Gene Ontology

Дано: набор белков или генов

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Откуда их взять?

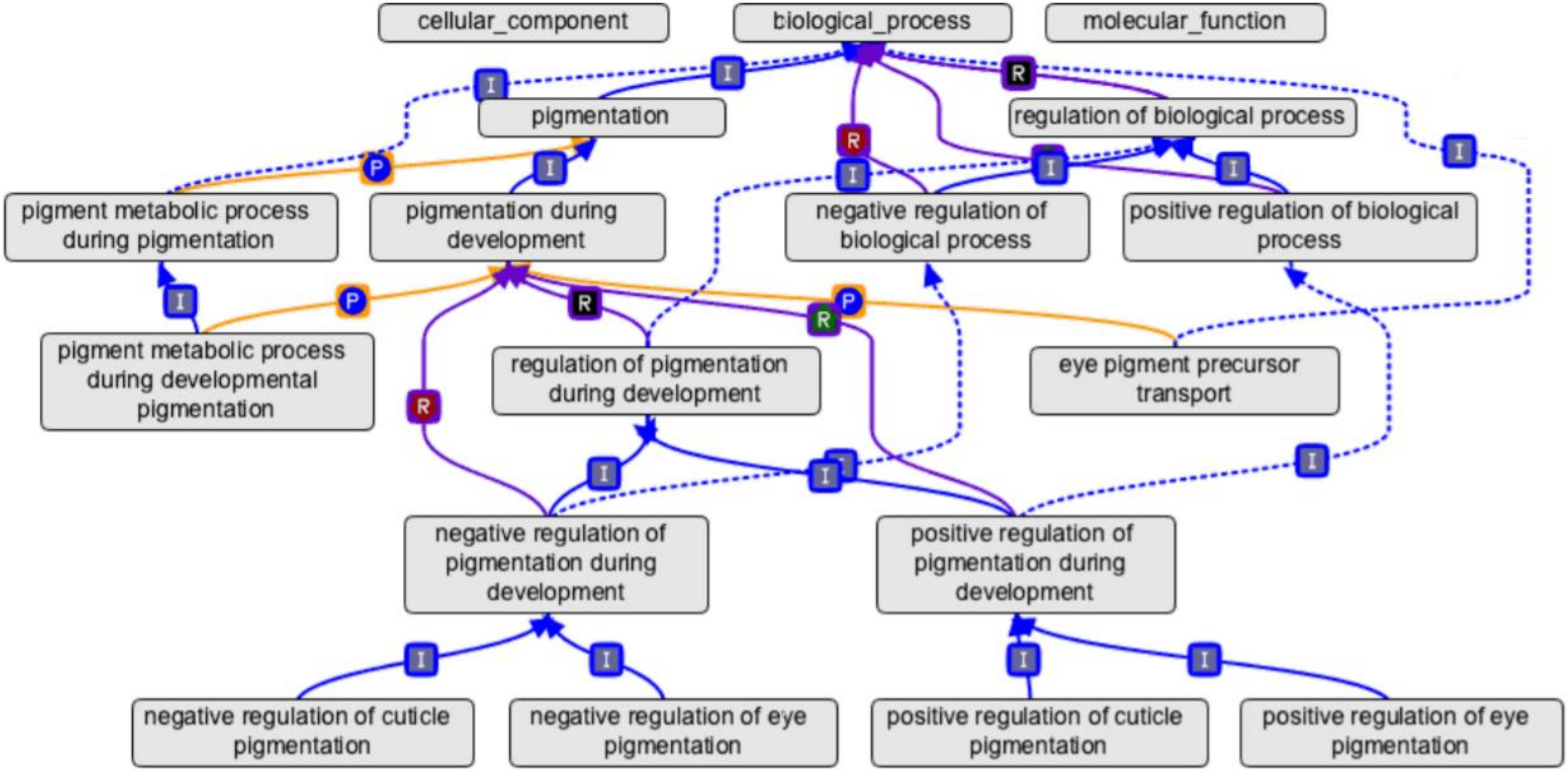
Экспрессия
Дифференциальная экспрессия
Масспектрометрия
Любимый набор
…

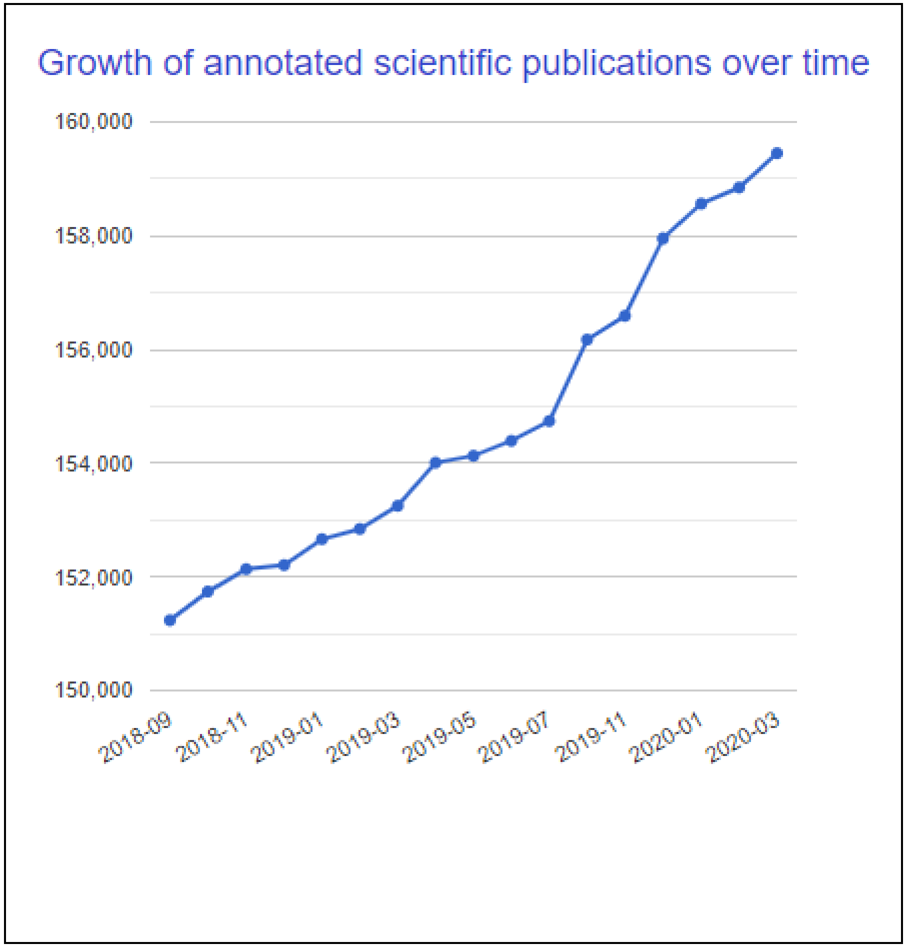
Что дальше делать?

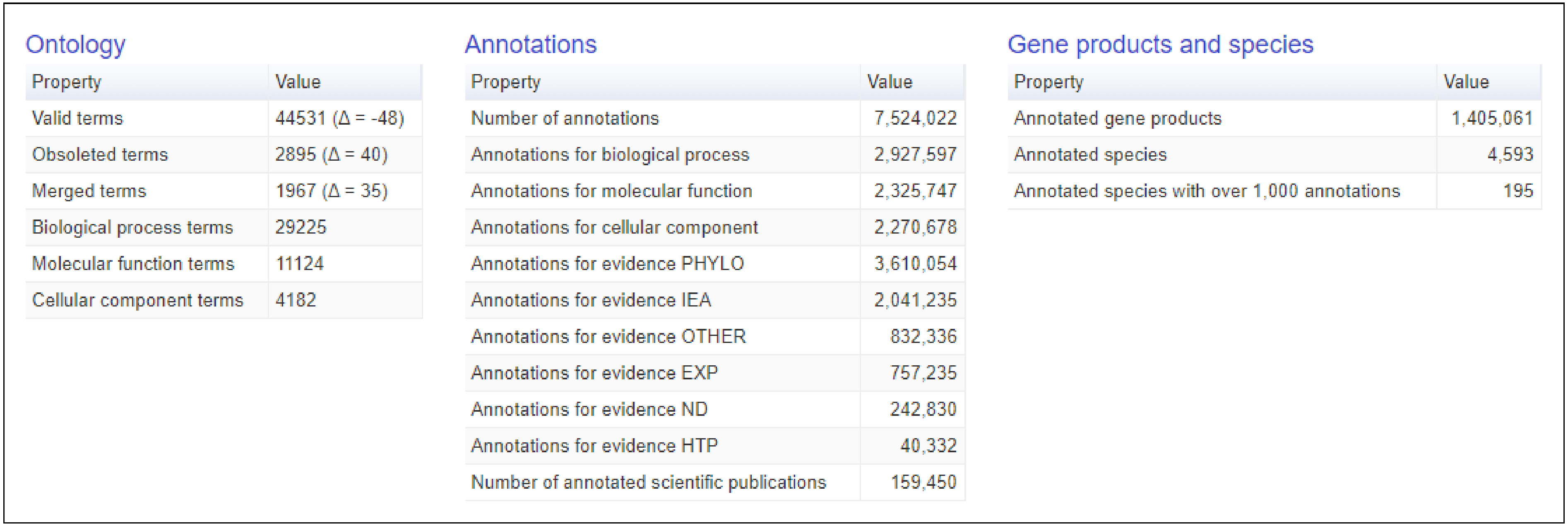
Gene Ontology – GO

http://geneontology.org/

База данных GO представляет собой граф биологических терминов, соединенных различными отношениями


cellular_component
biological_process
molecular_function
pigmentation
regulation of biological process
pigment metabolic process during pigmentation
pigmentation during development
negative regulation of biological process
positive regulation of biological process
pigment metabolic process during developmental pigmentation
regulation of pigmentation during development
eye pigment precursor transport
negative regulation of pigmentation during development
positive regulation of pigmentation during development
negative regulation of cuticle pigmentation
negative regulation of eye pigmentation
positive regulation of cuticle pigmentation
positive regulation of eye pigmentation
I
P
R


Growth of annotated scientific publications over time
160,000
158,000
156,000
154,000
152,000
150,000
2018-09
2018-11
2019-01
2019-03
2019-05
2019-07
2019-11
2020-01
2020-03



Ontology

Property	Value
Valid terms	44531 (Δ = -48)
Obsoleted terms	2895 (Δ = 40)
Merged terms	1967 (Δ = 35)
Biological process terms	29225
Molecular function terms	11124
Cellular component terms	4182

Annotations

Property	Value
Number of annotations	7,524,022
Annotations for biological process	2,927,597
Annotations for molecular function	2,325,747
Annotations for cellular component	2,270,678
Annotations for evidence PHYLO	3,610,054
Annotations for evidence IEA	2,041,235
Annotations for evidence OTHER	832,336
Annotations for evidence EXP	757,235
Annotations for evidence ND	242,830
Annotations for evidence HTP	40,332
Number of annotated scientific publications	159,450

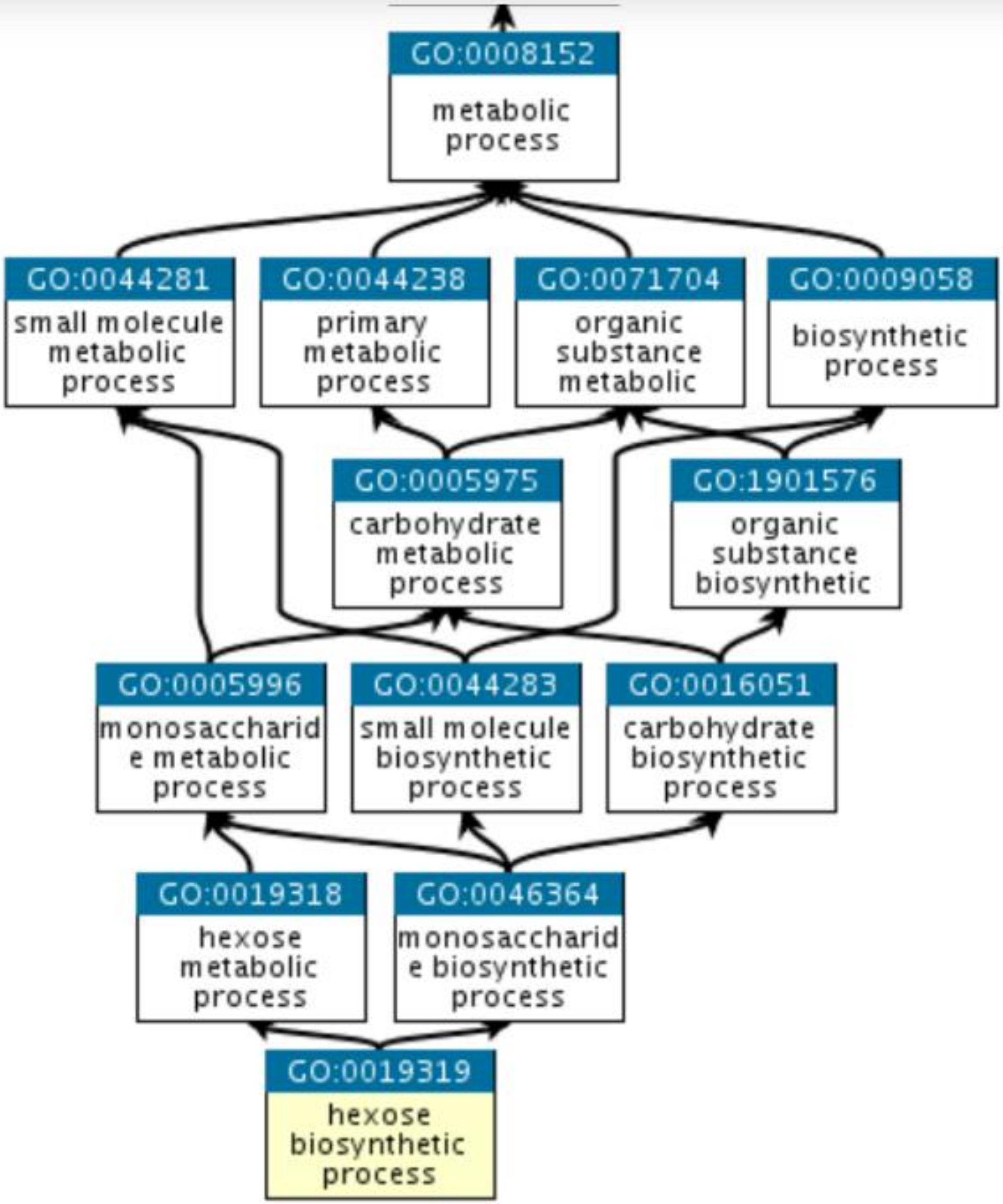
Gene products and species

Property	Value
Annotated gene products	1,405,061
Annotated species	4,593
Annotated species with over 1,000 annotations	195

Молекулярные функции (англ. molecular function) — специфическая активность генного продукта на молекулярном уровне, например, связывание углеводов илиАТФазная активность.

