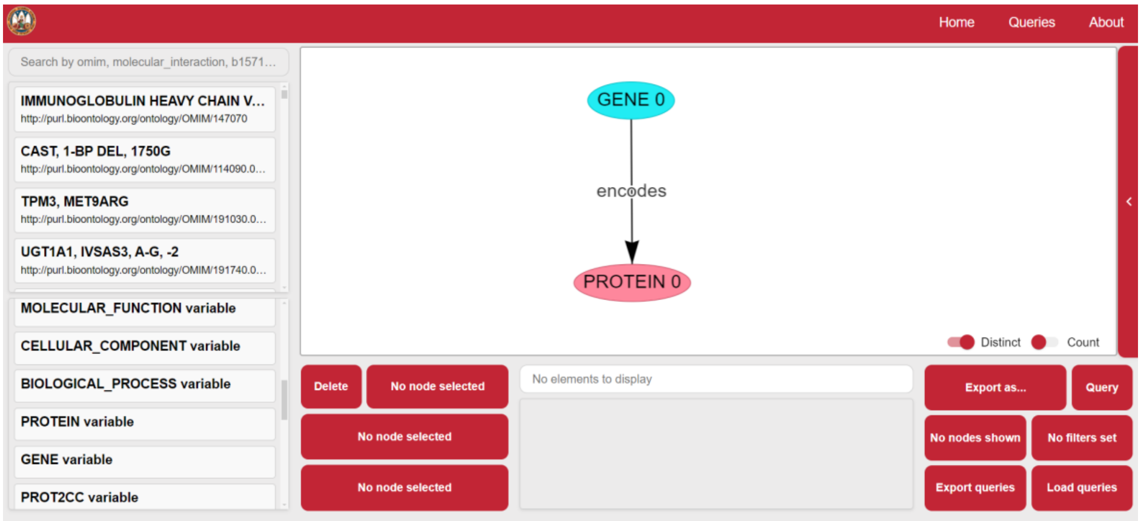
INTUITION Tutorial

1. Introduction

INTUITION is a web application for user friendly SPARQL query building. In this way, users can exploit RDF knowledge graphs without advanced knowledge in SPARQL query language.

INTUITION analyses the knowledge network of an accessible endpoint, in this case BioGateway (http://ssb4.nt.ntnu.no:23122/sparql), and allows building queries graphically by representing nodes (entities) and edges (properties).

RDF knowledge graphs represent entities through uniform resource identifiers (URIs), and information through triples or statements that represent a directional relationship between two entities, similar to a sentence: <subject> <predicate> <object>. For example: <Gene> <encodes> <Protein>. The SPARQL query language also uses this pattern to build queries. These queries can be complex by linking multiple triples and including operations. A tutorial for building SPARQL queries in BioGateway (BGW) is available in this repository (https://github.com/juan-mulero/cisreg). INTUITION uses this same design for query development.



Search by omim, molecular_interaction, b1571...

IMMUNOGLOBULIN HEAVY CHAIN V...
http://purl.bioontology.org/ontology/OMIM/147070

CAST, 1-BP DEL, 1750G
http://purl.bioontology.org/ontology/OMIM/114090.0...

TPM3, MET9ARG
http://purl.bioontology.org/ontology/OMIM/191030.0...

UGT1A1, IVSAS3, A-G, -2
http://purl.bioontology.org/ontology/OMIM/191740.0...

MOLECULAR_FUNCTION variable

CELLULAR_COMPONENT variable

BIOLOGICAL_PROCESS variable

PROTEIN variable

GENE variable

PROT2CC variable

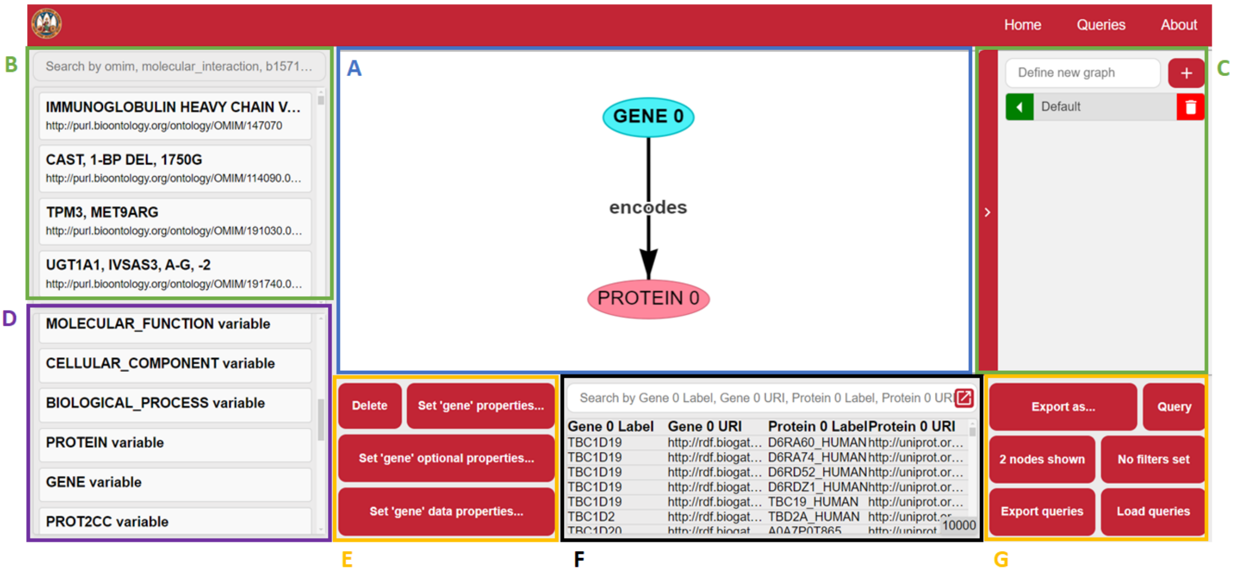
No elements to display

2. Design

In INTUITION we distinguish different sections:

A- Query building screen.
B- Entity browser (Currently deactivated).
C- Graph builder (Used for queries that use union clauses).
D- Variable selection (Main types of entities in the network).
E- Properties selection:
  - Object properties: relations between entities. Their inclusion acts as a filter.
  - Data properties: attributes of the entities. Their inclusion acts as a filter.
  - Optional properties: relations between entities. Their inclusion does not act as a filter (optional).

F- Output screen.
G- Query builder:
  - Query: runs the query.
  - Export as: exports the query results.
  - Nodes shown: output editor. Allow to indicate which variables are shown in the output screen, and to create bindings, i.e., to define variables.
  - Filters set: allow adding filters.
  - Export query: export the designed query.
  - Load query: to load a previously designed query.


Home
Queries
About
B
Search by omim, molecular_interaction, b1571...
A
GENE 0
encodes
PROTEIN 0
C
Define new graph
Default
D
MOLECULAR_FUNCTION variable
CELLULAR_COMPONENT variable
BIOLOGICAL_PROCESS variable
PROTEIN variable
GENE variable
PROT2CC variable
Delete
Set 'gene' properties...
Set 'gene' optional properties...
Set 'gene' data properties...
Search by Gene 0 Label, Gene 0 URI, Protein 0 Label, Protein 0 URI
10000
Export as...
Query
2 nodes shown
No filters set
Export queries
Load queries
E
F
G

IMMUNOGLOBULIN HEAVY CHAIN V...
http://purl.bioontology.org/ontology/OMIM/147070

CAST, 1-BP DEL, 1750G
http://purl.bioontology.org/ontology/OMIM/114090.0...

TPM3, MET9ARG
http://purl.bioontology.org/ontology/OMIM/191030.0...

UGT1A1, IVSAS3, A-G, -2
http://purl.bioontology.org/ontology/OMIM/191740.0...

