GO, KEGG и все-все-все

Анастасия Жарикова, Юлия Алешина

5 апреля 2024 - ФББ МГУ

ДАНО

• Набор интересных белков или генов

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- Набор интересных белков или генов
- Откуда такой набор можно взять?

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- Набор интересных белков или генов
- Откуда такой набор можно взять?
- Экспрессионный профиль
- Дифференциальная экспрессия
- Масспектрометрия
- Данные из статей
- Любимый набор

...

Что дальше делать?

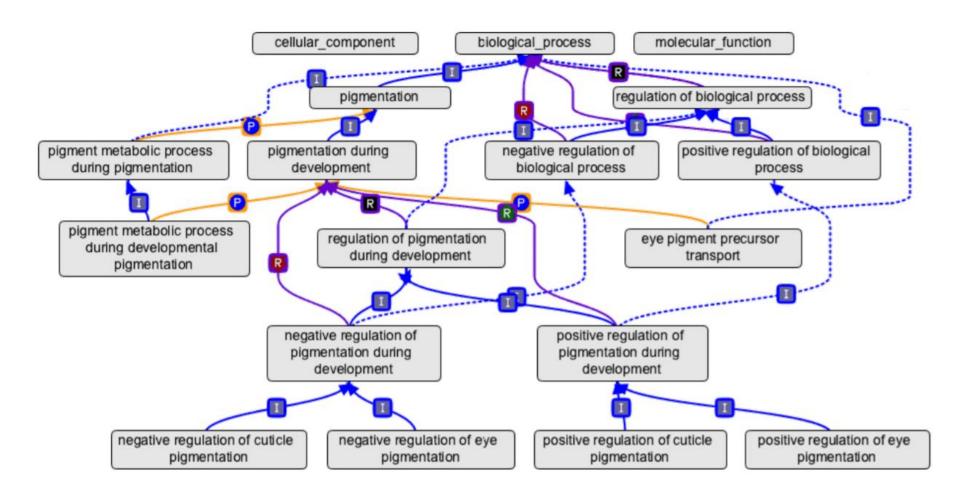


GENE ONTOLOGY - GO

http://geneontology.org/

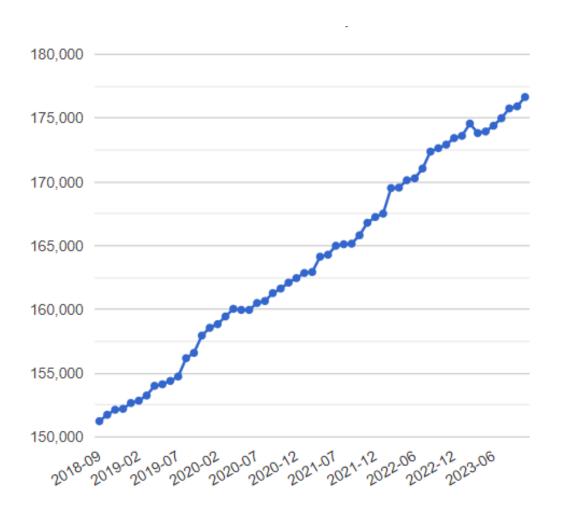
• База данных GO представляет собой граф биологических терминов, соединенных различными отношениями







КОЛИЧЕСТВО ПУБЛИКАЦИЙ, В КОТОРЫХ ИСПОЛЬЗУЕТСЯ GO





Ontology

Property	Value
Valid terms	42442 ($\Delta = -327$)
Obsoleted terms	5287 (Δ = 397)
Merged terms	2440 (Δ = 0)
Biological process terms	27186
Molecular function terms	11198
Cellular component terms	4058

Annotations

Property	Value
Number of annotations	7,655,937
Annotations for biological process	2,833,885
Annotations for molecular function	2,459,729
Annotations for cellular component	2,362,323
Annotations for evidence PHYLO	3,819,045
Annotations for evidence IEA	1,714,824
Annotations for evidence OTHER	858,807
Annotations for evidence EXP	955,756
Annotations for evidence ND	248,947
Annotations for evidence HTP	58,558
Number of annotated scientific publications	176,659

Gene products and species

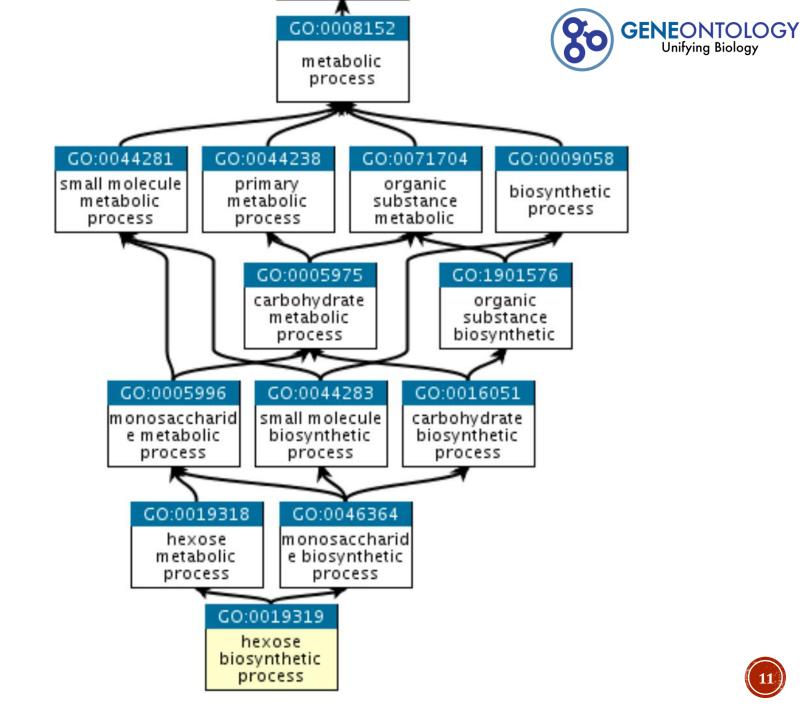
Property	Value
Annotated gene products	1,537,348
Annotated species	5,387
Annotated species with over 1,000 annotations	188



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.

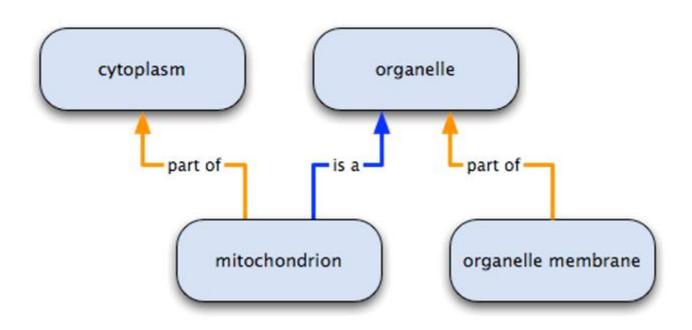
Клеточные компоненты (англ. cellular component) — части клетки или внеклеточного пространства, где осуществляется функция генного продукта, например, ядроили рибосома.



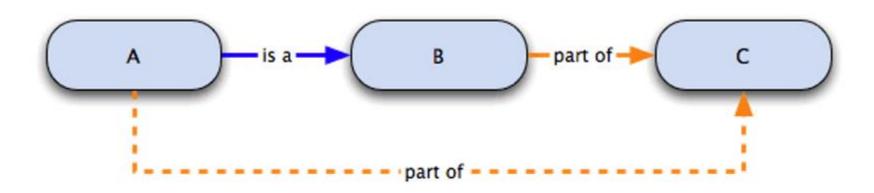


Термин GO (GO term) – узел графа – может иметь любое количество связей с любыми другими узлами

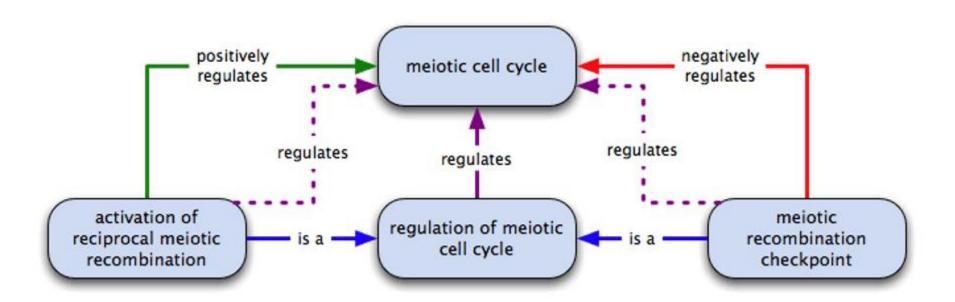
Отношения между узлами – ребра графа бывают разного типа











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 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)



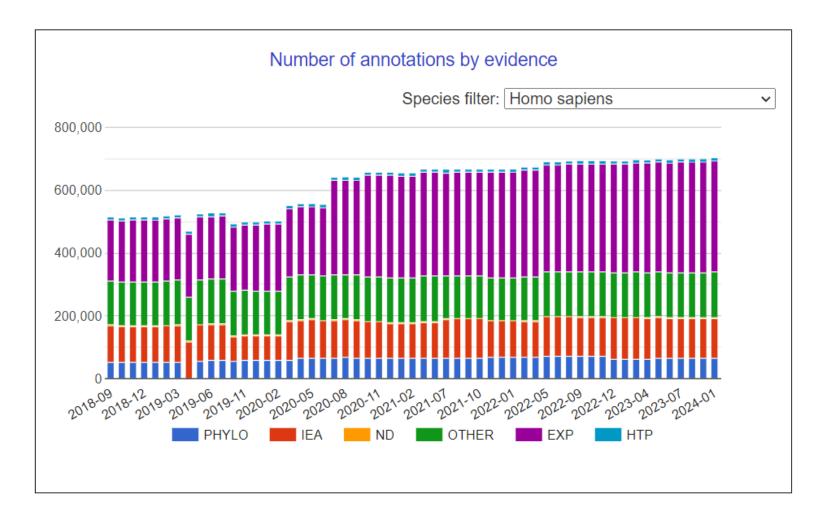




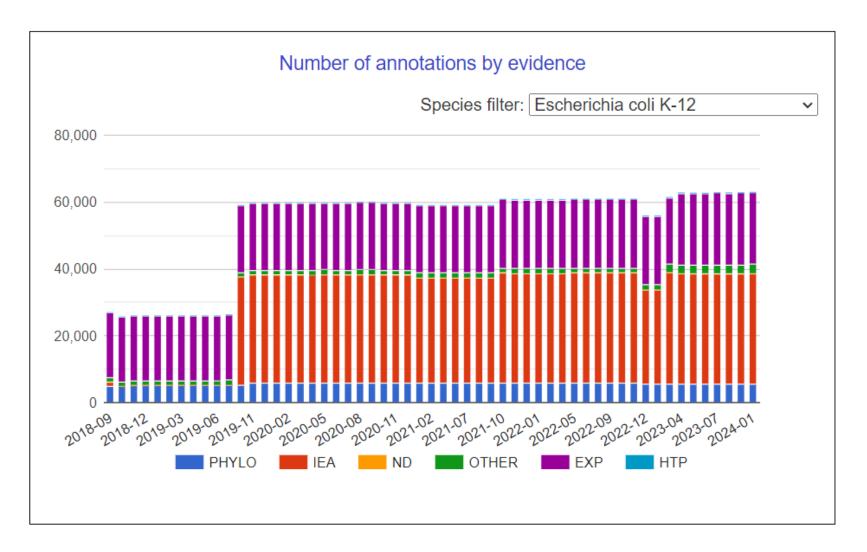


Gene/product	Gene/product name	Annotation qualifier	GO class (direct)	Annotation extension	Contributor	Organism	Evidence	Evidence with	PANTHER family	Type Isofor
Fcer1g	Fc fragment of IgE receptor Ig		positive regulation of type IIa hypersensitivity		RGD	Rattus norvegicus	ISO	RGD:10572	high affinity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