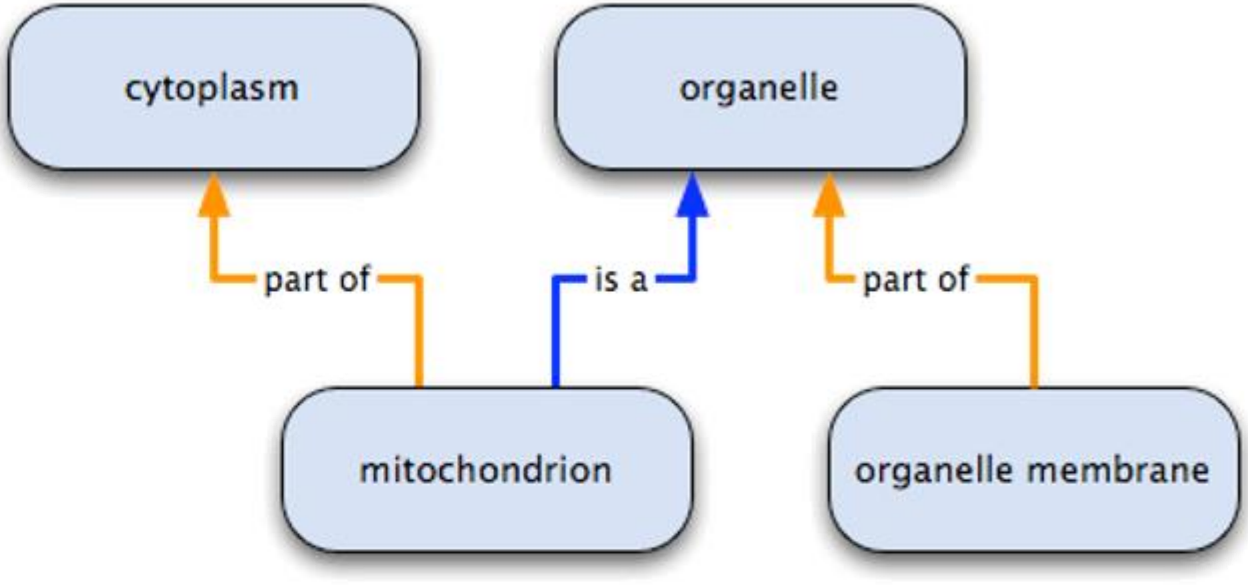
Биологические процессы (англ. biological process) — сложные явления, необходимые для жизнедеятельности организмов и происходящие благодаря осуществлению последовательности молекулярных функций, например, митоз или биосинтез пуринов.

Клеточные компоненты (англ. cellular component) — части клетки или внеклеточного пространства, где осуществляется функция генного продукта, например, ядроили рибосома.


GO:0008152
metabolic process
GO:0044281
small molecule metabolic process
GO:0044238
primary metabolic process
GO:0071704
organic substance metabolic
GO:0009058
biosynthetic process
GO:0005975
carbohydrate metabolic process
GO:1901576
organic substance biosynthetic
GO:0005996
monosaccharide metabolic process
GO:0044283
small molecule biosynthetic process
GO:0016051
carbohydrate biosynthetic process
GO:0019318
hexose metabolic process
GO:0046364
monosaccharide biosynthetic process
GO:0019319
hexose biosynthetic process

Термин GO (GO term) – узел графа – может иметь любое количество связей с любыми другими узлами

Отношения между узлами – ребра графа бывают разного типа



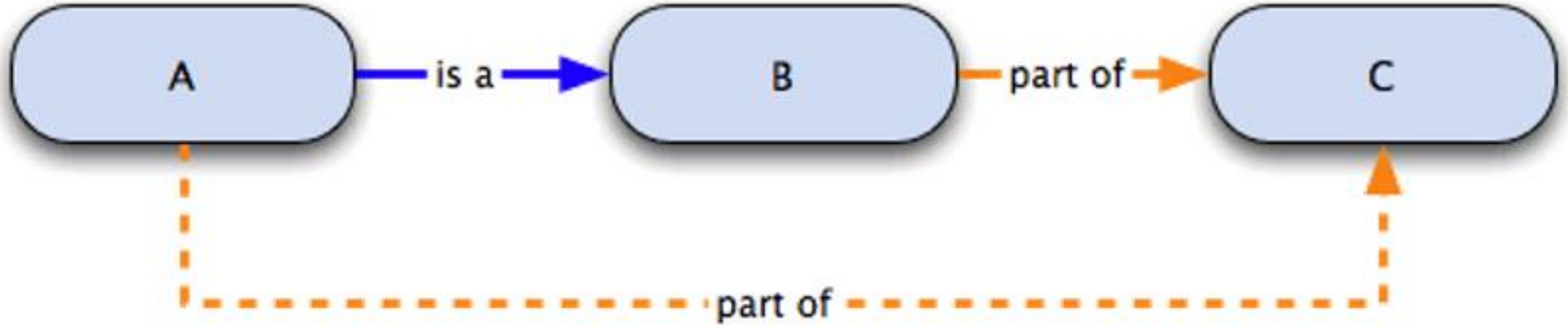
A *is a* B

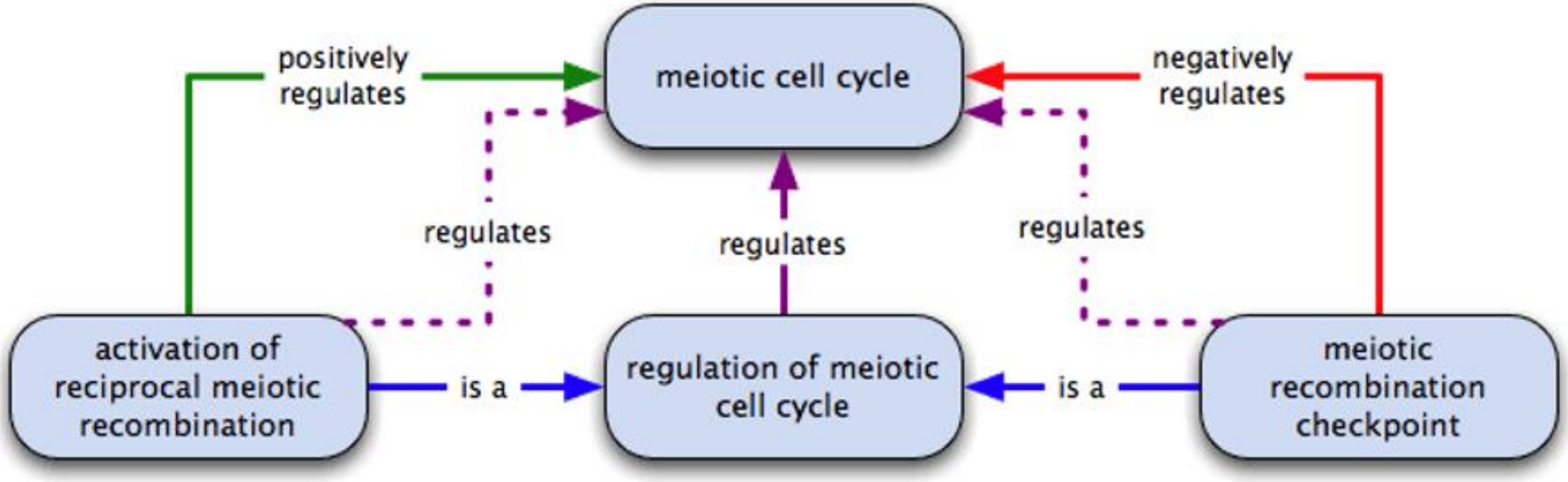
B *part of* C

Значит, A *part of* C

→ → Указанные непосредственно

⇢ Логически вытекающее





meiotic cell cycle

positively regulates

negatively regulates

regulates

regulates

regulates

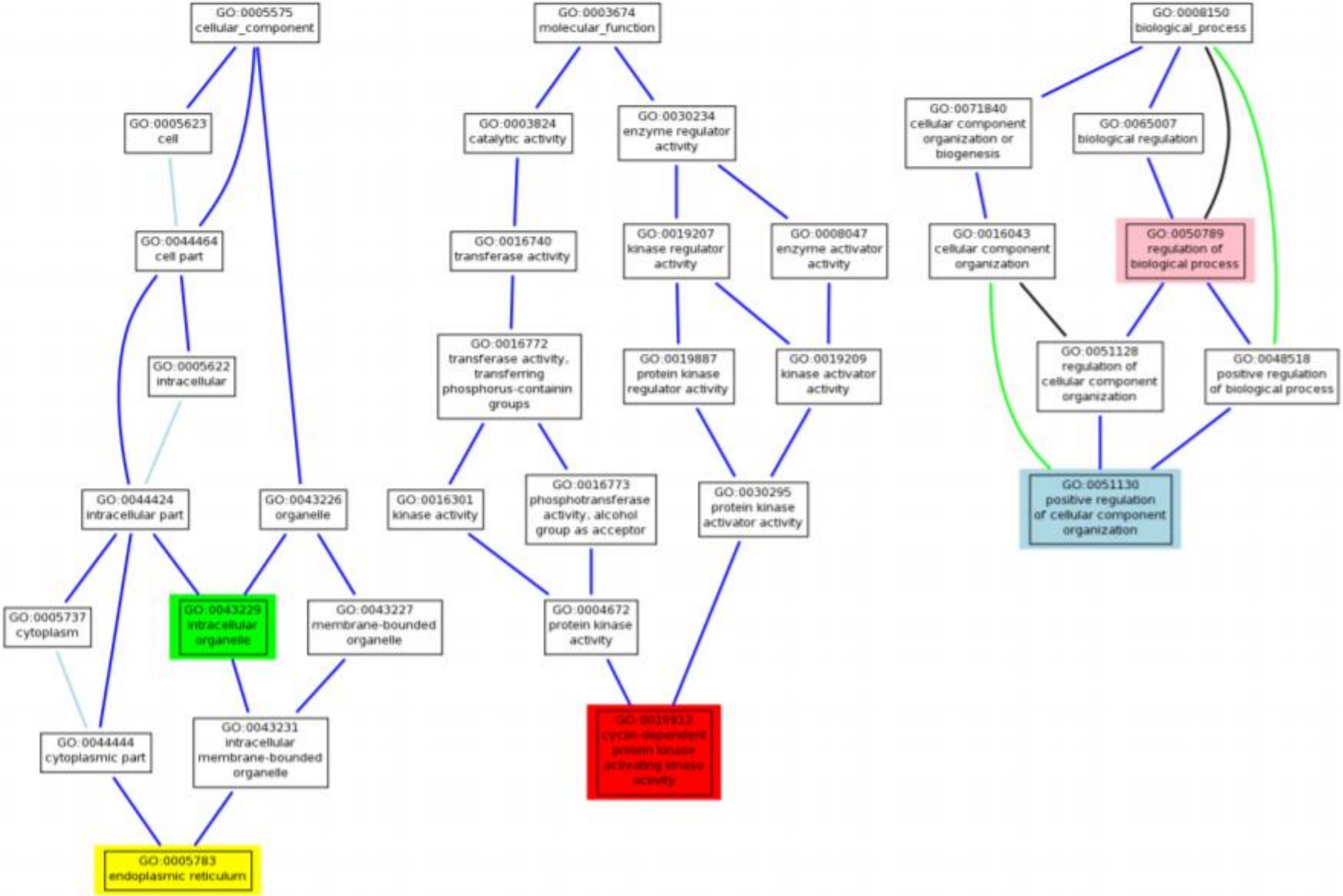
activation of reciprocal meiotic recombination

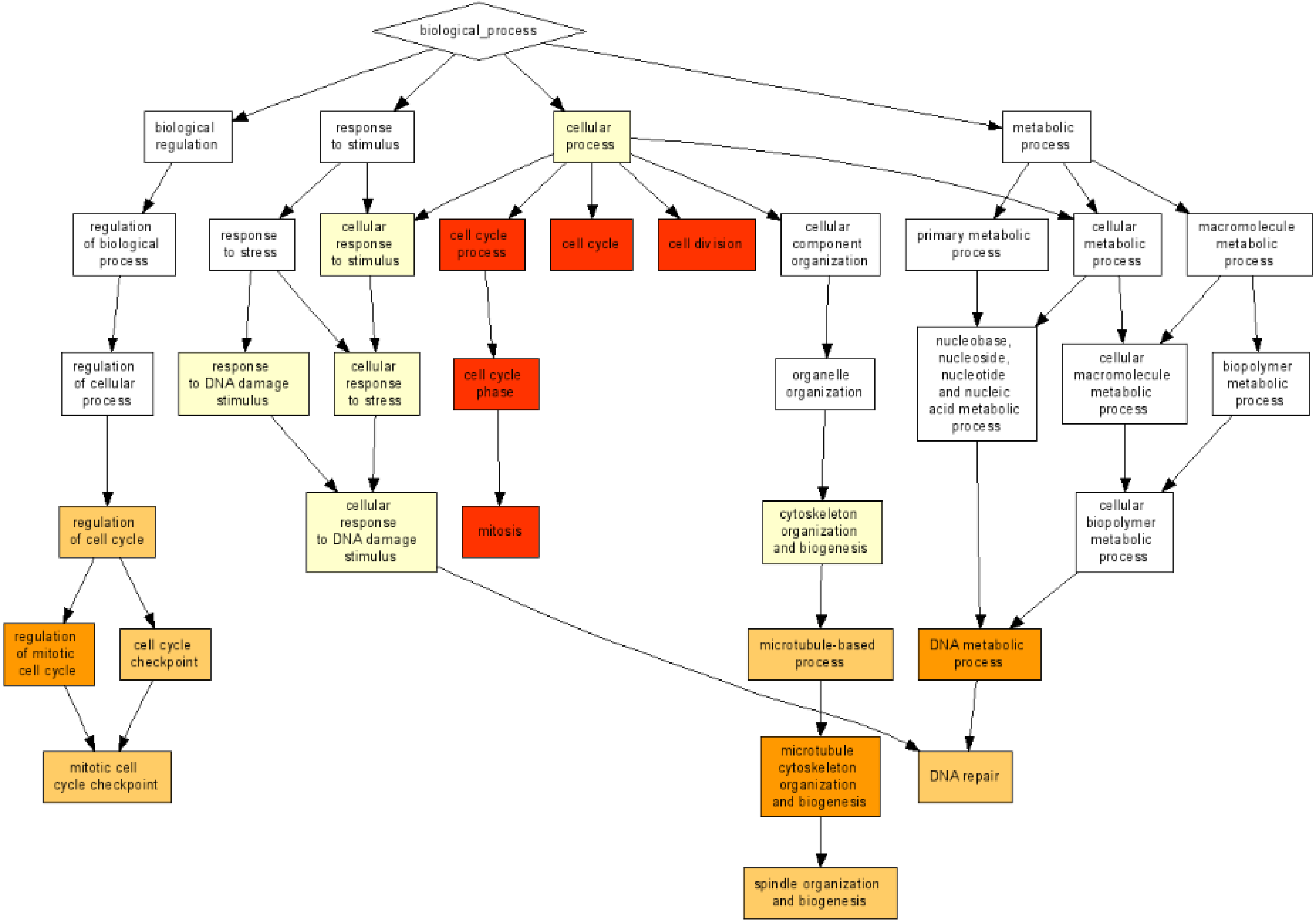
is a

regulation of meiotic cell cycle

is a

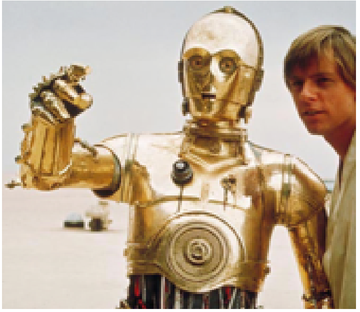
meiotic recombination checkpoint


GO:0005575 cellular_component
GO:0003674 molecular_function
GO:0008150 biological_process
GO:0005623 cell
GO:0003824 catalytic activity
GO:0030234 enzyme regulator activity
GO:0071840 cellular component organization or biogenesis
GO:0065007 biological regulation
GO:0044464 cell part
GO:0016740 transferase activity
GO:0019207 kinase regulator activity
GO:0008047 enzyme activator activity
GO:0016043 cellular component organization
GO:0050789 regulation of biological process
GO:0005622 intracellular
GO:0016772 transferase activity, transferring phosphorus-containin groups
GO:0019887 protein kinase regulator activity
GO:0019209 kinase activator activity
GO:0051128 regulation of cellular component organization
GO:0048518 positive regulation of biological process
GO:0044424 intracellular part
GO:0043226 organelle
GO:0016301 kinase activity
GO:0016773 phosphotransferase activity, alcohol group as acceptor
GO:0030295 protein kinase activator activity
GO:0051130 positive regulation of cellular component organization
GO:0005737 cytoplasm
GO:0043229 intracellular organelle
GO:0043227 membrane-bounded organelle
GO:0004672 protein kinase activity
GO:0044444 cytoplasmic part
GO:0043231 intracellular membrane-bounded organelle
GO:0019912 cyclin-dependent protein kinase activating kinase activity
GO:0005783 endoplasmic reticulum


