

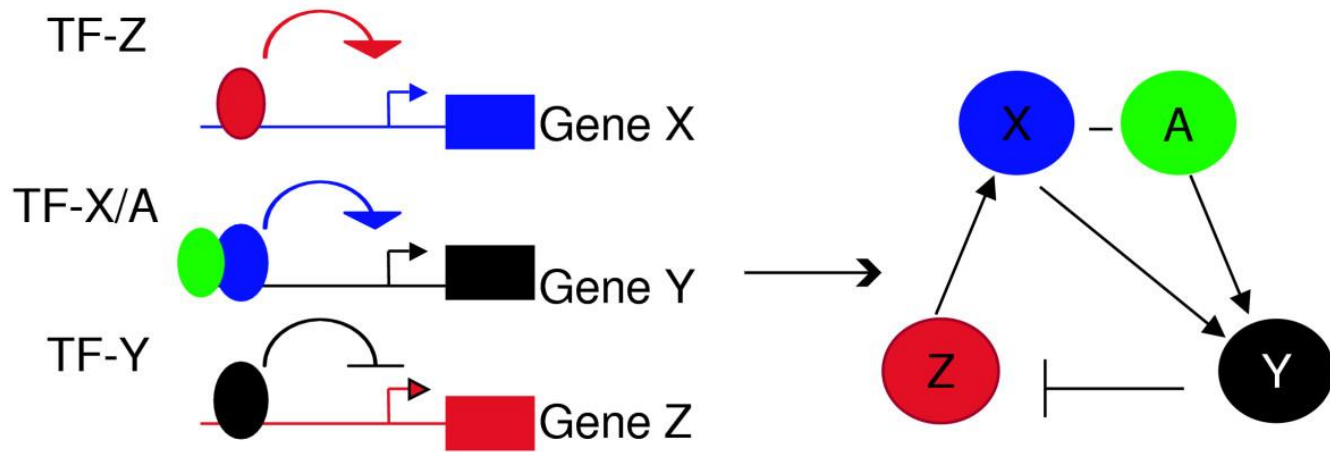
Лекция №4

1. Генные сети в эпоху
высокопроизводительного
секвенирования

2. Базы данных по генным сетям

к.б.н., с.н.с. лаб. эволюционной биоинформатики
и теоретической генетики Игнатьева Е.В.

Транскрипционные регуляторные сети (Transcription regulatory networks)



Транскрипционные регуляторные сети содержат узлы, обозначающие одновременно два вида объектов:

- 1) гены, относящиеся к рассматриваемой системе;
- 2) транскрипционные факторы, регулирующие экспрессию генов.

Типы связей (ребер) в транскрипционных регуляторных сетях:

- Стрелки отображают активацию (подавление) экспрессии гена транскрипционным фактором,
- Линии отображают белок-белковые взаимодействия

При отображении транскрипционных регуляторных сетей не принято изображать отдельно ген и отдельно белок !!!

Итоги: возможные экспериментальные подходы для получения данных для реконструкции транскрипционных регуляторных сетей (TRN)



Подход 1. Выявление сайтов чувствительности к ДНКазе-I в геноме и предсказание сайтов связывания транскрипционных факторов в районах ДНК, соответствующих сайтам чувствительности к ДНКазе-I

Подход 2. Оценка эффекта выключения активности транскрипционных факторов различными способами (siRNA и т.д.).

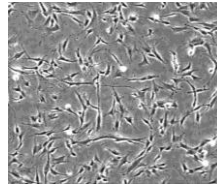
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Подход 2: Реконструкция транскрипционных регуляторных сетей (TRN) на основе исследования эффектов выключения генов с помощью siRNA (метод)

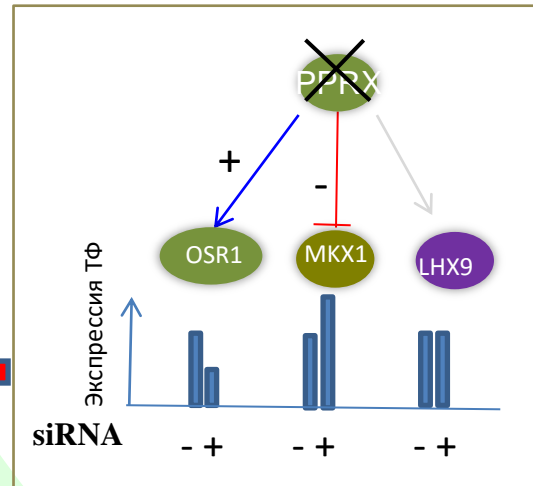
Анализ данных консорциума FANTOM5 по экспрессии в различных типах клеток человека (методика CAGE)

Список 18 транскрипционных факторов с повышенной экспрессией в фибробластах (fibroblast-enriched transcription factors)



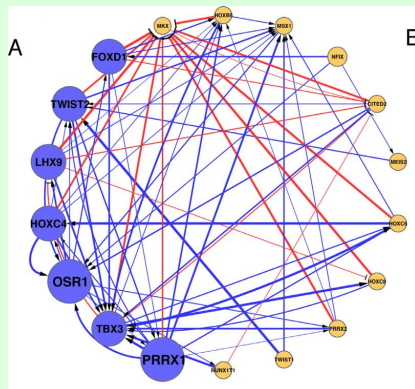
Эксперимент с поочередным выключением каждого из 18-ти ТФ с помощью siRNA

siRNA (= малые интерферирующие РНК) могут быть искусственно введены в клетки для нокдауна определённого гена.



Выявление генов, экспрессия которых меняется наиболее сильно в ответ на вмешательство siRNA .
= Это гены мишени, регулируемые исследуемыми ТФ

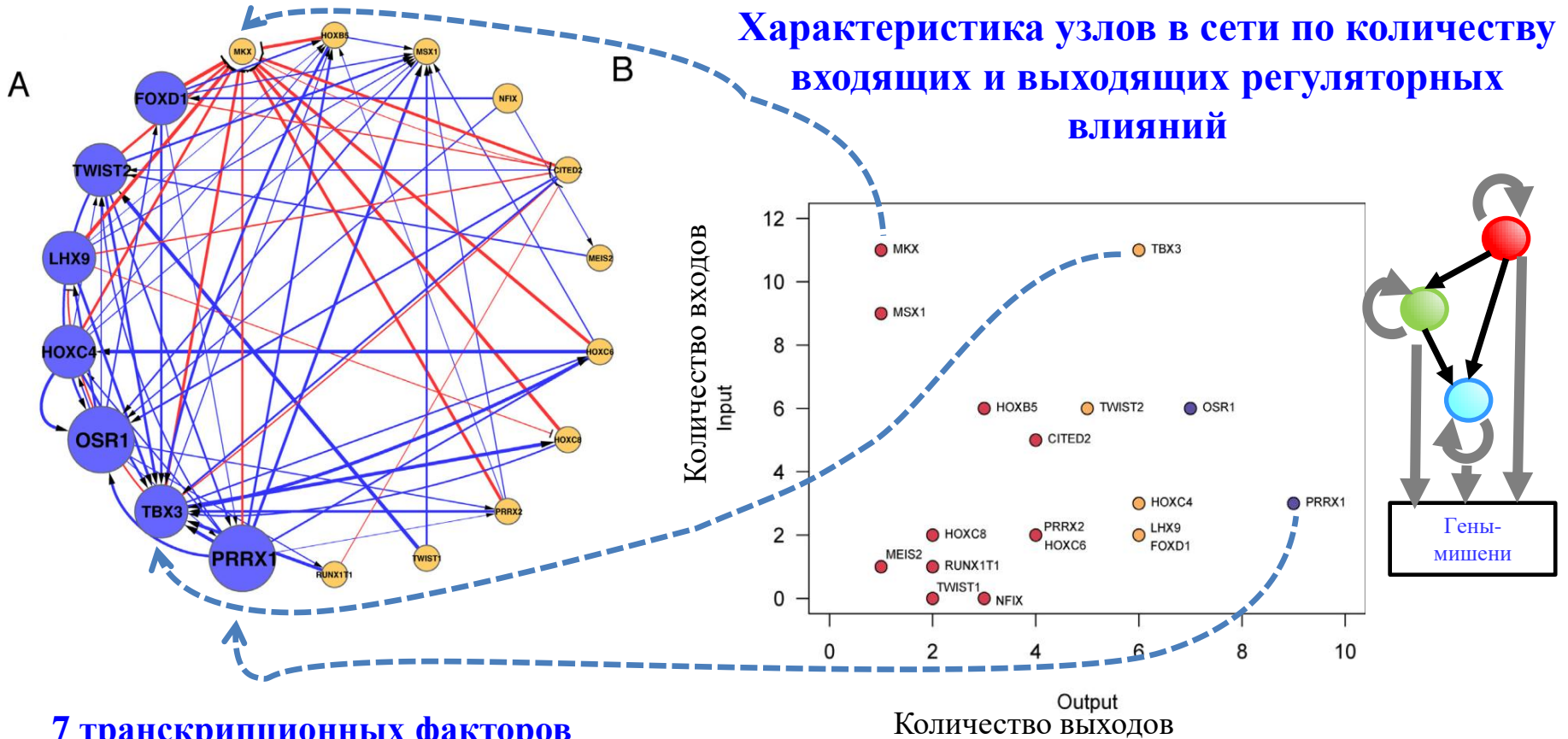
Фибробласт-специфичная сеть транскрипционной регуляции (TRN)



7 транскрипционных факторов с наибольшей значимостью + 11 других факторов

Подход 2: Реконструкция транскрипционных регуляторных сетей (TRN) на основе исследования эффектов выключения генов с помощью siRNA (результаты)

Фибробласт-специфичная сеть транскрипционной регуляции (TRN)

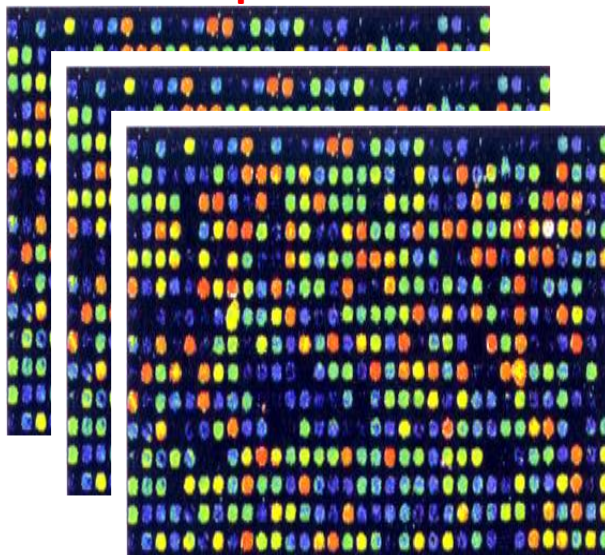


7 транскрипционных факторов с наибольшей значимостью + 11 других факторов

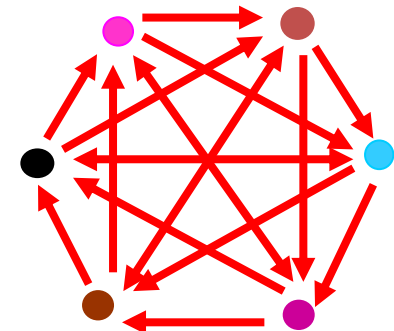
Задача в общем виде:

Реконструкция графов регуляторных генных сетей на основе данных по экспрессионным ДНК-чипам

Дано: Экспериментальные данные по уровням экспрессии генов в нескольких временных точках



Надо построить:



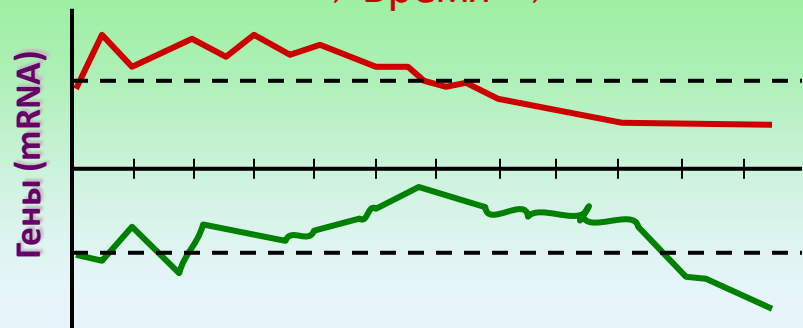
Граф взаимодействий между генами

концентрация i -го гена в j -й временной точке

→ Время →

$$X_{N \times M} := \begin{pmatrix} \chi_1^1 & \chi_1^2 & \dots & \chi_1^M \\ \chi_2^1 & \chi_2^2 & \dots & \chi_2^M \\ \vdots & \vdots & \ddots & \vdots \\ \chi_N^1 & \chi_N^2 & \dots & \chi_N^M \end{pmatrix}$$

→ Время →



Один из этапов теоретического подхода: выявление кластеров генов с контрастными экспрессионными характеристиками

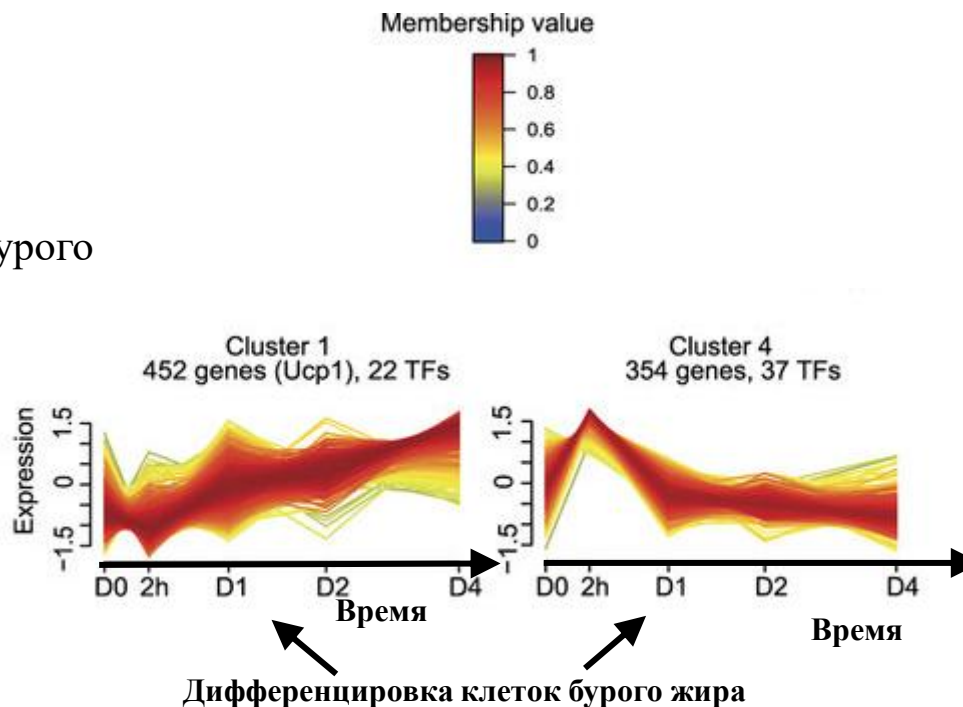
ГО термины:

Дифференцировка бурого жира

Клеточный ответ на инсулин

Биосинтез жирных кислот

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ГО термины:

Морфогенез

эпителиальной трубки

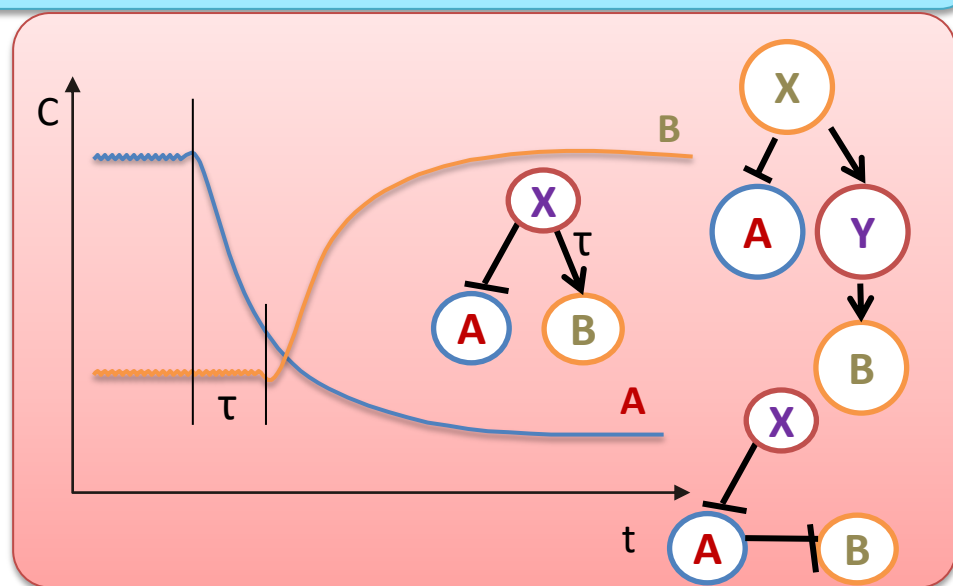
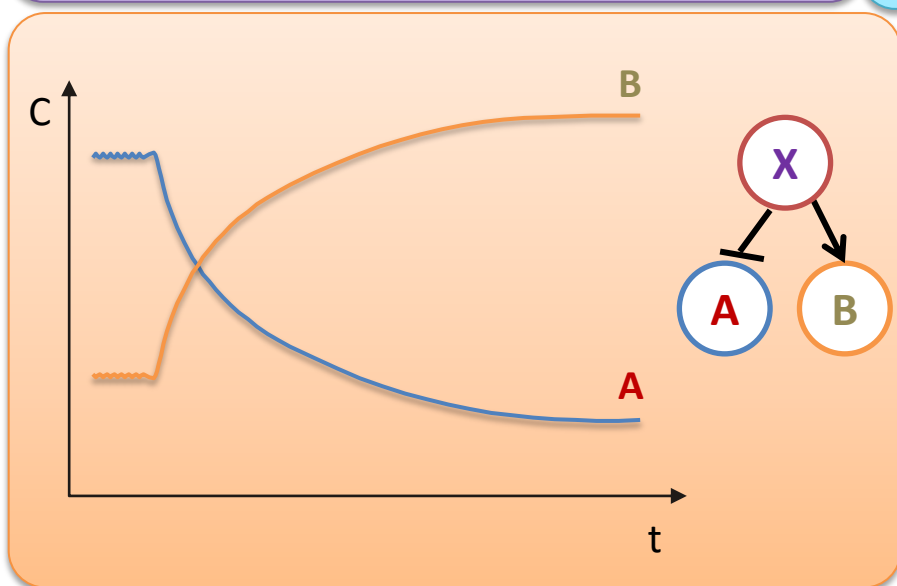
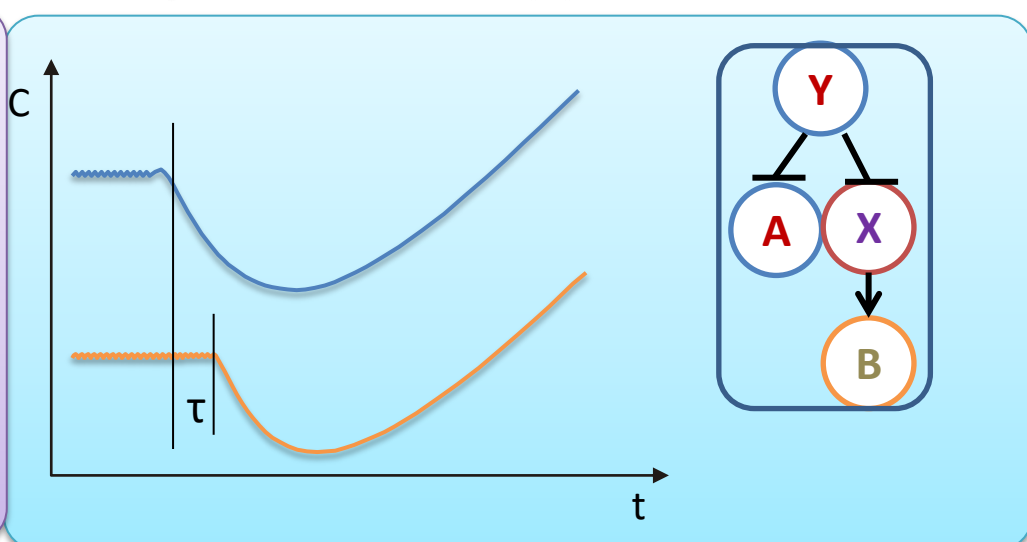
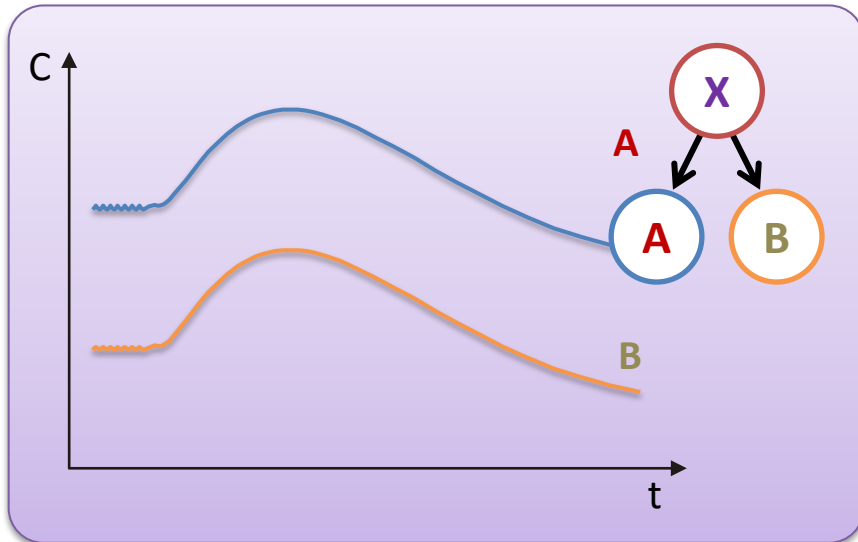
Пролиферация клеток

Дифференцировка

хондроцитов

.....

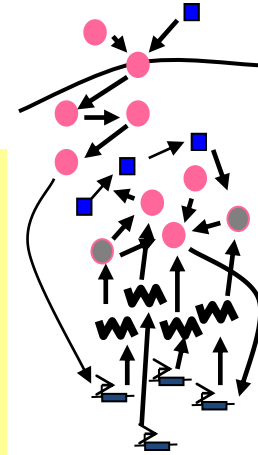
Построение гипотез о регуляторных взаимодействиях между генами основе данных по экспрессионным ДНК-чипам



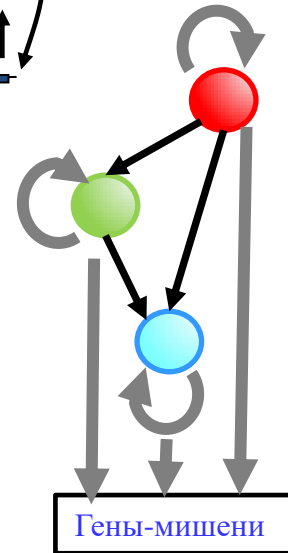
Результаты неоднозначны, необходима экспериментальная проверка !!!!

Генные сети, транскрипционные регуляторные сети- Что дальше ????

✓ **Генные сети** - молекулярно-генетические системы, обеспечивающие формирование фенотипических характеристик организмов (молекулярных, биохимических, структурных, морфологических, поведенческих и т.д.) на основе информации, закодированных в их геномах.



✓ **Транскрипционные регуляторные сети (TRN)** – сети, содержащие вершины, каждая из которых соответствует двум видам объектов:
1) гены, относящиеся к рассматриваемой системе;
2) транскрипционные факторы, кодируемые данными генами, и регулирующие экспрессию других генов из данной системы.



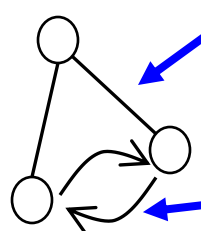
Сети взаимодействий между генами / белками

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Изображения генных сетей, а также любых сетей, являются графами.

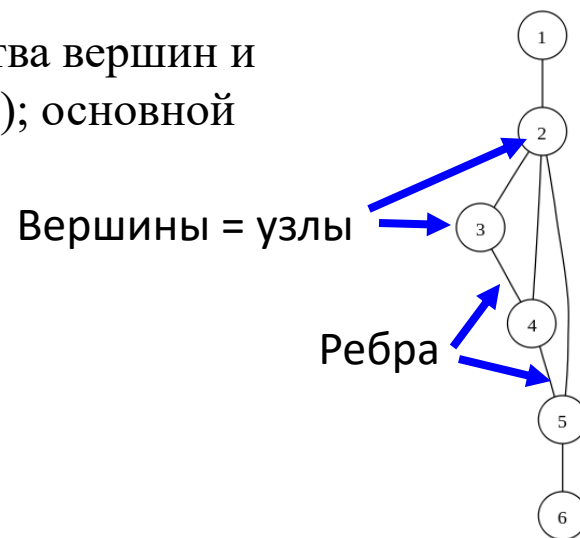
Граф (англ. *graph*) — совокупность непустого множества вершин и наборов пар вершин (связей между вершинами = ребер); основной объект изучения математической теории графов.

[https://ru.wikipedia.org/wiki/ Граф_\(математика\)](https://ru.wikipedia.org/wiki/Граф_(математика))



Неориентированное ребро соединяет неупорядоченную пару вершин

Ориентированное ребро (= дуга) соединяет упорядоченную пару вершин

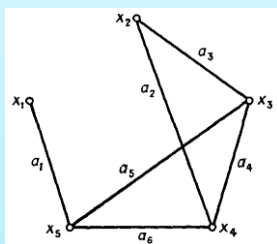


Вершины = узлы

Ребра

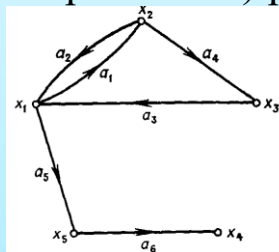
Классификация графов по типам входящих в них ребер

Неориентированный граф — это непустое множество вершин (=узлов) и неупорядоченных ребер



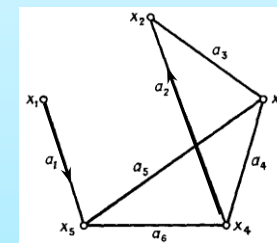
Пример неориентированного графа. x_1, x_2, x_3, x_4, x_5 — вершины графа. $a_1, a_2, a_3, a_4, a_5, a_6$ — ребра.

Ориентированный граф — это непустое множество вершин (=узлов) и упорядоченных (ориентированных) ребер (дуг)



Пример ориентированного графа. x_1, x_2, x_3, x_4, x_5 — вершины графа. $a_1, a_2, a_3, a_4, a_5, a_6$ — дуги.

Смешанный граф это граф, в котором некоторые рёбра могут быть ориентированными, а некоторые - неориентированными.

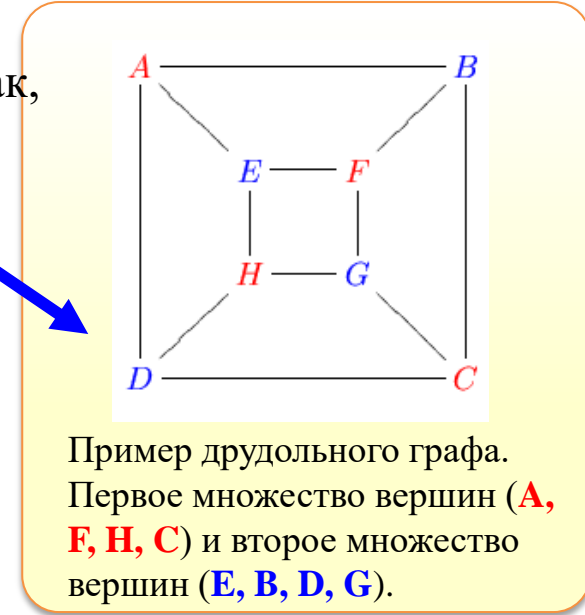


Пример смешанного графа. x_1, x_2, x_3, x_4, x_5 — вершины графа. a_1, a_2 — дуги. a_3, a_4, a_5, a_6 — ребра.

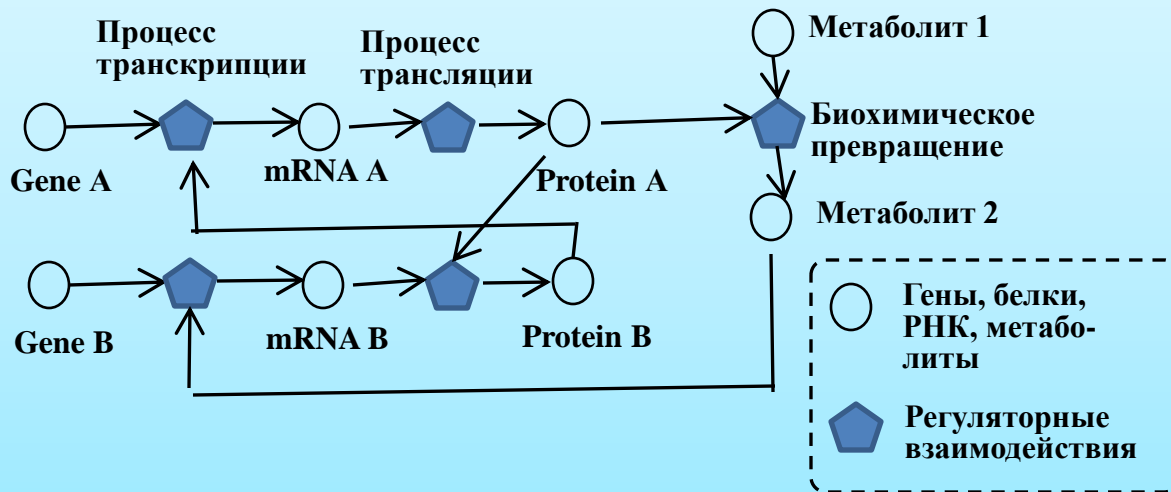
Классификация графов по типам входящих в них ребер

Граф называется двудольным, если его вершины можно разбить на два непересекающихся подмножества V_1 и V_2 так, что всякое ребро соединяет вершину из первого множества V_1 с вершиной из второго множества V_2 .

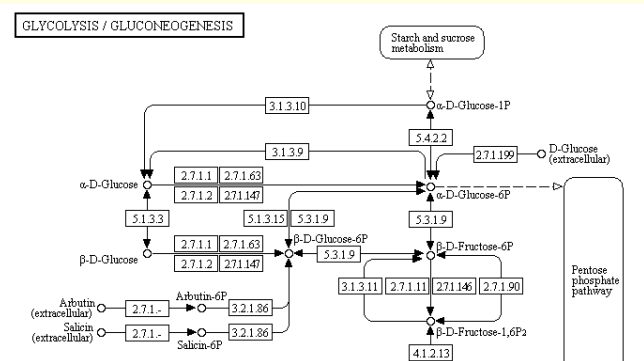
Граф называется k -дольным, если его вершины можно разбить на k непересекающихся подмножества V_1, V_2, \dots, V_k , так, так, что не будет ребер, соединяющих вершины одного и того же подмножества



Генную сеть можно представить в виде двудольного графа:
1-ый тип вершин – гены, белки, РНК, метаболиты
2-ой тип вершин – процессы и регуляторные взаимодействия

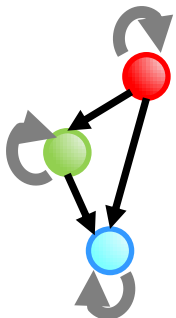
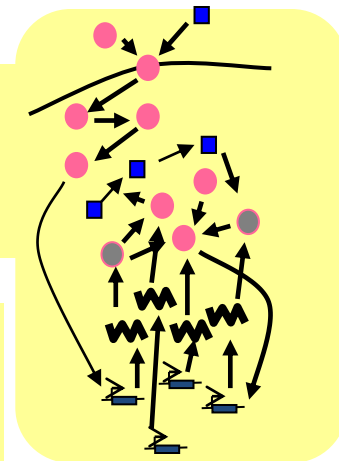


Представление данных о метаболическом пути в базе KEGG:
1-ый тип вершин – метаболиты
2-ой тип вершин – ферменты



Классификация сетей по типам вершин и связей

Генные сети – граф сети ориентированный либо смешанный и может включать вершины нескольких типов: гены, мРНК, белки, низкомолекулярные соединения, реакции



Транскрипционные регуляторные сети (TRN) граф сети ориентированный и включает вершины одного типа, обозначающие (одновременно !!!): 1) гены, относящиеся к рассматриваемой системе; 2) транскрипционные факторы, кодируемые данными генами и регулирующие экспрессию генов



Сети взаимодействий между генами / белками - граф сети неориентированный либо смешанный, включает вершины, одного типа, обозначающие гены и /или белки.

Ребро (связь) между вершинами сети может обозначать:

Белок-белковое взаимодействие

Гомологию между генами либо структурное сходство белков

Коэкспрессию

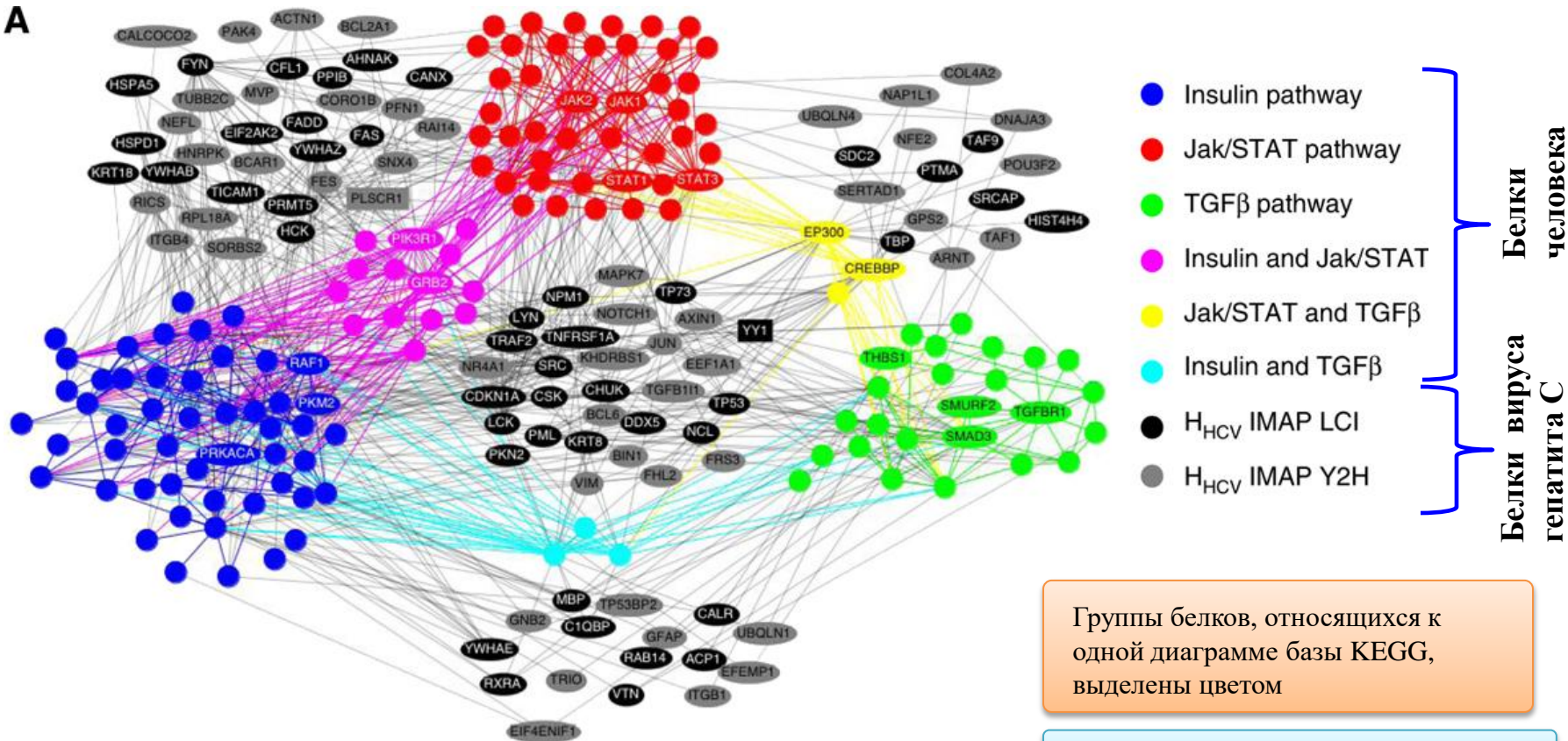
Принадлежность генов/белков к одному метаболическому-сигнальному пути