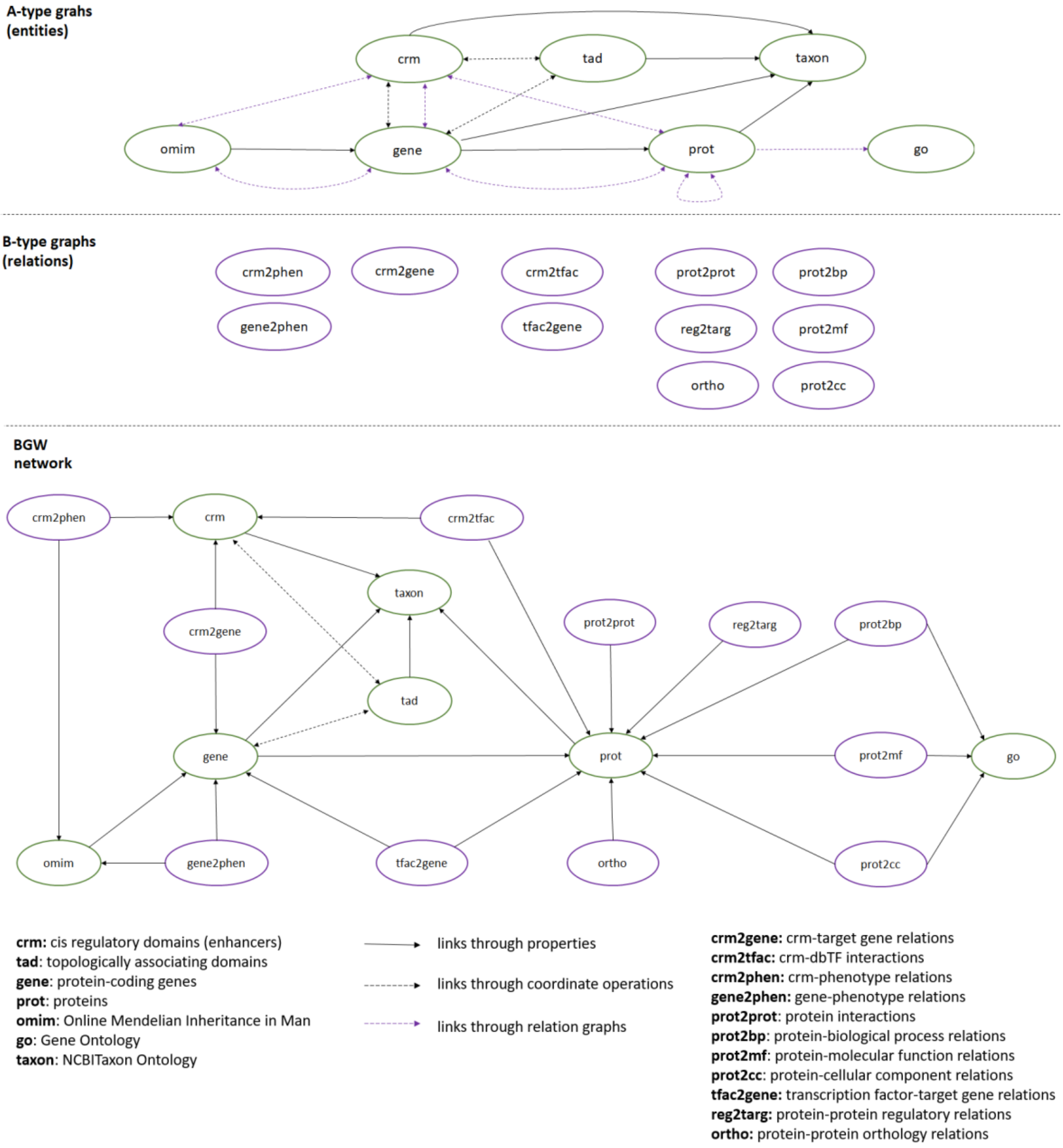
Gene 0 Label	Gene 0 URI	Protein 0 Label	Protein 0 URI
TBC1D19	http://rdf.biogat...	D6RA60_HUMAN	http://uniprot.or...
TBC1D19	http://rdf.biogat...	D6RA74_HUMAN	http://uniprot.or...
TBC1D19	http://rdf.biogat...	D6RD52_HUMAN	http://uniprot.or...
TBC1D19	http://rdf.biogat...	D6RDZ1_HUMAN	http://uniprot.or...
TBC1D19	http://rdf.biogat...	TBC19_HUMAN	http://uniprot.or...
TBC1D2	http://rdf.biogat...	TBD2A_HUMAN	http://uniprot.or...
TBC1D20	http://rdf.biogat	A0A7P0T865	http://uniprot

3. Variables and properties

Variables:

- CRM variable: cis regulatory module.
- Gene variable: genes.
- Protein variable: proteins.
- OMIM variable: entities from OMIM ontology (mainly phenotypes).
- Molecular_interaction: entities from Molecular Interactions ontology (MI).
- crm2gene variable: relation between CRM and gene.
- gene2phen variable: relation between gene and phenotype.
- crm2phen variable: relation between CRM and phenotype.
- crm2tfac variable: relation between CRM and protein (transcription factor).
- Transcription factor variable: transcription factors (currently only proteins that interact with CRM).
- reg2targ variable: regulatory relation between proteins.
- prot2prot: molecular interaction relation between proteins.
- tfac2gene variable: relation between gene and protein.
- Database variable: databases.
- Chromosome variable: chromosomes.
- Reference_genome variable: genome assembly.
- TAD variable: topologically associated domain.
- Cellular_component variable: cellular components from Gene Ontology (GO).
- prot2cc variable: relation between protein and its cellular components.
- Molecular_function variable: molecular functions from GO.
- prot2mf: relation between protein and its molecular functions.
- Biological_process variable: biological processes from GO.
- prot2bp variable: relation between protein and its biological processes.
- Ortho variable: orthology relation between proteins.
- Root variable: top hierarchically class of NCBITaxon Ontology.
- Taxonomic_rank variable: top hierarchically class of NCBITaxon Ontology.

The properties are detailed with examples and their domains here.

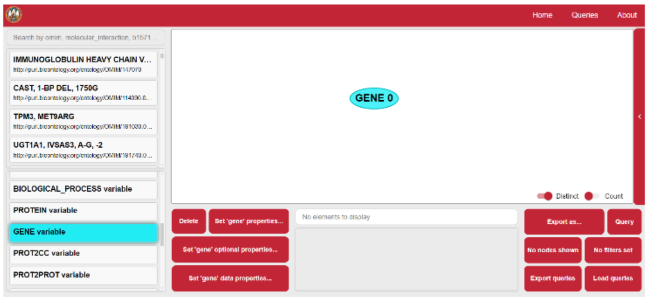

A-type grahs
(entities)
crm
tad
taxon
omim
gene
prot
go
B-type graphs
(relations)
crm2phen
crm2gene
crm2tfac
prot2prot
prot2bp
gene2phen
tfac2gene
reg2targ
prot2mf
ortho
prot2cc
BGW
network
crm2phen
crm
crm2tfac
taxon
crm2gene
prot2prot
reg2targ
prot2bp
tad
gene
prot
prot2mf
go
omim
gene2phen
tfac2gene
ortho
prot2cc
crm: cis regulatory domains (enhancers)
tad: topologically associating domains
gene: protein-coding genes
prot: proteins
omim: Online Mendelian Inheritance in Man
go: Gene Ontology
taxon: NCBITaxon Ontology
links through properties
links through coordinate operations
links through relation graphs
crm2gene: crm-target gene relations
crm2tfac: crm-dbTF interactions
crm2phen: crm-phenotype relations
gene2phen: gene-phenotype relations
prot2prot: protein interactions
prot2bp: protein-biological process relations
prot2mf: protein-molecular function relations
prot2cc: protein-cellular component relations
tfac2gene: transcription factor-target gene relations
reg2targ: protein-protein regulatory relations
ortho: protein-protein orthology relations

4. How to build a query

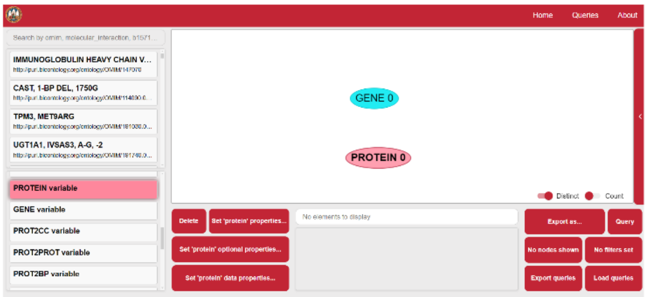
We take as an example the previous case: <Gene> <encodes> <Protein>.