biological_process
biological regulation
response to stimulus
cellular process
metabolic process
regulation of biological process
response to stress
cellular response to stimulus
cell cycle process
cell cycle
cell division
cellular component organization
primary metabolic process
cellular metabolic process
macromolecule metabolic process
regulation of cellular process
response to DNA damage stimulus
cellular response to stress
cell cycle phase
organelle organization
nucleobase, nucleoside, nucleotide and nucleic acid metabolic process
cellular macromolecule metabolic process
biopolymer metabolic process
regulation of cell cycle
cellular response to DNA damage stimulus
mitosis
cytoskeleton organization and biogenesis
cellular biopolymer metabolic process
regulation of mitotic cell cycle
cell cycle checkpoint
microtubule-based process
DNA metabolic process
mitotic cell cycle checkpoint
microtubule cytoskeleton organization and biogenesis
DNA repair
spindle organization and biogenesis

Типы достоверности

Inferred from Electronic Annotation (**IEA**)



Inferred from Sequence or structural Similarity (**ISS**)
- Inferred from Sequence Orthology (**ISO**)
- Inferred from Sequence Alignment (**ISA**)
- Inferred from Sequence Model (**ISM**)

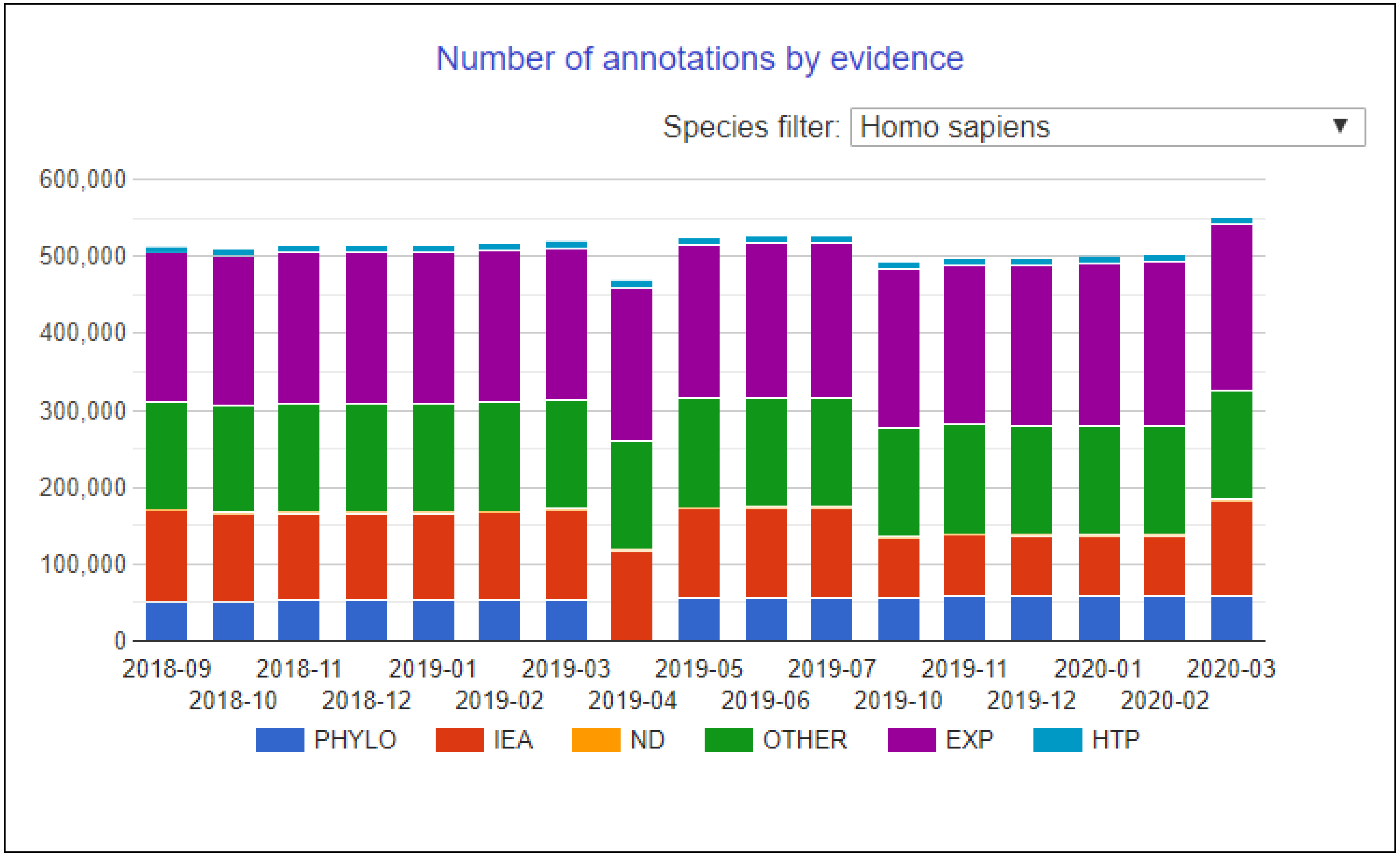
Inferred from Experiment (**EXP**)
- Inferred from Direct Assay (**IDA**)
- Inferred from Physical Interaction (**IPI**)
- Inferred from Mutant Phenotype (**IMP**)
- Inferred from Genetic Interaction (**IGI**)
- Inferred from Expression Pattern (**IEP**)

Traceable Author Statement (**TAS**)
Non-traceable Author Statement (**NAS**)

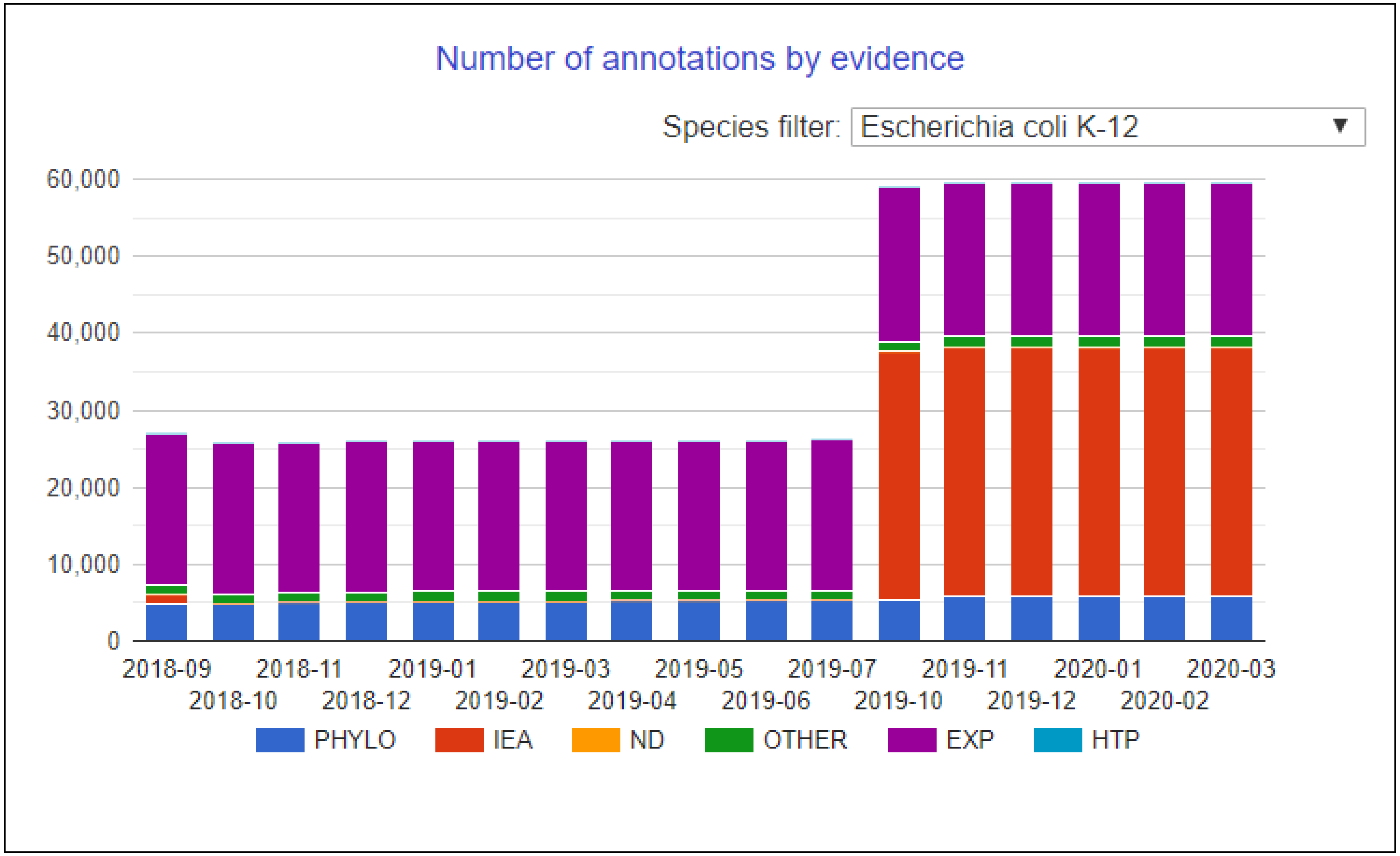
🟥 Плохо
🟨
🟩 Хорошо

http://geneontology.org/docs/guide-go-evidence-codes/

☐	Gene/product	Gene/product name	Annotation qualifier	GO class (direct)	Annotation extension	Contributor	Organism	Evidence	Evidence with	PANTHER family	Type	Isofor
☐	Fcer1g	Fc fragment of IgE receptor Ig		positive regulation of type IIa hypersensitivity		RGD	Rattus norvegicus	ISO	RGD:10572	high affinity immunoglobulin epsilon receptor gamma-subunit pthr16803	gene	
☐	Fcer1g	Fc fragment of IgE receptor Ig		positive regulation of type IIa hypersensitivity		RGD	Rattus norvegicus	ISO	RGD:10572	high affinity immunoglobulin epsilon receptor gamma-subunit pthr16803	gene	
☐	Fcer1g	Fc fragment of IgE receptor Ig		positive regulation of type IIa hypersensitivity		RGD	Rattus norvegicus	ISO	RGD:10572	high affinity immunoglobulin epsilon receptor gamma-subunit pthr16803	gene	
☐	Fcgr2a	Fc fragment of IgG receptor IIa		positive regulation of type IIa hypersensitivity		RGD	Rattus norvegicus	ISO	RGD:736451	immunoglobulin fc receptor pthr11481	gene	
☐	Fcgr2a	Fc fragment of IgG receptor IIa		positive regulation of type IIa hypersensitivity		RGD	Rattus norvegicus	ISO	RGD:736451	immunoglobulin fc receptor pthr11481	gene	
☐	Fcgr2a	Fc fragment of IgG receptor		regulation of antibody-		RGD	Rattus norvegicus	IMP		immunoglobulin fc receptor pthr11481	gene	



Species filter: Homo sapiens



Species filter: Escherichia coli K-12 ▼

GO Enrichment Analysis

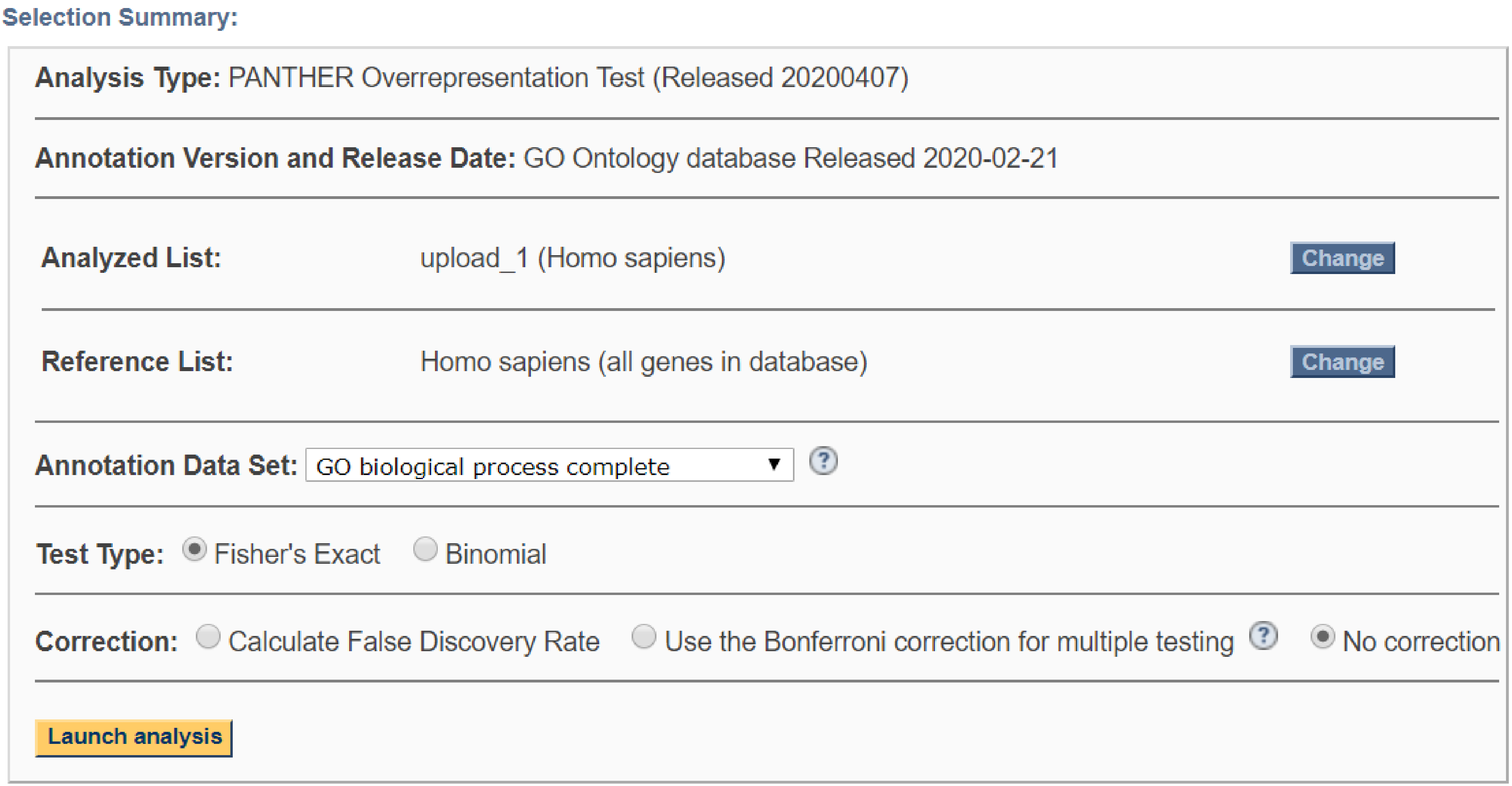
Powered by PANTHER

APOH
APP
CND2
COL3A1
COL5A2
CXCL6

biological process

Homo sapiens

Gene set example: genes up-regulated during formation of blood vessels/angiogenesis (source: msigdb) http://geneontology.org/docs/go-enrichment-analysis/