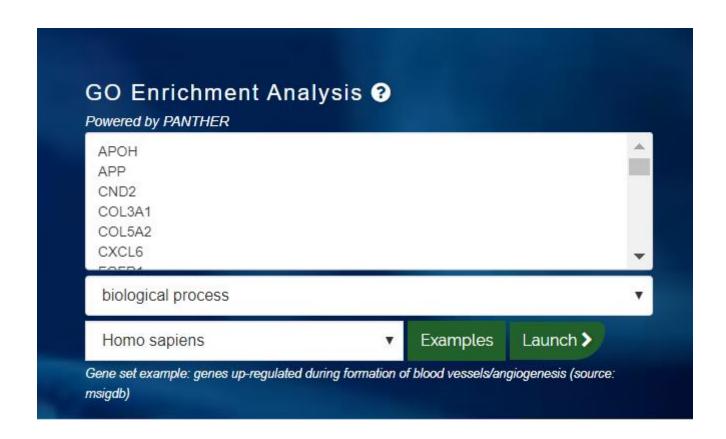










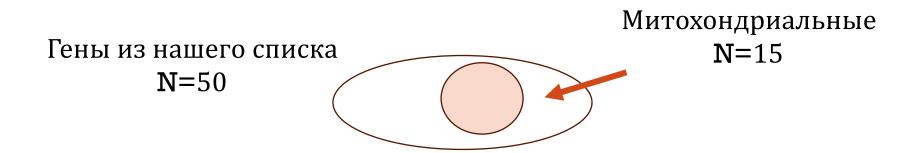


https://geneontology.org/

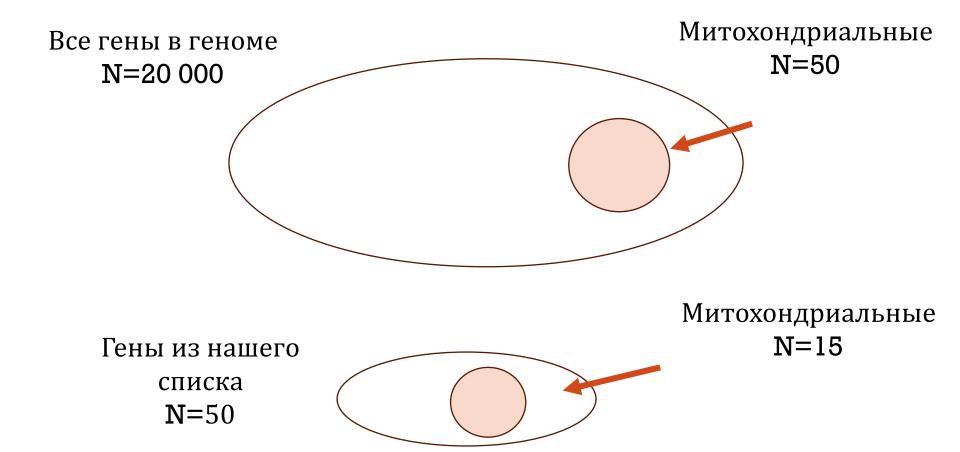
АНАЛИЗ ОБОГАЩЕНИЯ ТЕРМИНАМИ GO

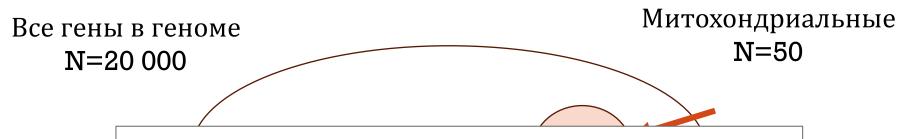
Есть список генов.

Перепредставлены ли в нем митохондриальные гены?



Это много или мало? С чем сравнить?

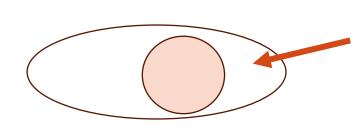




Насколько чаще гены из нашего списка попадают в категорию «митохондриальные», чем если бы мы их выбрали из всех генов случайно?

Митохондриальные **N=15**

Гены из нашего списка **N**=50



22

АНАЛИЗ ОБОГАЩЕНИЯ ТЕРМИНАМИ GO

- Для GO термина «митохондриальные» можно все гены разделить на:
 - Гены из нашего списка из GO термина «митохондриальные»
 - Гены из нашего списка вне GO термина «митохондриальные»
 - Все гены из базы (background) из GO термина «митохондриальные»
 - Все гены из базы (background) вне GO термина «митохондриальные»



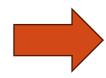
АНАЛИЗ ОБОГАЩЕНИЯ ТЕРМИНАМИ GO

• В GO тысячи терминов!

РАЗНЫЕ СЕРВИСЫ ИСПОЛЬЗУЮТ РАЗНЫЕ СТАТИСТИЧЕСКИЕ ТЕСТЫ

(Выбор теста зависит от задачи)

- Точный тест Фишера
- Биномиальный тест
- Критерий хи-квадрат
- и другие



P-value

http://geneontology.org/docs/go-enrichment-analysis/

Selection Summary:

Analysis Type: PANTHER	R Overrepresentation Test (Released 20200407)	
Annotation Version and	Release Date: GO Ontology database Released 2020-02-21	
Analyzed List:	upload_1 (Homo sapiens)	Change
Reference List:	Homo sapiens (all genes in database)	Change
Annotation Data Set: GC) biological process complete ▼ ②	
Test Type: Fisher's Ex	act O Binomial	
Correction: Calculate	False Discovery Rate Use the Bonferroni correction for multiple testing ③	No correction
Launch analysis		

СМОТРИМ ДИФФЕРЕНЦИАЛЬНУЮ ЭКСПРЕССИЮ В ОБРАЗЦАХ СПЕЦИФИЧЕСКОЙ ТКАНИ



Можно указать свой список генов, с которыми будут сравниваться частоты терминов (background list)

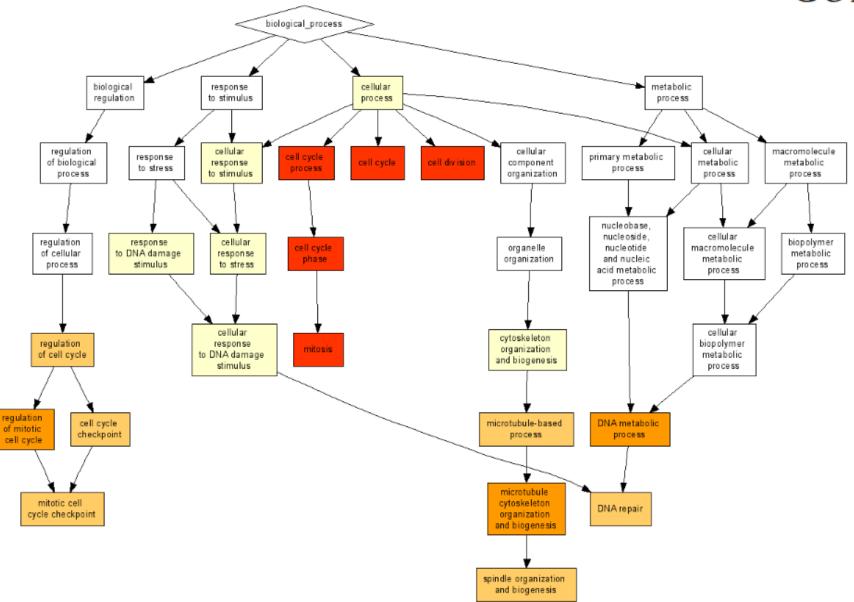
election Summary:	(Dacky		
Analysis Type: PANTHE	R Overrepresentation Test (Released 2024	40226)	
Annotation Version and	Release Date: GO Ontology database D0	DI: 10.5281/zenodo.105/6401 Relea	sed 2024-01-17
Analyzed List:	upload_1 (Homo sapiens)		Change
Reference List:	Homo sapiens (all genes in databa	se)	Change
Annotation Data Set: G	biological process complete 🔻 💿)	
Test Type: Fisher's E.	act O Binomial		
Correction: Calculate	False Discovery Rate O Use the Bonfe	erroni correction for multiple testing	
Launch analysis			





tep 1: Choose organism
Homo sapiens ▼ Step 2: Choose running mode
 Single ranked list of genes Two unranked lists of genes (target and background lists) Paste a ranked list of gene/protein names
Names should be separated by an <enter>. The preferred format is gene ymbol. Other supported formats are: gene and protein RefSeq, Uniprot, Unigene nd Ensembl.</enter>
Or upload a file: Выберите файл Файл не выбран
step 4: Choose an ontology
Process Function Component All
Search Enriched GO terms

GORILLA



https://davidbioinformatics.nih.gov/

U.S. Department of Health & Human Services

National Institutes of Health



Home Start Analysis Shortcut to DAVID Tools • Technical Center • Downloads & APIs • Terms of Service • About DAVID • About LHRI •

Overview

The **D**atabase for **A**nnotation, **V**isualization and **I**ntegrated **D**iscovery (**DAVID**) provides a comprehensive set of functional annotation tools for investigators to understand the biological meaning behind large lists of genes. These tools are powered by the comprehensive **DAVID Knowledgebase** built upon the DAVID Gene concept which pulls together multiple sources of functional annotations. For any given gene list, DAVID tools are able to:

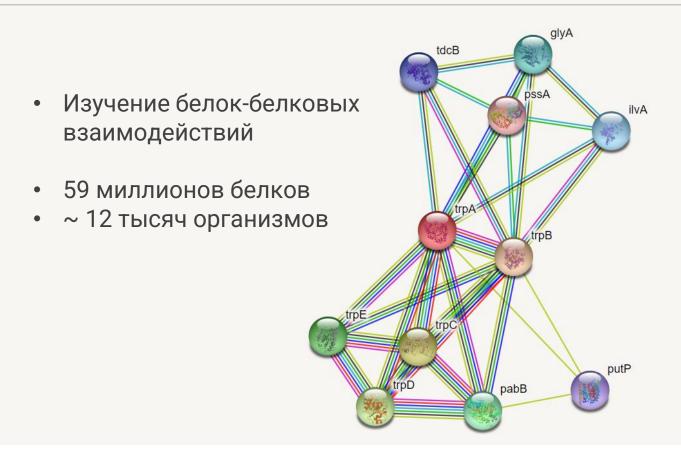
- ✓ Identify enriched biological themes, particularly GO terms
- ✓ Discover enriched functional-related gene groups
- Cluster redundant annotation terms
- ▼ Visualize genes on BioCarta & KEGG pathway maps
- ✓ Display related many-genes-to-many-terms on 2-D view.
- ▼ Search for other functionally related genes not in the list
- List interacting proteins
- Explore gene names in batch
- Link gene-disease associations
- Highlight protein functional domains and motifs
- Redirect to related literatures
- And more