1. Select the first node or subject, in this case Gene, in the variables section.
2. Select the second node or object, in this case Protein, in the variables section.
3. Select the object property that relates both entities, in this case "encodes".
4. Select in "Nodes shown" the data we want to show in the output, in this case Gene and Protein.
5. Click on "Query" to launch the query.
6. Click on "Export as" to download the data obtained. Click on "Export query" if you want to save the query as well.

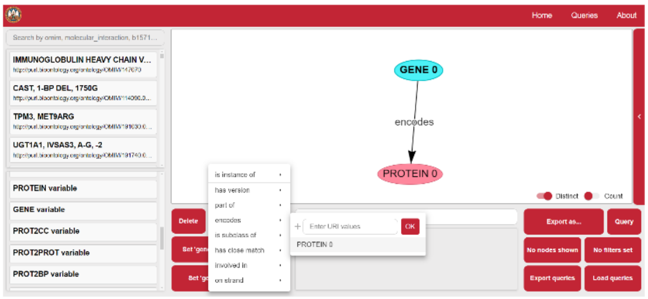
1.



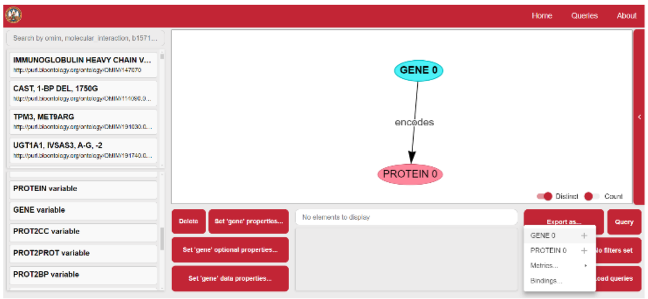
2.


GENE 0
PROTEIN 0
PROTEIN variable
GENE variable
PROT2CC variable
PROT2PROT variable
PROT2BP variable
Set 'protein' properties...
Set 'protein' optional properties...
Set 'protein' data properties...

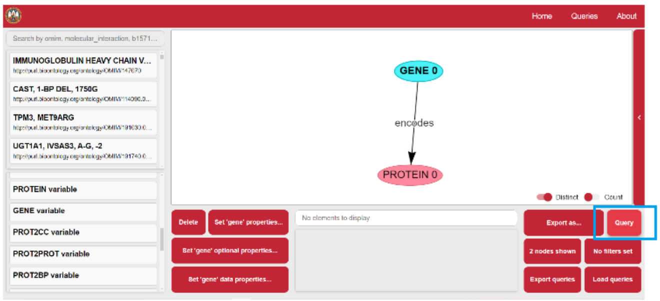
3.



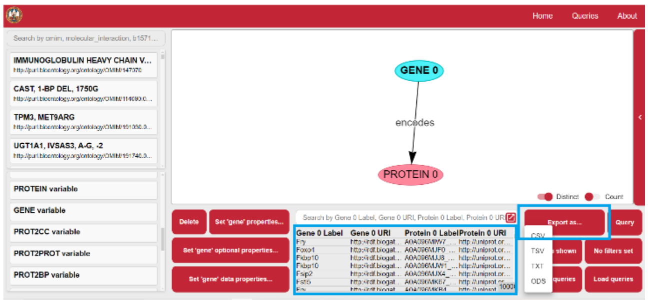
4.



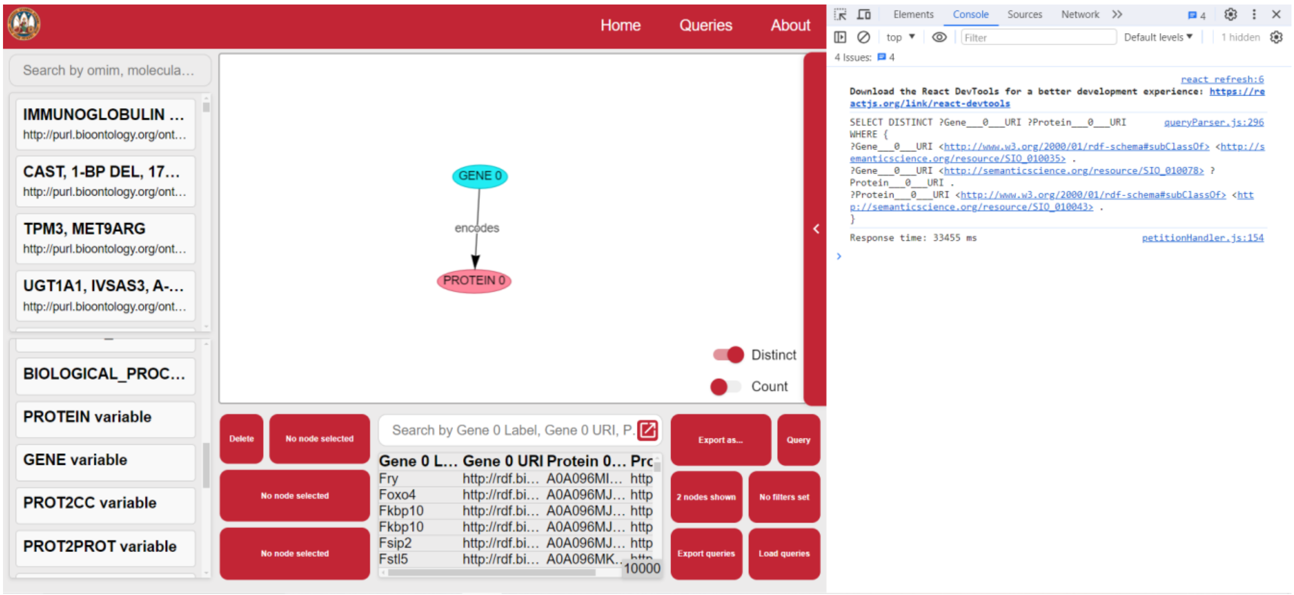
5.



6.



The generated SPARQL query can also be found by accessing the Console.



Gene 0 L...	Gene 0 URI	Protein 0...	Prc
Fry	http://rdf.bi...	A0A096MI...	http
Foxo4	http://rdf.bi...	A0A096MJ...	http
Fkbp10	http://rdf.bi...	A0A096MJ...	http
Fkbp10	http://rdf.bi...	A0A096MJ...	http
Fsip2	http://rdf.bi...	A0A096MJ...	http
Fstl5	http://rdf.bi...	A0A096MK...	http

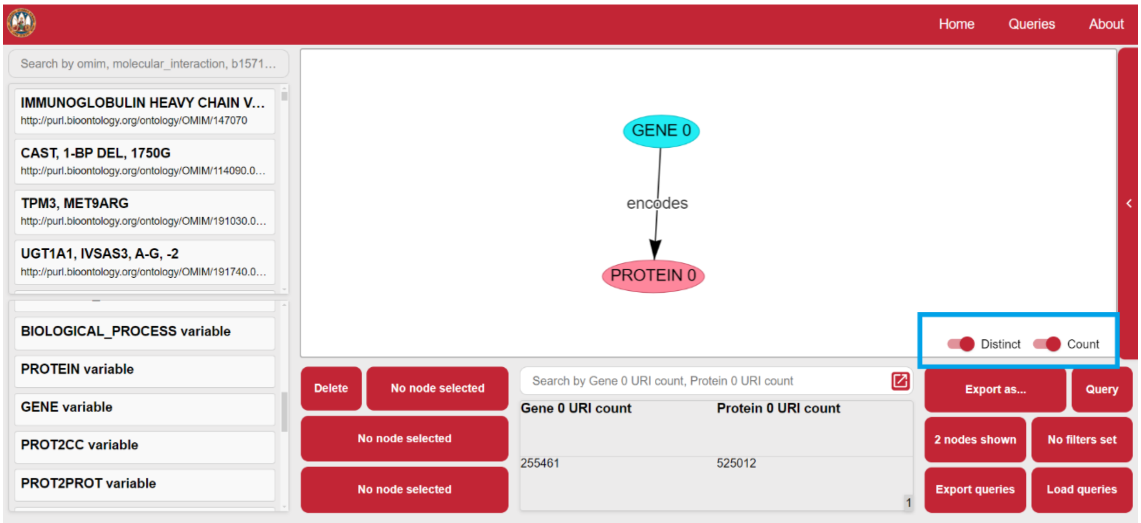
10000

```
                                                        react refresh:6
Download the React DevTools for a better development experience: https://re
actjs.org/link/react-devtools
SELECT DISTINCT ?Gene___0___URI ?Protein___0___URI       queryParser.js:296
WHERE {
?Gene___0___URI <http://www.w3.org/2000/01/rdf-schema#subClassOf> <http://s
emanticscience.org/resource/SIO_010035> .
?Gene___0___URI <http://semanticscience.org/resource/SIO_010078> ?
Protein___0___URI .
?Protein___0___URI <http://www.w3.org/2000/01/rdf-schema#subClassOf> <htt
p://semanticscience.org/resource/SIO_010043> .
}
Response time: 33455 ms                                 petitionHandler.js:154
>
```