Selection Summary:

Analysis Type: PANTHER Overrepresentation Test (Released 20200407)

Annotation Version and Release Date: GO Ontology database Released 2020-02-21

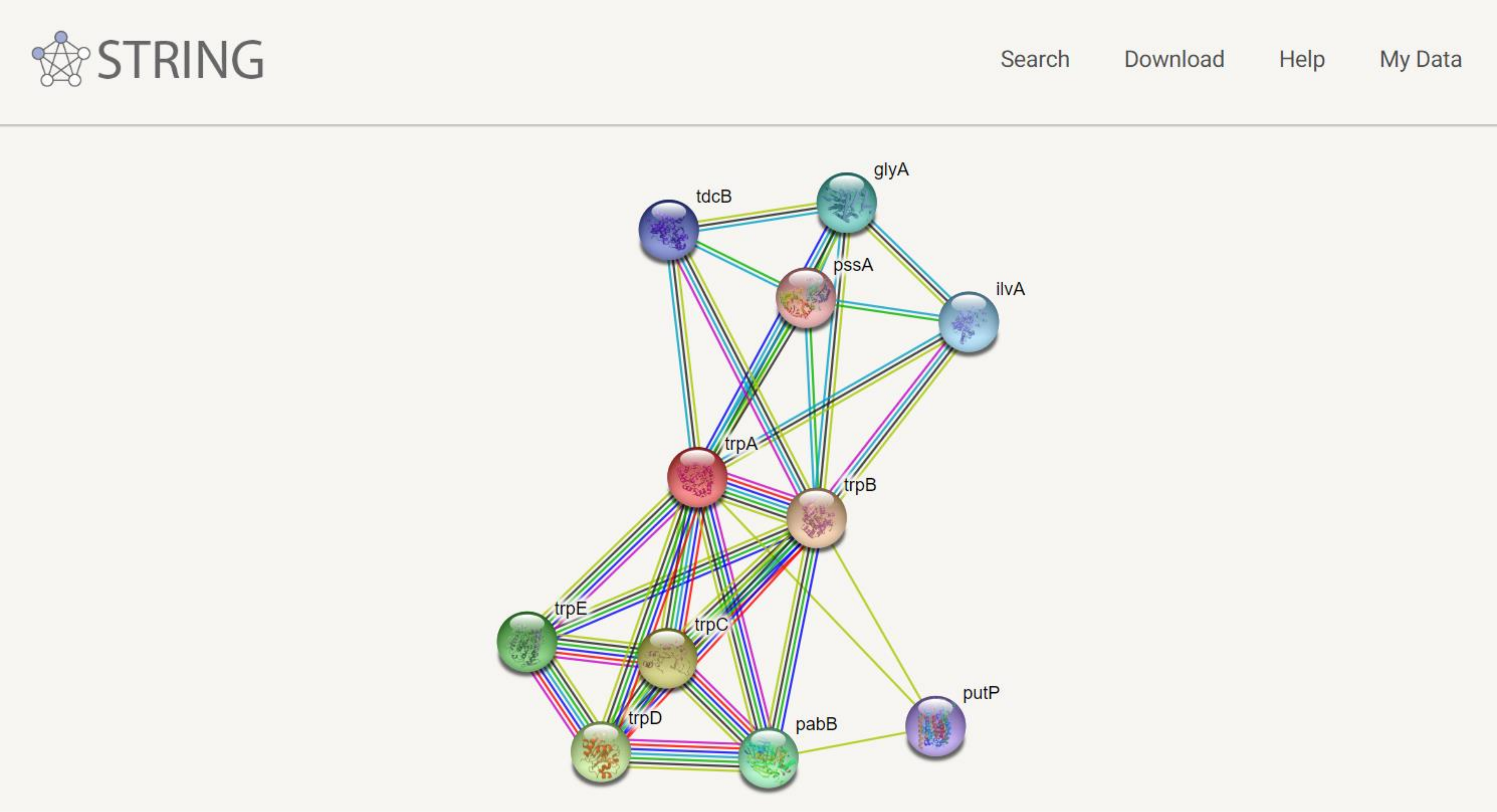
Analyzed List: upload_1 (Homo sapiens)

Reference List: Homo sapiens (all genes in database)

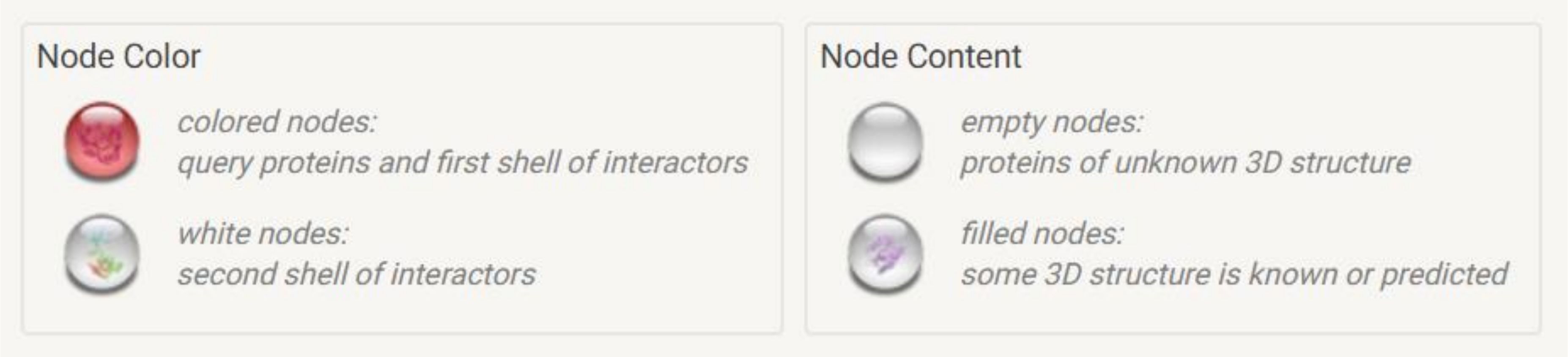
Annotation Data Set: GO biological process complete

Test Type: ● Fisher's Exact ○ Binomial

Correction: ○ Calculate False Discovery Rate ○ Use the Bonferroni correction for multiple testing ● No correction



https://string-db.org/



Node Color

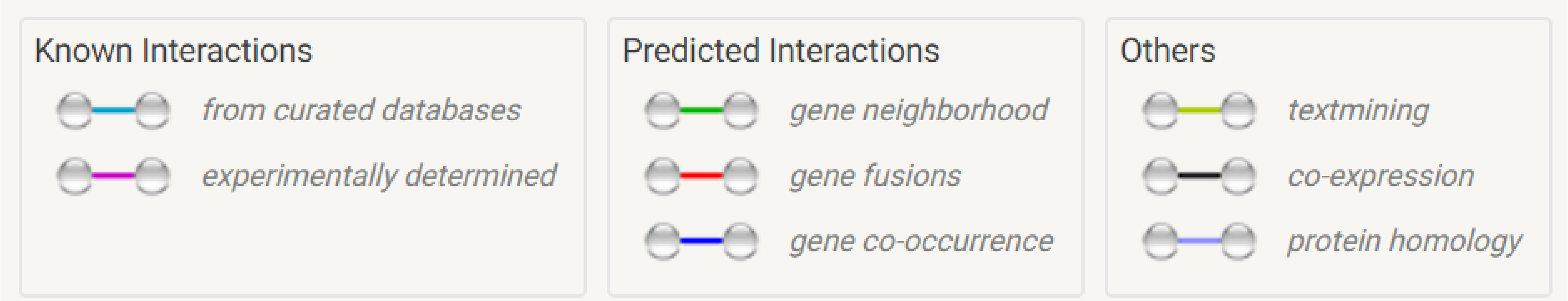
colored nodes:
query proteins and first shell of interactors

white nodes:
second shell of interactors

Node Content

empty nodes:
proteins of unknown 3D structure

filled nodes:
some 3D structure is known or predicted



Known Interactions

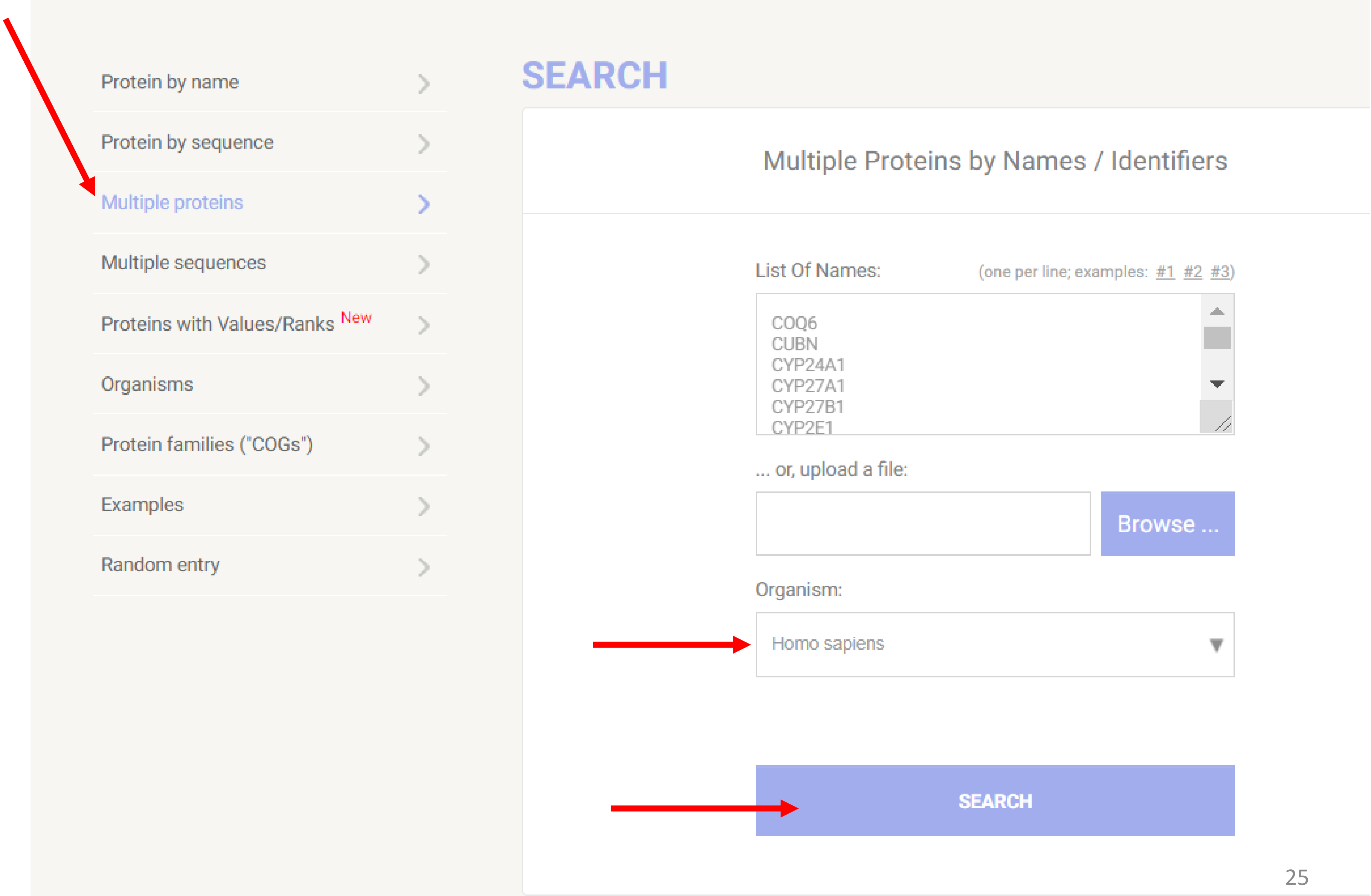
from curated databases
experimentally determined

Predicted Interactions

gene neighborhood
gene fusions
gene co-occurrence

Others

textmining
co-expression
protein homology



SEARCH

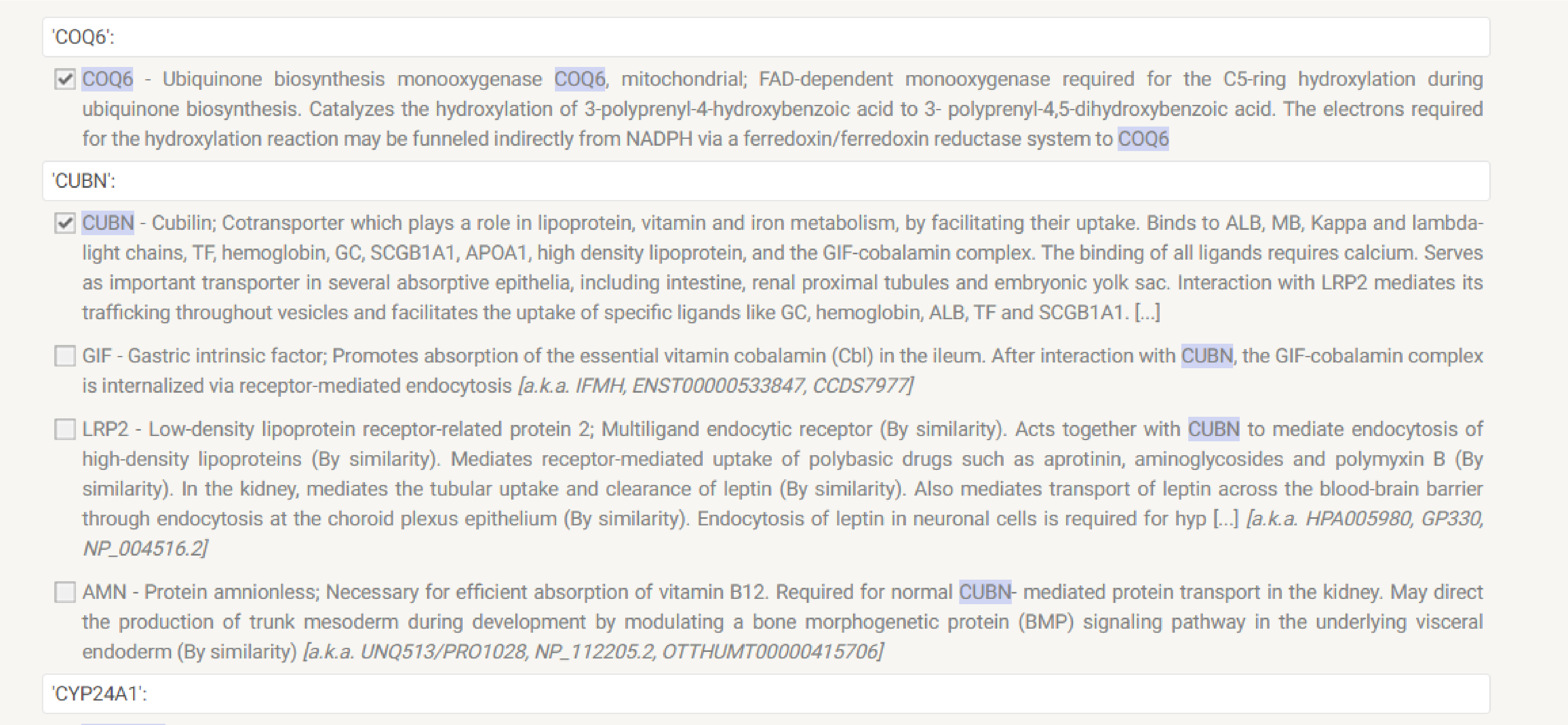
Multiple Proteins by Names / Identifiers