Только человек

Можно кластеризовать похожие термины аннотации

Можно смотреть ассоциации генов с болезнями





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

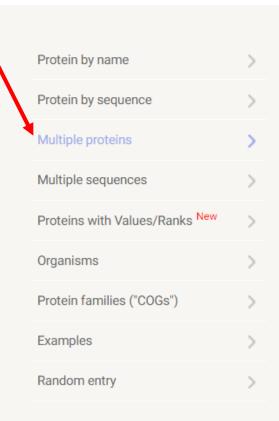


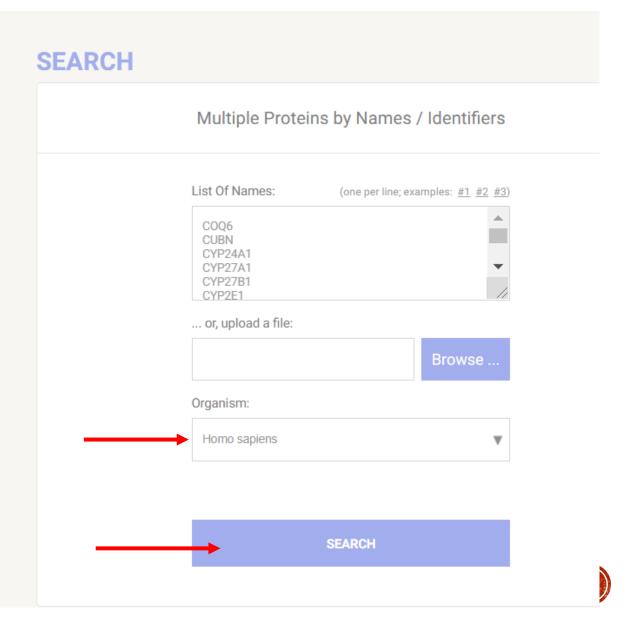
co-expression



protein homology





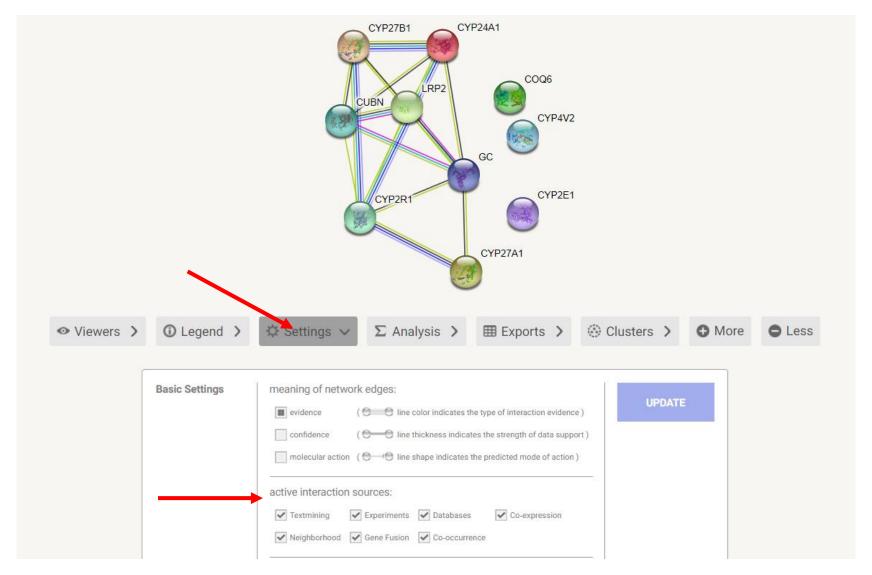




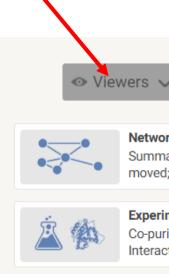
'C	OQ6':
~	COQ6 - Ubiquinone biosynthesis monooxygenase COQ6, mitochondrial; FAD-dependent monooxygenase required for the C5-ring hydroxylation during ubiquinone biosynthesis. Catalyzes the hydroxylation of 3-polyprenyl-4-hydroxybenzoic acid to 3- polyprenyl-4,5-dihydroxybenzoic acid. The electrons required for the hydroxylation reaction may be funneled indirectly from NADPH via a ferredoxin/ferredoxin reductase system to COQ6
'C	UBN':
✓	CUBN - Cubilin; Cotransporter which plays a role in lipoprotein, vitamin and iron metabolism, by facilitating their uptake. Binds to ALB, MB, Kappa and lambdalight 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/PR01028, NP_112205.2, OTTHUMT00000415706]

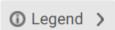
'CYP24A1':



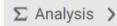


















Network

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

currently showing

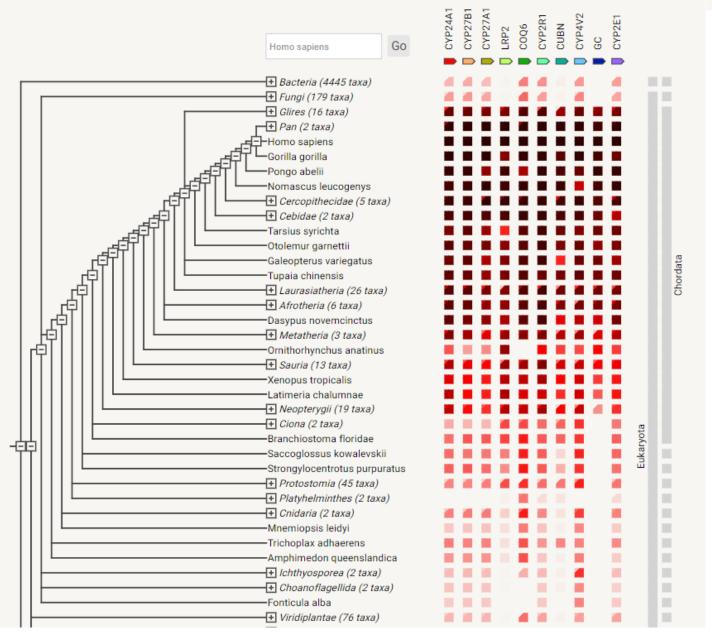
Automated, unsupervised textmining - searching for proteins that are frequently mentioned together.



Fusion

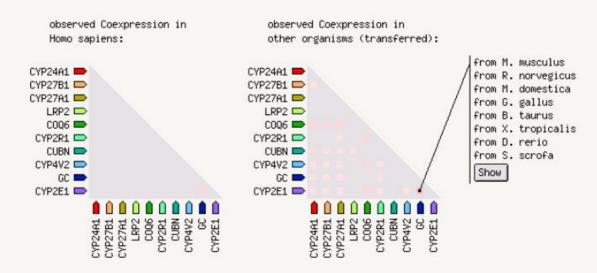
Genes that are sometimes fused into single open reading frames.



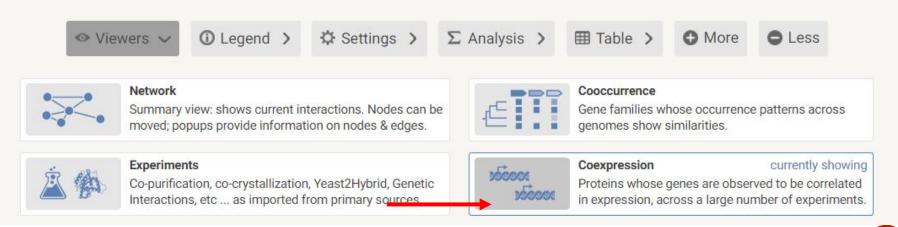


STRING

GENE COEXPRESSION



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



https://www.proteinatlas.org/

Было 2 года назад

THE HUMAN PROTEIN ATLAS

MENU HELP NEWS **SEARCH**ⁱ apob Search Fields » e.g. RBM3, insulin, CD36 SARS-CoV-2 relevant proteins TISSUE ATLAS **CELL ATLAS** PATHOLOGY ATLAS **BRAIN ATLAS BLOOD ATLAS** METABOLIC ATLAS

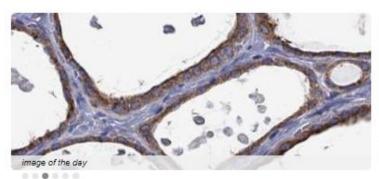
THE HUMAN PROTEIN ATLAS

The open access resource for human proteins
Search for specific genes/proteins or explore the 12 different sections

Search

e.g. ACE2, GFAP, EGFR

Search help



Exploring CLOCK: Our Inner Timekeeper

Our cells contain tiny molecular clocks that control a multitude of physiological and behavioral processes according to the circadian rhythm.



Wed, 27 Mar 2024

Different expression patterns in invasive and noninvasive PitNETs

Fields »

In a study published in the Journal of the Endocrine Society, transcriptomics analysis and radiological evaluation was used to explore the differences between invasive and noninvasive pituitary neuroendocrine tumors (PINETs) with respect to parasellar growth, bone invasiveness and vascularization.

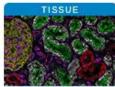


LISET PROTING

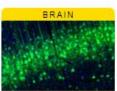
Thu, 4 Apr 2024

А теперь...

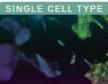
all news articles



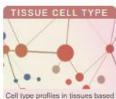
Protein and RNA profiles in tissues based on antibodies and transcriptomics



Protein and RNA profiles in brain based on microdissected regions



Single cell RNA profiles in tissues based on single cell RNA analysis



Cell type profiles in tissues base on deconvolution of bulk transcriptomics



Protein and RNA profiles in human cancers based on antibodies and transcriptomics



Protein levels in blood in patients with diseases

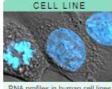




Blood protein levels in healthy individuals and the human secretome



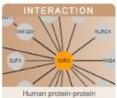
Spatial, subcellular protein profiles in human cells based on antibodies



RNA profiles in human cell lines with best models for human cancers

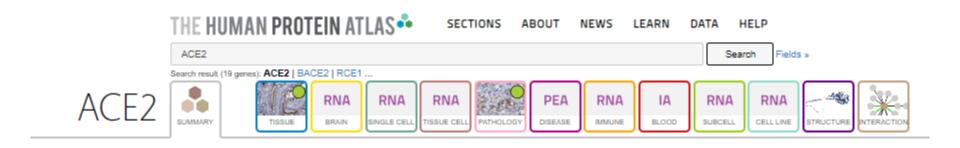


3D-structures of human proteins with antibody-binding sites and genetic variants



Human protein-protein interactions and metabolic enzyme profiles





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

















BLOOD

RNA SUBCELL







PROTEIN SUMMARY

GENE INFORMATION

RNA DATA

ANTIBODY DATA



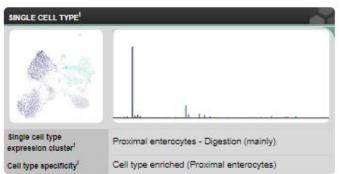
Tissue expression cluster

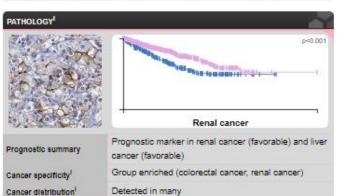
Tissue specificity

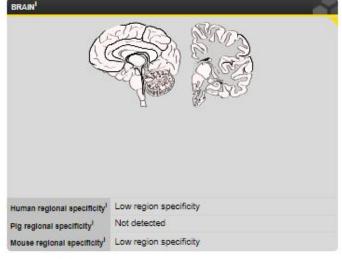
Protein expression

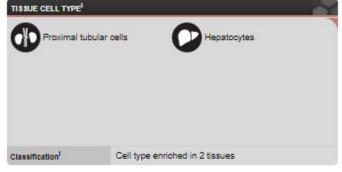
Kidney & Intestine - Metabolism (mainly) Tissue enhanced (gallbladder, intestine, kidney) Membranous expression in proximal renal tubules, intestinal tract, seminal vesicle, epididymis, exocrine

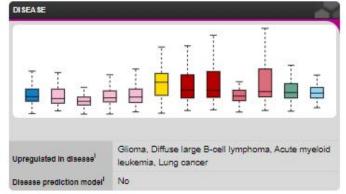
pancreas and gallbladder. Expressed in Sertoli and Leydig cells, and trophoblasts. Membranous expression in ciliated cells in nasal mucosa, bronchus, and fallopian tube. Expressed in endothelial cells and pericytes in many tissues.