5. Filters and other clauses

5.1. DISTINCT and COUNT

By default, the queries include the DISTINCT clause to avoid duplicate results. This can be desactivated clicking on the Distinct button, in the Query building screen. You can also activate the Count button if you want to include this clause in the query.

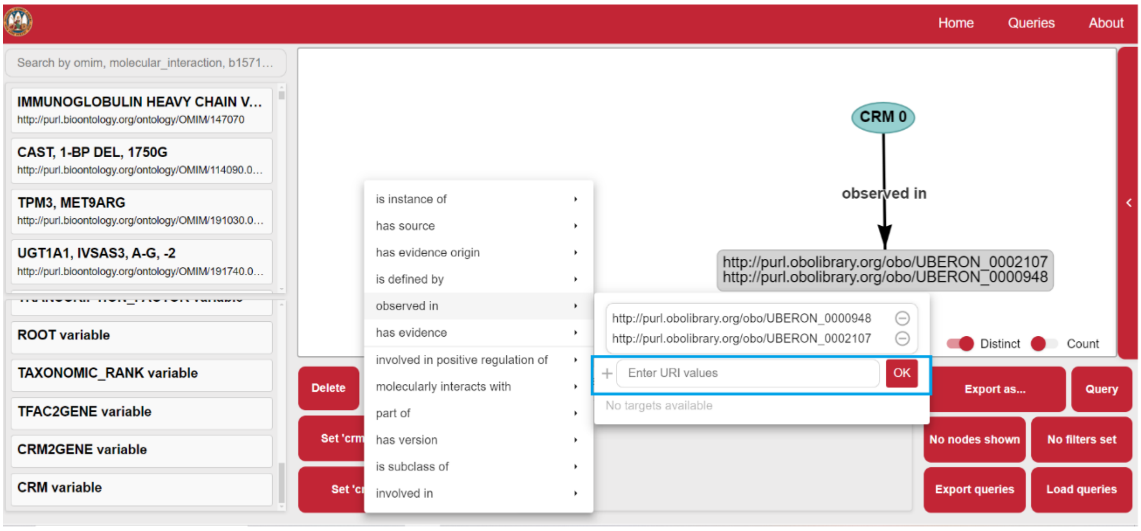

Home
Queries
About
Search by omim, molecular_interaction, b1571...
IMMUNOGLOBULIN HEAVY CHAIN V...
http://purl.bioontology.org/ontology/OMIM/147070
CAST, 1-BP DEL, 1750G
http://purl.bioontology.org/ontology/OMIM/114090.0...
TPM3, MET9ARG
http://purl.bioontology.org/ontology/OMIM/191030.0...
UGT1A1, IVSAS3, A-G, -2
http://purl.bioontology.org/ontology/OMIM/191740.0...
BIOLOGICAL_PROCESS variable
PROTEIN variable
GENE variable
PROT2CC variable
PROT2PROT variable
GENE 0
encodes
PROTEIN 0
Distinct
Count
Delete
No node selected
No node selected
No node selected
Search by Gene 0 URI count, Protein 0 URI count
Export as...
Query
2 nodes shown
No filters set
Export queries
Load queries
1

Gene 0 URI count	Protein 0 URI count
255461	525012

5.2. VALUES

This clause permits the assignment of one or more values to a specific variable. For example, cis regulatory modules identified in two tissues of interest. First we indicate the subject node (CRM variable), then we include in the corresponding object property (observed in) the values to be included. Click on "+" to include values and click on OK when all values are listed.

Since RDF resources are represented through URIs, the input values for filtering must be URIs. We are working on the use of labels for the next release version.

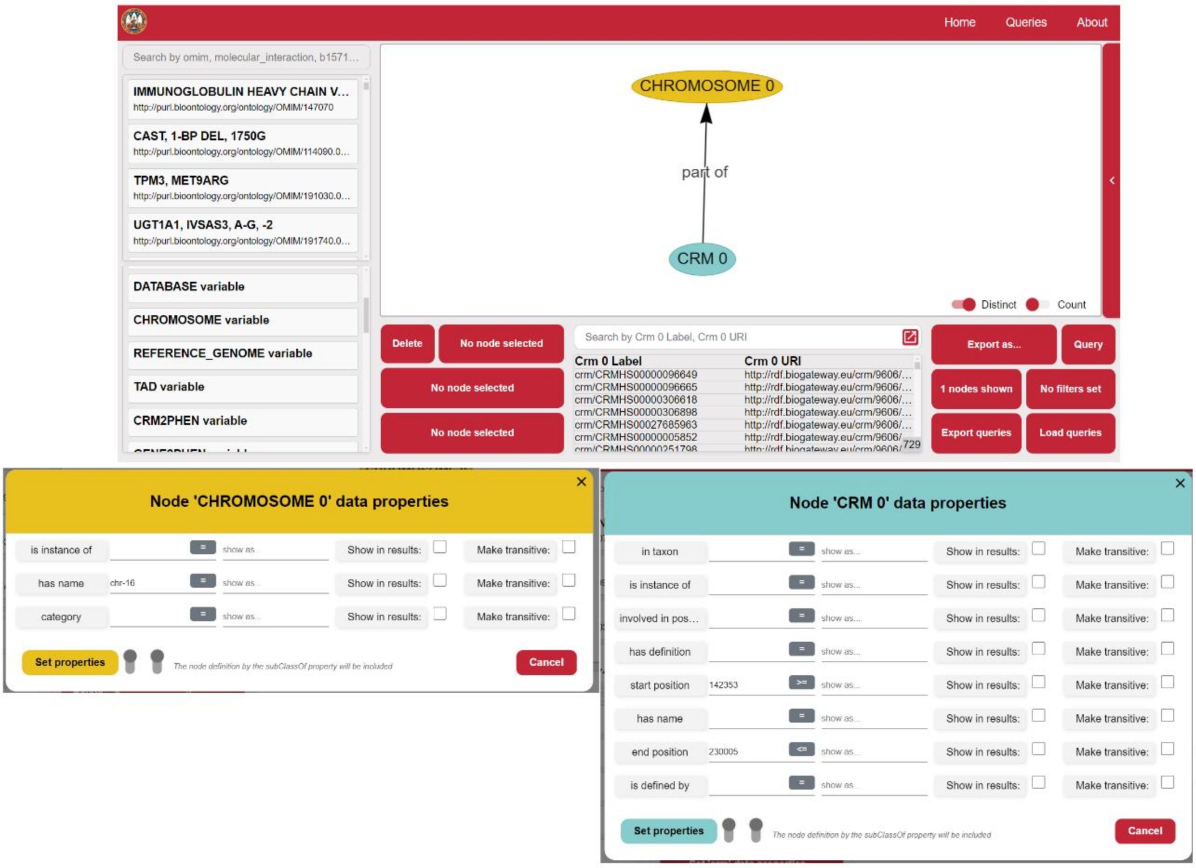


http://purl.obolibrary.org/obo/UBERON_0002107
http://purl.obolibrary.org/obo/UBERON_0000948

http://purl.obolibrary.org/obo/UBERON_0000948
http://purl.obolibrary.org/obo/UBERON_0002107

5.3. Filters of properties

Clicking on "data properties" we can also filter attributes. If the value is a string we can use the operator "=" to indicate an exact value, or the operator "⊆" to indicate a substring contained in the string. If the value is numeric we can use the operators =, >, ≥, <, ≤. For example, we filter the variables chromosome and CRM to obtain the enhancers that overlap at certain coordinates.