List Of Names: (one per line; examples: #1 #2 #3)

COQ6
CUBN
CYP24A1
CYP27A1
CYP27B1
CYP2E1

... or, upload a file:

Organism: Homo sapiens



'COQ6':

☑ COQ6 - Ubiquinone biosynthesis monooxygenase COQ6, mitochondrial; FAD-dependent monooxygenase required for the C5-ring hydroxylation during ubiquinone biosynthesis. Catalyzes the hydroxylation of 3-polyprenyl-4-hydroxybenzoic acid to 3- polyprenyl-4,5-dihydroxybenzoic acid. The electrons required for the hydroxylation reaction may be funneled indirectly from NADPH via a ferredoxin/ferredoxin reductase system to COQ6

'CUBN':

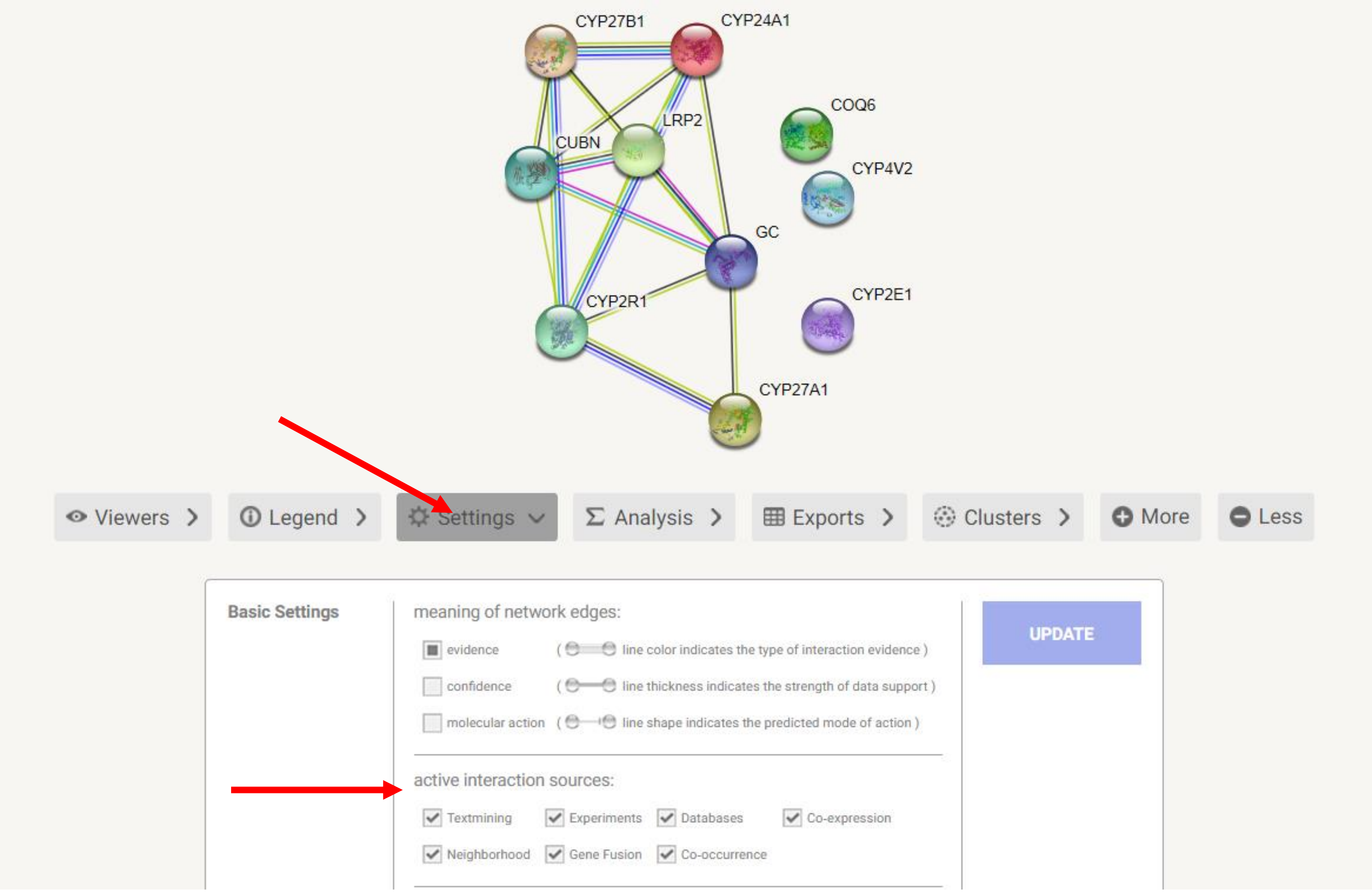
☑ CUBN - Cubilin; Cotransporter which plays a role in lipoprotein, vitamin and iron metabolism, by facilitating their uptake. Binds to ALB, MB, Kappa and lambda-light chains, TF, hemoglobin, GC, SCGB1A1, APOA1, high density lipoprotein, and the GIF-cobalamin complex. The binding of all ligands requires calcium. Serves as important transporter in several absorptive epithelia, including intestine, renal proximal tubules and embryonic yolk sac. Interaction with LRP2 mediates its trafficking throughout vesicles and facilitates the uptake of specific ligands like GC, hemoglobin, ALB, TF and SCGB1A1. [...]

☐ GIF - Gastric intrinsic factor; Promotes absorption of the essential vitamin cobalamin (Cbl) in the ileum. After interaction with CUBN, the GIF-cobalamin complex is internalized via receptor-mediated endocytosis *[a.k.a. IFMH, ENST00000533847, CCDS7977]*

☐ LRP2 - Low-density lipoprotein receptor-related protein 2; Multiligand endocytic receptor (By similarity). Acts together with CUBN to mediate endocytosis of high-density lipoproteins (By similarity). Mediates receptor-mediated uptake of polybasic drugs such as aprotinin, aminoglycosides and polymyxin B (By similarity). In the kidney, mediates the tubular uptake and clearance of leptin (By similarity). Also mediates transport of leptin across the blood-brain barrier through endocytosis at the choroid plexus epithelium (By similarity). Endocytosis of leptin in neuronal cells is required for hyp [...] *[a.k.a. HPA005980, GP330, NP_004516.2]*

☐ AMN - Protein amnionless; Necessary for efficient absorption of vitamin B12. Required for normal CUBN- mediated protein transport in the kidney. May direct the production of trunk mesoderm during development by modulating a bone morphogenetic protein (BMP) signaling pathway in the underlying visceral endoderm (By similarity) *[a.k.a. UNQ513/PRO1028, NP_112205.2, OTTHUMT00000415706]*

'CYP24A1':



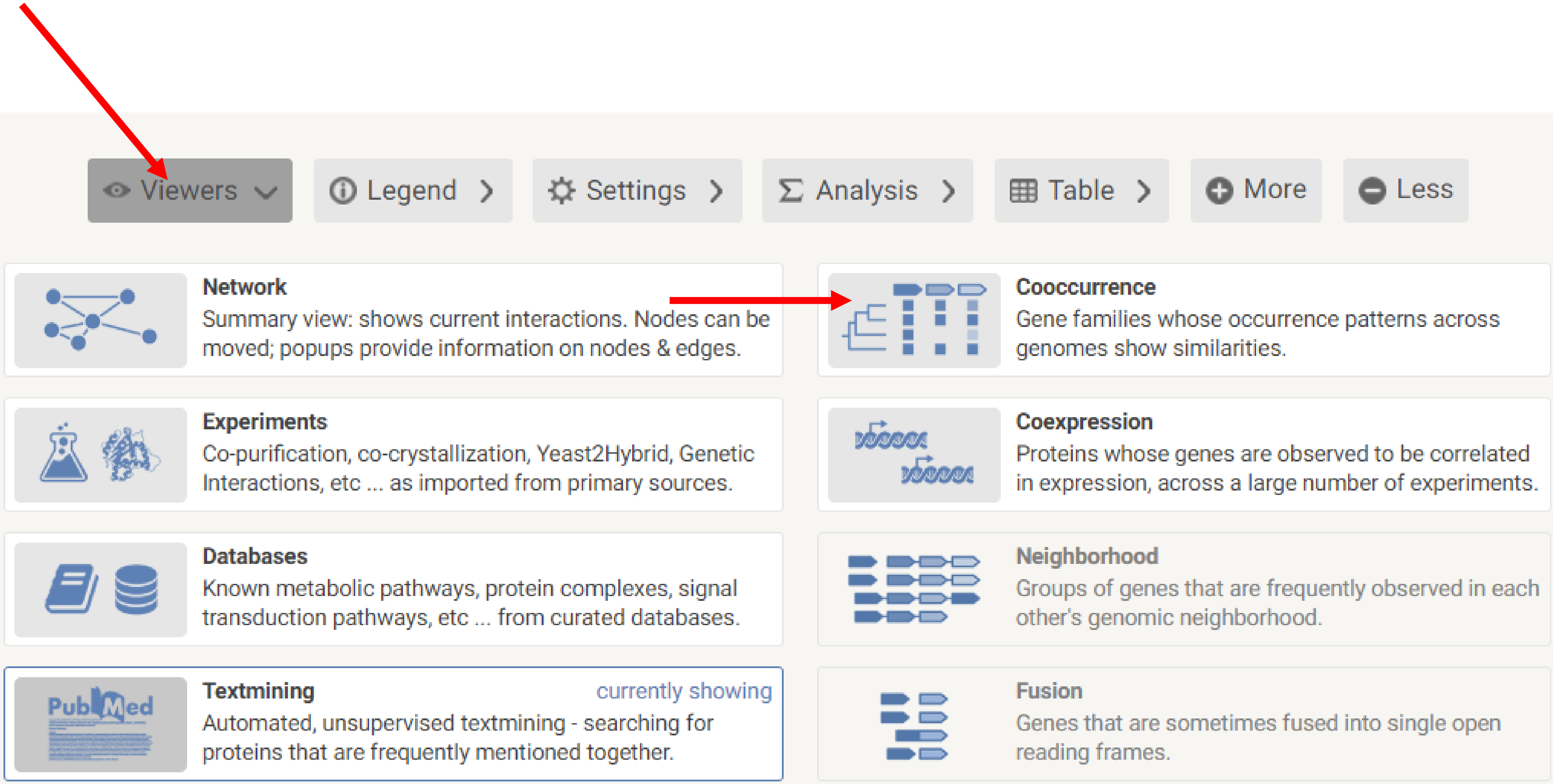
Basic Settings

meaning of network edges:

■ evidence (line color indicates the type of interaction evidence)
☐ confidence (line thickness indicates the strength of data support)
☐ molecular action (line shape indicates the predicted mode of action)

active interaction sources:

☑ Textmining ☑ Experiments ☑ Databases ☑ Co-expression
☑ Neighborhood ☑ Gene Fusion ☑ Co-occurrence



Network
Summary view: shows current interactions. Nodes can be moved; popups provide information on nodes & edges.

Cooccurrence
Gene families whose occurrence patterns across genomes show similarities.

Experiments
Co-purification, co-crystallization, Yeast2Hybrid, Genetic Interactions, etc ... as imported from primary sources.

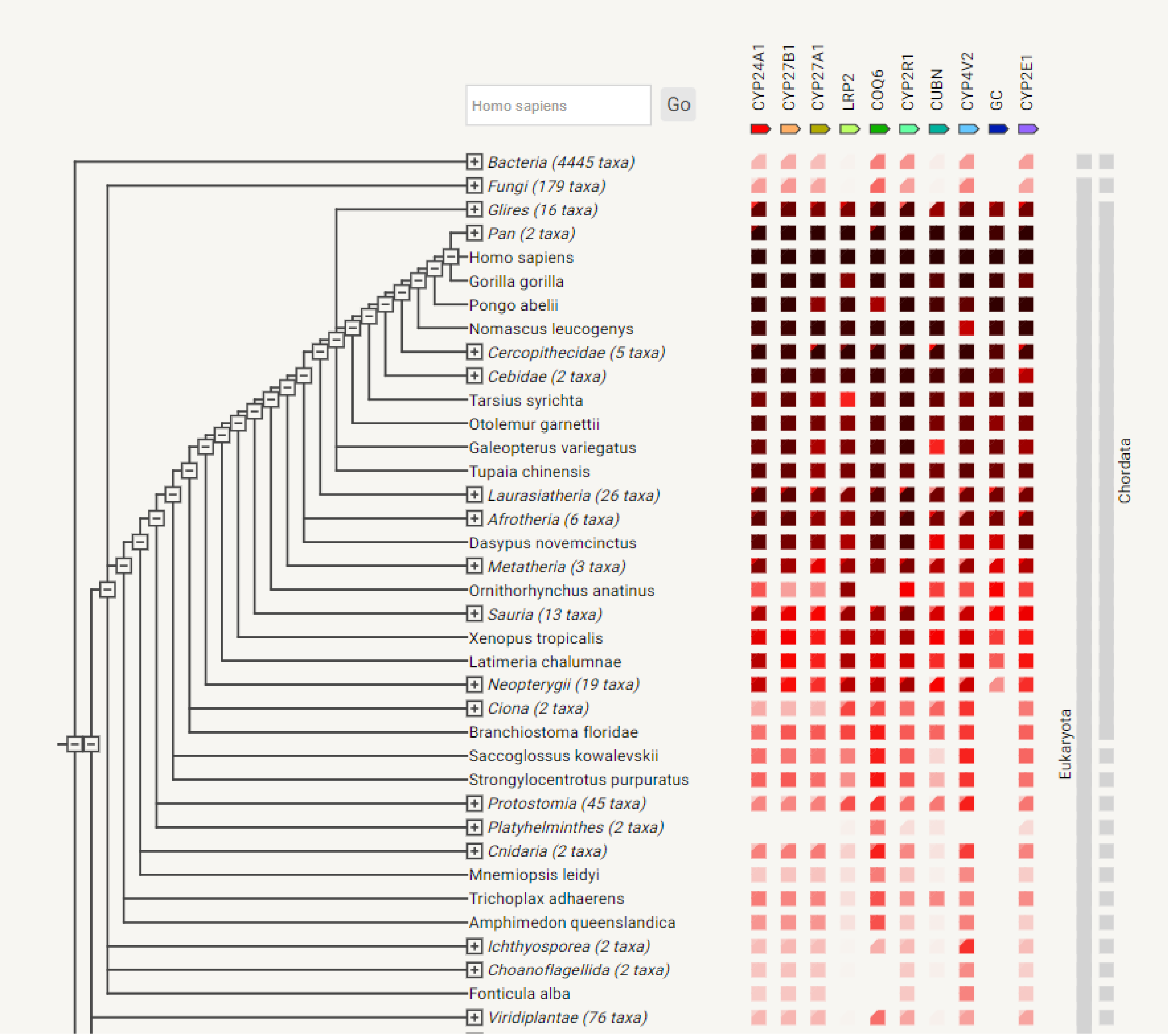
Coexpression
Proteins whose genes are observed to be correlated in expression, across a large number of experiments.