Совместную встречаемость в текстах статей

Сети взаимодействий между генами / белками широко используются для представления данных полногеномных исследований

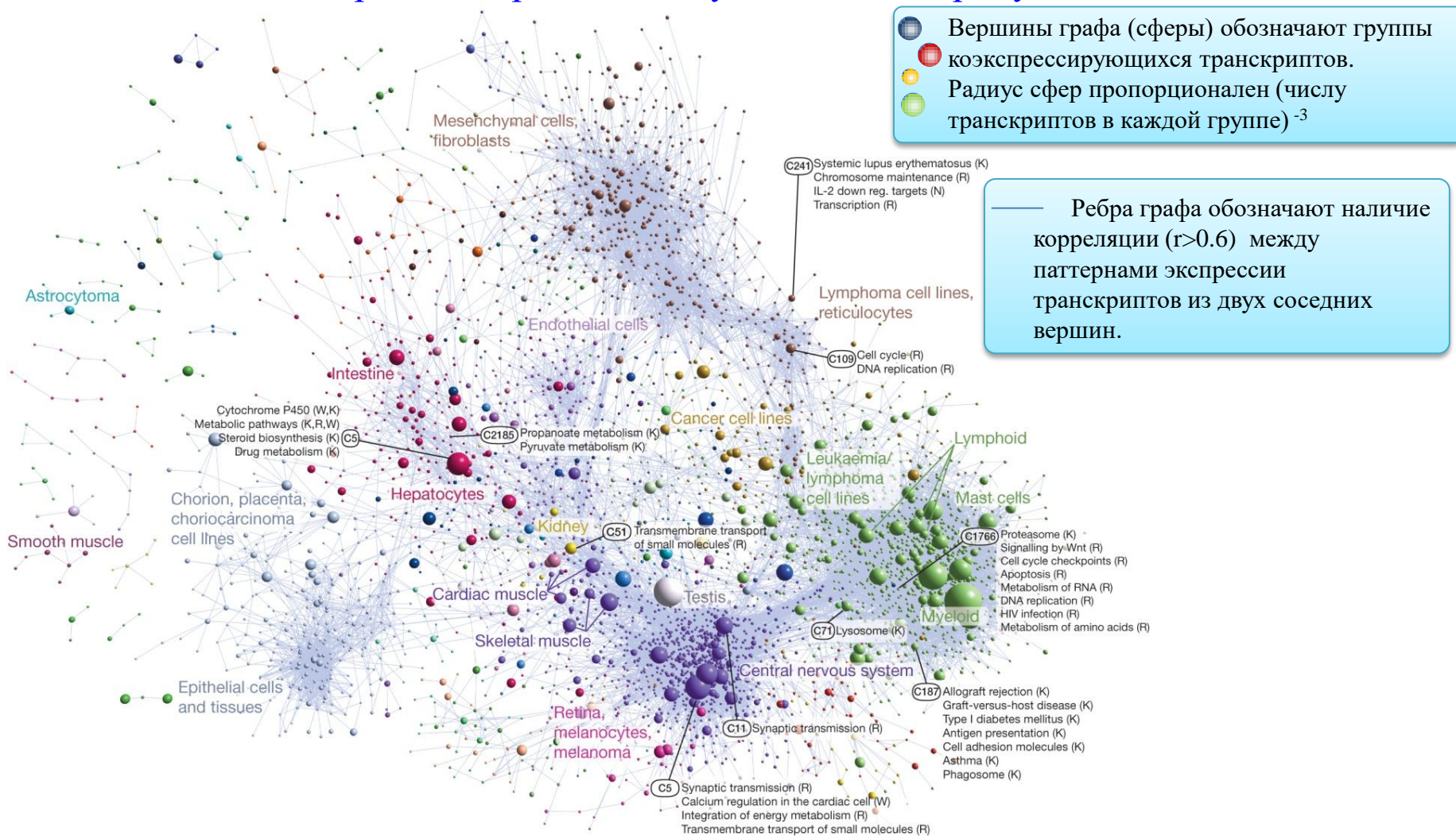
Пример №1: представление сети белок-белковых взаимодействий между белками человека, имеющими взаимодействия с белками вируса гепатита С

A



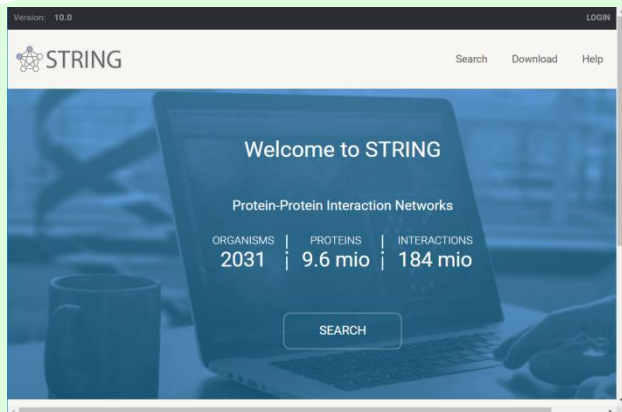
Сети взаимодействий между генами / белками широко используются для представления данных полногеномных исследований

Пример №2: представление коэкспрессирующихся генов/транскриптов человека на основе анализа паттернов экспрессии, полученных консорциумом FANTOM



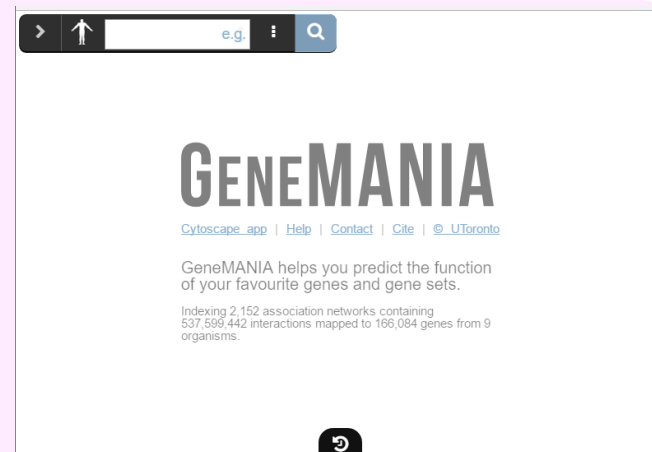
Как строить сети взаимодействий между генами / белками ??

Интернет-доступные информационные компьютерные системы, позволяющие экстрагировать данные по связям различных типов между генами/белками

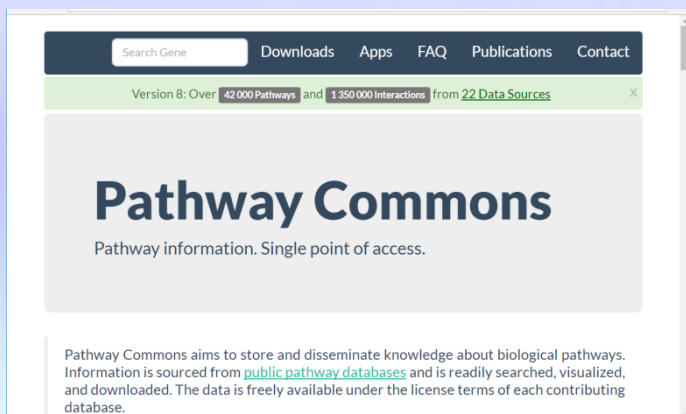


STRING - functional protein association networks
string-db.org/

GeneMANIA
<http://genemania.org/>

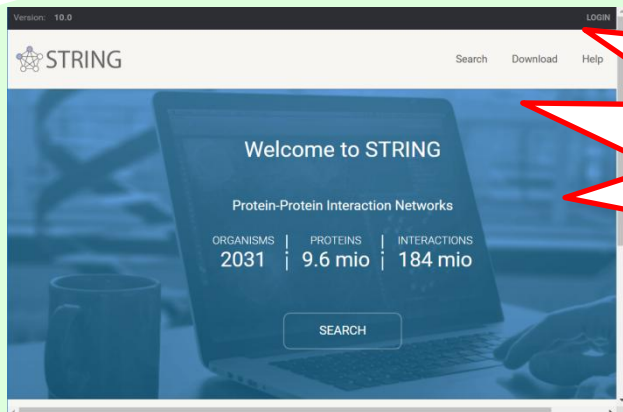


Pathway Commons - A Resource for Biological Pathway Analysis
<http://www.pathwaycommons.org/>



Как строить сети взаимодействий между генами / белками ??

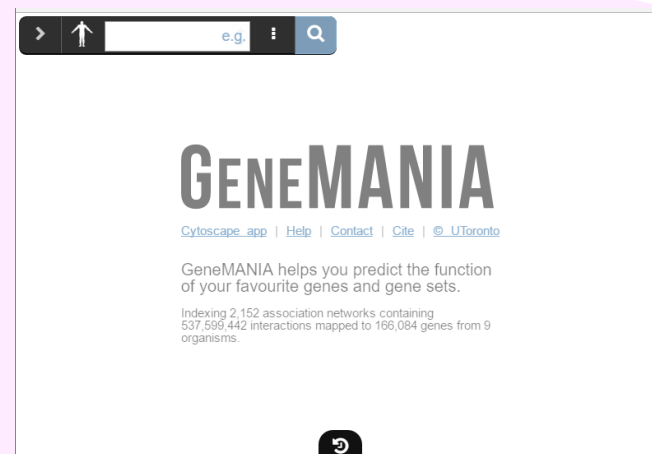
Интернет-доступные информационные компьютерные системы, позволяющие экстрагировать данные по связям различных типов между генами/белками



STRING - functional protein
association networks
string-db.org/

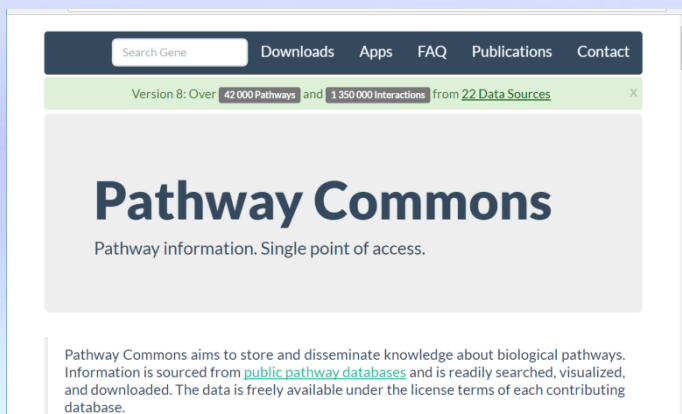
GeneMANIA

<http://genemania.org/>



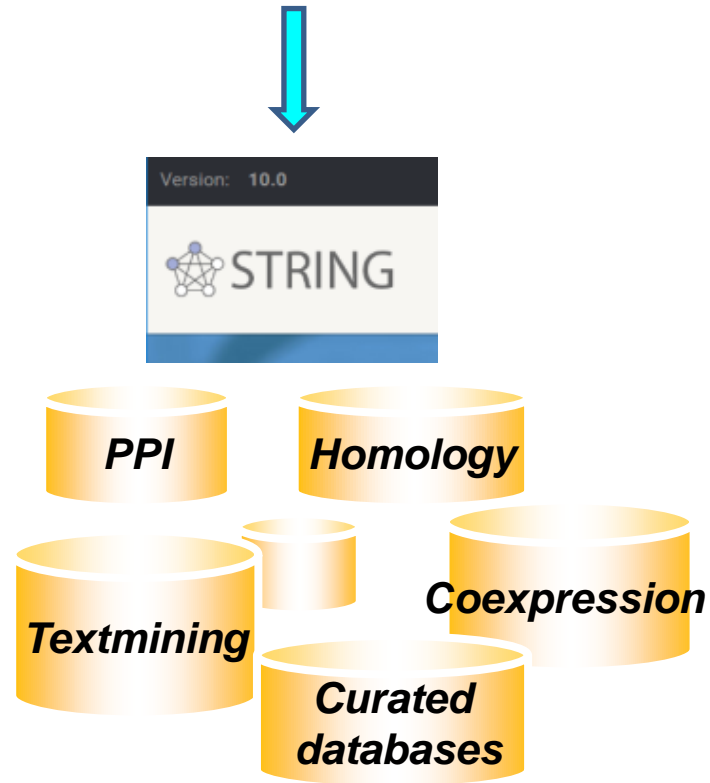
Pathway Commons - A Resource for Biological
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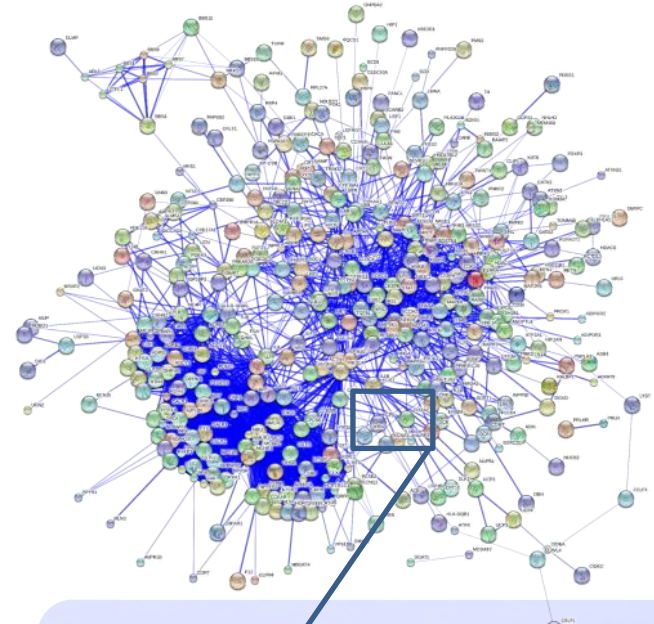


Программно-информационный инструмент STRING (<http://string-db.org/>)

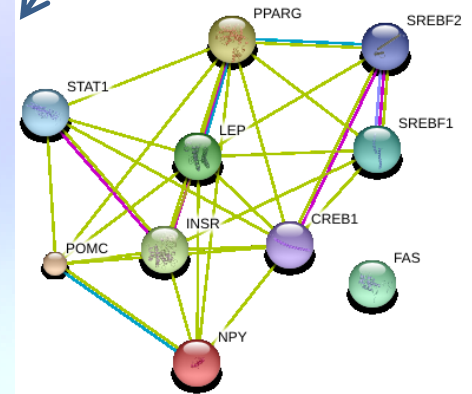
Дано: список ~500 генов человека



Общий вид сети взаимодействий между генами, вовлеченными в регуляцию массы тела



Фрагмент сети



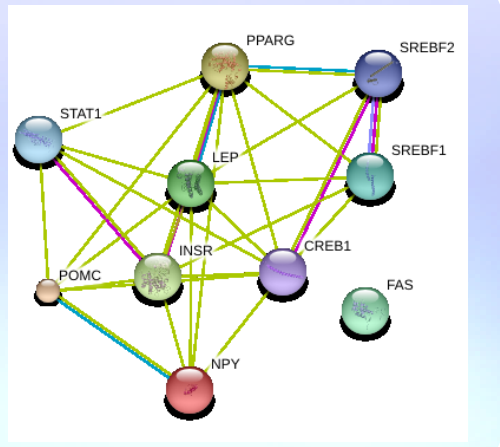
Базы данных взаимодействий между генами

849 видов организмов с пометкой “core”

1184 видов организмов с пометкой “periphery”

Сеть, реконструированная системой STRING, включает взаимодействия разных типов

Фрагмент сети



active interaction sources:

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

minimum required interaction score:

medium confidence (0.400)

- highest confidence (0.900)
- high confidence (0.700)
- medium confidence (0.400)
- low confidence (0.150)
- custom value

2nd shell: - none -

quick change:

Условные обозначения

Known Interactions

- from curated databases
- experimentally determined

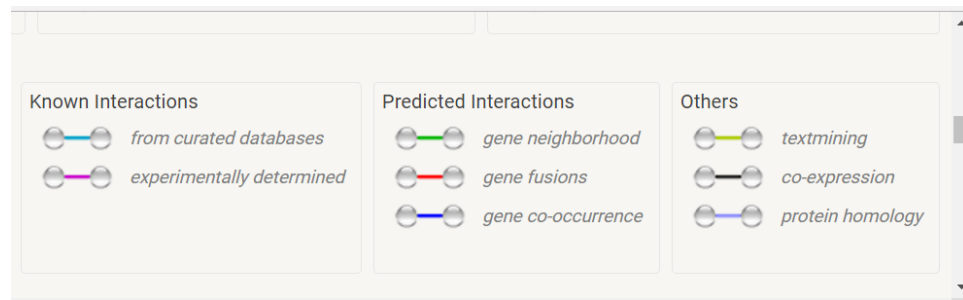
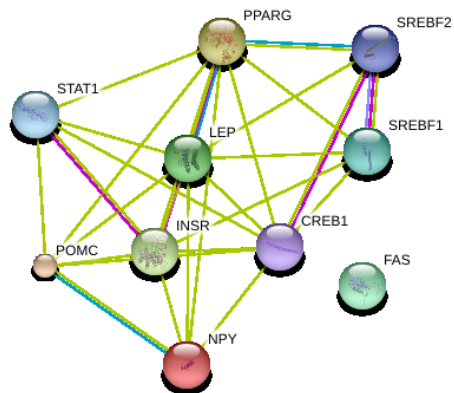
Predicted Interactions

- gene neighborhood
- gene fusions
- gene co-occurrence

Others

- textmining
- co-expression
- protein homology

Основные типы взаимодействий в системе STRING



Experimentally determined - белок-белковые взаимодействия из баз данных (базы, входящие в IMEx consortium (HPRD, MINT, etc.), а также BioGRID)

From curated databases - совместная встречаемость в метаболических и сигнальных путях

Textmining – встречаемость в абстрактах и текстах статей

Coexpression – сходные паттерны экспрессии генов

Protein homology – структурное сходство белков (например, семейства белков)



STRING: данные можно скачать в тестовом виде !!

string-db.org/cgi/download.pl?UserId=KZzQJ_H2iEpx&sessionId=aTOEaFhHbX0Z

STRING Search Download Help My Data

DOWNLOAD

FILES TOO LARGE?