IMMUNOGLOBULIN HEAVY CHAIN V...
http://purl.bioontology.org/ontology/OMIM/147070

CAST, 1-BP DEL, 1750G
http://purl.bioontology.org/ontology/OMIM/114090.0...

TPM3, MET9ARG
http://purl.bioontology.org/ontology/OMIM/191030.0...

UGT1A1, IVSAS3, A-G, -2
http://purl.bioontology.org/ontology/OMIM/191740.0...

DATABASE variable
CHROMOSOME variable
REFERENCE_GENOME variable
TAD variable
CRM2PHEN variable

Crm 0 Label	Crm 0 URI
crm/CRMHS00000096649	http://rdf.biogateway.eu/crm/9606/...
crm/CRMHS00000096665	http://rdf.biogateway.eu/crm/9606/...
crm/CRMHS00000306618	http://rdf.biogateway.eu/crm/9606/...
crm/CRMHS00000306898	http://rdf.biogateway.eu/crm/9606/...
crm/CRMHS00027685963	http://rdf.biogateway.eu/crm/9606/...
crm/CRMHS00000005852	http://rdf.biogateway.eu/crm/9606/
crm/CRMHS00000251798	http://rdf.biogateway.eu/crm/9606/

Node 'CHROMOSOME 0' data properties

is instance of		=	show as	Show in results:	□	Make transitive: □
has name	chr-16	=	show as	Show in results:	□	Make transitive: □
category		=	show as...	Show in results:	□	Make transitive: □

Set properties — The node definition by the subClassOf property will be included — Cancel

Node 'CRM 0' data properties

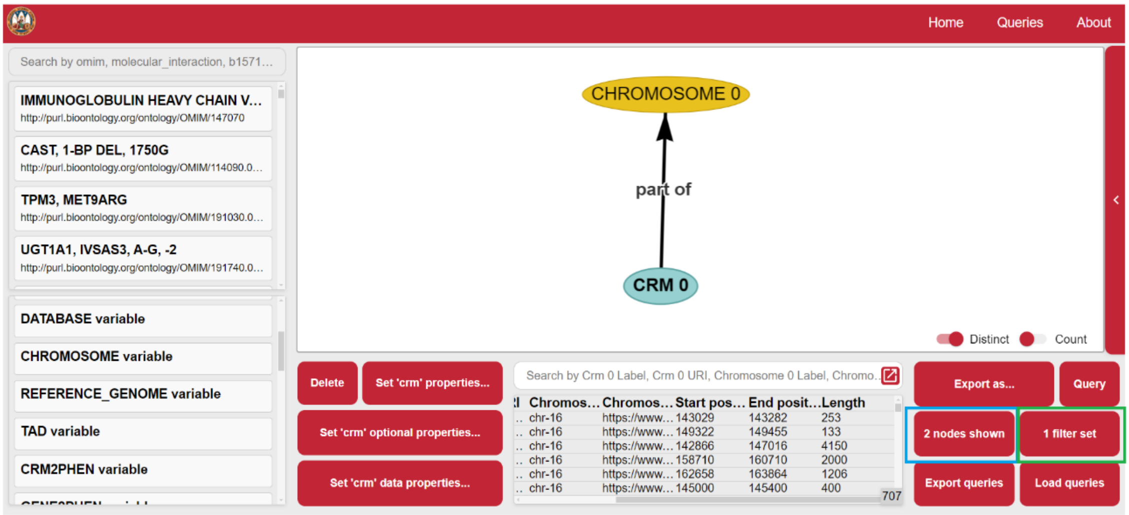
in taxon		=	show as...	Show in results:	□	Make transitive: □
is instance of		=	show as...	Show in results:	□	Make transitive: □
involved in pos...		=	show as...	Show in results:	□	Make transitive: □
has definition		=	show as...	Show in results:	□	Make transitive: □
start position	142353	>=	show as...	Show in results:	□	Make transitive: □
has name		=	show as...	Show in results:	□	Make transitive: □
end position	230005	<=	show as...	Show in results:	□	Make transitive: □
is defined by		=	show as...	Show in results:	□	Make transitive: □

Set properties — The node definition by the subClassOf property will be included — Cancel

Varaibles can also be filtered clicking on “Filters set” button.

5.4. Creating and filtering variables

INTUITION supports the generation and filtering of new variables. This functionality is implemented in "Nodes shown" > "Bindings" button. For example, by subtracting the end and start positions of the CRMs we obtain the length of the sequences in a new variable. Then, we can filter this new variable in the “Filters set” button.



Search by omim, molecular_interaction, b1571...

IMMUNOGLOBULIN HEAVY CHAIN V...
http://purl.bioontology.org/ontology/OMIM/147070

CAST, 1-BP DEL, 1750G
http://purl.bioontology.org/ontology/OMIM/114090.0...

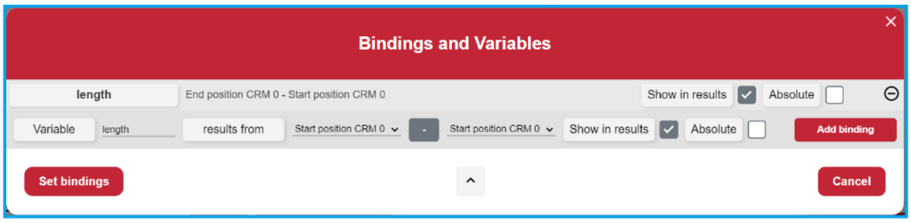
TPM3, MET9ARG
http://purl.bioontology.org/ontology/OMIM/191030.0...

UGT1A1, IVSAS3, A-G, -2
http://purl.bioontology.org/ontology/OMIM/191740.0...

Search by Crm 0 Label, Crm 0 URI, Chromosome 0 Label, Chromo...

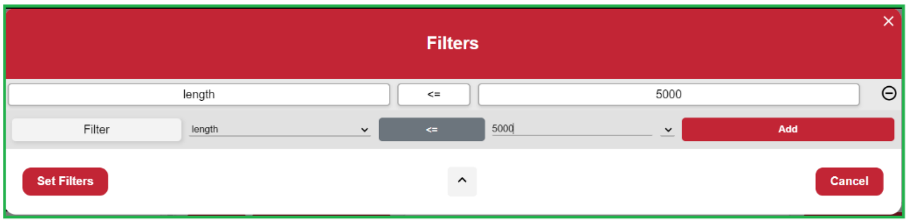
:I	Chromos...	Chromos...	Start pos...	End posit...	Length
..	chr-16	https://www...	143029	143282	253
..	chr-16	https://www...	149322	149455	133
..	chr-16	https://www...	142866	147016	4150
..	chr-16	https://www...	158710	160710	2000
..	chr-16	https://www...	162658	163864	1206
..	chr-16	https://www...	145000	145400	400

707



length | End position CRM 0 - Start position CRM 0 | Show in results ☑ | Absolute □