Databases
Known metabolic pathways, protein complexes, signal transduction pathways, etc ... from curated databases.

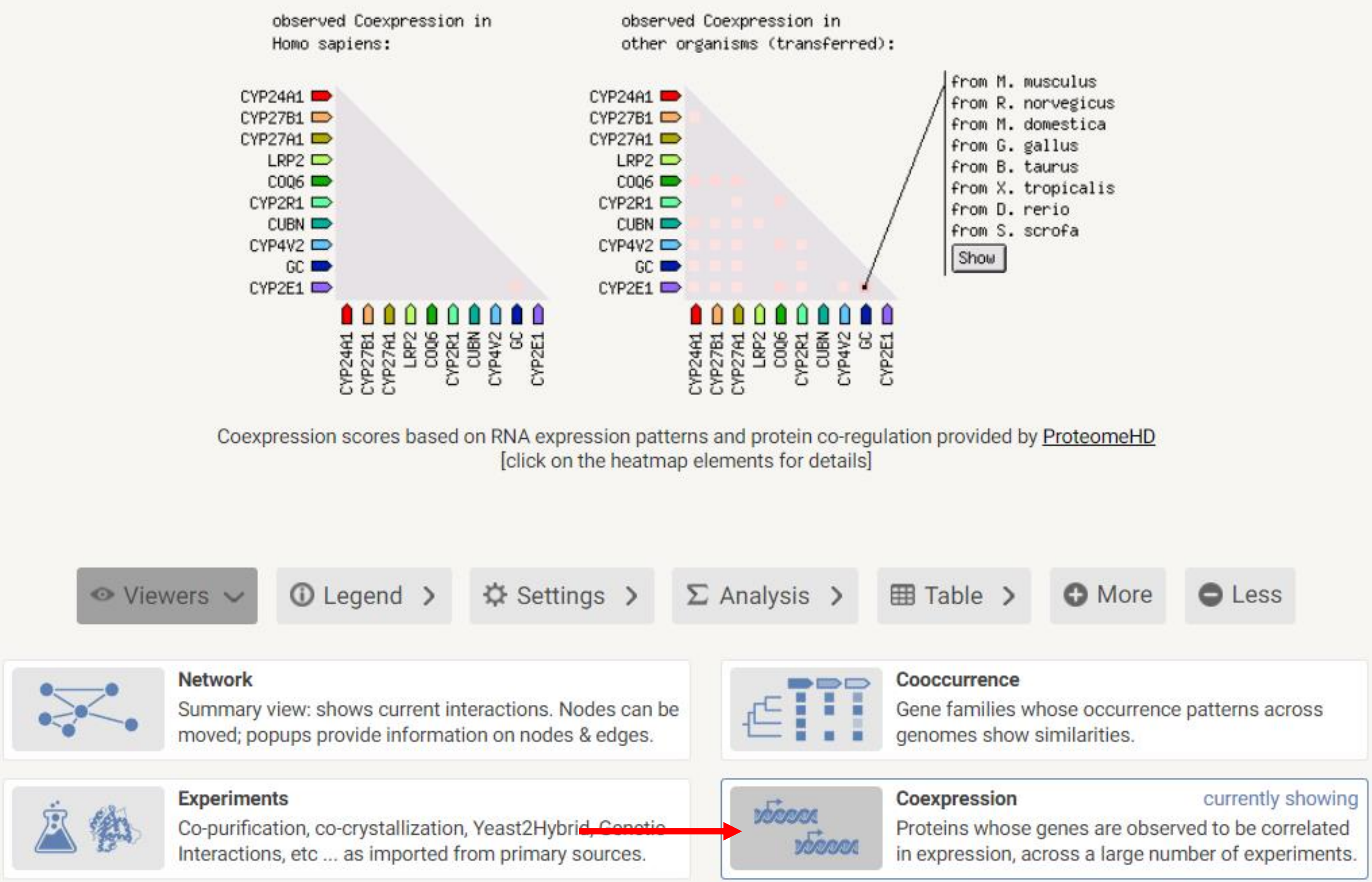
Neighborhood
Groups of genes that are frequently observed in each other's genomic neighborhood.

Textmining
Automated, unsupervised textmining - searching for proteins that are frequently mentioned together.

Fusion
Genes that are sometimes fused into single open reading frames.


Homo sapiens
Go
CYP24A1
CYP27B1
CYP27A1
LRP2
COQ6
CYP2R1
CUBN
CYP4V2
GC
CYP2E1
Bacteria (4445 taxa)
Fungi (179 taxa)
Glires (16 taxa)
Pan (2 taxa)
Homo sapiens
Gorilla gorilla
Pongo abelii
Nomascus leucogenys
Cercopithecidae (5 taxa)
Cebidae (2 taxa)
Tarsius syrichta
Otolemur garnettii
Galeopterus variegatus
Tupaia chinensis
Laurasiatheria (26 taxa)
Afrotheria (6 taxa)
Dasypus novemcinctus
Metatheria (3 taxa)
Ornithorhynchus anatinus
Sauria (13 taxa)
Xenopus tropicalis
Latimeria chalumnae
Neopterygii (19 taxa)
Ciona (2 taxa)
Branchiostoma floridae
Saccoglossus kowalevskii
Strongylocentrotus purpuratus
Protostomia (45 taxa)
Platyhelminthes (2 taxa)
Cnidaria (2 taxa)
Mnemiopsis leidyi
Trichoplax adhaerens
Amphimedon queenslandica
Ichthyosporea (2 taxa)
Choanoflagellida (2 taxa)
Fonticula alba
Viridiplantae (76 taxa)
Chordata
Eukaryota

GENE COEXPRESSION



Coexpression scores based on RNA expression patterns and protein co-regulation provided by ProteomeHD
[click on the heatmap elements for details]

Network
Summary view: shows current interactions. Nodes can be moved; popups provide information on nodes & edges.

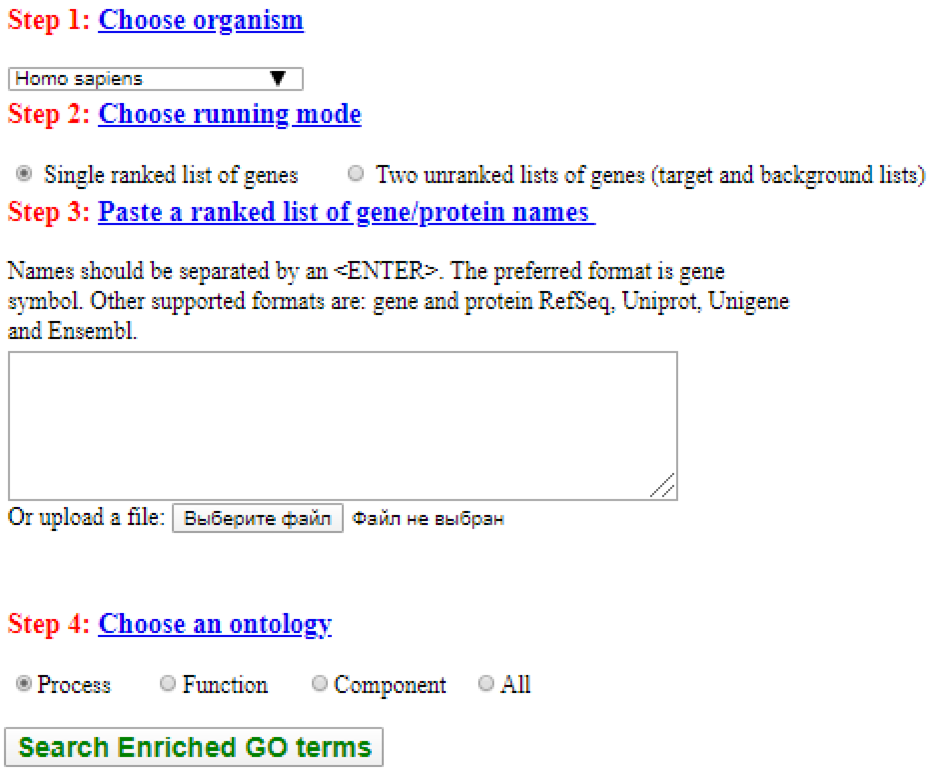
Cooccurrence
Gene families whose occurrence patterns across genomes show similarities.

Experiments
Co-purification, co-crystallization, Yeast2Hybrid, Genetic Interactions, etc ... as imported from primary sources.

Coexpression currently showing
Proteins whose genes are observed to be correlated in expression, across a large number of experiments.

GORILLA

***G**ene **O**ntology en**RI**chment ana**L**ysis and visua**L**iz**A**tion tool*



Step 1: Choose organism

Homo sapiens ▼

Step 2: Choose running mode

● Single ranked list of genes ○ Two unranked lists of genes (target and background lists)

Step 3: Paste a ranked list of gene/protein names

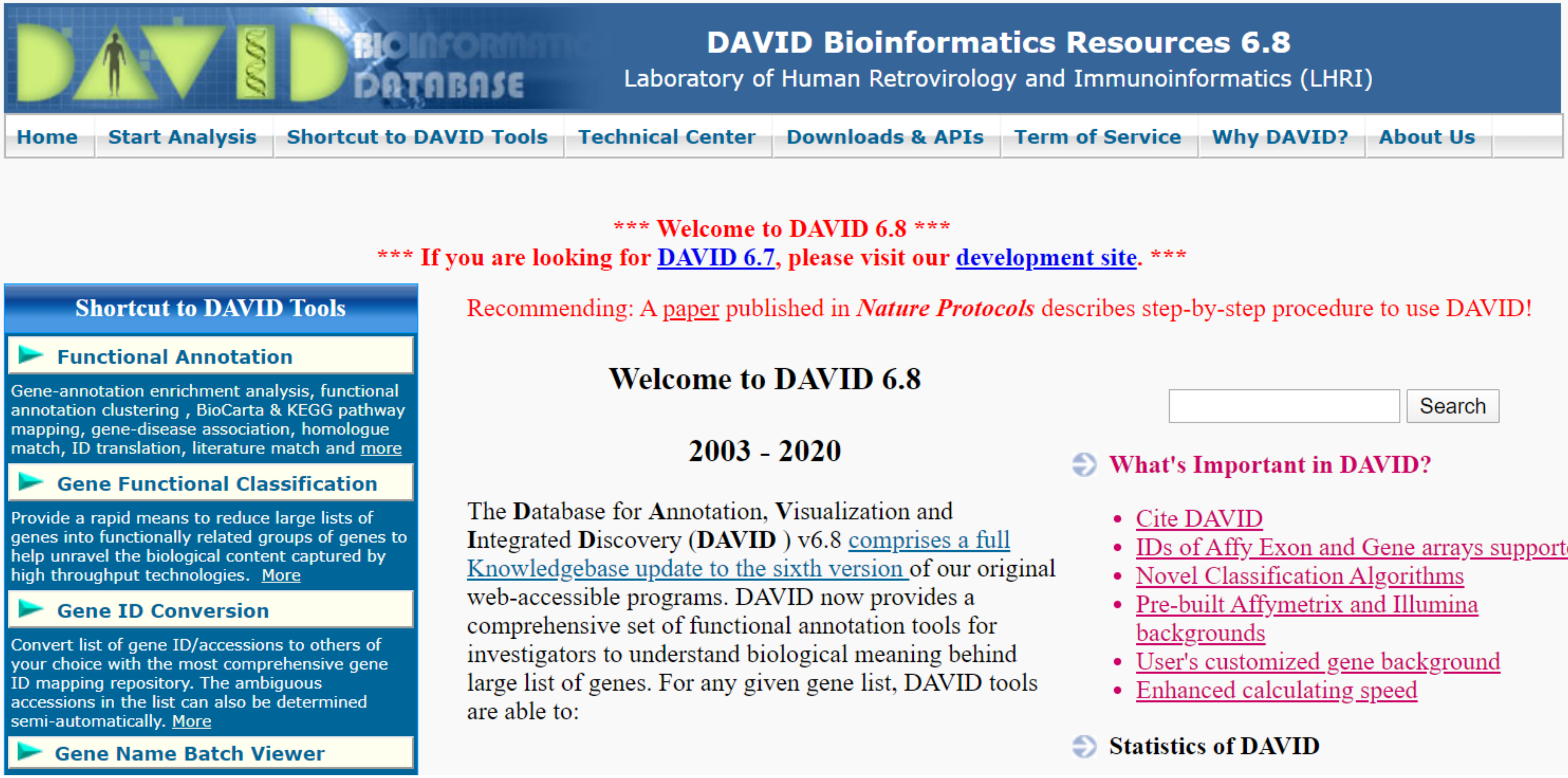
Names should be separated by an <ENTER>. The preferred format is gene symbol. Other supported formats are: gene and protein RefSeq, Uniprot, Unigene and Ensembl.

Or upload a file: Выберите файл Файл не выбран

Step 4: Choose an ontology

● Process ○ Function ○ Component ○ All

https://david.ncifcrf.gov/



DAVID Bioinformatics Resources 6.8

Laboratory of Human Retrovirology and Immunoinformatics (LHRI)

***** Welcome to DAVID 6.8 *****

***** If you are looking for DAVID 6.7, please visit our development site. *****

Shortcut to DAVID Tools

Functional Annotation

Gene-annotation enrichment analysis, functional annotation clustering , BioCarta & KEGG pathway mapping, gene-disease association, homologue match, ID translation, literature match and more

Gene Functional Classification

Provide a rapid means to reduce large lists of genes into functionally related groups of genes to help unravel the biological content captured by high throughput technologies. More

Gene ID Conversion

Convert list of gene ID/accessions to others of your choice with the most comprehensive gene ID mapping repository. The ambiguous accessions in the list can also be determined semi-automatically. More

Gene Name Batch Viewer

Recommending: A paper published in ***Nature Protocols*** describes step-by-step procedure to use DAVID!