Some of the files below can be made smaller (prior to download), by restricting the data to one organism of interest. Choose an organism here:

INTERACTION DATA

File	Description	Access
protein.links.v10.txt.gz (11 Gb)	protein network data (scored links between proteins)	
protein.links.detailed.v10.txt.gz (16.7 Gb)	protein network data (incl. subscores per channel); commercial entities require a license.	
protein.links.full.v10.txt.gz (17.8 Gb)	protein network data (incl. distinction: direct vs. interologs); all users require a license	license required
protein.actions.v10.txt.gz (5 Gb)	interaction types for protein links (bugfix update 27.01.2017)	
COG.links.v10.txt.gz (107.1 Mb)	association scores between orthologous groups	
COG.links.detailed.v10.txt.gz (163.2 Mb)	association scores (incl. subscores per channel); commercial entities require a license.	

ACCESSORY DATA

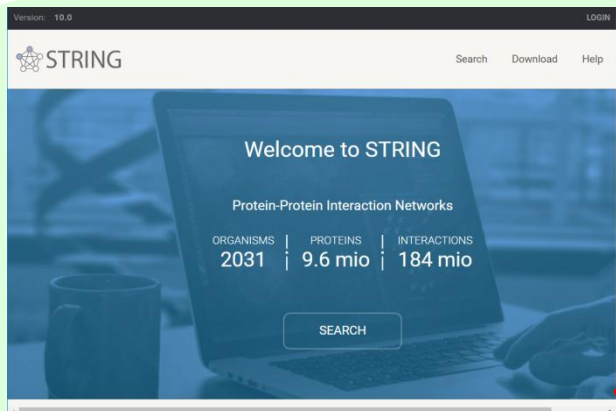
File	Description	Access
protein.sequences.v10.fa.gz (2.2 Gb)	sequences of the proteins in STRING (can be used as a blast db)	
COG.mappings.v10.txt.gz (127.6 Mb)	orthologous groups (COGs,NOGs,KOGs,...) and their proteins	
species.mappings.v10.txt.gz (19.1 Mb)	presence / absence of orthologous groups in species	
species.v10.txt (141.8 Kb)	organisms in STRING	
species.tree.v10.txt (46.5 Kb)	STRING tree of species	
protein.aliases.v10.txt.gz (636.2 Mb)	aliases for STRING proteins: locus names, accessions, descriptions...	
psicquic-mitab_2.5.v10.tar (3.4 Gb)	protein network data in PSI-MI MITAB2.5 (PSICQUIC) format	
mapping_files (download directory)	separate identifier mapping files, for several frequently used name_spaces...	

FULL DATABASE DUMPS

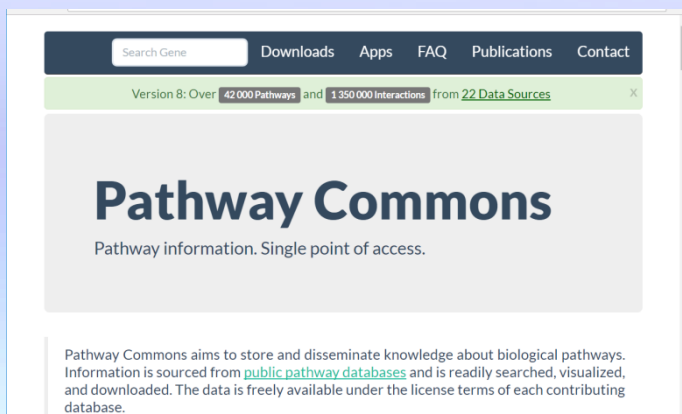
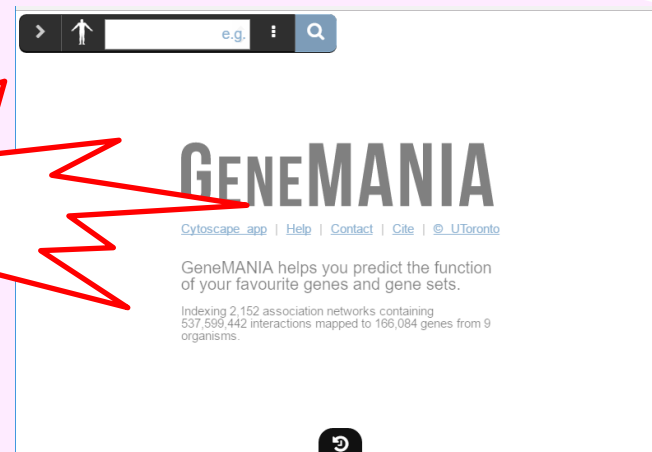
File	Description	Access
database.schema.v10.pdf (119.1 Kb)	STRING database schema	
items.schema.v10.sql.gz (4.5 Gb)	full database, part I: the players (proteins, species, COGs,...)	license required
network.schema.v10.sql.gz (21.4 Gb)	full database, part II: the networks (nodes, edges, scores,...)	license required
evidence.schema.v10.sql.gz (301.9 Gb)	full database, part III: interaction evidence (datasets, abstracts, predictions, ...)	license required
homology.schema.v10.sql.gz (459.7 Gb)	full database, part IV: homology data (all-against-all SIMAP similarity searches)	license required

Как строить сети взаимодействий между генами / белками ??

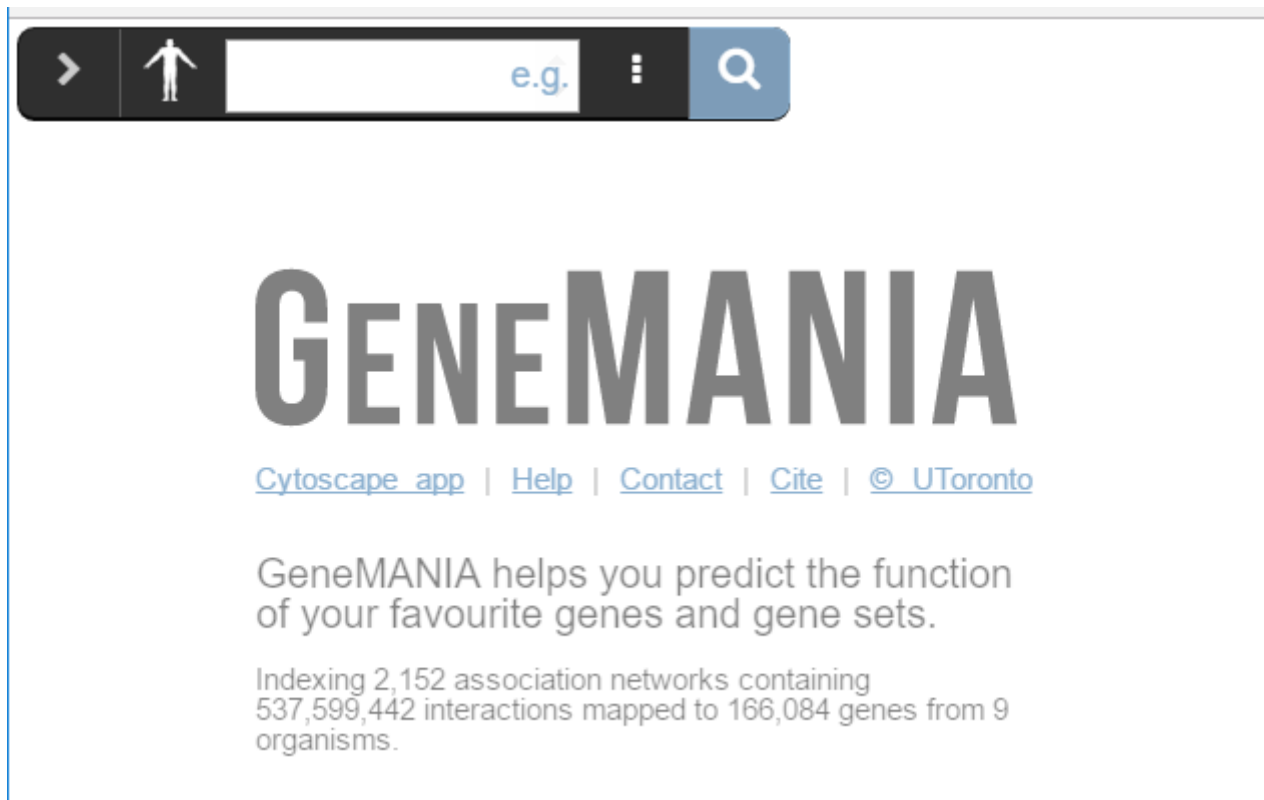
Интернет-доступные информационные компьютерные системы, позволяющие экстрагировать данные по связям различных типов между генами/белками



STRING - functional protein association networks
string-db.org/



Pathway Commons - A Resource for Biological Pathway Analysis
<http://www.pathwaycommons.org/>

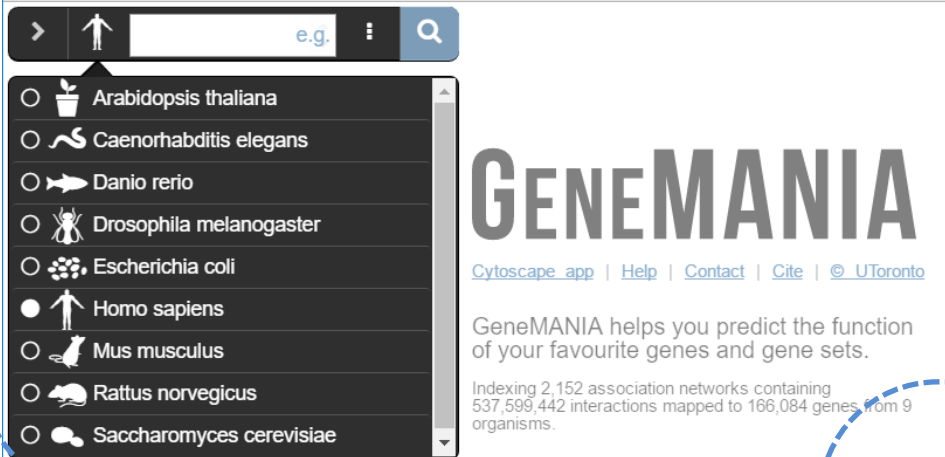


Ресурс, позволяющий определять функциональность генов и наборов генов. Имеет две реализации: Интернет-доступную, а также как плагин системы Cytoscape

GeneMania

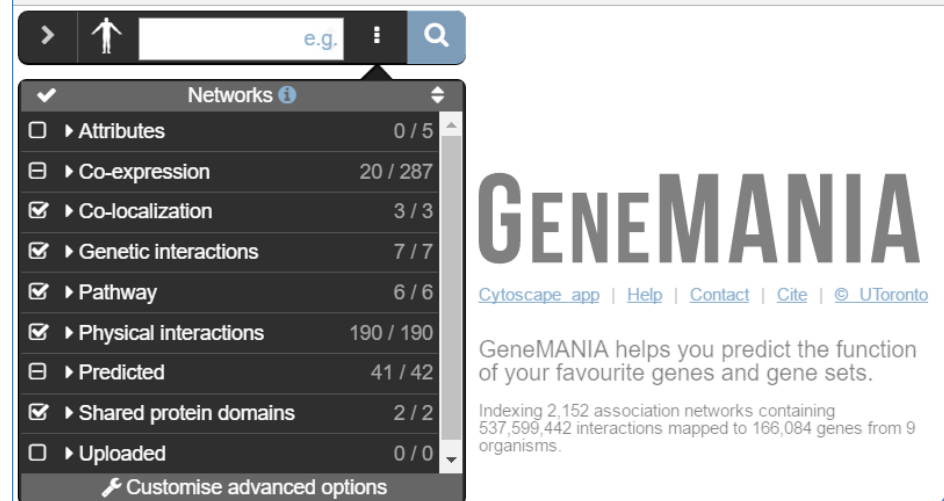
<http://genemania.org/>

Ресурс, позволяет работать с 9-ю видами организмов



The screenshot shows the top navigation bar of the GeneMania website. A search bar contains the text "e.g.". Below the search bar, a dropdown menu is open, listing nine species with their respective icons: Arabidopsis thaliana, Caenorhabditis elegans, Danio rerio, Drosophila melanogaster, Escherichia coli, Homo sapiens, Mus musculus, Rattus norvegicus, and Saccharomyces cerevisiae. The main content area features the "GENEMANIA" logo, navigation links for "Cytoscape app", "Help", "Contact", "Cite", and "© UToronto". Below the logo, a text block states: "GeneMANIA helps you predict the function of your favourite genes and gene sets. Indexing 2,152 association networks containing 537,599,442 interactions mapped to 166,084 genes from 9 organisms."

А также выбирать (комбинировать) данные различных типов:

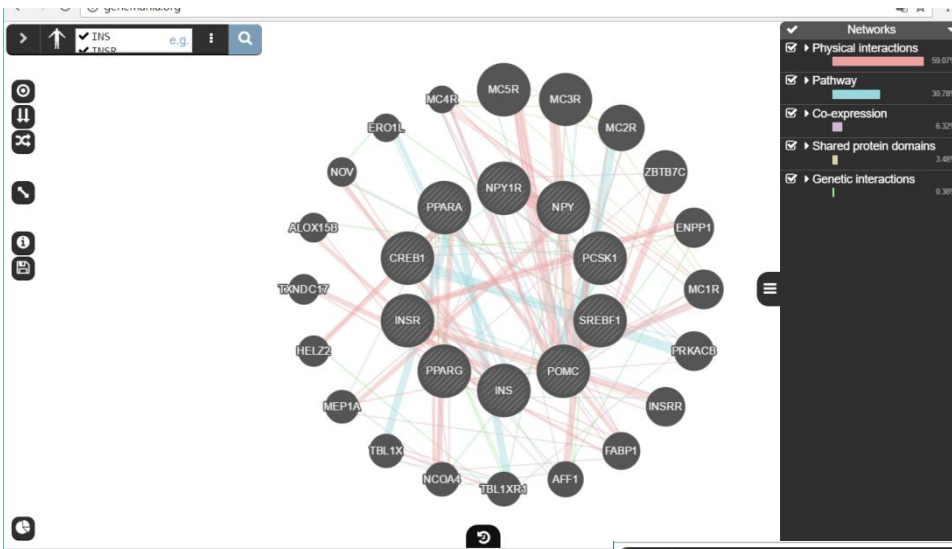


The screenshot shows the same GeneMania website interface as the previous image, but with the "Networks" dropdown menu open. The menu lists various network types with checkboxes and counts: Attributes (0 / 5), Co-expression (20 / 287), Co-localization (3 / 3), Genetic interactions (7 / 7), Pathway (6 / 6), Physical interactions (190 / 190), Predicted (41 / 42), Shared protein domains (2 / 2), and Uploaded (0 / 0). A "Customise advanced options" link is visible at the bottom of the menu. The main content area remains the same, displaying the "GENEMANIA" logo and the same introductory text as in the previous screenshot.

Результат тестового запроса к GeneMania

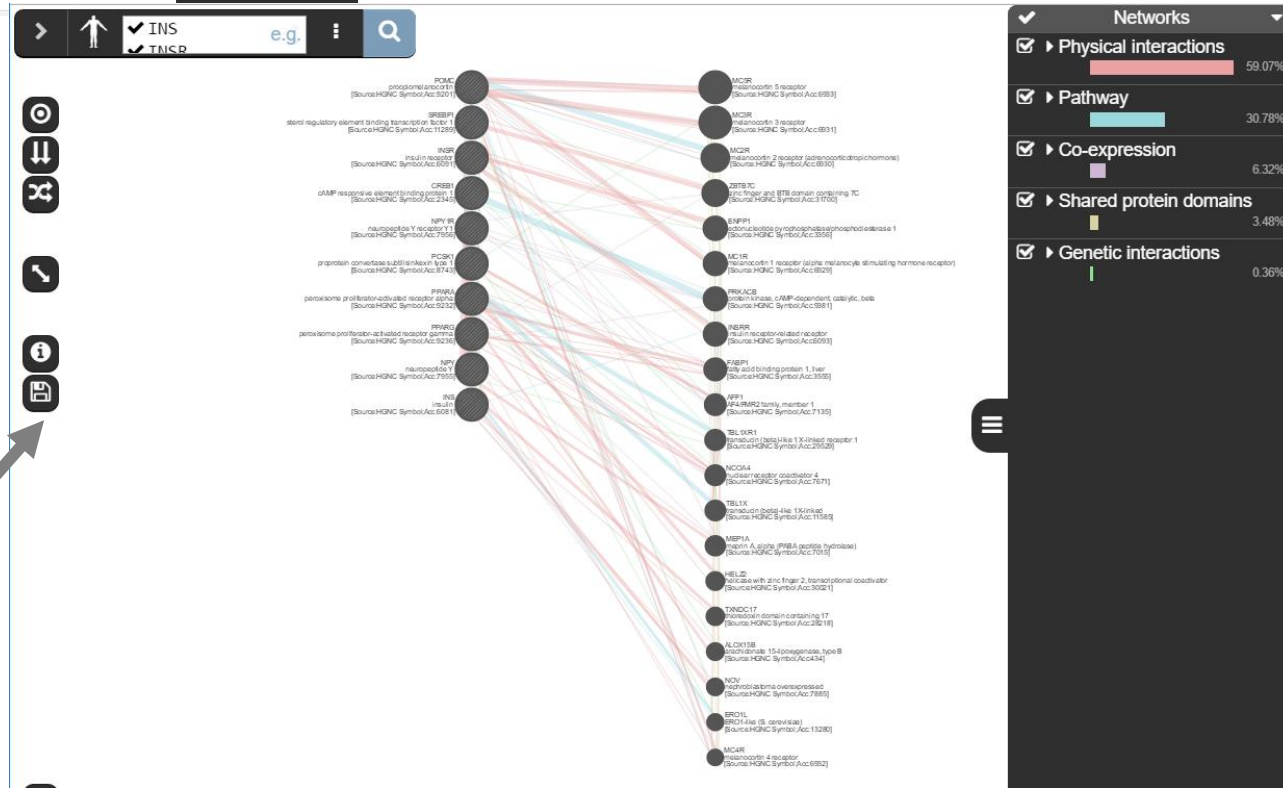
Запрос содержал 10 генов человека:
INS, INSR, POMC, SREBF1, PPARG, PPARA, NPY, NPY1R, PCSK1, CREB1

Система построила связи между 10-ю генами и дополнила список генов новыми генами, имеющими максимальное количество связей с генами из списка



Два способа представления полученного результата

Опция для сохранения данных в текстовом виде (таблица)



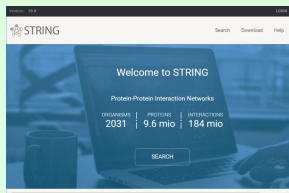
Как строить сети взаимодействий между генами / белками ??