Variable: length | results from: Start position CRM 0 - Start position CRM 0 | Show in results ☑ | Absolute □



length | <= | 5000

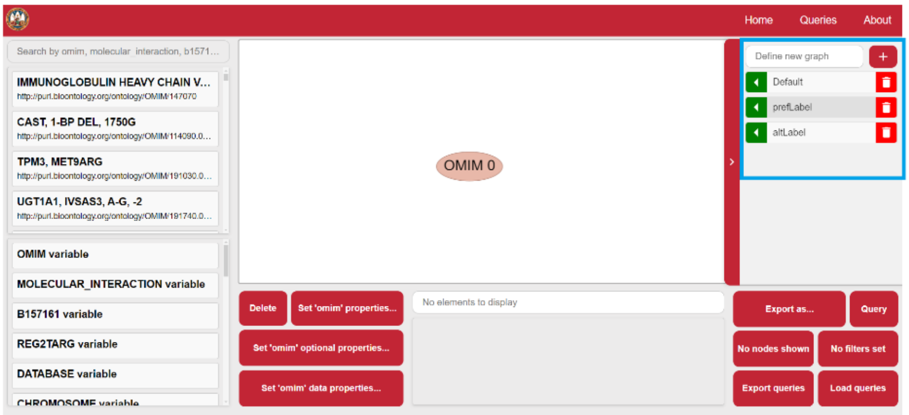
Filter: length | <= | 5000

5.5. UNION

INTUITION also allows the use of the UNION clause of SPARQL. UNION merges subqueries through common variables in both queries. We illustrate its use through a use case. For example, we retrieve the OMIM entities that contain the string "breast cancer" as a name or synonym. To do that:

1. In the Graph builder section, we create the graphs belonging to each of the subqueries, and we include an OMIM node in each of them. In the example, the graphs are "prefLabel" for the main label query and "altLabel" for the query of the synonym.
2. In each of the graphs we define the variable "label" according to the appropriate dataproperties ("has name" and "has synonym" properties, respectively). For this, we use the "show as" functionality, which enables to rename the variables, in this case under the common variable called "label".
3. We return to the main graph where we will join the two subqueries. For this, we include the subgraphs clicking on the green flap of each of the subgraphs.
4. Select one of the subgraphs represented as nodes and click on "Define union".
5. In "Node shown" we select the variables to be shown and in "Filters set" we filter the variable "label".
6. Run the query (Query).

1.


Home
Queries
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IMMUNOGLOBULIN HEAVY CHAIN V...
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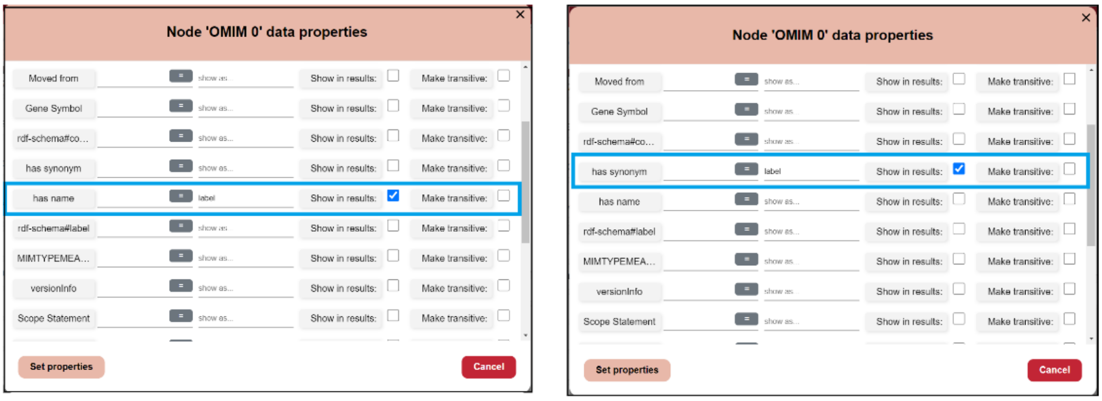
http://purl.bioontology.org/ontology/OMIM/114090.0...
TPM3, MET9ARG
http://purl.bioontology.org/ontology/OMIM/191030.0...
UGT1A1, IVSAS3, A-G, -2
http://purl.bioontology.org/ontology/OMIM/191740.0...
OMIM variable
MOLECULAR_INTERACTION variable
B157161 variable
REG2TARG variable
DATABASE variable
CHROMOSOME variable
OMIM 0
Define new graph
Default
prefLabel
altLabel
Delete
Set 'omim' properties...
Set 'omim' optional properties...
Set 'omim' data properties...
No elements to display
Export as...
Query
No nodes shown
No filters set
Export queries
Load queries

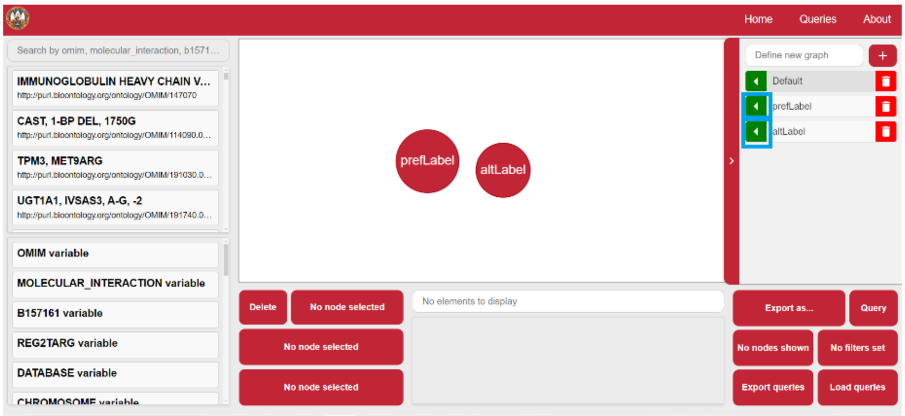
2.



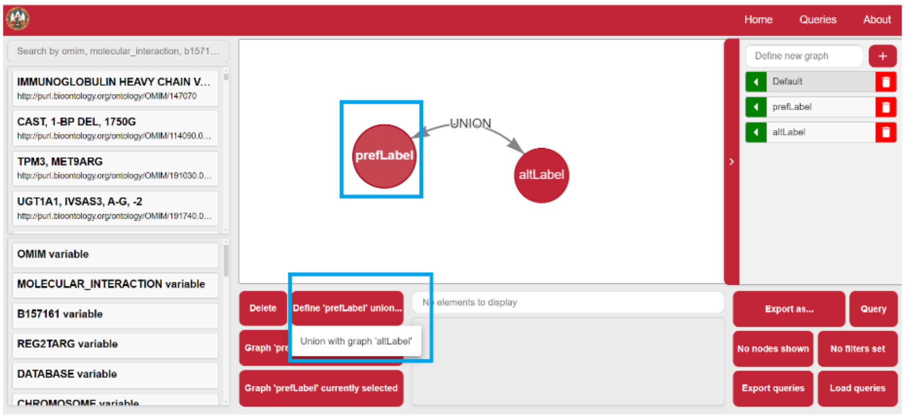
has name = label Show in results: ☑ Make transitive: □

has synonym = label Show in results: ☑ Make transitive: □

3.



4.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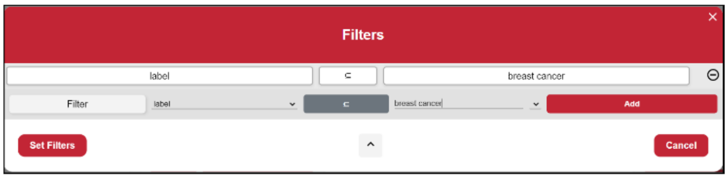
http://purl.bioontology.org/ontology/OMIM/114090.0...
TPM3, MET9ARG
http://purl.bioontology.org/ontology/OMIM/191030.0...
UGT1A1, IVSAS3, A-G, -2
http://purl.bioontology.org/ontology/OMIM/191740.0...
OMIM variable
MOLECULAR_INTERACTION variable
B157161 variable
REG2TARG variable
DATABASE variable
CHROMOSOME variable
UNION
prefLabel
altLabel
Define new graph
Default
prefLabel
altLabel
Delete
Define 'prefLabel' union...
Union with graph 'altLabel'
Graph 'pre
Graph 'prefLabel' currently selected
No elements to display
Export as...
Query
No nodes shown
No filters set
Export queries
Load queries

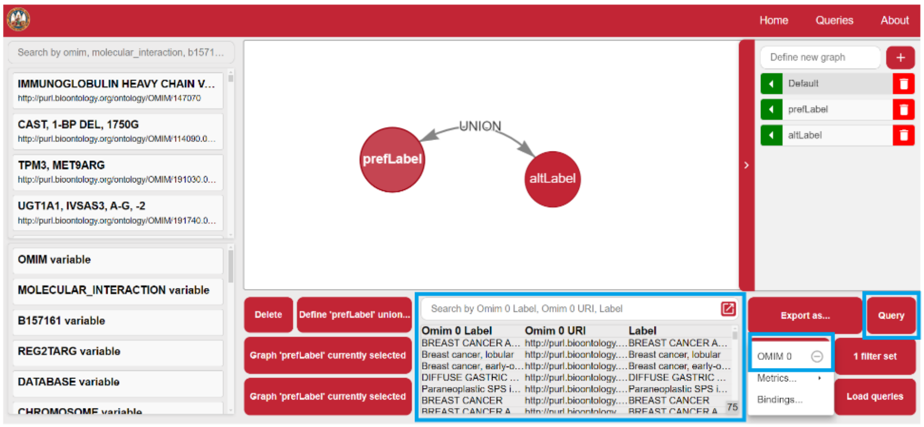
5.



label ⊂ breast cancer

Filter label ⊂ breast cancer

6.