RNA SUBCELL







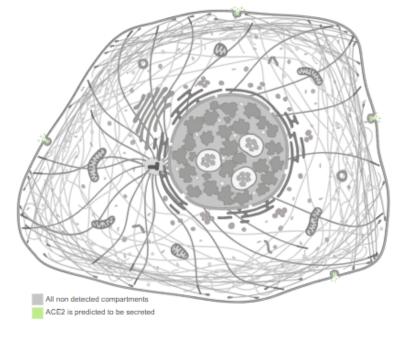
RNA EXPRESSION

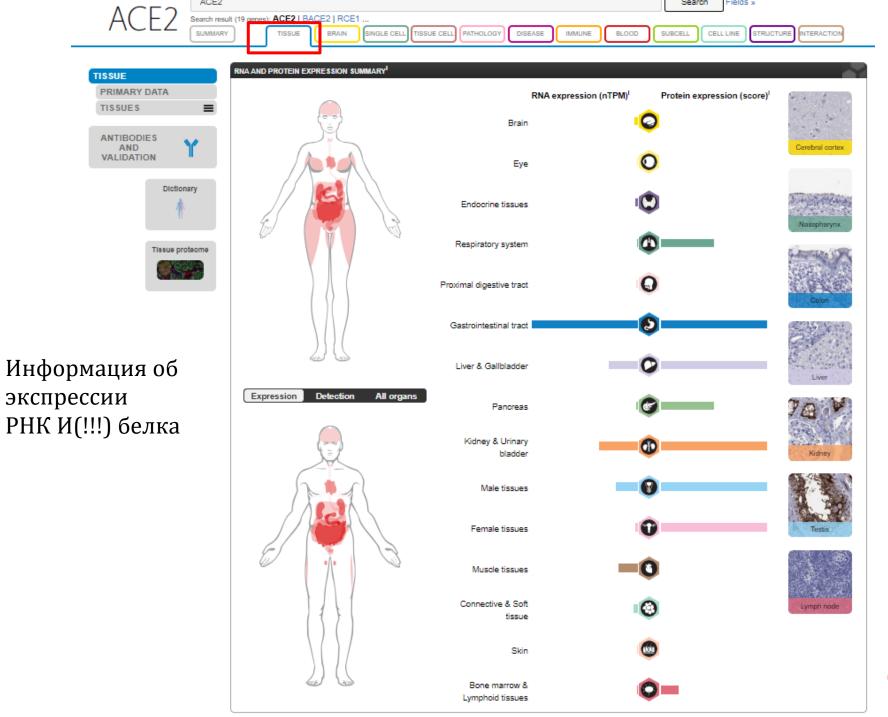


Subcellular proteome

GENERAL INFORMATION								
Gene name ^l	ACE2							
Gene description	Angiotensin converting enzyme 2							
Protein class ^I	Enzymes Metabolic proteins Transporters							
Predicted location	Secreted, Membrane							
Number of transcripts ¹	9							

HUMAN PROTEIN ATLA	HUMAN PROTEIN ATLAS INFORMATION ¹					
Main location ¹	Not available (Failed to get Reactome Data)					
Extracellular location	Protein predicted to be secreted					
Reliability score	Pending cell analysis.					











RNA BRAIN

SIN

RNA RNA



PEA DISEASE

RNA

IA BLOOD RNA

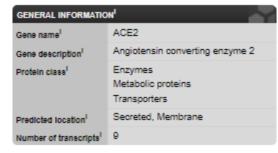
RNA CELL LINE



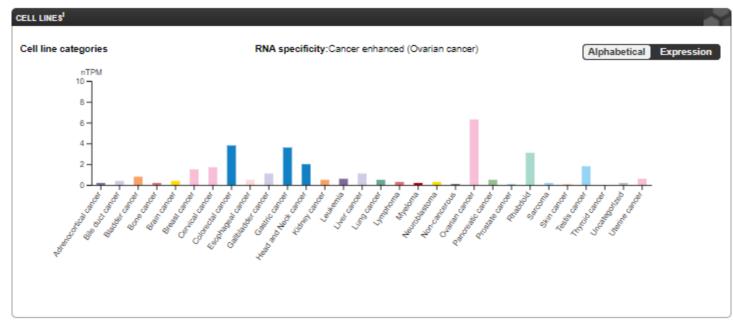


CELL LINE





HUMAN PROTEIN ATLAS INFORMATION						
Cell line expression cluster	Non-specific - Mitochondria (mainly)					
Cell line specificity ^l	Cancer enhanced (Ovarian cancer)					
Tau specificity score	0.72					
Cell line distribution	Detected in many					
Protein evidence ^l	Evidence at protein level					
Extracellular location ¹	Protein predicted to be secreted					







RNA BRAIN

RNA SINGLE CELL

RNA



PEA RNA DISEASE IMMUNE

IΑ BLOOD

RNA SUBCELL CELL LIN



PROTEIN STRUCTURE

ANTIBODIES AND VALIDATION



GENERAL INFORMATION ACE2 Gene name^l ACEH Synonyme Angiotensin converting enzyme 2 Gene description Enzymes Protein class Metabolic proteins Transporters Secreted, Membrane Predicted location¹ Evidence at protein level (all genes) Protein evidence

GENE INFORMATION Chromosome Х p22.2 Cytoband Chromosome location (bp) 15494568 - 15607238 Number of transcripts¹ ENSG00000130234 (version 109) Ensembl 59272 Entrez gene HGNC:13557 HGNC Q9BYF1 (UniProt - Evidence at protein level) UniProt NX_Q9BYF1 neXtProt GeneCarda ACE2









RNA







IΑ BLOOD

RNA

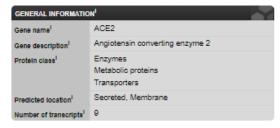
IMMUNE

RNA SUBCELL

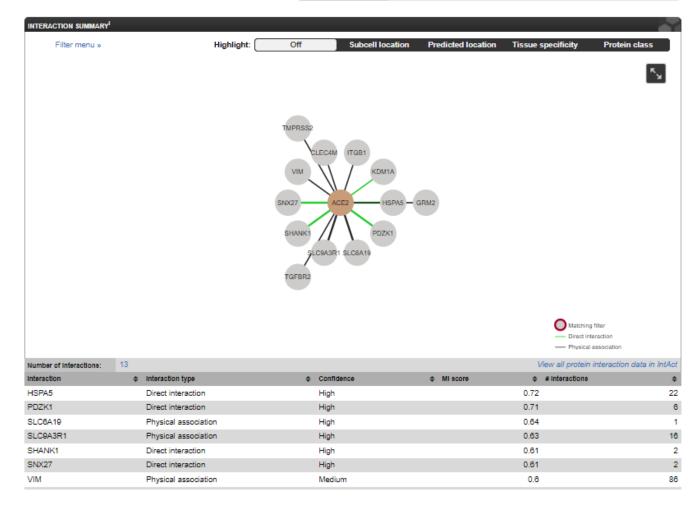
RNA CELL LINE



Protein Interactions



HUMAN PROTEIN ATLAS INFORMATION Tissue expression Kidney & Intestine - Metabolism (mainly) cluster (RNA) Tissue enhanced (gallbladder, intestine, kidney) Tissue specificity (RNA) Tau specificity score (RNA) Detected in many Tissue distribution (RNA) Evidence at protein level Protein evidence Subcellular location¹ Not available Secreted to blood Secretome annotation



Метаболические пути







KEGG ▼ Search Help

» Japanese

Classification

Pathway

Brite table

Organism

Compound Network

Drug (ATC)

KO (Function)

Disease (ICD)

Drug (Target)

Module

Brite

KEGG Home

Release notes Current statistics Plea from KEGG

KEGG Database

KEGG overview Searching KEGG KEGG mapping Color codes

KEGG Objects

Pathway maps Brite hierarchies KEGG DB links

KEGG Software KEGG API KGML

KEGG FTP Subscription

GenomeNet

DBGET/LinkDB

Feedback Copyright request

Kanehisa Labs

KEGG: Kyoto Encyclopedia of Genes and Genomes

KEGG is a database resource for understanding high-level functions and utilities of the biological system, such as the cell, the organism and the ecosystem, from molecular-level information, especially large-scale molecular datasets generated by genome sequencing and other high-throughput experimental technologies. See Release notes (April 1, 2020) for new and updated features.

Main entry point to the KEGG web service

KEGG2 KEGG Table of Contents [Update notes | Release history]

Data-oriented entry points

KEGG PATHWAY KEGG pathway maps

KEGG BRITE BRITE hierarchies and tables

KEGG MODULE KEGG modules

KEGG ORTHOLOGY KO functional orthologs [Annotation]

KEGG GENOME Genomes [Pathogen | Virus | Plant]

KEGG GENES Genes and proteins [SeqData]

KEGG COMPOUND Small molecules

KEGG GLYCAN Glycans

KEGG REACTION Biochemical reactions [RModule]

KEGG ENZYME Enzyme nomenclature
KEGG NETWORK Disease-related network elements

KEGG DISEASE Human diseases [Cancer]
KEGG DRUG Drugs [New drug approvals]

KEGG MEDICUS Health information resource [Drug labels search]

Organism-specific entry points

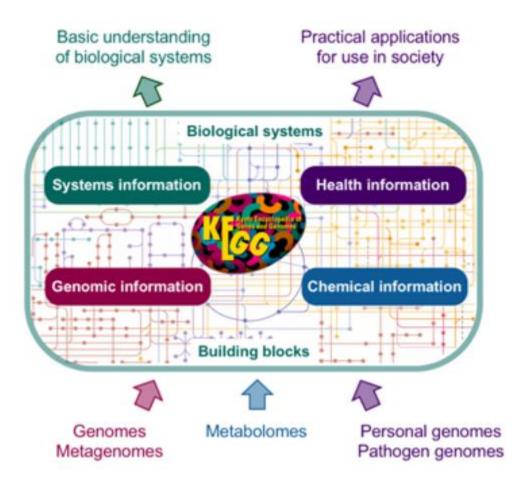
KEGG Organisms Enter org code(s) Go hsa hsa eco

Analysis tools

KEGG Mapper
BlastKOALA
BLAST-based KO annotation and KEGG mapping
GHOSTX-based KO annotation and KEGG mapping
KofamKOALA
HMM profile-based KO annotation and KEGG mapping

BLAST/FASTA Sequence similarity search

SIMCOMP Chemical structure similarity search



Current Statistics

KEGG Database	as of 2024/4/3	
Systems informat		
KEGG PATHWAY	Pathway maps, reference (total)	570 (1,152,602)
KEGG BRITE	Functional hierarchies, reference (total)	195 (384,000)
KEGG MODULE	KEGG modules	481
	Reaction modules	48
Genomic informat	<u>ion</u>	
KEGG ORTHOLOG	Y KEGG Orthology (KO) groups	26,696
KEGG GENES	Genes in KEGG organisms	52,674,035
	Addendum proteins	4,159
	Viral genes	688,823 377
KEGG GENOME	Viral mature peptides	
KEGG GENOME	KEGG organisms (1024 eukaryotes, 8366 bacteria, 432 archaea)	9,822
	KEGG selected viruses (T4 category)	359
	KEGG viruses (Vtax category)	14,384
Chemical informat	<u>tion</u>	
KEGG COMPOUND	Metabolites and other chemical substances	19,296
KEGG GLYCAN	Glycans	11,222
KEGG REACTION	Biochemical reactions	12,016
	Reaction class	3,194
KEGG ENZYME	Enzyme nomenclature	8,109
Health information	1	
KEGG NETWORK	Disease-related network elements	1,396
	Network variation maps	140
KEGG VARIANT	Human gene variants	1,328
KEGG DISEASE	Human diseases	2,705
KEGG DRUG	Drugs	12,369
5 111	Drug groups	2,462
Drug labels	1	40.057
KEGG MEDICUS	Japanese prescription drug labels from JAPIC Japanese OTC drug labels from JAPIC	13,357 10,545
KEGG MEDICUS	FDA prescription drug labels linked to DailyMed	33,365
KEGG MEDICOS	TDA prescription drug labels linked to DallyMed	33,363





Category	Database	Content	Color	
Customs	KEGG PATHWAY	KEGG pathway maps		
Systems information	KEGG BRITE	BRITE hierarchies and tables	K GG	
mormation	KEGG MODULE	KEGG modules	_	
	KEGG ORTHOLOGY (KO)	Functional orthologs	KEGG	
Genomic information	KEGG GENOME	KEGG organisms (complete genomes)	WE	
IIIIOIIIIatioii	KEGG GENES	Genes and proteins	N GG	
	KEGG SSDB	GENES sequence similarity	_	
	KEGG COMPOUND	Small molecules		
Chemical information	KEGG GLYCAN	Glycans	WE	
	KEGG REACTION	Biochemical reactions	v[ce	
	KEGG RCLASS	Reaction class		
	KEGG ENZYME	Enzyme nomenclature		
	KEGG NETWORK	Disease-related network elements		
Health information	KEGG VARIANT	Human gene variants		
	KEGG DISEASE	Human diseases	KF	
	KEGG DRUG	Drugs	66	
	KEGG DGROUP	Drug groups		
	KEGG ENVIRON	Health-related substances		