Интернет-доступные информационные компьютерные системы, позволяющие экстрагировать данные по связям различных типов между генами/белками

STRING - functional protein

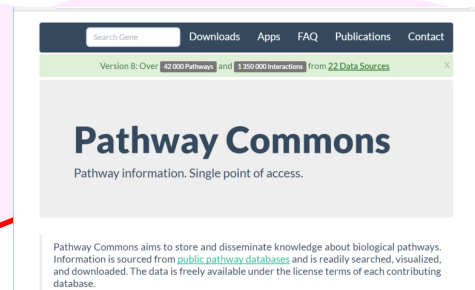
association networks

string-db.org/



GeneMANIA

<http://genemania.org/>



Pathway Commons

- A Resource for Biological Pathway Analysis

<http://www.pathwaycommons.org/>

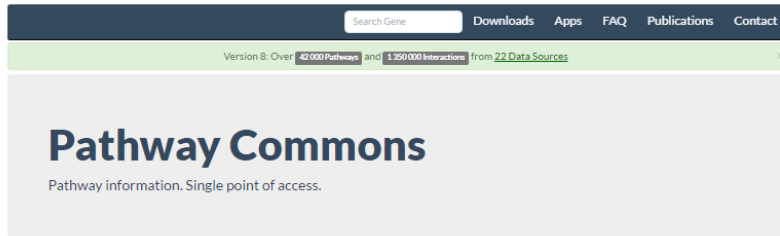


Cytoscape - Network Data
Integration, Analysis, and
Visualization in a Box

Pathway Commons

<http://www.pathwaycommons.org/>

Version 8: Over **42 000 Pathways** and **1 350 000 Interactions** from 22 Data Sources



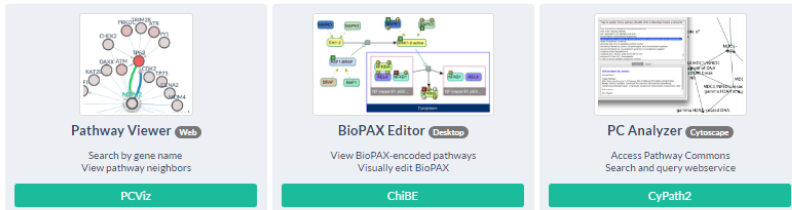
The screenshot shows the top navigation bar with a search box and links for Downloads, Apps, FAQ, Publications, and Contact. Below the navigation bar, a green banner displays the statistics: "Version 8: Over 42,000 Pathways and 1,350,000 Interactions from 22 Data Sources". The main heading "Pathway Commons" is followed by the tagline "Pathway information. Single point of access."

Pathway Commons aims to store and disseminate knowledge about biological pathways. Information is sourced from [public pathway databases](#) and is readily searched, visualized, and downloaded. The data is freely available under the license terms of each contributing database. [Pathway Commons, a web resource for biological pathway data](#). Cerami E et al. *Nucleic Acids Research* (2011).

Apps

Biologists

Visualize, Edit, and Analyze Pathways.

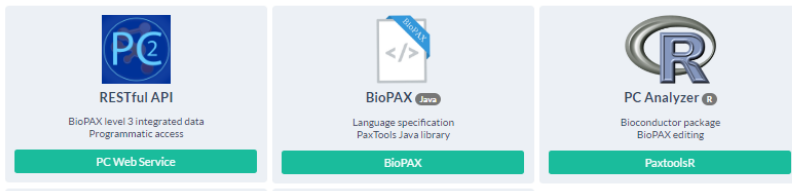


Three application cards are shown for biologists. Each card features a representative image, a title, a description, and a platform label. Below each card is a green button with the application name.

- Pathway Viewer** (Web): Search by gene name, View pathway neighbors. Platform: PCviz.
- BioPAX Editor** (Desktop): View BioPAX-encoded pathways, Visually edit BioPAX. Platform: ChIBE.
- PC Analyzer** (Cytoscape): Access Pathway Commons, Search and query webservice. Platform: CyPath2.

Computational Biologists & Software Developers

Build apps. Dig into BioPAX. Use R.



Three application cards are shown for computational biologists and software developers. Each card features a representative image, a title, a description, and a platform label. Below each card is a green button with the application name.

- RESTful API** (PC2): BioPAX level 3 integrated data, Programmatic access. Platform: PC Web Service.
- BioPAX** (Java): Language specification, PaxTools Java library. Platform: BioPAX.
- PC Analyzer** (R): Bioconductor package, BioPAX editing. Platform: PaxtoolsR.



Pathway Commons aims to store and disseminate knowledge about biological pathways. Information is sourced from public pathway databases and is readily searched, visualized, and downloaded. The data is freely available under the license terms of each contributing database.

Cerami EG1, Gross BE, Demir E, Rodchenkov I, Babur O, Anwar N, Schultz N, Bader GD, Sander C. Pathway Commons, a web resource for biological pathway data. *Nucleic Acids Res.* 2011 Jan;39(Database issue):D685-90.

Pathway Commons: источники данных (7) по сетям

Из всех ресурсов были взяты данные, относящиеся к виду *Homo sapiens*



Reactome v56 (only 'Homo sapiens.owl') 31-Mar-2016 (BIOPAX)

URI: <http://pathwaycommons.org/pc2/reactome>

All names (for data filtering): reactome

Contains: **2007** pathways, **14427** interactions, **35835** participants



NetPath 12/2011 (BIOPAX)

URI: <http://pathwaycommons.org/pc2/netpath>

All names (for data filtering): netpath

Contains: **27** pathways, **6347** interactions, **3266** participants



NCI Pathway Interaction Database: Pathway

NCI Curated Human Pathways from PID (final); 27-Jul-2015 (BIOPAX)

URI: <http://pathwaycommons.org/pc2/pid>

All names (for data filtering): pid,nci pathway interaction database: pathway

Contains: **745** pathways, **14707** interactions, **10531** participants



KEGG Pathway

KEGG 07/2011 (only human, hsa* files),
converted to BioPAX by BioModels

(<http://www.ebi.ac.uk/biomodels-main/>) team (BIOPAX)

URI: <http://pathwaycommons.org/pc2/kegg>

All names (for data filtering): kegg,kegg pathway

Contains: **122** pathways, **3566** interactions, **3355** participants



HumanCyc

HumanCyc 19.5; 27-Oct-2015;

under license from SRI International, www.biocyc.org (BIOPAX)

URI: <http://pathwaycommons.org/pc2/humancyc>

All names (for data filtering): humancyc,biocyc

Contains: **302** pathways, **7102** interactions, **5896** participants



PANTHER Pathway

PANTHER Pathways 3.4 on 18-May-2015

(auto-converted to human-only model) (BIOPAX)

URI: <http://pathwaycommons.org/pc2/panther>

All names (for data filtering): panther,panther pathway,pantherdb

Contains: **272** pathways, **4700** interactions, **6703** participants



WikiPathways

WikiPathways - Community Curated Human Pathways; 29/09/2015
(human) (BIOPAX)

URI: <http://pathwaycommons.org/pc2/wp>

All names (for data filtering): wikipathways

Contains: **333** pathways, **9758** interactions, **9584** participants

Pathway Commons : источники данных по связям и взаимодействиям в сетях

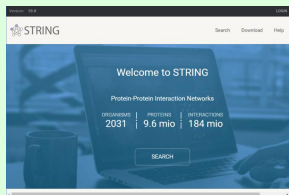
(<http://www.pathwaycommons.org/pc2/datasources>)

1. PhosphoSitePlus PhosphoSite Kinase-substrate information; 15-Mar-2016 (BIOPAX)
2. HPRD PSI-MI Release 9; 13-Apr-2010 (PSI_MI)
3. Database of Interacting Proteins DIP (human), 14-01-2016 (PSI_MI)
4. BioGRID Release 3.4.135 (human and the viruses), 24-Mar-2016 (PSI_MI)
5. IntAct (human only; 'negative' files removed), 16-Feb-2016 (PSI_MI)
6. IntAct Complex (human), 16-Feb-2016 (PSI_MI)
7. BIND (human), 15-Dec-2010 (PSI_MI)
8. CORUM (human), 17-Feb-2012 (PSI_MI)
9. Transcription Factor Target data from Collection 3 in MSigDB (originally from: TRANSFAC Public, by BIOBASE, QIAGEN); version 7.4 (BIOPAX)
10. Human miRNA-target gene relationships from MiRTarBase; v4.5, 01-NOV-2013 (converted 13-MAR-2015) (BIOPAX)
11. DrugBank v4.3 converted to BioPAX from the original XML dump (BIOPAX)
12. Recon X: Reconstruction of the Human Genome, converted from SBML; 2.03 (BIOPAX)
13. Comparative Toxicogenomics Database (human), 20150603 (BIOPAX)
14. Small Molecule Pathway Database 2.0, 07-Jul-2015 (BIOPAX)
15. INOH 4.0 (signal transduction and metabolic data), 22-MAR-2011 (BIOPAX)
16. ChEBI Ontology v138, 01-Apr-2016 (WAREHOUSE)
17. UniProtKB/Swiss-Prot (human), 16-Mar-2015 (WAREHOUSE)
18. Selected whole-source id-mapping files (to ChEBI) from UniChem (manually edited/fixed/sorted), 29-Dec-2015 (MAPPING)

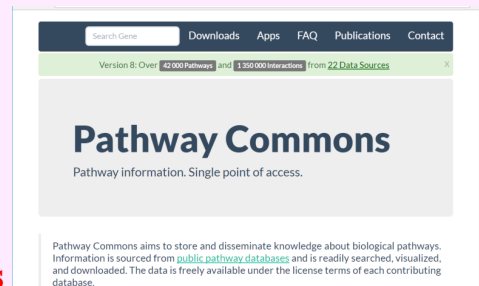
Как строить и анализировать сети взаимодействий между генами / белками ??

Интернет-доступные информационные компьютерные системы, позволяющие экстрагировать данные по связям различных типов между генами/белками

STRING - functional protein association networks
string-db.org/



GeneMANIA
<http://genemania.org/>



Pathway Commons

- A Resource for Biological Pathway Analysis

<http://www.pathwaycommons.org/>



Cytoscape - Network Data Integration, Analysis, and Visualization in a Box

Cytoscape - компьютерная система, предназначенная для визуализации сетей межмолекулярных взаимодействий (<http://www.cytoscape.org/>)



Области использования:

Биология

Социология (Social Science)

Общий комплексный сетевой анализ (General Complex Network Analysis)

Franz M1, Lopes CT1, Huck G1, Dong Y1, Sumer O1, Bader GD1 Cytoscape.js: a graph theory library for visualisation and analysis. *Bioinformatics*. 2016 Jan 15;32(2):309-11.

Lopes CT1, Franz M, Kazi F, Donaldson SL, Morris Q, Bader GD.

Cytoscape Web: an interactive web-based network browser. *Bioinformatics*. 2010 Sep 15;26(18):2347-8.

Cytoscape бесплатная компьютерная система, которую можно скачать и установить на персональном компьютере



Download Cytoscape 3.4.0

 for Windows (64 bit)

Please install **Java 8** first to use Cytoscape.
Java 6 & 7 are no longer supported

Problems? [Read this page first](#)

[Release Notes](#)

[Other Platforms](#)
[Old Versions](#)

[License Agreement](#)

Cytoscape is available as a platform-independent open-source Java application, released under the terms of the [LGPL](#).
By downloading Cytoscape, you agree that you have read the license agreement that follows and agree to its terms. If you don't agree, do not download Cytoscape.

Основные требования к компьютеру:

- **64-битная система**
- **Наличие Java 8**

Franz M1, Lopes CT1, Huck G1, Dong Y1, Sumer O1, Bader GD1 Cytoscape.js: a graph theory library for visualisation and analysis. *Bioinformatics*. 2016 Jan 15;32(2):309-11.

Lopes CT1, Franz M, Kazi F, Donaldson SL, Morris Q, Bader GD.

Cytoscape Web: an interactive web-based network browser. *Bioinformatics*. 2010 Sep 15;26(18):2347-8.

Достоинства системы *Cytoscape* (<http://www.cytoscape.org/>)



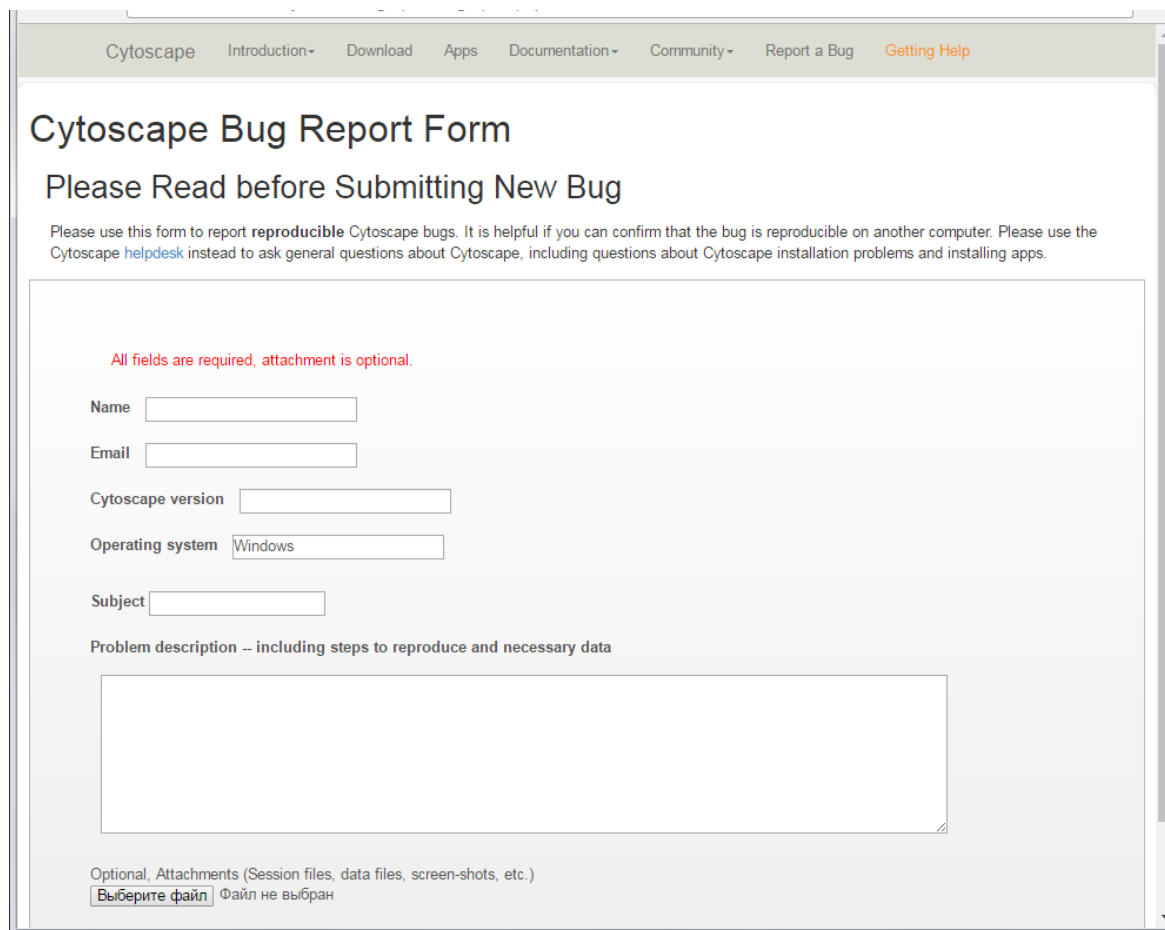
- *Cytoscape* - компьютерная программа (система), (компьютерная платформа), (пакет программ) **с открытым исходным кодом**, это позволяет компьютерным специалистам всего мира участвовать в развитии *Cytoscape*.
- Функционирует отлаженная система отслеживания ошибок.
- Большое количество возможностей для анализа, поскольку отлажен механизм добавления новых функциональных модулей программы в виде **плагинов** (**апплетов** = Apps (formerly called Plugins)).
- Каждый плагин описан в отдельной публикации в **рецензируемом журнале**.
- Одна из самых **цитируемых** программ (компьютерных систем)
- Есть возможность учитывать при визуализации дополнительные данные многих различных типов (функциональная аннотация, информация об уровне экспрессии генов и пр.)

Franz M1, Lopes CT1, Huck G1, Dong Y1, Sumer O1, Bader GD1 Cytoscape.js: a graph theory library for visualisation and analysis. *Bioinformatics*. 2016 Jan 15;32(2):309-11.

Lopes CT1, Franz M, Kazi F, Donaldson SL, Morris Q, Bader GD.

Cytoscape Web: an interactive web-based network browser. *Bioinformatics*. 2010 Sep 15;26(18):2347-8.

Cytoscape – функционирует отлаженная система отслеживания ошибок (багов) программы http://chianti.ucsd.edu/cyto_web/bugreport/bugreport.php



The image shows a web browser window displaying the Cytoscape Bug Report Form. The browser's address bar shows the URL http://chianti.ucsd.edu/cyto_web/bugreport/bugreport.php. The page has a navigation menu with links for Cytoscape, Introduction, Download, Apps, Documentation, Community, Report a Bug, and Getting Help. The main heading is "Cytoscape Bug Report Form" followed by "Please Read before Submitting New Bug". A paragraph of instructions explains that the form is for reporting reproducible bugs and that users should use the helpdesk for general questions. The form itself contains several input fields: Name, Email, Cytoscape version, Operating system (with "Windows" selected), and Subject. Below these is a large text area for the problem description. At the bottom, there is an optional attachment section with a file selection button labeled "Выберите файл" and the text "Файл не выбран".