Home
Queries
About
Search by omim, molecular_interaction, b1571...
IMMUNOGLOBULIN HEAVY CHAIN V...
http://purl.bioontology.org/ontology/OMIM/147070
CAST, 1-BP DEL, 1750G
http://purl.bioontology.org/ontology/OMIM/114090.0...
TPM3, MET9ARG
http://purl.bioontology.org/ontology/OMIM/191030.0...
UGT1A1, IVSAS3, A-G, -2
http://purl.bioontology.org/ontology/OMIM/191740.0...
OMIM variable
MOLECULAR_INTERACTION variable
B157161 variable
REG2TARG variable
DATABASE variable
CHROMOSOME variable
UNION
prefLabel
altLabel
Define new graph
Default
prefLabel
altLabel
Delete
Define 'prefLabel' union...
Graph 'prefLabel' currently selected
Graph 'prefLabel' currently selected
Search by Omim 0 Label, Omim 0 URI, Label
Export as...
Query
OMIM 0
Metrics...
Bindings...
1 filter set
Load queries
75

Omim 0 Label	Omim 0 URI	Label
BREAST CANCER A...	http://purl.bioontology....	BREAST CANCER A...
Breast cancer, lobular	http://purl.bioontology....	Breast cancer, lobular
Breast cancer, early-o...	http://purl.bioontology....	Breast cancer, early-o...
DIFFUSE GASTRIC ...	http://purl.bioontology....	DIFFUSE GASTRIC ...
Paraneoplastic SPS i...	http://purl.bioontology....	Paraneoplastic SPS i...
BREAST CANCER	http://purl.bioontology....	BREAST CANCER
BREAST CANCER A...	http://purl.bioontology...	BREAST CANCER A...

6. Use Cases

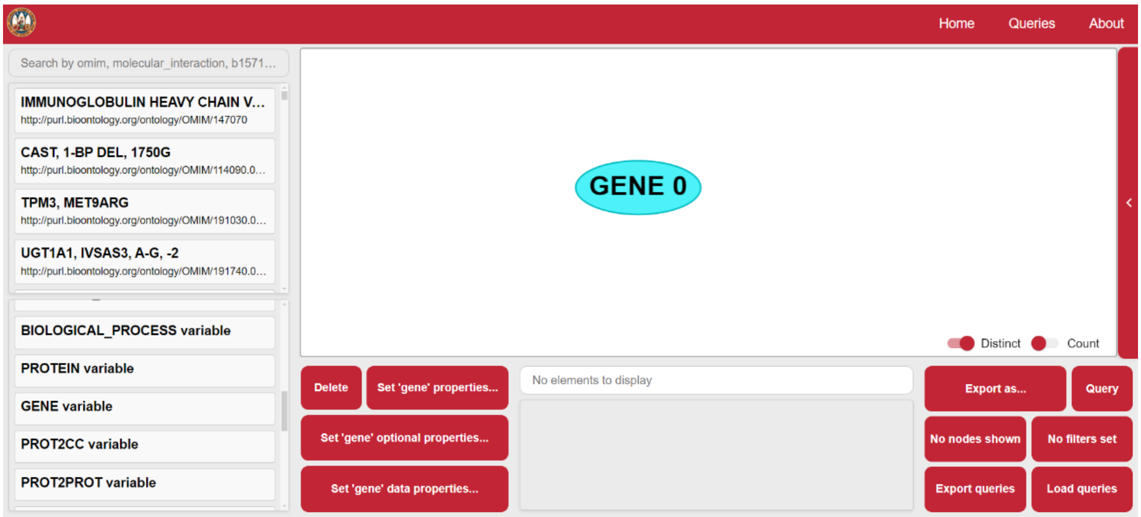
The following Use Cases were developed in the paper "*Analysis of the landscape of human enhancer sequences in biological databases*". The corresponding queries are attached for reproducibility and as examples of use.

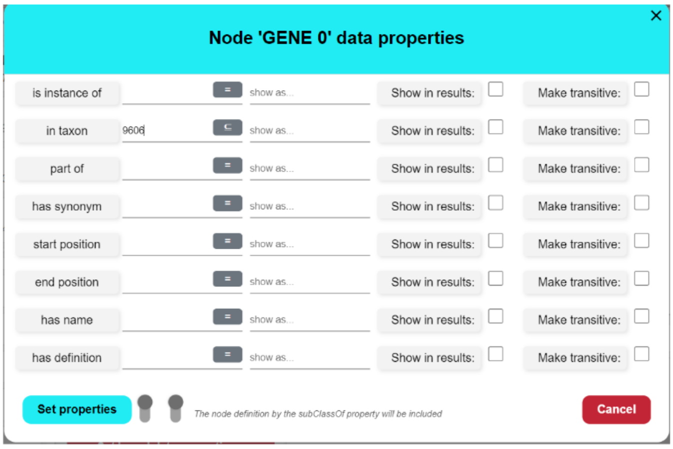
1. Use case 1: json files to load here.
2. Use case 2: json files to load here.
3. Use case 3: json files to load here.

7. Useful notes

7.1. Filtering by taxon

The resources in RDF are represented by URIs, so they must be used when the filtering involves a resource. This is the case for filtering by taxon (*in taxon* property). Since operating with URIs can be tedious, e.g. http://purl.obolibrary.org/obo/NCBITaxon_9606, the "content in" or "⊆" operator makes it easier to work with identifiers. The following example illustrates the filtering of human genes.


Home
Queries
About
Search by omim, molecular_interaction, b1571...
IMMUNOGLOBULIN HEAVY CHAIN V...
http://purl.bioontology.org/ontology/OMIM/147070
CAST, 1-BP DEL, 1750G
http://purl.bioontology.org/ontology/OMIM/114090.0...
TPM3, MET9ARG
http://purl.bioontology.org/ontology/OMIM/191030.0...
UGT1A1, IVSAS3, A-G, -2
http://purl.bioontology.org/ontology/OMIM/191740.0...
BIOLOGICAL_PROCESS variable
PROTEIN variable
GENE variable
PROT2CC variable
PROT2PROT variable
GENE 0
Distinct
Count
Delete
Set 'gene' properties...
Set 'gene' optional properties...
Set 'gene' data properties...
No elements to display
Export as...
Query
No nodes shown
No filters set
Export queries
Load queries