Chemical information category is collectively called KEGG LIGAND Health information category integrated with drug labels is called KEGG MEDICUS



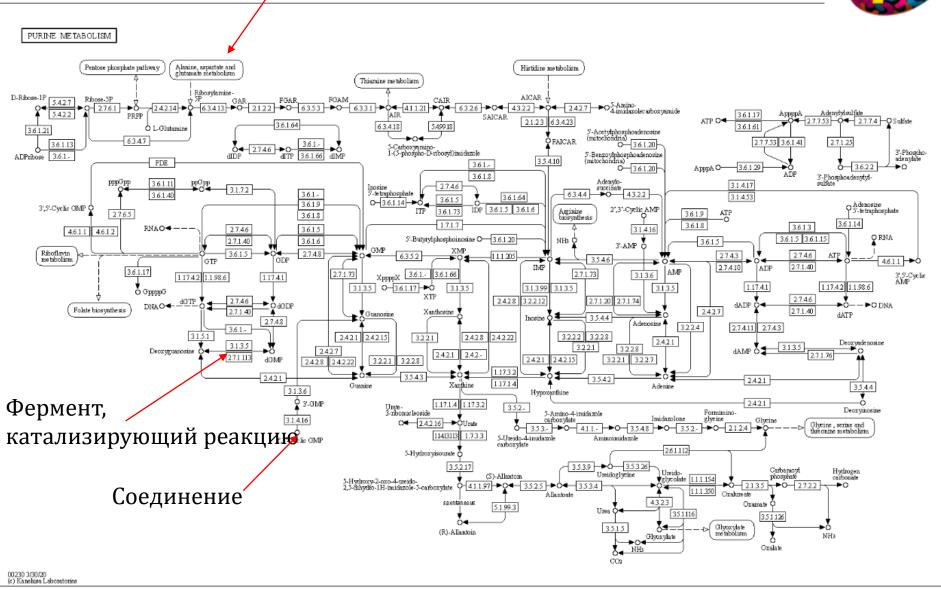
Pathway Maps

KEGG PATHWAY is a collection of manually drawn pathway maps representing our knowledge on the molecular interaction, reaction and relation networks for:

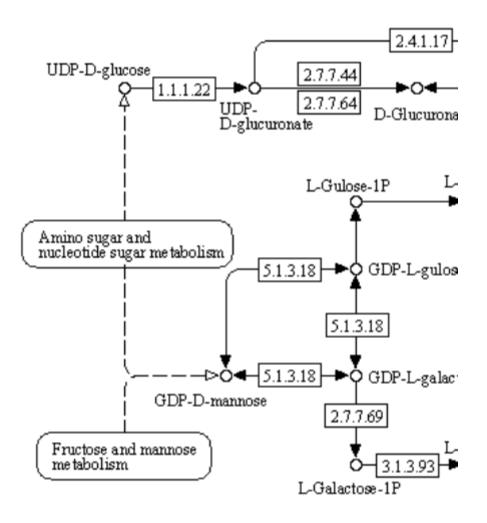
- 1. Metabolism
 - Global/overview Carbohydrate Energy Lipid Nucleotide Amino acid Other amino Glycan Cofactor/vitamin Terpenoid/PK Other secondary metabolite Xenobiotics Chemical structure
- 2. Genetic Information Processing
- 3. Environmental Information Processing
- 4. Cellular Processes
- 5. Organismal Systems
- 6. Human Diseases
- 7. Drug Development

Другой метаболический путь











ENZYME: 2.7.7.4



Help

	Help						
Entry	EC 2.7.7.4 Enzyme						
Name	sulfate adenylyltransferase; ATP-sulfurylase; adenosine-5'-triphosphate sulfurylase; adenosinetriphosphate sulfurylase; adenylylsulfate pyrophosphorylase; ATP sulfurylase; ATP-sulfurylase; sulfurylase;						
Class	Transferases; Transferring phosphorus-containing groups; Nucleotidyltransferases BRITE hierarchy						
Sysname	ATP:sulfate adenylyltransferase						
Reaction(IUBMB)	ATP + sulfate = diphosphate + adenylyl sulfate [RN:R00529]						
Reaction(KEGG)	R00529; (other) R04929 Reaction						
Substrate	ATP [CPD:C00002]; sulfate [CPD:C00059]						
Product	<pre>diphosphate [CPD:C00013]; adenylyl sulfate [CPD:C00224]</pre>						
Comment	The human phosphoadenosine-phosphosulfate synthase (PAPS) system is a bifunctional enzyme (fusion product of two catalytic activities). In a first step, sulfate adenylyltransferase catalyses the formation of adenosine 5'-phosphosulfate (APS) from ATP and inorganic sulfate. The second step is catalysed by the adenylylsulfate kinase portion of 3'-phosphoadenosine 5'-phosphosulfate (PAPS) synthase, which involves the formation of PAPS from enzyme-bound APS and ATP. In contrast, in bacteria, yeast, fungi and plants, the formation of PAPS is carried out by two individual polypeptides, sulfate adenylyltransferase (EC 2.7.7.4) and adenylyl-sulfate kinase (EC 2.7.1.25).						
	led 0 = 3 + 1 + 1 + 1 + 1 + 1 + 1 + 1 + 1 + 1 +						

All links

```
Pathway (16)
  KEGG PATHWAY (14)
  KEGG MODULE (2)
Chemical substance (6)
  KEGG COMPOUND (6)
Chemical reaction (4)
  KEGG REACTION (2)
  KEGG RCLASS (2)
Gene (106612)
  KEGG ORTHOLOGY (5)
  KEGG GENES (8508)
  KEGG MGENES (61373)
  RefGene (36726)
Protein sequence (77269)
  UniProt (40770)
  SWISS-PROT (457)
  RefSeq(pep) (35969)
  PDBSTR (54)
  PMD (19)
DNA sequence (141864)
  RefSeq(nuc) (127520)
  GenBank (7103)
   EMBL (7241)
3D Structure (24)
  PDB (24)
Protein domain (9)
  InterPro (8)
  Pfam (1)
All databases (325804)
Download RDF
```

КОД ФЕРМЕНТА

- Класс код первого уровня: 1-7. Номер одного из семи главных классов ферментов
- **Подкласс** код второго уровня. Номер характеризует основные виды субстратов, участвующих в данном виде химических реакций.
- **Под-подкласс** код третьего уровня. Номер определяет более частные подгруппы, отличающиеся природой химических соединений доноров или акцепторов, участвующих в данной подгруппе реакций.
- **Код четвертого уровня** все ферменты, относящиеся к данному под-подклассу получают свои порядковые номера.
- Пример: глюкозоксидаза 1.1.3.4
- **КФ 1** Оксидоредуктазы
- **КФ 1.1** Алкогольоксидоредуктазы
- КФ 1.1.3 Оксидоредуктазы, окисляющие группу СН-ОН и восстанавливающие кислород.
- **КФ 1.1.3.4** Оксидоредуктазы, окисляющие глюкозу в присутствии кислорода. Всего известно 3 глюкозоксидазы из разных организмов.



ОСНОВНЫЕ КЛАССЫ ФЕРМЕНТОВ

• Коды первого уровня

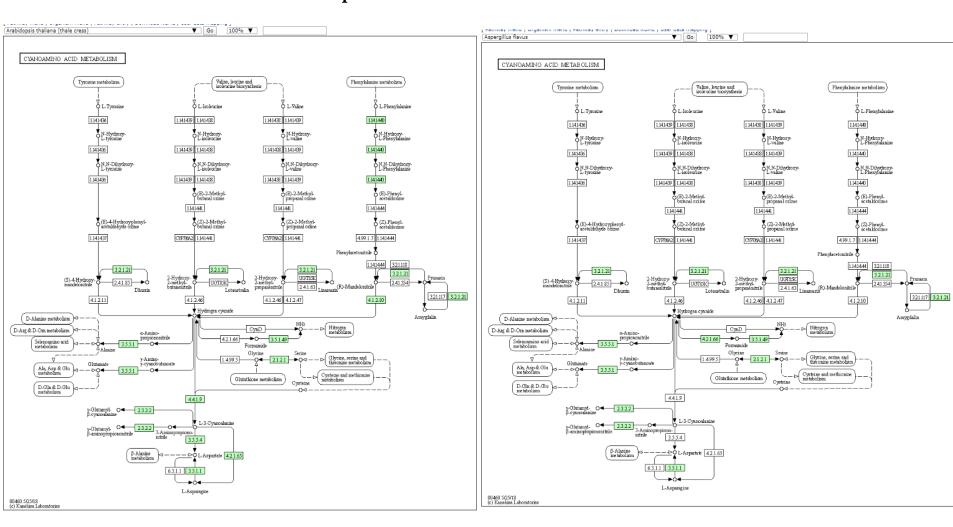
Класс	Катализируемая реакция	Тип реакции	Важнейшие подклассы
КФ 1 Оксидоредуктазы	Окислительно-восстановительные реакции. Перенос атомов Н и О или электронов от одного субстрата на другой	$AH + B \rightarrow A + BH$ (восстановленный) $A + O \rightarrow AO$ (окисленный)	дегидрогеназа, оксидаза, пероксидаза, редуктаза, монооксидаза, диоксигеназа
КФ 2 Трансферазы	Перенос функциональной группы от одного субстрата на другой. Это может быть метильная, ацильная, фосфатная группа или аминогруппа.	$AB + C \rightarrow A + BC$	аминотрансфераза, фосфотрансфераза, С1-трансфераза, гликозилтрансфераза
КФ 3 Гидролазы	Образование двух продуктов из одного субстрата в результате гидролиза.	$AB + H_2O \rightarrow AOH$ $+ BH$	эстераза, гликозил-гидролаза, пептидаза, амидаза
КФ 4 Лиазы (синтазы)	Негидролитическое добавление или удаление группы к или от субстрата. Образование C-C, C-N, C-O или C-S связи.	RCOCOOH → RCOH + CO ₂	С-О-лиаза, С-S-лиаза, С-N-лиаза, С-С-лиаза
КФ 5 Изомеразы	Внутримолекулярная перестановка, то есть изомеризация молекулы субстрата.	$AB \rightarrow BA$	эпимераза, цис-транс-изомераза, внутримолекулярная оксидоредуктаза и др.
КФ 6 <i>Лигазы</i> (синтетазы)	Соединение двух молекул в результате синтеза новой C-O, C-S, C-N или C-C связи, сопряжённое с одновременным гидролизом АТФ.	$X + Y + ATP \rightarrow XY$ + ADP + Pi	С-О-лигаза, С-S-лигаза, С-N-лигаза, С-С-лигаза
КФ 7 Транслоказы	Перенос ионов или молекул через мембраны или их разделение в мембранах.	$AB + C_{[side 1]} \rightarrow$ $AB^* + C_{[side 2]}$	EC 7.1 - транслокация H ⁺ ; EC 7.2 - транслокация неорганических катионов и их хелатов; EC 7.3 - транслокация неорганических анионов; EC 7.4 - транслокация аминокислот и пептидов; EC 7.5 - транслокация углеводов и их производных; EC 7.6 - транслокация других соединений. ^[2]







Сравнительная геномика





ПОИСК ОТ ОРГАНИЗМА

VE						
Kicc	Search KEGG	•	for	neurospora crassa	Go	Clear

Database: KEGG - Search term: neurospora crassa

KEGG GENES

cmi:CMM 2688

no KO assigned | (GenBank) unnamed protein product; putative acetyl xylan esterase (XP_330314.1| hypothetical protein [Neurospora crassa]; AAC39371.1| acetyl xylan esterase II precursor [Penicillium purpurogenum])., pfam01083, Cutinase, Cutinase.; Conserved hypothetical protein

vg:1449901

no KO assigned | (RefSeq) MSV087, MseVgp087; Melanoplus sanguinipes entomopoxvirus; ORF MSV087 putative thioredoxin, similar to Neurospora crassa GB:D45892

vg:1449935

no KO assigned | (RefSeq) MSV144, MseVgp144; Melanoplus sanguinipes entomopoxvirus; ORF MSV144 putative ubiquitin, similar to Neurospora crassa GB:U01220