Cytoscape Introduction Download Apps Documentation Community Report a Bug Getting Help

Cytoscape Bug Report Form

Please Read before Submitting New Bug

Please use this form to report **reproducible** Cytoscape bugs. It is helpful if you can confirm that the bug is reproducible on another computer. Please use the Cytoscape [helpdesk](#) instead to ask general questions about Cytoscape, including questions about Cytoscape installation problems and installing apps.

All fields are required, attachment is optional.

Name

Email

Cytoscape version

Operating system

Subject

Problem description -- including steps to reproduce and necessary data

Optional, Attachments (Session files, data files, screen-shots, etc.)

Файл не выбран

Cytoscape App Store – сайт, интегрирующий все плагины (апплеты)

<http://apps.cytoscape.org/>

Тематический
каталог
плагинов



The screenshot displays the Cytoscape App Store interface. At the top, there is a navigation bar with the Cytoscape logo, the text 'Cytoscape App Store', and links for 'Submit an App', 'Search the App Store', and 'Sign In'. The main content area is divided into several sections:

- Categories:** A vertical list of categories on the left side, including 'collections', 'data visualization', 'network generation', 'graph analysis', 'online data import', 'network analysis', 'clustering', 'integrated analysis', 'utility', 'enrichment analysis', 'data integration', 'systems biology', 'layout', 'visualization', 'ontology analysis', 'network comparison', 'local data import', 'pathway database', 'import', and 'core app'. A red arrow points from the external text to this section.
- Newest Releases:** A section titled 'Newest Releases' with a 'Get Started with the App Store' button. It features a grid of app cards, each with an icon, name, description, and a '3.0+' rating badge. The apps shown are Rene, EClizer, CytoMCS, ClueGO, CluePedia, and PCM.
- Top Downloaded Apps:** A section titled 'Top Downloaded Apps' showing a grid of app cards. The apps shown are ClueGO, BiNGO, GeneMANIA (highlighted with a red dashed border), CluePedia, AgilentLiteratureSearch, and MCODE.

Плагины Cytoscape получают путевку в жизнь в форме публикации в рецензируемом журнале.

NCBI Resources How To Sign in to NCBI

PubMed (Cytoscape[Title]) AND (plugin[Title] OR App[Title] OR applic[Title]) Search

Format: Summary Sort by: Most Recent Per page: 20

Filters: Manage Filters

Send to Find related data Database: Select

Search results
Items: 1 to 20 of 78

1. [A Cytoscape app for motif enumeration with ISMAGS.](#)
Van Parys T, Melckenbeeck I, Houbraken M, Audenaert P, Pickavet M, Demeester P, Van de Peer Y. *Bioinformatics*. 2017 Feb 1;33(3):461-463. doi: 10.1093/bioinformatics/btw626. No abstract available. PMID: 28158465 [Similar articles](#)

2. [MORO: a Cytoscape app for relationship analysis between modularity and robustness in large-scale biological networks](#)
Truong CD, Tran TD, Kwon YK. *BMC Syst Biol*. 2016 Dec 23;10(Suppl 4):122. doi: 10.1186/s12918-016-122-3. PMID: 28155725 **Free PMC Article** [Similar articles](#)

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The Author(s) *BMC Bioinformatics* 2017, **18**(Suppl 1):28
DOI 10.1186/s12859-016-1427-5

BMC Bioinformatics

RESEARCH Open Access

Orthoscape: a cytoscape application for grouping and visualization KEGG based gene networks by taxonomy and homology principles

Zakhar Sergeevich Mustafin^{1†}, Sergey Alexandrovich Lashin^{1,2†}, Yury Georgievich Matushkin¹, Konstantin Vladimirovich Gunbin¹ and Dmitry Arkadievich Afonnikov^{1,2}

From The International Conference on Bioinformatics of Genome Regulation and Structure (Systems Biology (BGRS/SB-2016) Novosibirsk, Russia. 29 August-2 September 2016

Abstract

Background: There are many available software tools for visualization and analysis of biological networks. Among them, Cytoscape (<http://cytoscape.org/>) is one of the most comprehensive packages, with many plugins and applications which extends its functionality by providing analysis of protein-protein interaction, gene regulatory and gene co-expression networks, metabolic, signaling, neural as well as ecological-type networks including food webs, communities networks etc. Nevertheless, only three plugins tagged 'network evolution' found in Cytoscape official app store and in literature. We have developed a new Cytoscape 3.0 application Orthoscape aimed to facilitate evolutionary analysis of gene networks and visualize the results.

Results: Orthoscape aids in analysis of evolutionary information available for gene sets and networks by highlighting: (1) the orthology relationships between genes; (2) the evolutionary origin of gene network components; (3) the evolutionary pressure mode (diversifying or stabilizing, negative or positive selection) of orthologous groups in general and/or branch-oriented mode. The distinctive feature of Orthoscape is the ability to control all data analysis steps via

Возможности Cytoscape



В области молекулярной биологии, системной биологии, геномики и протеомики:
Принимать (загружать) данные о молекулярным и генетическим взаимодействиям в стандартных форматах:

Simple interaction file (SIF or .sif format)

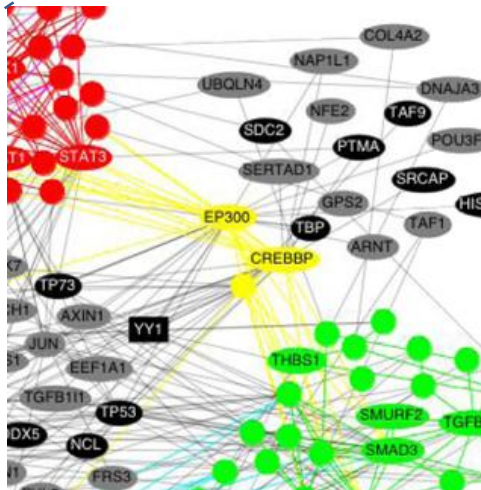
Nested network format (NNF or .nnf format)

Graph Markup Language (GML or .gml format)

XGMML (extensible graph markup and modelling language).





SBML, BioPAX, PSI-MI Level 1 and 2.5, GraphML, Delimited text, Excel Workbook (.xls, .xlsx)

Интегрировать данные о взаимодействиях с функциональной аннотацией объектов и связей



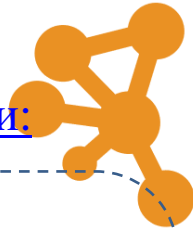
Условные обозначения

Толщина линии соответствует уровню достоверности белок-белкового взаимодействия

-  Jak/STAT
-  Jak/STAT and TGFb
-  TGFb
-  Белок вируса HCV

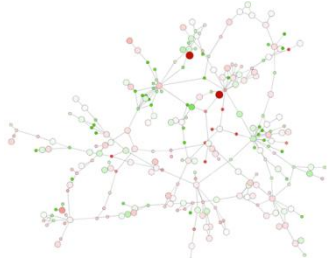
Фрагмент диаграммы, отображающей белок-белковые взаимодействия между белками вируса гепатита С и белками человека

Возможности Cytoscape (продолжение)

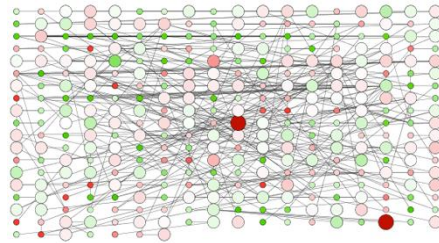


В области молекулярной биологии, системной биологии, геномики и протеомики;

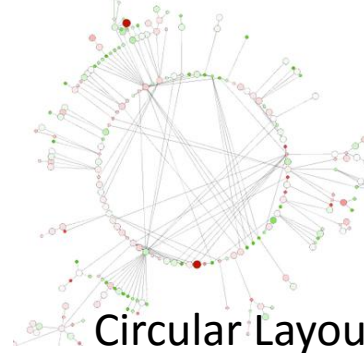
Визуализация информации в различных режимах



Organic Layout



Grid Layout

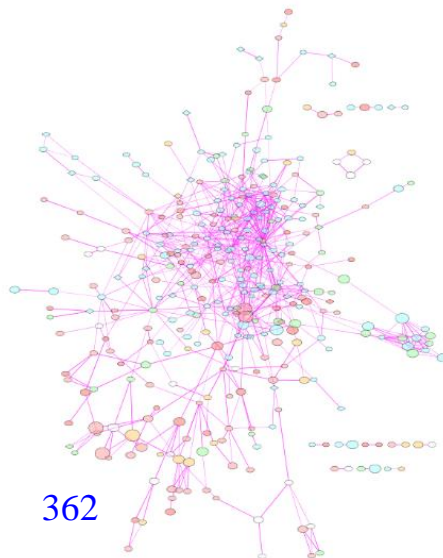


Circular Layout



GroupAttributesLayout

Анализировать и моделировать на основе плагинов



Число вершин 362



Кластеризация
с помощью
программы
MCODE
(плагин Cytoscape)

Rank	Cluster	Details
1		Score: 8,222 Nodes: 10 Edges: 37
2		Score: 3,333 Nodes: 4 Edges: 5
3		Score: 3,333 Nodes: 4 Edges: 5
4		Score: 3 Nodes: 3 Edges: 3
5		Score: 3 Nodes: 3 Edges: 3
6		Score: 3 Nodes: 3 Edges: 3
7		Score: 2,889 Nodes: 10 Edges: 13
		Score: 2,778 Nodes: 19

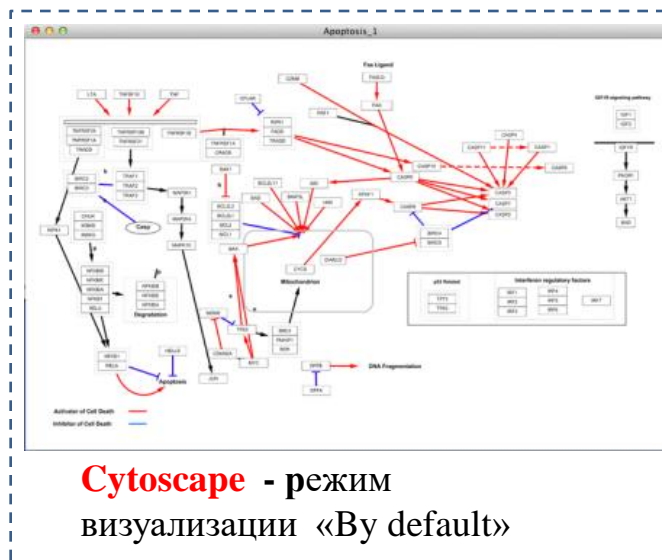
Возможности Cytoscape (продолжение)



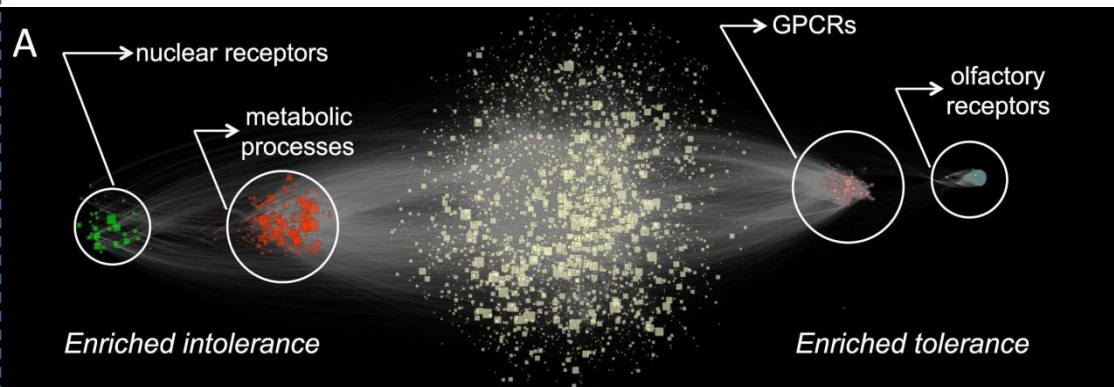
В области молекулярной биологии, системной биологии, геномики и протеомики:

Визуализировать и анализировать данные о генных сетях человека (таких как WikiPathways, Reactome, KEGG).

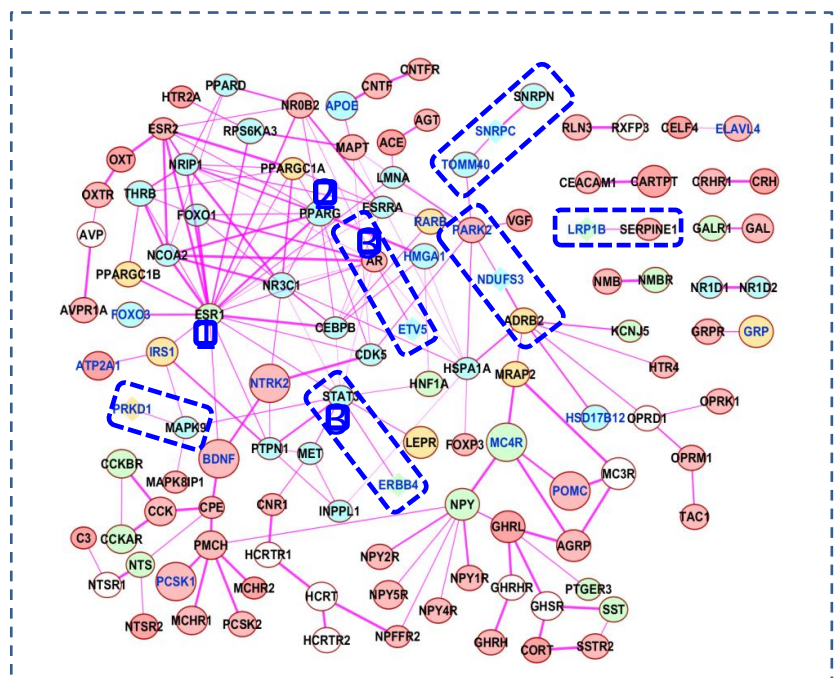
Диаграмма
Апоптозис из
WikiPathways



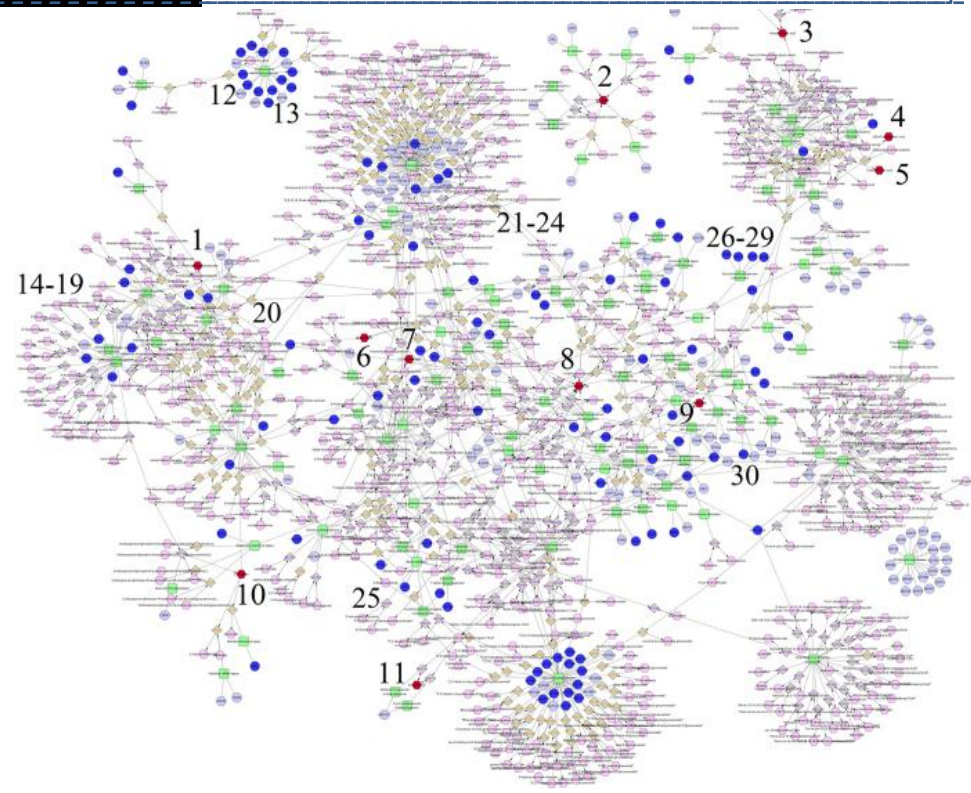
Примеры визуализации данных с помощью Cytoscape



Rackham OJ, Shihab HA, Johnson MR, Petretto E. EvoTol: a protein-sequence based evolutionary intolerance framework for disease-gene prioritization. *Nucleic Acids Res.* 2015;43(5):e33.



Ignatieva EV, Afonnikov DA, Saik OV, Rogaev EI, Kolchanov NA. A compendium of human genes regulating feeding behavior and body weight, its functional characterization and identification of GWAS genes involved in brain-specific PPI network. *BMC Genet.* 2016;17(Suppl 3):158.



A Comprehensive Analysis of Metabolomics and Transcriptomics in Cervical Cancer. Yang et al, *Sci Rep.* 2017; 7: 43353

Возможности Cytoscape (продолжение)



Общий комплексный сетевой анализ

- Может применяться в любых отраслях знаний, где используется сетевое представление данных.
- Подсчет статистики по различным характеристикам сетей
- Поиск кратчайшего пути между вершинами
- Выявление кластеров с использованием нескольких алгоритмов
- Может быть использован совместно с другими популярными программами для анализа графов (igraph, Pajek, or GraphViz)

Часть 2.

Представление генных сетей
в базах данных.

Как построить генную сеть ?



