdf.metanetx.org/mnet/seed_Opt85962_1

Programmatic access

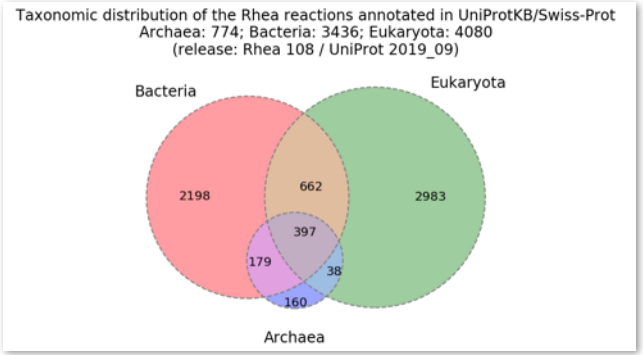
jupyter

SPARQL

+

python

SPARQLWrapper
pandas
matplotlib
matplotlib_venn
[...]



Rhea reactions used in UniProtKB/Swiss-Prot annotation (release: Rhea 108 / UniProt 2019_09)

		label	count	pct
category				
domain	archaea	857	8.6%
domain	bacteria	3334	33.6%
domain	eukaryota	4221	42.5%
domain	viruses	187	1.9%

Jupyter notebook: rhea_tutorial_SWAT4HCLS_2019.ipynb

2.1 Python Libraries

```
from SPARQLWrapper import SPARQLWrapper, JSON
import pandas as pd
from pandas.io.json import json_normalize
```

2.2 SPARQL endpoints

```
sparql_uniprot_url = "https://sparql.uniprot.org/sparql/"
sparql_rhea_url = "https://sparql.rhea-db.org/sparql"
```

2.3 Python functions

```
def sparql2pandas(sparql_query, sparql_service_url):
    """
    Use SPARQLWrapper to query a SPARQL endpoint (sparql_service_url) with a given SPARQL query string
    (sparql_query) that uses SELECT query form.
    Return the SPARQL query result as a pandas Dataframe.
    """
    #
    # run the SPARQL query
    #
    sparql=SPARQLWrapper(sparql_service_url)
    sparql.setQuery(sparql_query)
    sparql.setReturnFormat(JSON)
    res = sparql.query().convert()
```

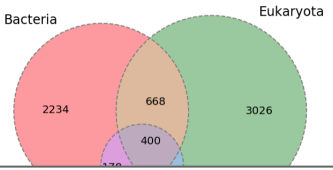
3.1 Q1: Retrieve all Rhea reactions (approved or preliminary) and their chemical equation

```
sparql_Q1="""
#endpoint: https://sparql.rhea-db.org/sparql

PREFIX rh:<http://rdf.rhea-db.org/>

SELECT ?reaction ?reactionEquation
WHERE {
  ?reaction rdfs:subClassOf rh:Reaction .
  ?reaction rh:status ?status .
  VALUES ?status {rh:Approved rh:Preliminary}
  ?reaction rh:equation ?reactionEquation .
}
ORDER BY ?reaction
"""
print(sparql_Q1)
```

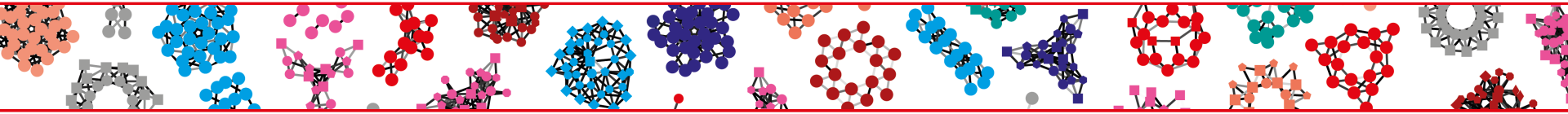
4.1.2 Compute Venn diagram using matplotlib and matplotlib_venn python libraries

```
import matplotlib.pyplot as plt
from matplotlib_venn import venn3
from matplotlib_venn import venn3_circles

set_A = set(df_up_rh[df_up_rh.domainName == 'Archaea']['rhReaction'].drop_duplicates())
set_B = set(df_up_rh[df_up_rh.domainName == 'Bacteria']['rhReaction'].drop_duplicates())
set_E = set(df_up_rh[df_up_rh.domainName == 'Eukaryota']['rhReaction'].drop_duplicates())

nb_A = len(set_A)
nb_B = len(set_B)
nb_E = len(set_E)
nb_all = len(set_A | set_B | set_E)

title = 'Taxonomic distribution of the Rhea reactions annotated in UniProtKB/Swiss-Prot\n'
title += 'Rhea reactions: in Archaea=%s ; in Bacteria=%s; in Eukaryota=%s\n' % (nb_A, nb_B, nb_E)

# Plot Venn diagram
v=venn3([set_B,set_E,set_A], set_labels = ('Bacteria','Eukaryota', '\nArchaea'))
c=venn3_circles([set_B,set_E,set_A], linestyle='dashed', linewidth=1, color="grey")
plt.title(title)

plt.show();
```