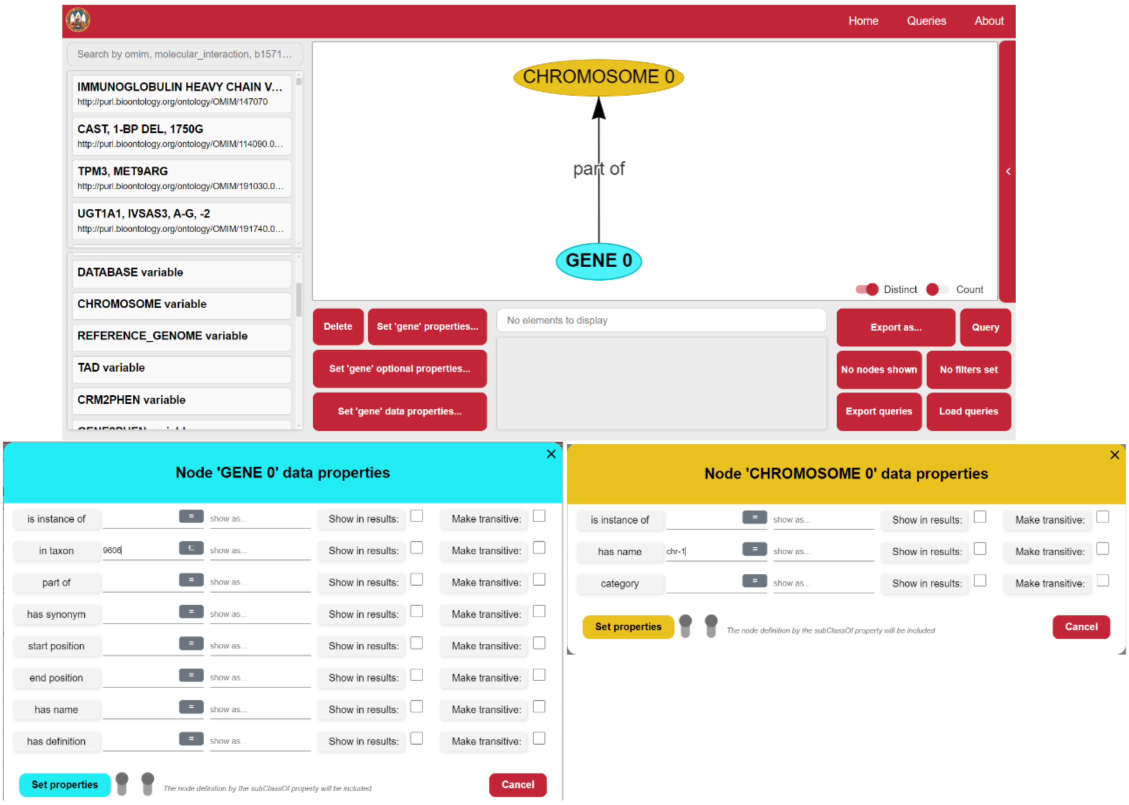
Node 'GENE 0' data properties

is instance of		=	show as...	Show in results: □	Make transitive: □
in taxon	9606	⊆	show as...	Show in results: □	Make transitive: □
part of		=	show as...	Show in results: □	Make transitive: □
has synonym		=	show as...	Show in results: □	Make transitive: □
start position		=	show as...	Show in results: □	Make transitive: □
end position		=	show as...	Show in results: □	Make transitive: □
has name		=	show as...	Show in results: □	Make transitive: □
has definition		=	show as...	Show in results: □	Make transitive: □

The node definition by the subClassOf property will be included

7.2. Filtering by chromosome

Chromosomes are resources that have labels. Therefore, chromosomes can be filtered through their labels. Strings can be filtered in INTUITION using the "=" (exact value) or "⊆" (contained in) operators. The default configuration of string filtering is not case-sensitive. The following example filters human genes on chromosome 1.



Home
Queries
About
Search by omim, molecular_interaction, b1571...
IMMUNOGLOBULIN HEAVY CHAIN V...
http://purl.bioontology.org/ontology/OMIM/147070
CAST, 1-BP DEL, 1750G
http://purl.bioontology.org/ontology/OMIM/114090.0...
TPM3, MET9ARG
http://purl.bioontology.org/ontology/OMIM/191030.0...
UGT1A1, IVSAS3, A-G, -2
http://purl.bioontology.org/ontology/OMIM/191740.0...
DATABASE variable
CHROMOSOME variable
REFERENCE_GENOME variable
TAD variable
CRM2PHEN variable
CHROMOSOME 0
part of
GENE 0
Distinct
Count
Delete
Set 'gene' properties...
Set 'gene' optional properties...
Set 'gene' data properties...
No elements to display
Export as...
Query
No nodes shown
No filters set
Export queries
Load queries

Node 'GENE 0' data properties

is instance of		=	show as...	Show in results: □	Make transitive: □
in taxon	9606	⊆	show as...	Show in results: □	Make transitive: □
part of		=	show as...	Show in results: □	Make transitive: □
has synonym		=	show as...	Show in results: □	Make transitive: □
start position		=	show as...	Show in results: □	Make transitive: □
end position		=	show as...	Show in results: □	Make transitive: □
has name		=	show as...	Show in results: □	Make transitive: □
has definition		=	show as...	Show in results: □	Make transitive: □

The node definition by the subClassOf property will be included

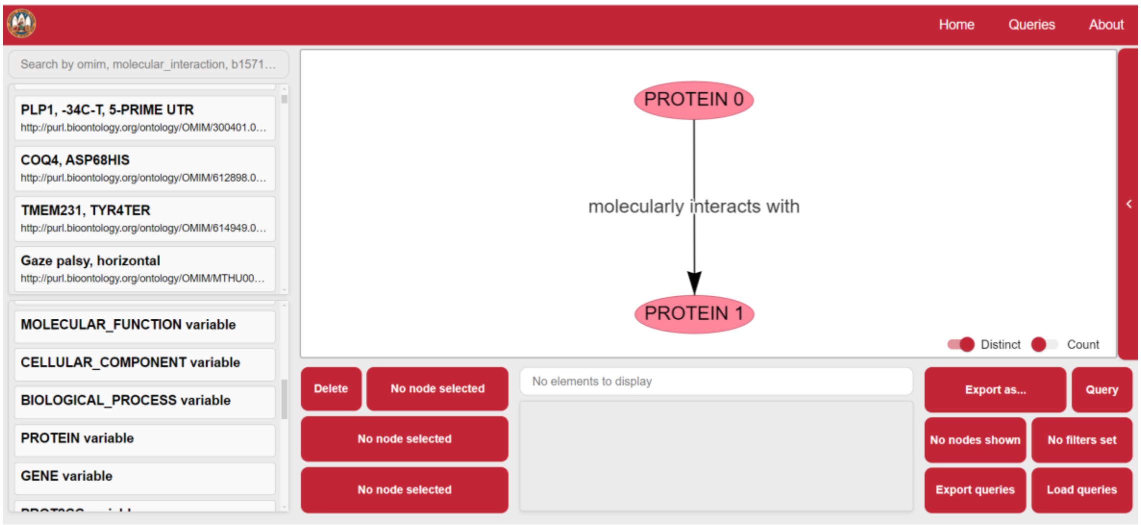
Node 'CHROMOSOME 0' data properties

is instance of		=	show as...	Show in results: □	Make transitive: □
has name	chr-1	=	show as...	Show in results: □	Make transitive: □
category		=	show as...	Show in results: □	Make transitive: □

The node definition by the subClassOf property will be included

7.3. Numbering of variables

Queries can involve different variables. These queries can require the use of an entity as different variables, for example the protein-protein interaction involves two different proteins, and therefore two different variables. INTUITION permits to include the same variable more than once. These nodes are listed starting from 0. The counter is reset when the application is refreshed, not when the query is deleted.


Home
Queries
About
Search by omim, molecular_interaction, b1571...
PLP1, -34C-T, 5-PRIME UTR
http://purl.bioontology.org/ontology/OMIM/300401.0...
COQ4, ASP68HIS
http://purl.bioontology.org/ontology/OMIM/612898.0...
TMEM231, TYR4TER
http://purl.bioontology.org/ontology/OMIM/614949.0...
Gaze palsy, horizontal
http://purl.bioontology.org/ontology/OMIM/MTHU00...
MOLECULAR_FUNCTION variable
CELLULAR_COMPONENT variable
BIOLOGICAL_PROCESS variable
PROTEIN variable
GENE variable
PROTEIN 0
molecularly interacts with
PROTEIN 1
Distinct
Count
Delete
No node selected
No node selected
No node selected
No elements to display
Export as...
Query
No nodes shown
No filters set
Export queries
Load queries