Welcome to DAVID 6.8

2003 - 2020

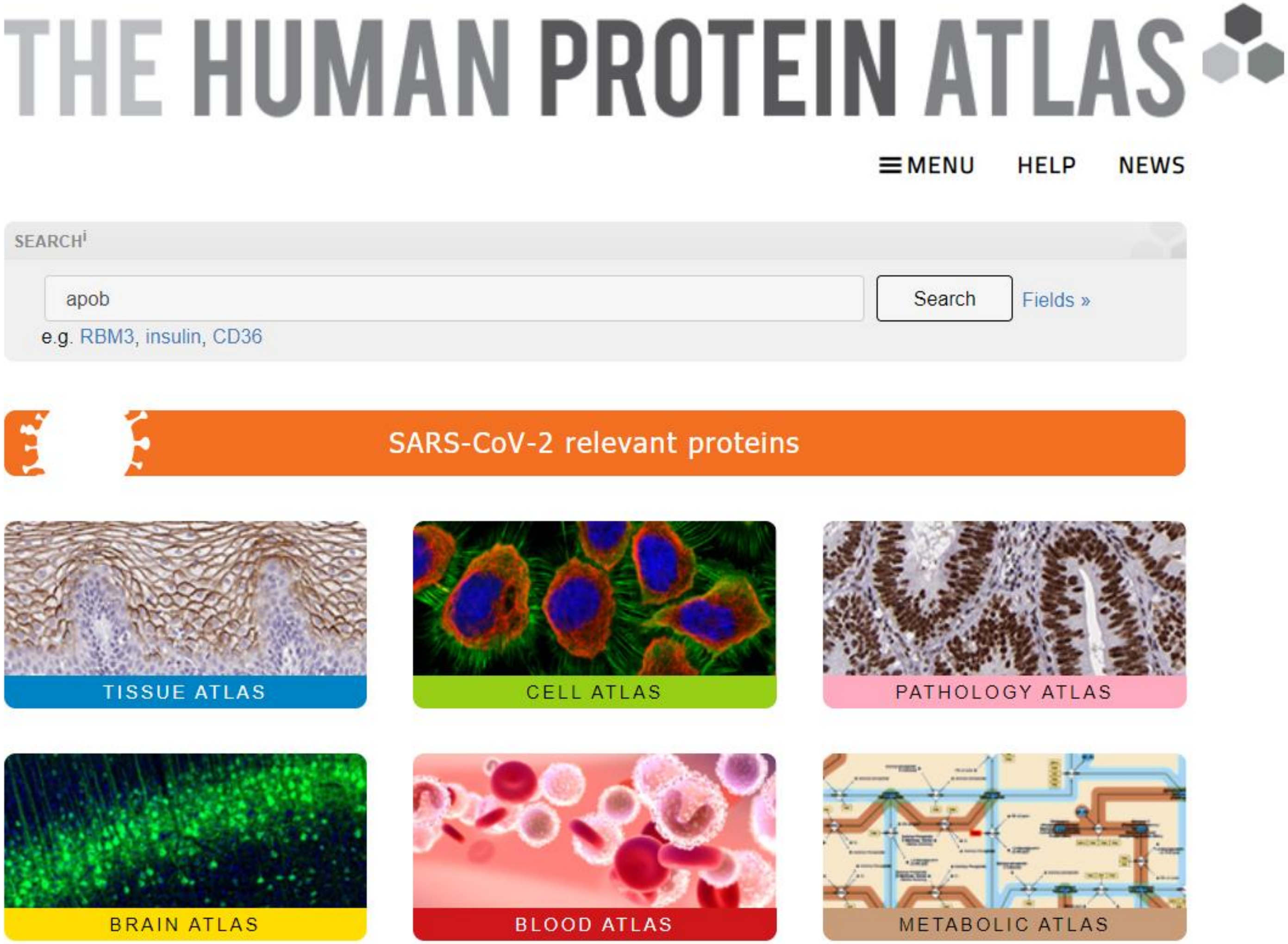
The **D**atabase for **A**nnotation, **V**isualization and **I**ntegrated **D**iscovery (**DAVID**) v6.8 comprises a full Knowledgebase update to the sixth version of our original web-accessible programs. DAVID now provides a comprehensive set of functional annotation tools for investigators to understand biological meaning behind large list of genes. For any given gene list, DAVID tools are able to:

What's Important in DAVID?

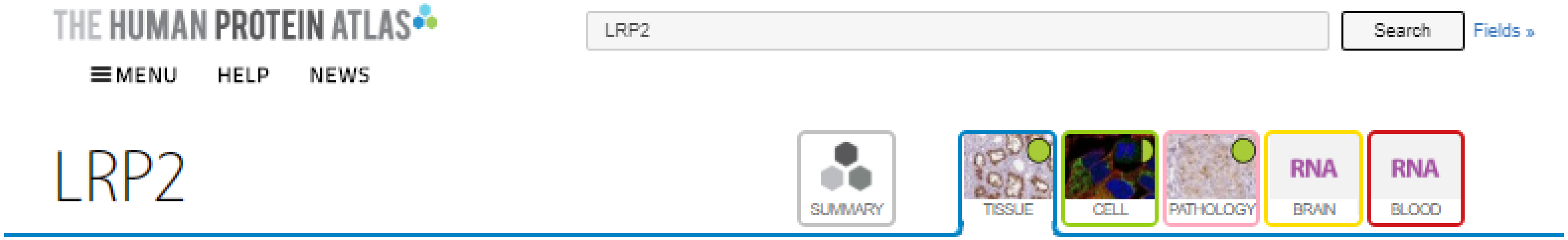
- Cite DAVID
- IDs of Affy Exon and Gene arrays supported
- Novel Classification Algorithms
- Pre-built Affymetrix and Illumina backgrounds
- User's customized gene background
- Enhanced calculating speed

Statistics of DAVID

https://www.proteinatlas.org/

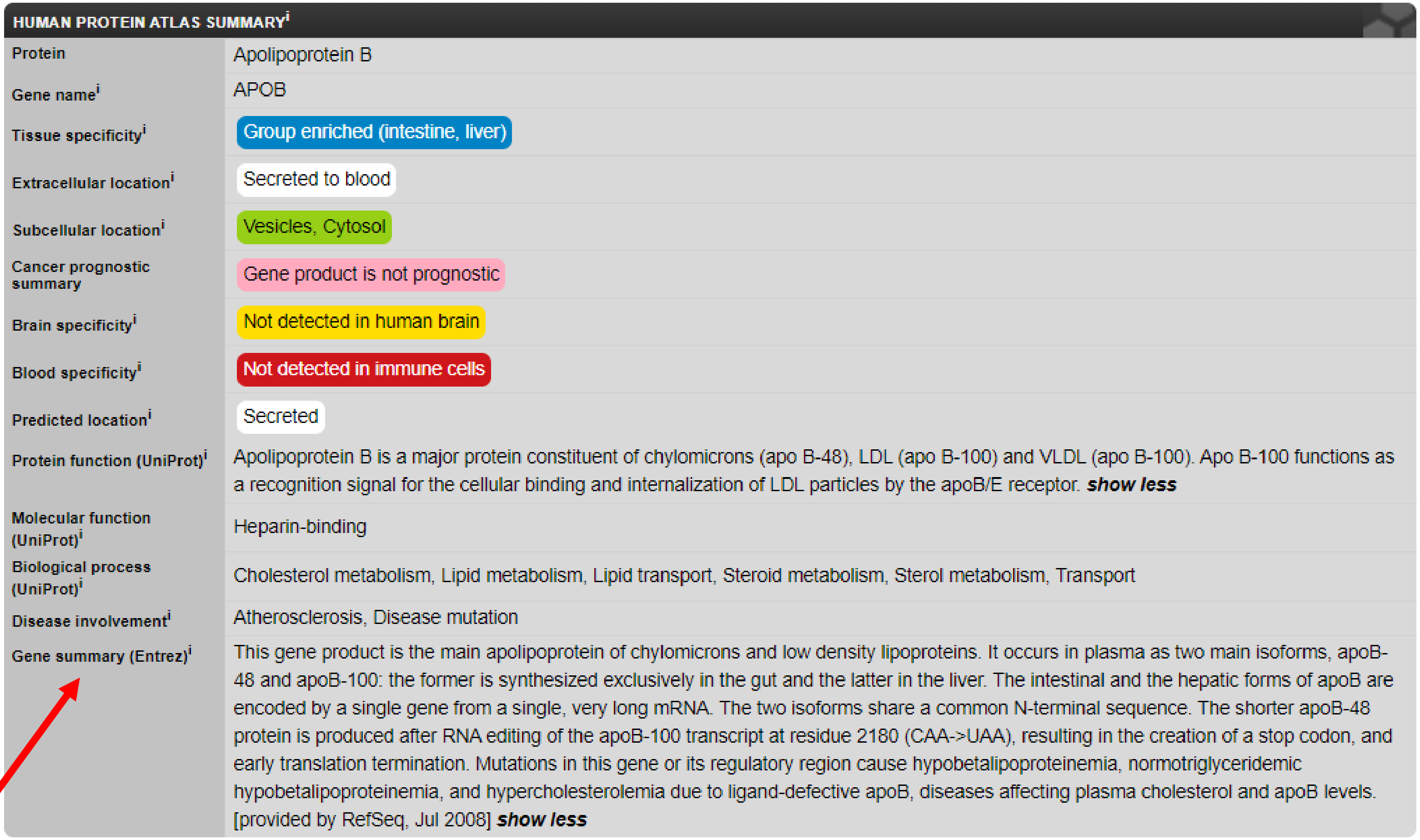


SEARCH: apob


THE HUMAN PROTEIN ATLAS
MENU
HELP
NEWS
Search
Fields »
SUMMARY
TISSUE
CELL
PATHOLOGY
RNA
BRAIN
RNA
BLOOD

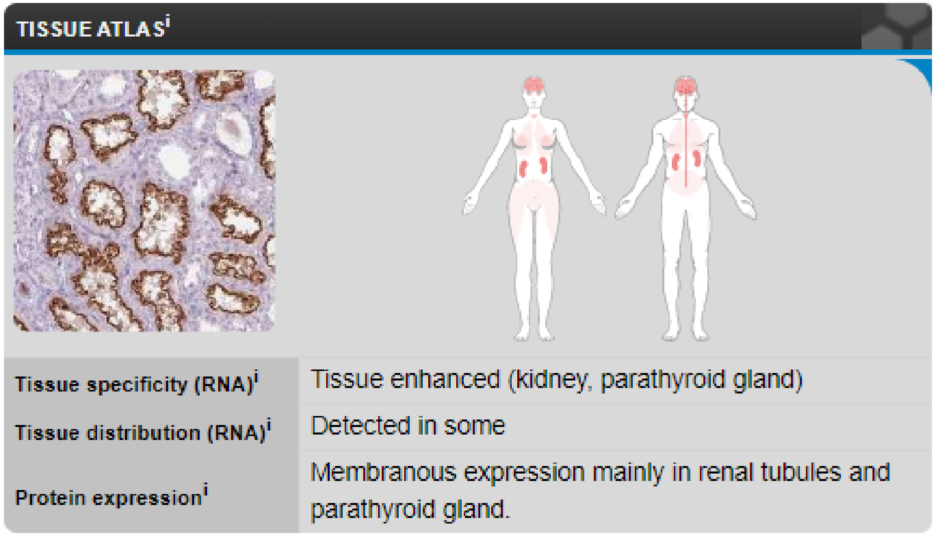
LRP2

LRP2



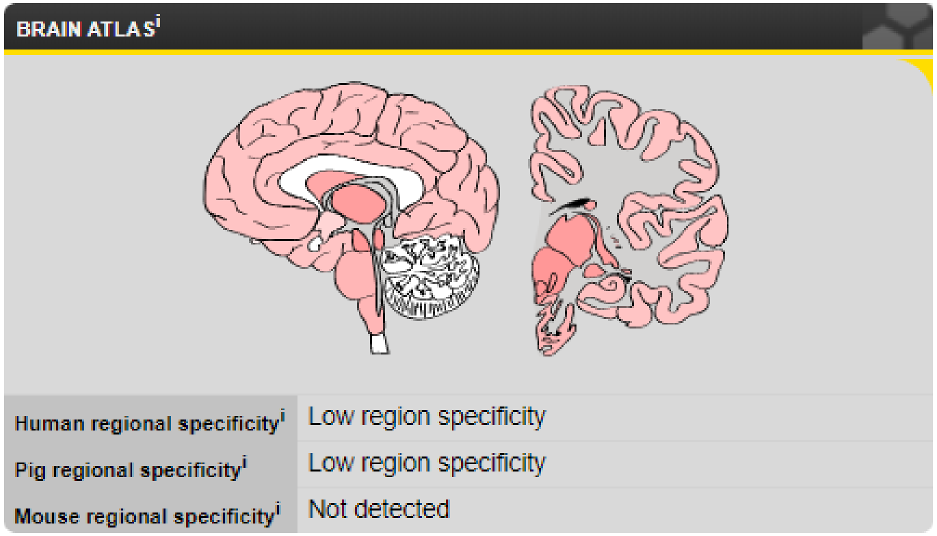
HUMAN PROTEIN ATLAS SUMMARY

Protein	Apolipoprotein B
Gene name	APOB
Tissue specificity	Group enriched (intestine, liver)
Extracellular location	Secreted to blood
Subcellular location	Vesicles, Cytosol
Cancer prognostic summary	Gene product is not prognostic
Brain specificity	Not detected in human brain
Blood specificity	Not detected in immune cells
Predicted location	Secreted
Protein function (UniProt)	Apolipoprotein B is a major protein constituent of chylomicrons (apo B-48), LDL (apo B-100) and VLDL (apo B-100). Apo B-100 functions as a recognition signal for the cellular binding and internalization of LDL particles by the apoB/E receptor. ***show less***
Molecular function (UniProt)	Heparin-binding
Biological process (UniProt)	Cholesterol metabolism, Lipid metabolism, Lipid transport, Steroid metabolism, Sterol metabolism, Transport
Disease involvement	Atherosclerosis, Disease mutation
Gene summary (Entrez)	This gene product is the main apolipoprotein of chylomicrons and low density lipoproteins. It occurs in plasma as two main isoforms, apoB-48 and apoB-100: the former is synthesized exclusively in the gut and the latter in the liver. The intestinal and the hepatic forms of apoB are encoded by a single gene from a single, very long mRNA. The two isoforms share a common N-terminal sequence. The shorter apoB-48 protein is produced after RNA editing of the apoB-100 transcript at residue 2180 (CAA->UAA), resulting in the creation of a stop codon, and early translation termination. Mutations in this gene or its regulatory region cause hypobetalipoproteinemia, normotriglyceridemic hypobetalipoproteinemia, and hypercholesterolemia due to ligand-defective apoB, diseases affecting plasma cholesterol and apoB levels. [provided by RefSeq, Jul 2008] ***show less***



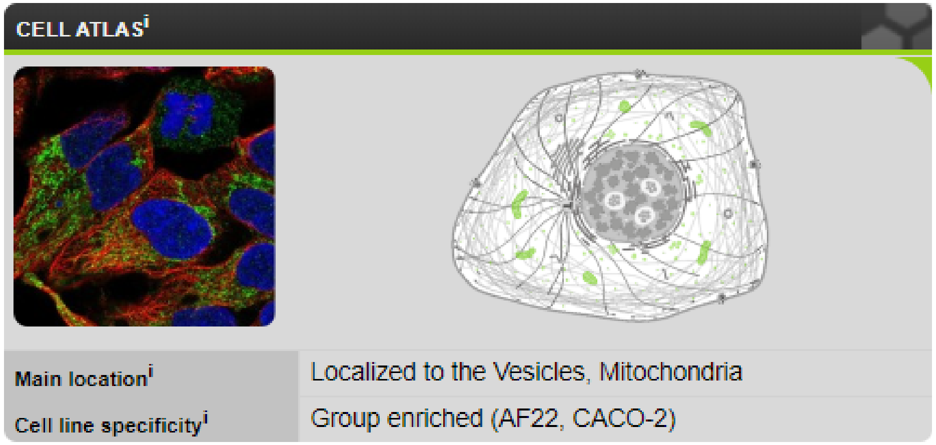
TISSUE ATLAS

Tissue specificity (RNA)	Tissue enhanced (kidney, parathyroid gland)
Tissue distribution (RNA)	Detected in some
Protein expression	Membranous expression mainly in renal tubules and parathyroid gland.