KEGG GENOME

T01034

ncr, 367110; Neurospora crassa OR74A

KEGG MGENES

T30455:18971

similarity to hypothetical protein CAD21257.1 - neurospora crassa

T30456:15058

similarity to hypothetical protein CAD21257.1 - neurospora crassa

T30579:1733

similarity to hypothetical protein CAD21257.1 - neurospora crassa

KEGG ENZYME

3.1.30.1

Aspergillus nuclease S1; endonuclease S1 (Aspergillus); single-stranded-nucleate endonuclease; deoxyribonuclease S1; deoxyribonuclease S1; nuclease S1; Neurospora crassa single-strand specific endonuclease; S1 nuclease; single-strand endodeoxyribonu • • •





KEGG

GENOME: Neurospora crassa

	Help							
Entry	T01034 Complete Genome							
Name	ncr, 367110							
Definition	Neurospora crassa OR74A							
Category	Reference genome							
Annotation	yes Show organism							
Taxonomy	TAX:367110							
Lineage	Eukaryota; Fungi; Dikarya; Ascomycota; Pezizomycotina; Sordariomycetes; Sordariomycetidae; Sordariales; Sordariaceae; Neurospora							
	Taxonomy							
Data source	RefSeq (Assembly:GCF_000182925.2) BioProject:132							
Original DB	Broad							
Statistics	Number of protein genes: 9758							
	Number of RNA genes: 416							
Created	2007							
Reference	PMID:12712197							
Authors	Galagan JE, Calvo SE, Borkovich KA, Selker EU, Read ND, Jaffe D, FitzHugh W, Ma LJ, Smirnov S, Purcell S, et al.							
Title	The genome sequence of the filamentous fungus Neurospora crassa.							
Journal	Nature 422:859-68 (2003)							
	DOI:10.1038/nature01554							

```
All links
Ontology (43)
   KEGG BRITE (43)
Pathway (297)
   KEGG PATHWAY (119)
   KEGG MODULE (178)
Genome (1)
   ASSEMBLY (1)
Gene (15422)
   KEGG GENES (10174)
   KEGG MGENES (613)
   RefGene (4635)
Literature (1)
   PubMed (1)
Taxonomy (1)
   TAX (1)
All databases (15765)
Download RDF
```

DBGET integrated database retrieval system



REACTOME

https://reactome.org/







Pathway Browser

Visualize and interact with Reactome biological pathways



Analysis Tools

Merges pathway identifier mapping, over-representation, and expression analysis



ReactomeFIViz

Designed to find pathways and network patterns related to cancer and other types of diseases

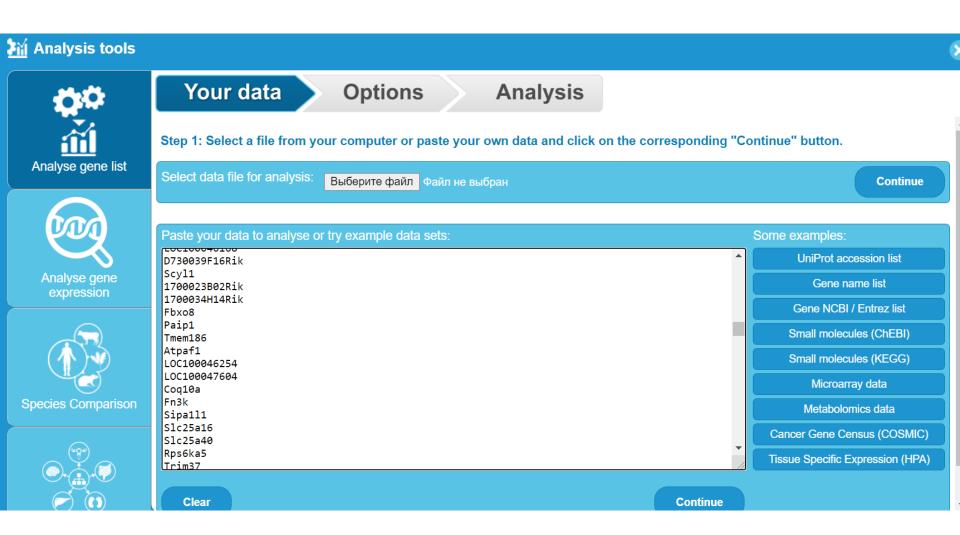


Documentation

Information to browse the database and use its principal tools for data analysis





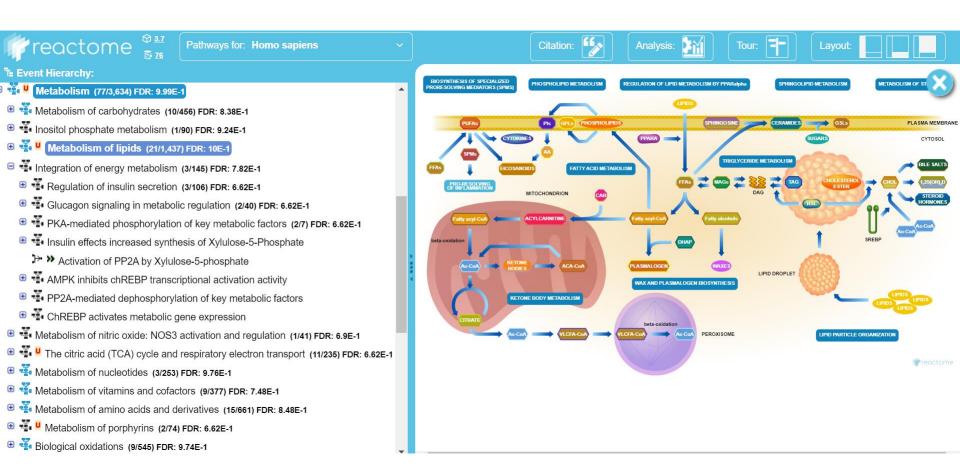




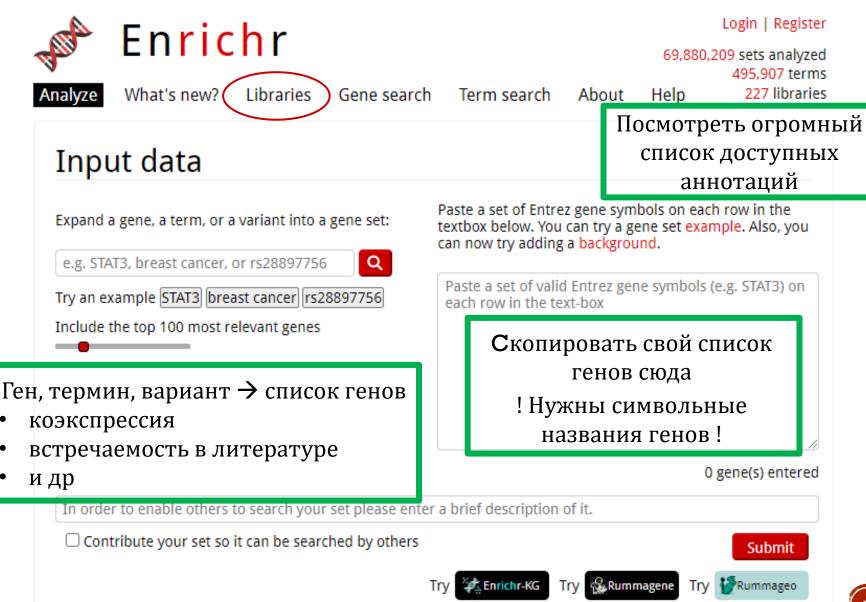


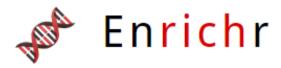






https://maayanlab.cloud/Enrichr/





69,881,391 sets analyzed 495,907 terms

Analyze

What's new?

Libraries

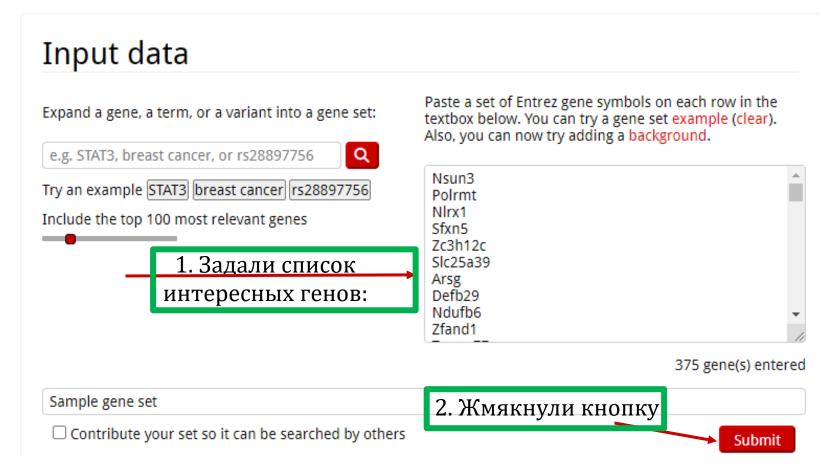
Gene search

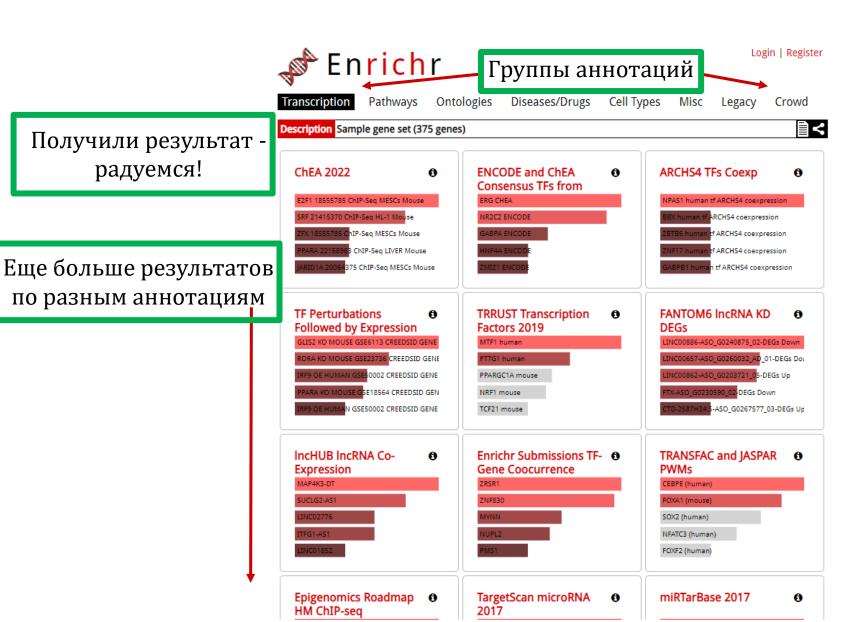
Term search

About

Help

227 libraries





радуемся!

Изучили результаты по нужным аннотациям!



Выбрали группу аннотаций

Login | Register

Transcription Pathways Ontologies Diseases/Drugs Cell Types Misc Legacy Crowd

Description Sample gene set (375 genes)



COVID-19 Related Gene Sets 2021

Bar Graph

Table Clustergram

Appyter

٠



SVG PNG JPG

Click the bars to sort. Now sorted by p-value ranking.