1 Эксперт-биолог строит сеть на основе анализа научных публикаций

2 Экспериментально-теоретический подход: эксперимент на основе ОМИКСНЫХ ТЕХНОЛОГИЙ + теоретический анализ

Эксперимент по ДНК-аза I футпринтингу в 41 типе клеток человека + компьютерное предсказание 475 типов ССТФ

Сети регуляторных транскрипционных взаимодействий для 41 типов клеток человека



Neph S., et al., Cell, 2012, 1, 1274–1286

3 Теоретический подход: экстракция данных из Интернет-ресурсов, интеграция, анализ

Данные баз данных OMIM, PubMed, Human Protein Atlas, ресурсов STRING, GeneMANIA, TSEA + анализ системой Cytoscape

Специфичная для мозга сеть белок-белковых взаимодействий, между продуктами генов, участвующих в регуляции массы тела человека



Ignatieva EV, Afonnikov DA, Saik OV, Rogaev EI, Kolchanov NA.. BMC Genet. 2016;17(S3):158.

Информационные источники для реконструкции генной сети

Информация об объектах генной сети:

Гены

EntrezGene
Ensembl
GeneCards

Белки

UniProtKB
PDB
NCBI Protein

миРНК

miRBase
miRDB
miRTarBase

Метаболиты

ChEBI HMDB
KEGG COMPOUND
KEGG DRUG

Межмолекулярные взаимодействия

Тр.фактор->ген

TRRUST TRRD
GTRD
The Interactome

миРНК->ген

miRTarBase
miRBase

Белок-белковые

BioGRID
GeneMANIA
STRING

Публикации из PubMed

Данные, полученные на основе омиксных технологий

Генные сети и пути регуляции сложных биологических процессов

Функциональные модули генной сети

Метаболические пути

MetaCyc

KEGG Pathway
PANTHER Pathway
BioCarta
SMPDB
ConsensusPathDB
Reactome
NDEx

Пути передачи сигналов

NetPath
Spike
InnateDB
WikiPathways
SIGNOR

ANDSystem

GeneNet



Список генов, метаболических процессов, путей сигнальной трансдукции и т.п.



Новая генная сеть

Информационные ресурсы, полезные для реконструкции сетей могут содержать:

- Характеристики объектов, являющихся компонентами генной сети (гены, белки, мРНК, миРНК, метаболиты и т.д.) (*EntrezGene, UniProtKB, miRBase, KEGG COMPOUND*)
- Данные о взаимодействиях между объектами в генной сети (регуляторные (ТФ->ген мишень - *The Interactome*), белок-белковые (*BioGRID*), РНК-белковые, влияние низкомолекулярных соединений на активность белков)
- Данные о структурных модулях генной сети (метаболические пути, сигнальные пути - *KEGG Pathway, Reactome, WikiPathways*)
- Диаграммы генных сетей (*WikiPathways, GeneNet*)

Сведения о базах данных по метаболическим и сигнальным на Вэб-сайте журнала NAR (http://www.oxfordjournals.org/nar/database/c/)

NAR Database Summary Paper

[Nucleotide Sequence Databases](#)
[RNA sequence databases](#)
[Protein sequence databases](#)
[Structure Databases](#)
[Genomics Databases \(non-vertebrate\)](#)
[Metabolic and Signaling Pathways](#)

[ChemProt](#)

[Enzymes and enzyme nomenclature](#)

[Metabolic pathways](#)

[BiGG Models](#)

[BioCarta Pathways](#)

[BioCyc](#)

[Bionemo](#)

[BioSilico](#)

[CeCaFDB](#)

[ClusterMine360](#)

[EAWAG-BBD](#)

[ECMDB](#)

[HMDB - The Human Metabolome Database](#)

[iPAVS](#)

[KaPPA-View](#)

[KEGG - Kyoto Encyclopedia of Genes and Genomes](#)

[KEGG LIGAND Database](#)

[LAMP](#)

[MedicCyc](#)

[MetaboLights](#)

[Metabolomics Workbench](#)

[MetaCrop](#)

[MetaCyc](#)

[MMCD](#)

[MMMDB](#)

[MNXref/MetaNetX](#)

[MODOMICS](#)

[Pathguide](#)

[Pathway Commons](#)

[PMAP](#)

[Reactome](#)

[Rhea](#)

[RNApathwaysDB](#)

[SMPDB](#)

[SYSTEMONAS](#)

[UniPathway](#)

[WholeCellKB - Model Organism Databases for Comprehensive Whole-Cell Models](#)

[WikiPathways](#)

[YMDB](#)

[Protein-protein interactions](#)

[Signalling pathways](#)

[Human and other Vertebrate Genomes](#)

[Human Genes and Diseases](#)

- ▶ [Compilation Paper](#)
- ▶ [Category List](#)
- ▶ [Alphabetical List](#)
- ▶ [Category/Paper List](#)
- ▶ [Search Summary Paper](#)

NAR Database Summary Paper

[Nucleotide Sequence Databases](#)
[RNA sequence databases](#)
[Protein sequence databases](#)
[Structure Databases](#)
[Genomics Databases \(non-vertebrate\)](#)
[Metabolic and Signaling Pathways](#)

[ChemProt](#)

[Enzymes and enzyme nomenclature](#)

[Metabolic pathways](#)

[Protein-protein interactions](#)

[Signalling pathways](#)

[AgingChart](#)

[CGDB](#)

[CR Cistrome](#)

[KBDock](#)

[NetworkKIN](#)

[P2CS](#)

[pathDIP](#)

[PepCyber: P~Pep](#)

[PhosPhAt](#)

[PID](#)

[PRRDB](#)

[Quorumpeps](#)

[RegPhos](#)

[REPAIRtoire](#)

[SigMol](#)

[SIGNOR](#)

[SPIKE](#)

[UCSD-Nature Signaling Gateway Molecule Pages](#)

[XTalkDB](#)

[Human and other Vertebrate Genomes](#)

[Human Genes and Diseases](#)

[Microarray Data and other Gene Expression Databases](#)

[Proteomics Resources](#)

[Other Molecular Biology Databases](#)

[Organelle databases](#)

[Plant databases](#)

[Immunological databases](#)

[Cell biology](#)

- ▶ [Compilation Paper](#)
- ▶ [Category List](#)
- ▶ [Alphabetical List](#)
- ▶ [Category/Paper List](#)
- ▶ [Search Summary Papers](#)

Характеристика информационных ресурсов, полезных для реконструкции сетей

Игнатъева Е.В., Афонников Д.А., Колчанов Н.А.
Интернет-доступные информационные ресурсы по
геномным сетям, включающие данные по человеку и
животным. Вавиловский журнал генетики и
селекции. 2017; 21(8):895-902

http://www.bionet.nsc.ru/vogis/download/06_Ignatjeva.pdf

27 информационных ресурсов.

- 1) типы накопленной информации;
- 2) способы представления информации;
- 3) способы наполнения баз данных;
- 4) основные источники информации;
- 5) про-граммные средства, позволяющие осуществлять поиск и анализ данных

Информационное содержание баз в 2017 г.
описано в ПРИЛОЖЕНИИ

<http://www.bionet.nsc.ru/vogis/download/pict-2017-21/appx13.pdf>

Таблица 1. Интернет-доступные базы данных по геномным сетям, метаболическим и сигнальным путям, путям регуляции других биологических процессов и молекулярно-генетическим взаимодействиям (представлены в алфавитном порядке)

Название базы	Способ наполнения или источник данных	Тип данных	Ссылка
ANDSystem	БД, ААТ	ББВ, РВ, коэкспрессия, участие белков в биологических процессах по данным UniProt-GOA, использование вещества для лечения заболевания, ассоциации «ген-заболевание»	http://www.bionet.sccc.ru/andvisio/
BiGG Models	P	МП	http://bigg.ucsd.edu/
BioCarta	P	МП, ППС, ПРБП, заболевания	https://cgap.nci.nih.gov/Pathways/BioCarta_Pathways
BioCyc	P, БД, КП	МП	https://biocyc.org/
BioGRID	P	ББВ, ГВ	https://thebiogrid.org/
ConsensusPathDB	P, БД	МП, ППС, ПРБП, ББВ, РВ, ГВ	http://cpdb.molgen.mpg.de/
GeneMANIA	ААТ, БД, КП	ББВ, ГВ, коэкспрессия, связи между генами/белками, предсказанные компьютерными методами	http://genemania.org/
GeneNet	P	Структурно-функциональная организация ГС, ППС, МП	http://www.mgs.bionet.nsc.ru/mgs/gnw/genenet/
GTRD	КАОД	ДНК-белковые взаимодействия	http://gtrd.biouml.org
InnateDB	P, БД	ППС	http://www.innatedb.ca/
The Interactome	КАОД	Тканеспецифические СТР	http://www.regulatorynetworks.org/
KEGG PATHWAY	P	МП, ППС, ПРБП, заболевания, лекарства	http://www.genome.ad.jp/kegg
miRBase	КАОД, КП, P	РВ	http://www.mirbase.org/
MetaCyc	P	МП	http://metacyc.org/
NDEX	БД, P	МП, ППС, ПРБП, ББВ, РВ	http://www.ndexbio.org/#/
NetPath	P	ППС человека	http://www.netpath.org/
PANTHER Pathway	P, БД	МП, ППС	http://pantherdb.org/
Pathway Commons	БД	ББВ, РВ	http://www.pathwaycommons.org/
Reactome	P	МП, ППС, пути транспорта молекул в клетке и репликации ДНК	http://www.reactome.org/
SIGNOR	P	ППС и регуляторные взаимодействия между их участниками, ПРБП, заболевания	http://signor.uniroma2.it/
SMPDB	P	МП, ППС, ПРБП, заболевания	http://smpdb.ca/
SPIKE	P, БД	ППС человека	http://www.cs.tau.ac.il/~spike/
STRING	P, ААТ, БД, КП	ББВ, коэкспрессия, связи между генами/белками, предсказанные компьютерными методами	string-db.org/
TRED	P, БД, КП	СТР, РВ	http://rulai.csh.edu/TRED
TRRD	P	РВ, ДНК-белковые взаимодействия	http://www.mgs.bionet.nsc.ru/mgs/gnw/trrd/
TRRUST	ААТ, P	СТР, РВ	http://www.grnpedia.org/trrust
WikiPathways	P	МП, ППС, ПРБП, заболевания	https://www.wikipathways.org/index.php/WikiPathways

Примечание. Способы наполнения: P – ручное аннотирование научных публикаций; ААТ – автоматический анализ текстов; БД – импорт из других баз данных; КП – компьютерные предсказания; КАОД – компьютерный анализ данных, полученных высокоскоростными экспериментальными методами. Типы данных: ББВ – белок-белковые взаимодействия; ГВ – генетические взаимодействия; МП – метаболические пути; ППС – пути передачи сигналов; ПРБП – пути регуляции биологических процессов на клеточном и организменном уровне; РВ – регуляторные взаимодействия (транскрипционный фактор – регулируемый ген либо миРНК – регулируемый ген); СТР – сети транскрипционной регуляции. Более подробное описание баз данных со ссылками на наиболее свежие публикации представлено в Приложении 2.

В лекции № 4 будет дана характеристика баз данных по генным сетям, а также по метаболическим и сигнальным путям:

1) GeneNet – ИЦиГ СО РАН , г.Новосибирск
<http://www.mgs.bionet.nsc.ru/mgs/gnw/genenet/>

2) KEGG Kyoto encyclopedia of genes and genomes:
integrated suite of databases on genes, proteins, and metabolic pathways
<http://www.genome.ad.jp/kegg>

3) MetaCyc Metabolic Database <http://metacyc.org/>
+ BioCyc (Database Collection) <https://biocyc.org/>

4) Reactome <http://www.reactome.org/>

5) WikiPathways <http://www.wikipathways.org/index.php/WikiPathways>

7) Signor <http://signor.uniroma2.it/>

8) SPIKE <http://www.cs.tau.ac.il/~spike/>

8) BioCarta https://cgap.nci.nih.gov/Pathways/BioCarta_Pathways

GeneNet: публикация в Nucleic Acids Research 2005

*Nucleic Acids Research, 2005, Vol. 33, Database issue D425–D427
doi:10.1093/nar/gki077*

GeneNet in 2005

**E. A. Ananko*, N. L. Podkolodny, I. L. Stepanenko, O. A. Podkolodnaya,
D. A. Rasskazov, D. S. Miginsky, V. A. Likhoshvai, A. V. Ratushny,
N. N. Podkolodnaya and N. A. Kolchanov**

Institute of Cytology and Genetics, Siberian Branch of the Russian Academy of Sciences,
Lavrentiev Avenue 10, Novosibirsk 630090, Russia

Received September 15, 2004; Revised and Accepted October 8, 2004

ABSTRACT

The GeneNet system is designed for collection and analysis of the data on gene and metabolic networks

of the manifold data on the expression and changes in the concentration of macromolecular interactions, enzymatic

GeneNet in 2005

**E. A. Ananko*, N. L. Podkolodny, I. L. Stepanenko, O. A. Podkolodnaya,
D. A. Rasskazov, D. S. Miginsky, V. A. Likhoshvai, A. V. Ratushny,
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Received September 15, 2004; Revised and Accepted October 8, 2004

ABSTRACT

The GeneNet system is designed for collection and analysis of the data on gene and metabolic networks, signal transduction pathways and kinetic characteristics of elementary processes. In the past 2 years, the GeneNet structure was considerably improved: (i) the current version of the database is now implemented using ORACLE®; (ii) the capacities to describe the structure of the protein complexes and the interactions between the units are increased; (iii) two tables with kinetic constants and more detailed descriptions of certain reactions were added; and (iv) a module for kinetic modelling was supplemented. The current SRS release of the GeneNet database contains 37 graphical maps of gene networks, as well as descriptions of 1766 proteins, 1008 genes, 241 small molecules and 2524 relationships between gene network units, and 552 kinetic constants. Information distributed between 16 inter-linked tables was obtained by annotating 1900 journal publications. SRS release of the GeneNet database, the graphical viewer and the modelling section are available at <http://www.mgsa-bionet.nsc.ru/mgsa/gw/genenet/>.

INTRODUCTION

Systematic arrangement and analysis of a variety of data subjects present a challenge. The GeneNet system (1) was developed to respond to the challenge. The widely available specialised databases, such as KEGG (2), BioCarta (<http://www.biocarta.com/index.asp>), BIND (3), TRANSPATH (4) and MetaCyc (5), among others, are concerned with metabolic or signal transduction pathways. The GeneNet workbench is more versatile, enabling the description of functions and regulation of complicated biological systems on the basis

*Nucleic Acids Research, 2005, Vol. 33, Database issue D425–D427
doi:10.1093/nar/gki077*

of the manifold data on the expression regulation of genes and changes in the concentration of their products, the macromolecular interactions, enzymatic reactions, the effects of external agents, signal transduction pathways, to name a few. The GeneNet diagrams represent mainly the structural-functional organization of the gene network (1) that controls particular processes in eukaryotes (6). The GeneNet's task is not to give a detailed description of protein-protein interactions or of the gene or protein structure; all this is available from the other established databases. The intention is to describe, in more detail, the relationships between the gene network units and regulatory influences on the relationships (7). The information from the GeneNet database is further used in the developing of kinetic computer models of various biological processes (8).

GeneNet MODULES

The GeneNet system consists of the following functional modules:

- (i) a database that compiles information on the structural and functional organization of the gene and metabolic networks, their elementary units (proteins, genes, RNAs, small molecules, etc.) and elementary interactions between the units (1);
- (ii) a graphical viewer that allows display of the structure of the gene network and interactions of its units as a two-dimensional graph;
- (iii) a section of computer modeling of gene networks;
- (iv) software for analysis of the graph structure of gene network and its functional characteristics (9);
- (v) a graphical editor enabling the construction of new diagrams and to modify the existing ones, to add new information to the database.

It should be noted that the user can request the software for analysis and the graphical editor in the GeneNet licensed version only. For this reason, the descriptions of these tools are omitted here. Furthermore, the licensed GeneNet version

*To whom correspondence should be addressed. Tel: +7 382 331319; Fax: +7 382 331279; Email: ananko@ngs.nsc.ru

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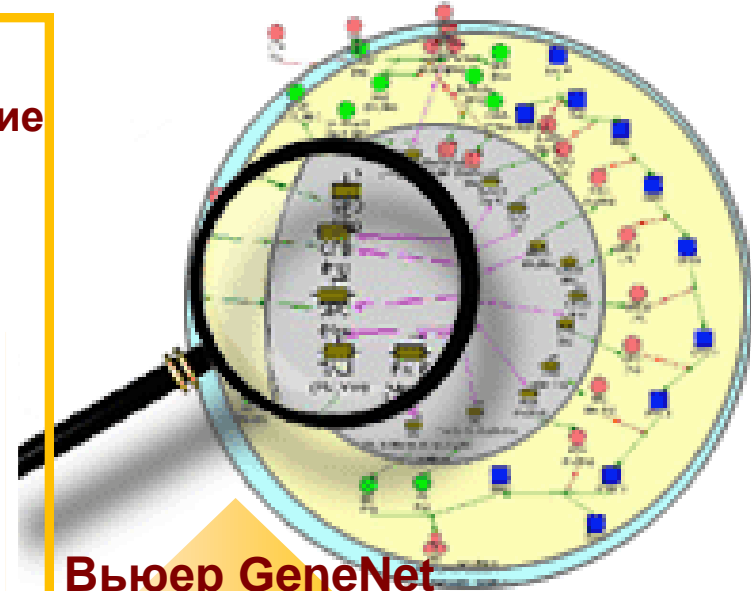
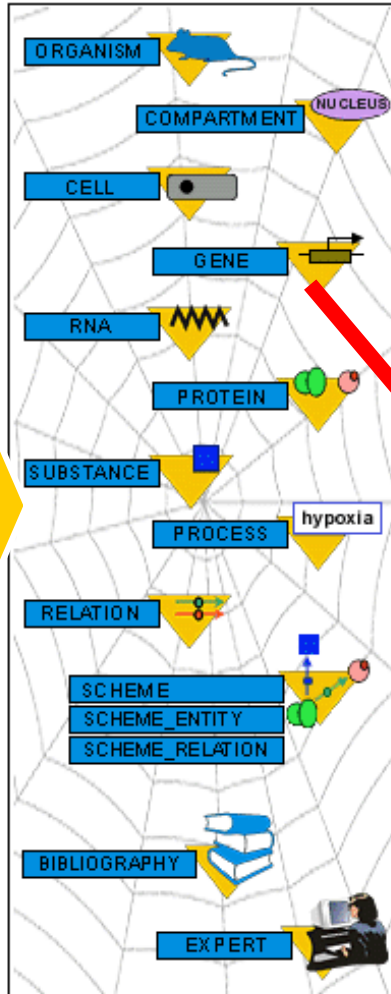
Технология GeneNet: основные модули, которыми пользуются разработчики базы