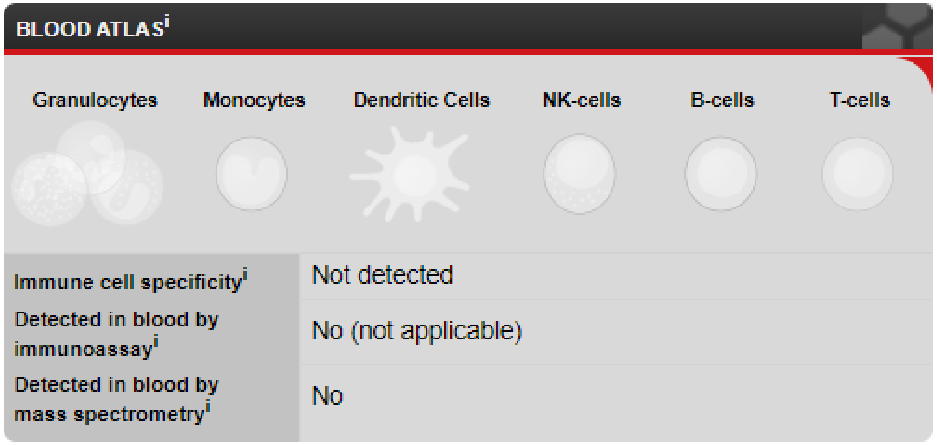
BRAIN ATLAS

Human regional specificity	Low region specificity
Pig regional specificity	Low region specificity
Mouse regional specificity	Not detected



CELL ATLAS

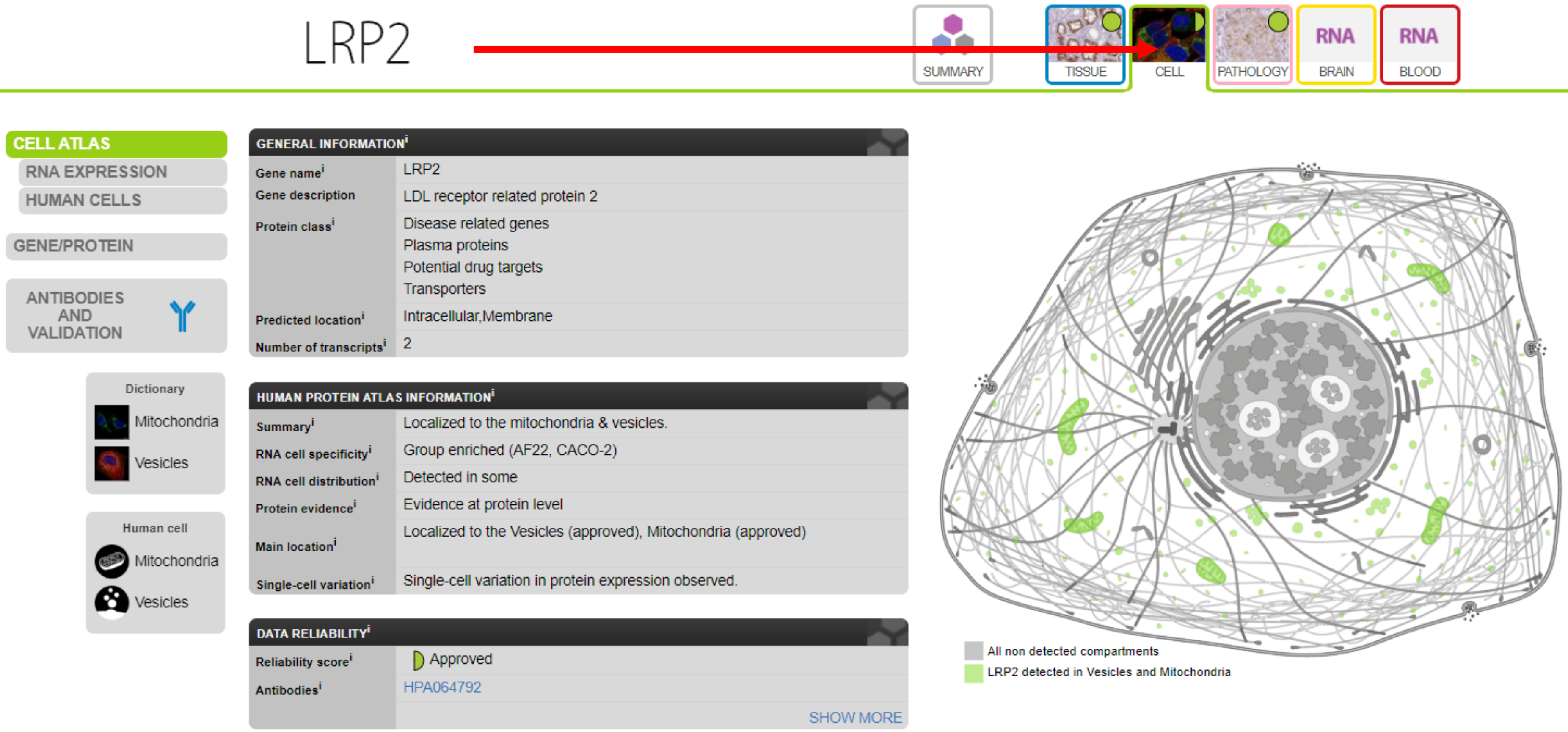
Main location	Localized to the Vesicles, Mitochondria
Cell line specificity	Group enriched (AF22, CACO-2)



BLOOD ATLAS

Immune cell specificity	Not detected
Detected in blood by immunoassay	No (not applicable)
Detected in blood by mass spectrometry	No

Ваш ID может быть специфичен для какой-либо ткани, может присутствовать везде или нигде не быть детектирован



LRP2

GENERAL INFORMATION

Gene name	LRP2
Gene description	LDL receptor related protein 2
Protein class	Disease related genes Plasma proteins Potential drug targets Transporters
Predicted location	Intracellular,Membrane
Number of transcripts	2

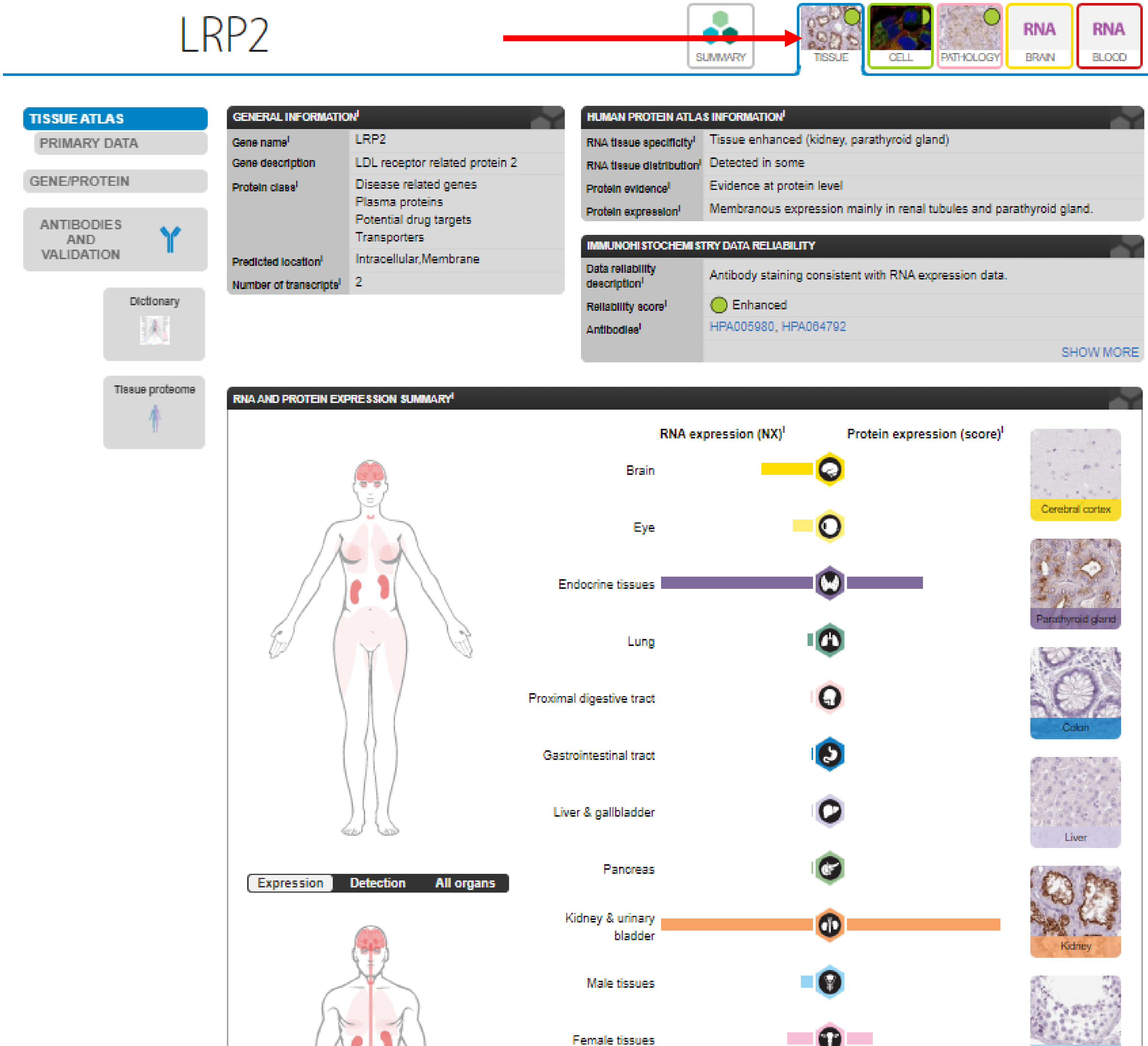
HUMAN PROTEIN ATLAS INFORMATION

Summary	Localized to the mitochondria & vesicles.
RNA cell specificity	Group enriched (AF22, CACO-2)
RNA cell distribution	Detected in some
Protein evidence	Evidence at protein level
Main location	Localized to the Vesicles (approved), Mitochondria (approved)
Single-cell variation	Single-cell variation in protein expression observed.

DATA RELIABILITY

Reliability score	Approved
Antibodies	HPA064792

⬜ All non detected compartments
🟩 LRP2 detected in Vesicles and Mitochondria



GENERAL INFORMATION

Gene name	LRP2
Gene description	LDL receptor related protein 2
Protein class	Disease related genes Plasma proteins Potential drug targets Transporters
Predicted location	Intracellular,Membrane
Number of transcripts	2

HUMAN PROTEIN ATLAS INFORMATION

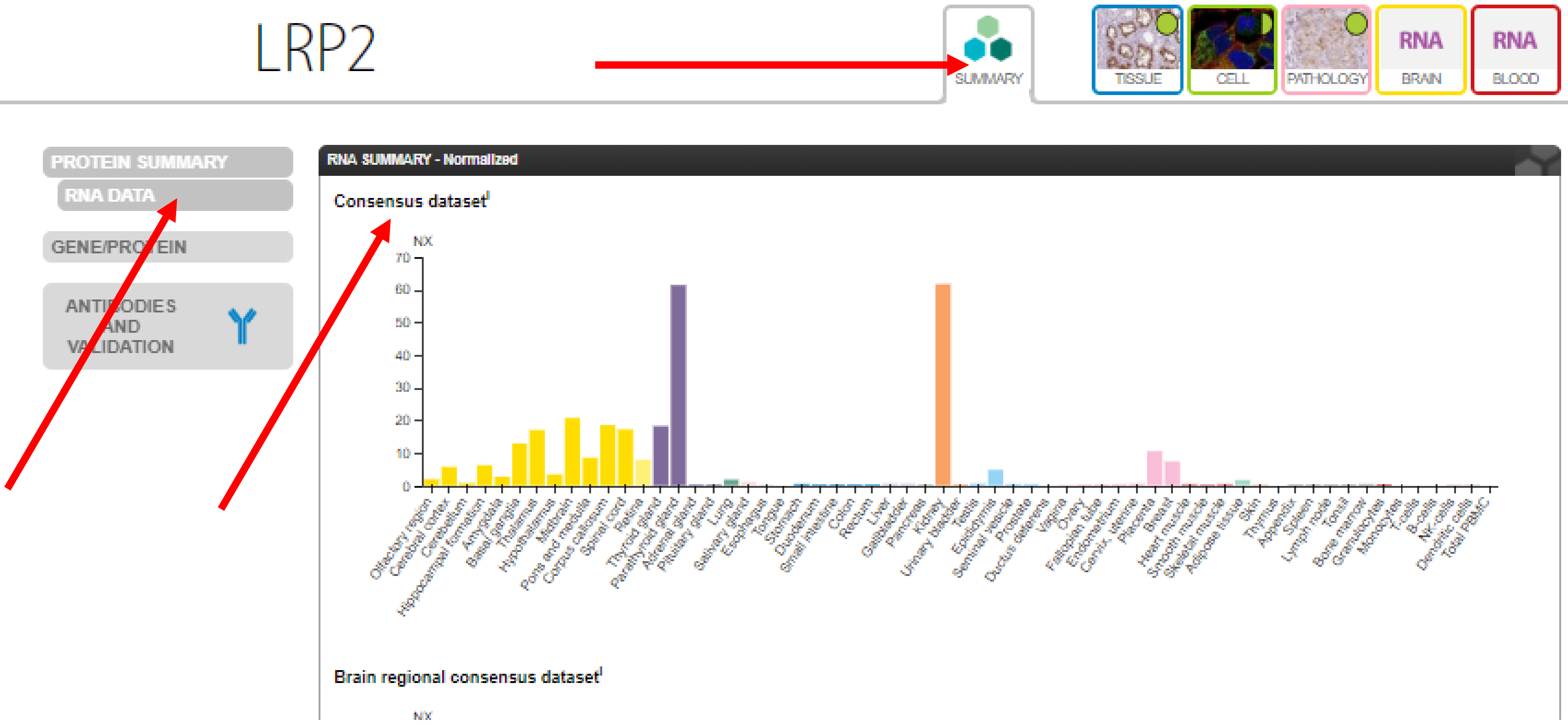
RNA tissue specificity	Tissue enhanced (kidney, parathyroid gland)
RNA tissue distribution	Detected in some
Protein evidence	Evidence at protein level
Protein expression	Membranous expression mainly in renal tubules and parathyroid gland.

IMMUNOHISTOCHEMISTRY DATA RELIABILITY

Data reliability description	Antibody staining consistent with RNA expression data.
Reliability score	● Enhanced
Antibodies	HPA005980, HPA064792

SHOW MORE

RNA AND PROTEIN EXPRESSION SUMMARY



RNA SUMMARY - Normalized

Consensus dataset

Brain regional consensus dataset