500 genes down-regulated by MHV-A59 in murine liver cells from GSE146074 5d

447 genes down-regulated by SARS-CoV-2 infection in Vero E6 cells from GSE153940

Top 500 up genes for SARS-CoV-2 infection in Rhesus macaques at Group 2 dose in PBMCs at 10 DPI from GSE15

500 genes down-regulated by SARS-CoV-2 in A549-ACE2 cells from GSA154613 terfenadine

Top 500 down genes for SARS-CoV-2 infection in Rhesus macaques at Group 1 dose in PBMCs at 4 DPI from GSE1

COVID19-Nsp13 protein host PPI from Krogan

500 genes down-regulated by SARS-CoV-2 in mouse Kidney cells at 7 dpi from GSE162113

Top 500 downregulated genes in mouse kidney with SARS-CoV-2 infection (Day 7) from GEO GSE162113

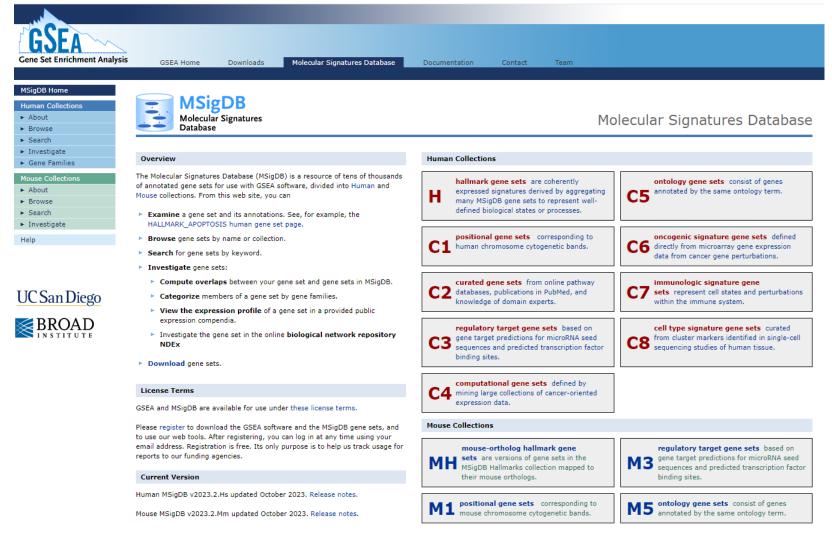
332 proteins enriched in AP-MS using various SARS-CoV-2 proteins as bait from Gordon et al. (2020)

COVID19-All 332 protein host PPI from Krogan

Обогащенные категории

> Выбрали вид представления результатов

http://www.gsea-msigdb.org/gsea/msigdb/collections.jsp



Аннотированные гены человека и и мыши сгруппированы по 9 и 6 коллекциям

Можно скачать все сразу, либо отдельные коллекции или аннотации внутри коллекций.



Коллекции включают в себя и широко известные GO, KEGG, Reactome... так и более специализированные коллекции:

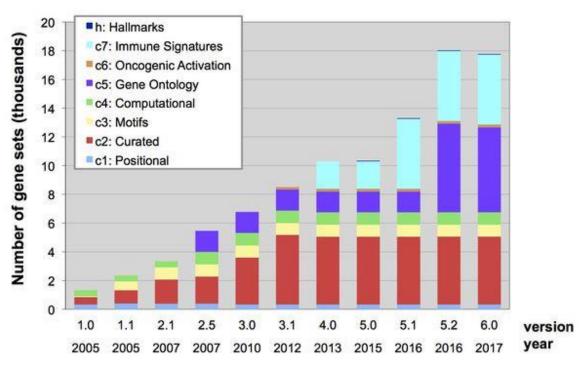
- связанные с иммунной системой
 - раком
 - вакцинами...

Есть и маркеры клеточных типов, собранные по нескольким scRNA-seq публикациям.

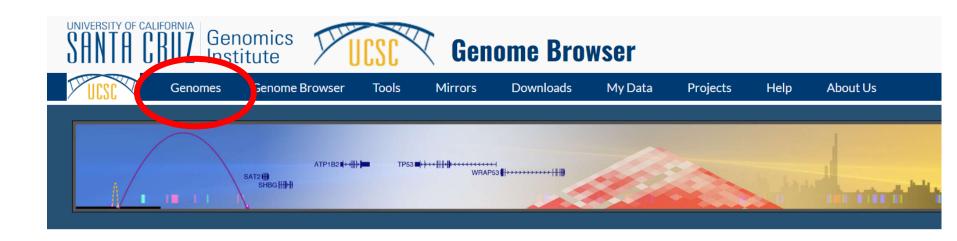
На этом же сайте можно скачать ПО для GSEA анализа.

Так же можно использовать веб-сервис

https://www.genepattern.org/



https://genome.ucsc.edu/



Search genes, data, help docs and more...

Tools



- Genome Browser Interactively visualize genomic data
- BLAT Rapidly align sequences to the genome
- In-Silico PCR Rapidly align PCR primer pairs to the genome
- Table Browser Download and filter data from the Genome Browser
- LiftOver Convert genome coordinates between assemblies
- REST API Returns data requested in JSON format
- Variant Annotation Integrator Annotate genomic variants
- More tools...

News

Mar. 26, 2024 - New gnomAD v4 Constraint Metric
Mar. 07, 2024 - New Prediction Scores super track

Search

Mar. 05, 2024 - New JASPAR tracks: Human (hg1§

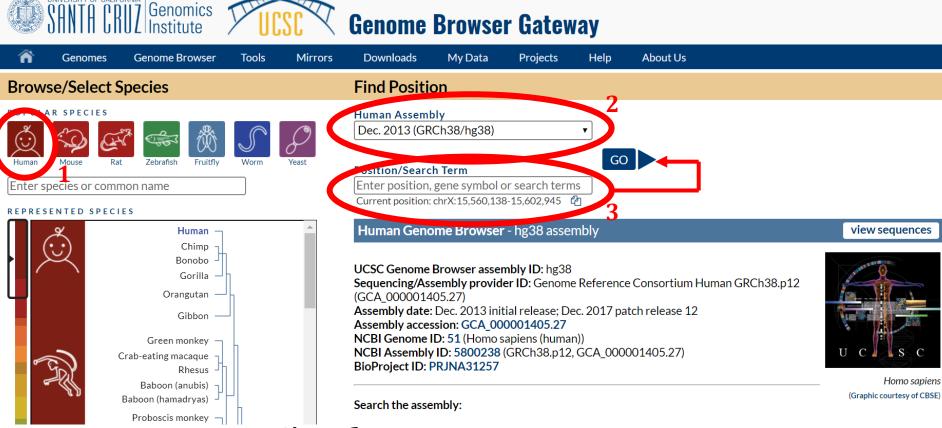
Mar. 01, 2024 - AbSplice Prediction Scores for hg

Feb. 21, 2024 - New DECIPHER Dosage Sensitivit

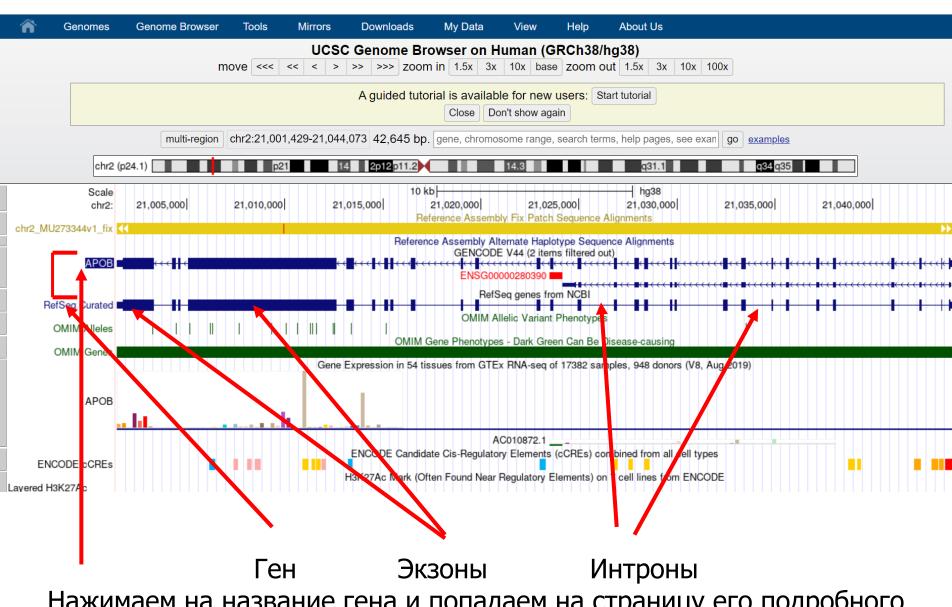
Feb. 14 2024 - New GENCODE gene tracks: V45 (I

More news... Subscrib



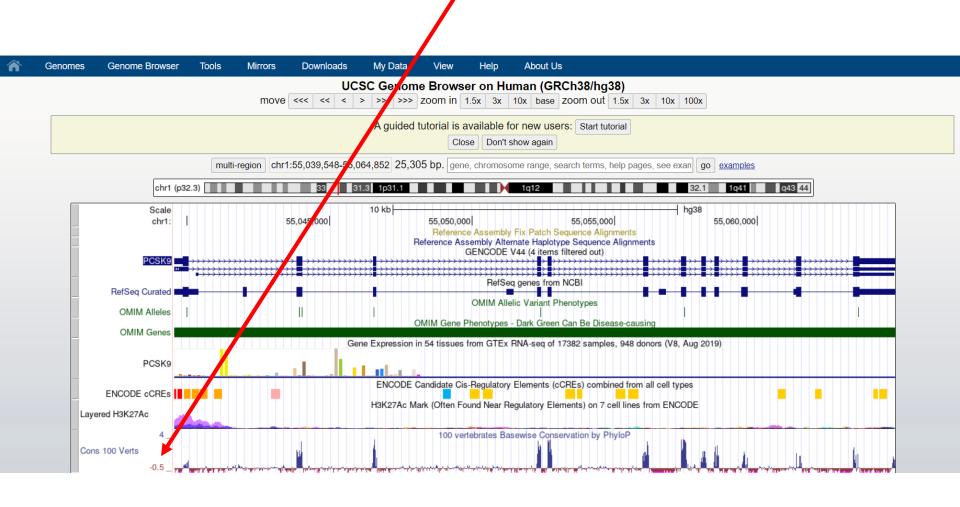


- 1) Выбираем человека Human
- 2) Версия генома человека GRCh38/hg38
- 3) В раздел Position/Search Term вводим название своего гена или координаты локуса

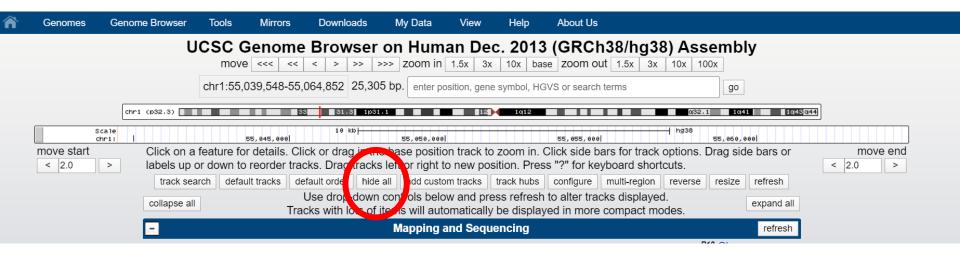


Нажимаем на название гена и попадаем на страницу его подробного описания

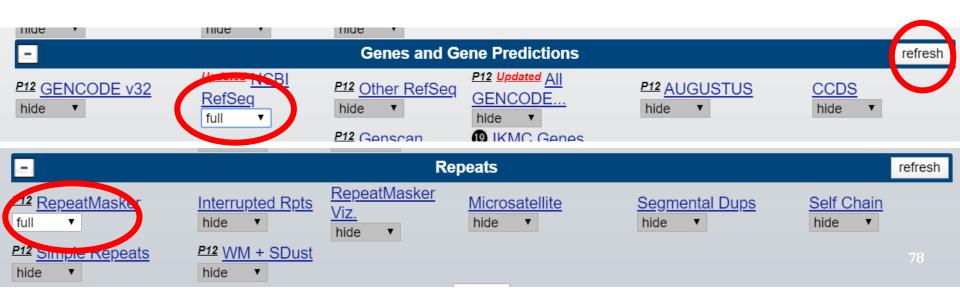
Обратите внимание на трек консервативности