Taxonomic distribution of the Rhea reactions annotated in UniProtKB/Swiss-Prot
Rhea reactions: in Archaea=777 ; in Bacteria=3480; in Eukaryota=4132



Overview



Summary

- **How to query metabolic data across multiple data source :**

Source	Description	web site	SPAQRL endpoint
Rhea	chemical reactions	https://www.rhea-db.org/	https://sparql.uniprot.org/sparql/
UniProt	protein sequences and annotations	https://www.uniprot.org/	https://sparql.rhea-db.org/sparql
Bgee	expression data	https://bgee.org/	hosted by http://biosoda.expasy.org/
MetaNetX	reconcilied metabolic networks	https://www.metanetx.org/	https://rdf.metanetx.org/

  - Do simple chemical and reaction searches
  - Do structural search using InChiKey
  - How to use ASK for QC
  - How to link chemical data to enzymes, subcellular location or anatomic entities
  - How to enter in the world of metabolic models

- **Programmatic access in Python**

- **Conclusion: very powerful** but... still some technical issues to be resolved

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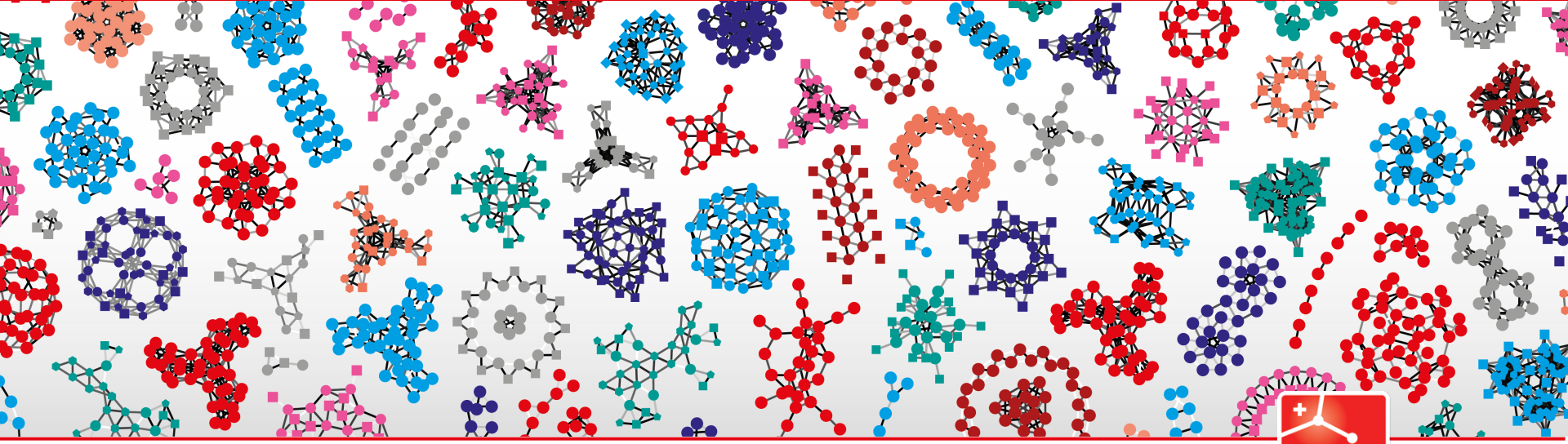
Web: https://www.rhea-db.org/

SPARQL: https://sparql.rhea-db.org/sparql

Email support: rhea-reaction@sib.swiss

Twitter: @rhea_db



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Thank you for your attention

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