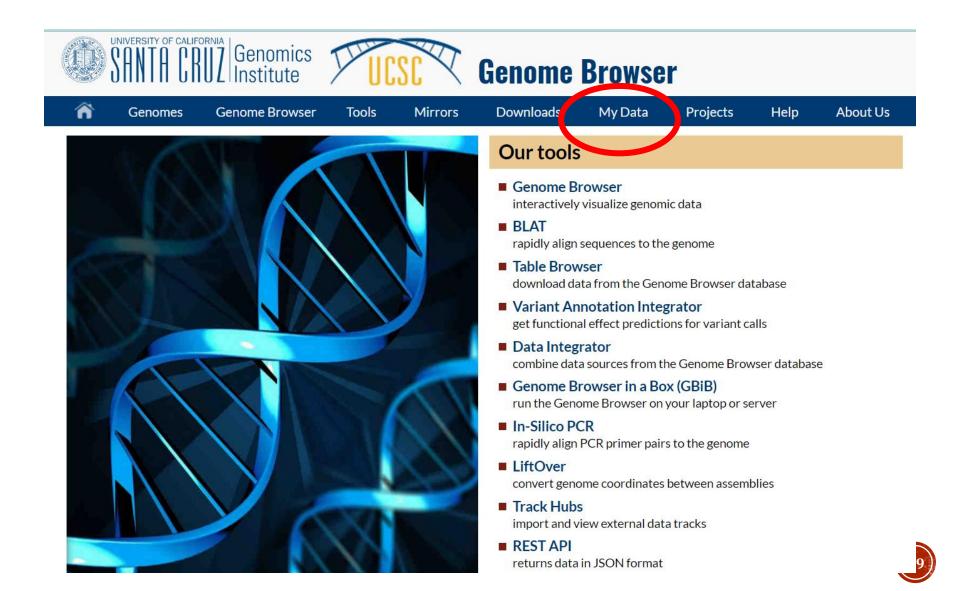
Можно спрятать все треки



Открыть только некоторые



https://genome.ucsc.edu/



https://genome.ucsc.edu/

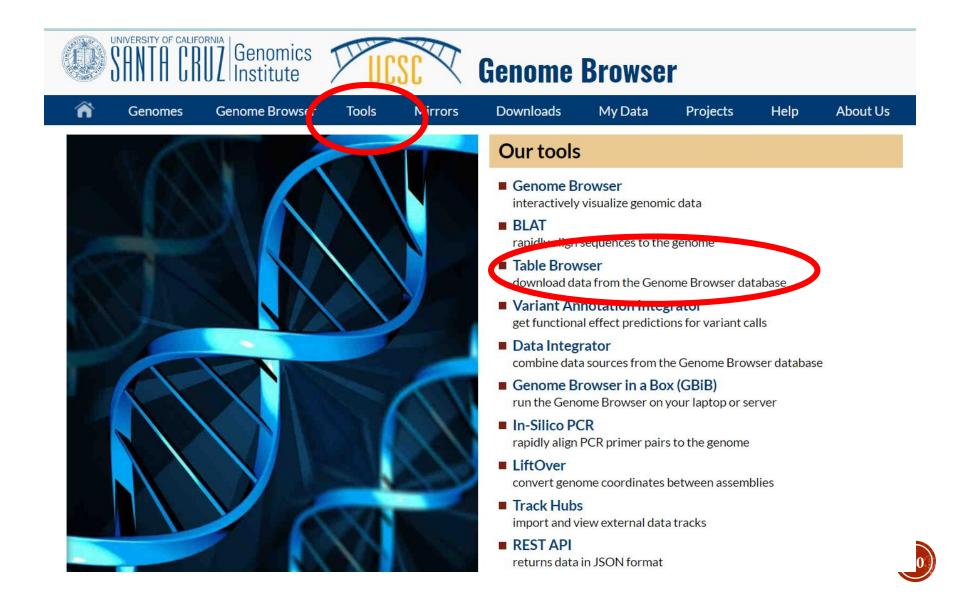


Table Browser

clade: Mammal

Use this program to retrieve the data associated with a track in text format, to calculate intersections between tracks, and to retrieve DNA sequence covered by a track. For help in using this application see <u>Using the Table Browser</u> for a description of the controls in this form, and the <u>User's Guide</u> for general information and sample queries. For more complex queries, you may want to use <u>Galaxy</u> or our <u>public MySQL server</u>. To examine the biological function of your set through annotation enrichments, send the data to <u>GREAT</u>. Refer to the <u>Credits</u> page for the list of contributors and usage restrictions associated with these data. All tables can be downloaded in their entirety from the <u>Sequence and Annotation Downloads</u> page.

assembly: Dec. 2013 (GRCh38/hg38) ~

group: Comparative Genomics ✓ tı	rack: Conservation	~	add custom tracks	track hubs	
table: Cons 100 Verts (phyloP100way)	✓ describe table	e schema			
region: ● genome ○ position chr1:8,916,757-8,919,018 lookup define regions					
filter: create					
subtrack merge: create					
intersection: create					
correlation: create					
output format: data points V Send out	put to 🗌 <u>Galaxy</u> 🗀	GREAT			
output file: repmask.mm10.bed	(leave blank t	o keep out	put in browser)		
file type returned: • plain text ogzip compressed					

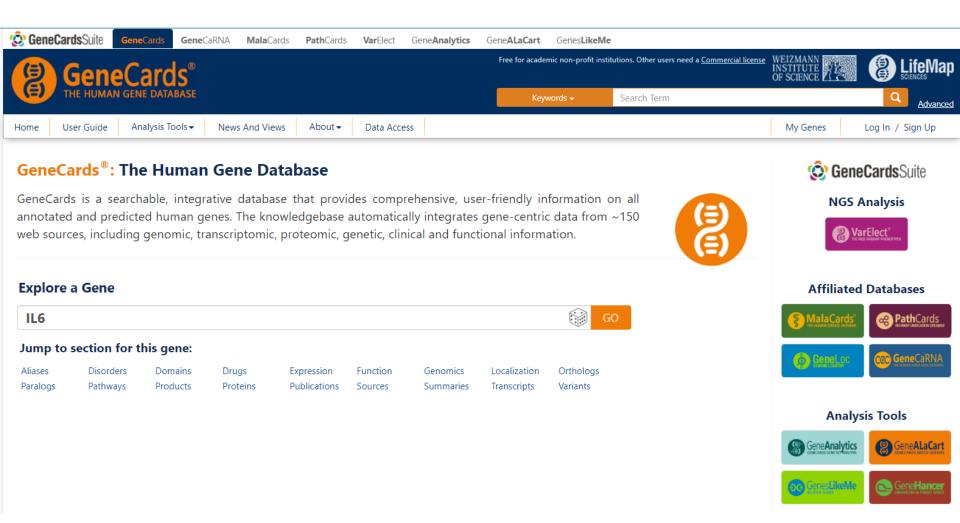
Note: to return more than 100,000 lines, change the filter setting (above). The entire data set may be available for download as a very large file that contains the original data values (not compressed into the wiggle format) -- see the Downloads page.

get output summary/statistics

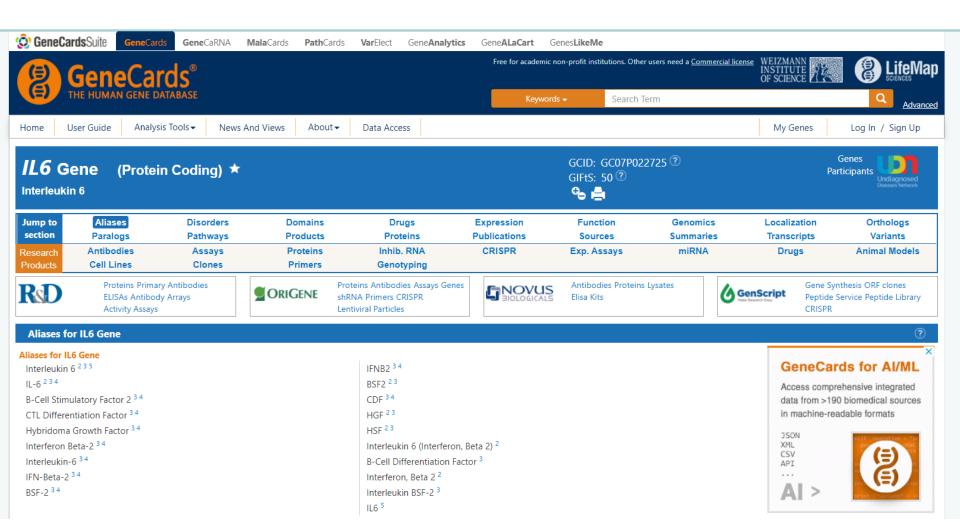
To reset all user cart settings (including custom tracks), click here.

✓ genome: Human

https://www.genecards.org/

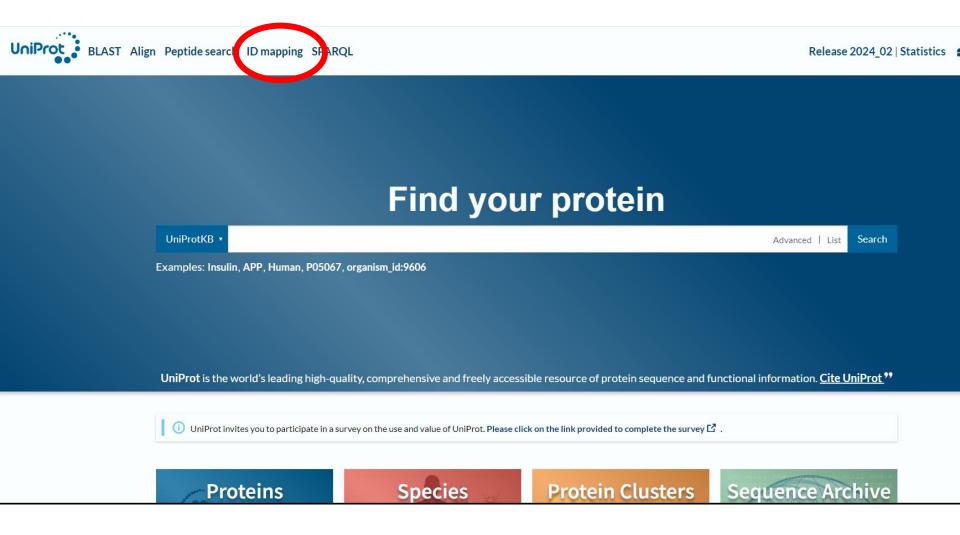








https://www.uniprot.org/





Retrieve/ID mapping

Enter one of more IDs (100,000 max). You may also load from a text file. Separate IDs by whitespace (space, tab, newline) or commas.

P31946	
① Your input contains 1 ID	
From database To database	
UniProtKB AC/ID ▼ Gene Name ▼	

Указываем базы данных



ID mapping 1 result found for UniProtKB_AC-ID → Gene_Name

API Request

Overview

Input Parameters

Download View: Cards ○ Table ◎ ♠ Resubmit

1 | D was mapped to 1 result

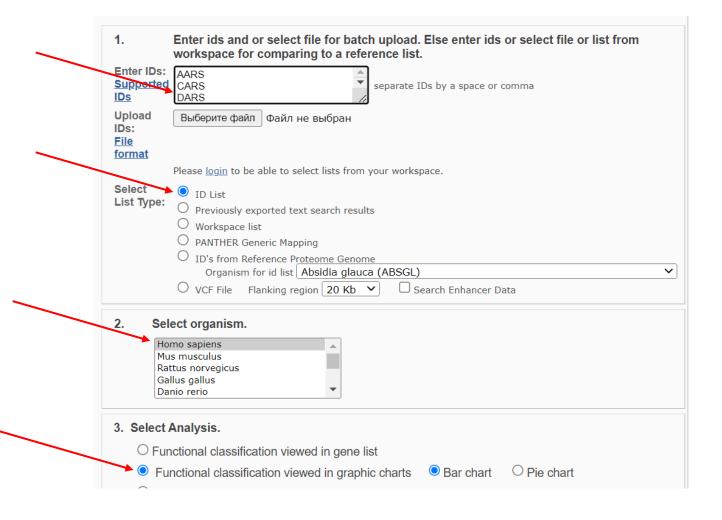
From To

P31946 YWHAB





http://www.pantherdb.org/





http://www.pantherdb.org/