Статьи из журналов с описанием экспериментов

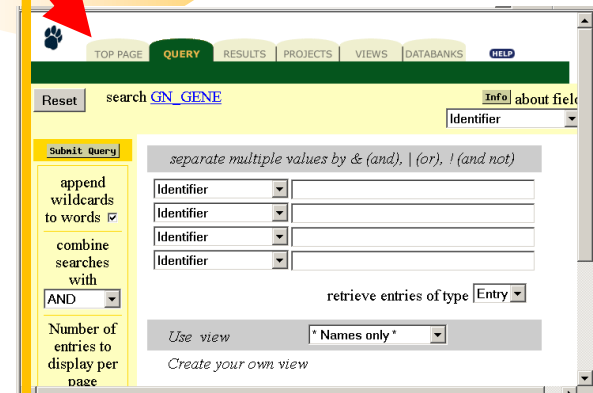


Графический редактор GeneEd для внесения **НОВОЙ** информации

База данных (текстовое описание объектов, связей, диаграмм)



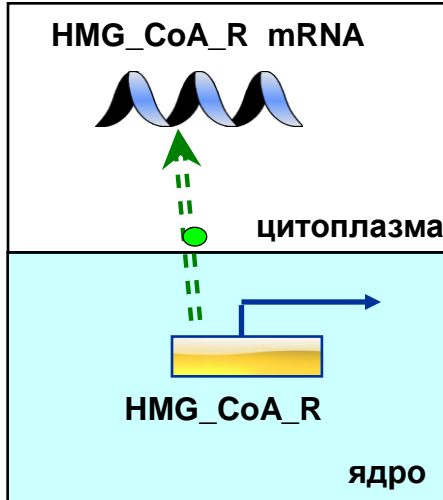
Вьюер GeneNet = редактор GeneEd, у которого отключена опция редактирования



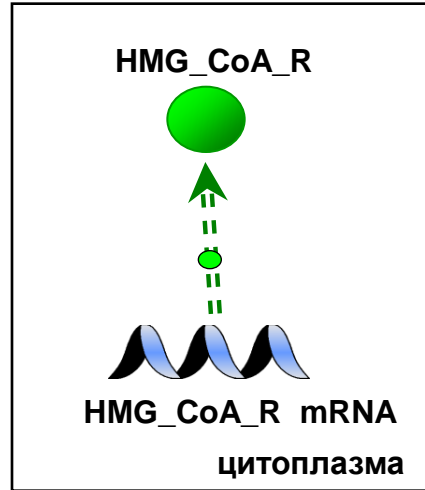
Доступ к информации через поисковую систему SRS

GeneNet: примеры графического изображения элементарных процессов (повторение)

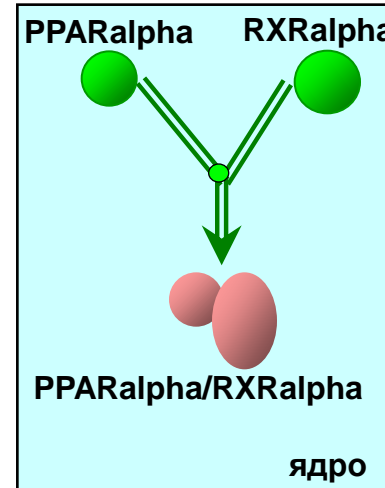
Транскрипция



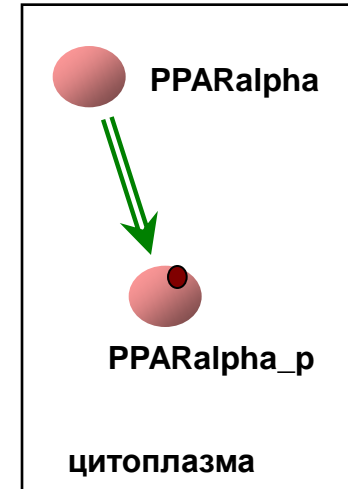
Трансляция



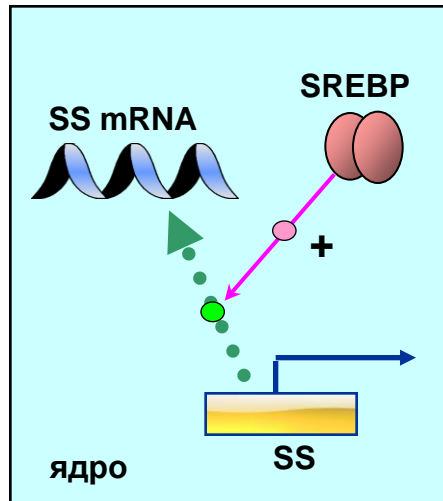
Мультимеризация белка



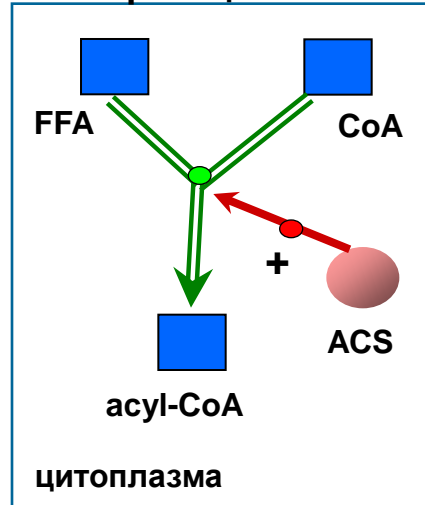
Фосфорилирование белка



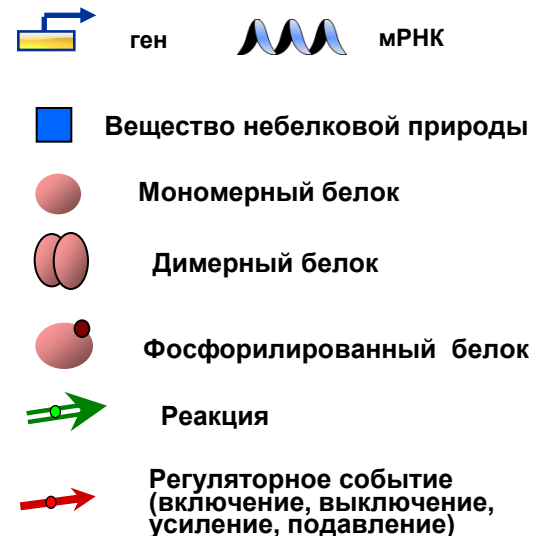
Активация транскрипции



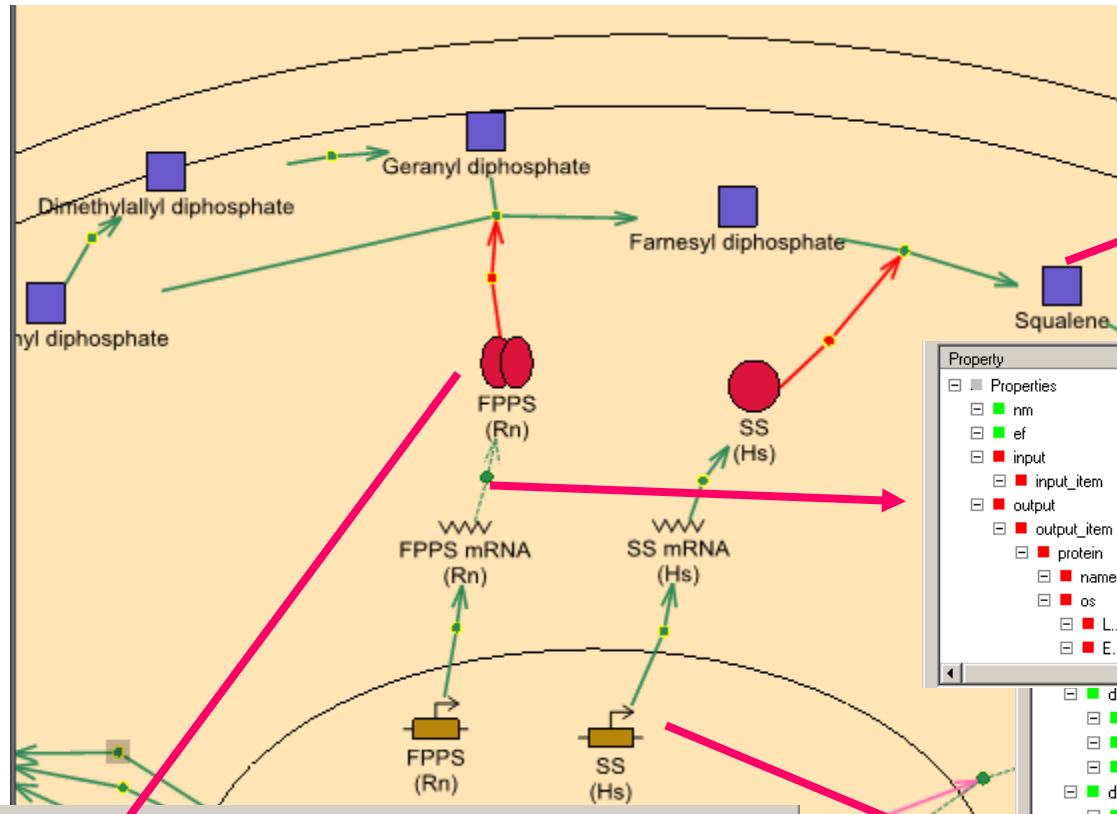
Ферментативная реакция



Условные обозначения:



БАЗА GeneNet (ИЦиГ СО РАН): представление данных в графическом редакторе



Property	Value
[-] Properties	
[-] sn	Squalene
[-] nm	Squalene

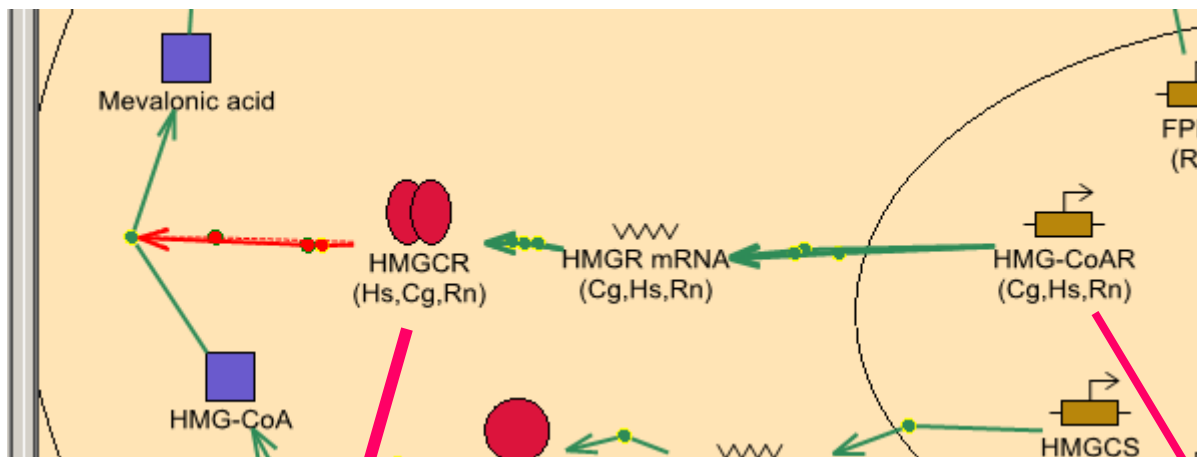
Property	Value
[-] Properties	
[-] nm	reaction
[-] ef	indirect
[-] input	
[-] input_item	
[-] output	
[-] output_item	
[-] protein	
[-] name	farnesyl diphosphate synthase
[-] os	
[-] L...	Rattus norvegicus
[-] E...	rat

Comment
Object properties
short name
full name
Organism Species
Species Latin name
Species English name
DataBase Reference
Database name
accession number of the ...
identifier of the entry in th...
DataBase Reference
Database name
accession number of the ...
identifier of the entry in th...
DataBase Reference
Database name
accession number of the ...
identifier of the entry in th...
Inducer
full name
Cell
short name
description
Organism Species
Species Latin name
Species English name
Cell
short name
description

Property	Value
[-] Properties	
[-] sn	FPPS
[-] nm	farnesyl diphosphate synthase
[-] sy	geranyl-diphosphate: isopentenyl-diphosphate ger...
[-] os	
[-] Latin	Rattus norvegicus
[-] English	rat
[-] dbref	

[-] dbref	
[-] name	EMBL
[-] ac	U18994
[-] id	HS189941
[-] dbref	
[-] name	SWISS-PROT
[-] ac	P37268
[-] id	FDFT_HUMAN
[-] inducer	
[-] name	cholesterol (repression)
[-] cell	
[-] sn	HepG2
[-] de	HepG2 hepatoma cell line
[-] os	
[-] Latin	Homo sapiens
[-] English	human
[-] cell	
[-] sn	liver
[-] de	liver

представление данных об объектах разных видов в графическом редакторе



Hs	: HMGCR	: HMG-CoA reductase	: 3-hydroxy-3-methylglutaryl-CoA reductase
Cg	: HMGCR	: HMG-CoA reductase	: 3-hydroxy-3-methylglutaryl-CoA reductase
Rn	: HMGCR	: HMG-CoA reductase	: 3-hydroxy-3-methylglutaryl-CoA reductase

Cg	: HMG-CoAR	: HMG-CoA reductase gene
Hs	: HMG-CoAR	: HMG-CoA reductase gene
Rn	: HMG-CoAR	: HMG-CoA reductase gene

Группа одноименных (гомологичных) объектов разных видов (гены, мРНК, белки) представлены на диаграмме в базе GeneNet одним образом. Имеется возможность просмотреть текстовую информацию о каждом объекте

Интернет-доступная версия GeneNet

<http://www.mgs.bionet.nsc.ru/mgs/gnw/genenet/>

Gene Networks

HOME DNA RNA PROTEIN GENENETWORKS MAP

[an error occurred while processing this directive]

The **GeneNet** system is designed for formalized description and automated visualization of gene networks. The GeneNet system includes: database on gene network components, Java program for the data visualization.

ACCESS to GeneNet

- [SRS access](#)
- [GeneNet browser](#)
- [Start GeneNet Viewer](#)
- [Start GeneNet Modelling](#)

General information

- [Main principles](#)
- [How to cite GeneNet](#)
- [Publications](#)
- [Reports on the conferences](#)
- [GeneNet Workgroup](#)
- [Acknowledgments](#)
- [FAQ](#)
- [Thesaurus on organs and tissues in mammals](#)

About the GeneNet viewer

- [Levels of the gene network representation](#)
- [Hierarchical description of a gene network structure](#)
- [Component images](#)

About the GeneNet database

- [Database format](#)
- [Example of SRS query](#)

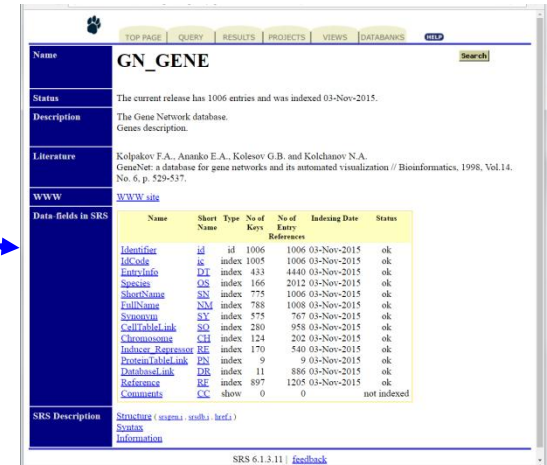
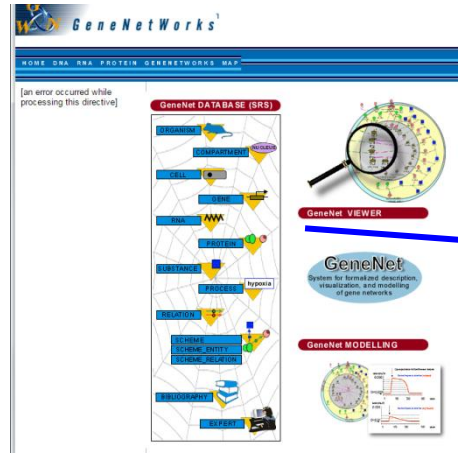
Current release

- [Versions info](#)
- [Information contents](#)
- [GeneNet functional sections](#)

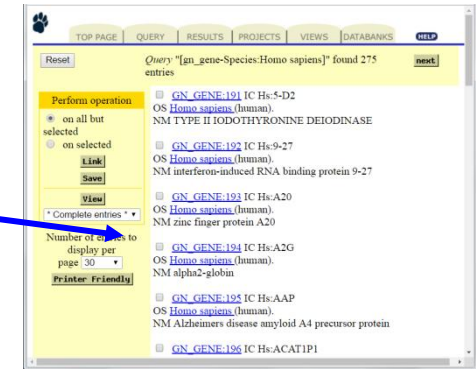
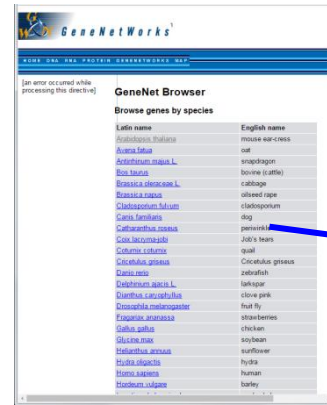
2017_02.htm ^ Показать все ×

Интернет-доступная версия GeneNet: основные модули

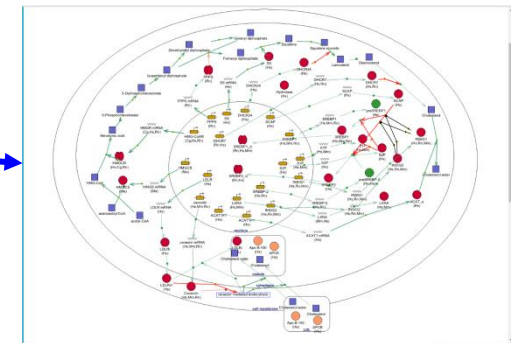
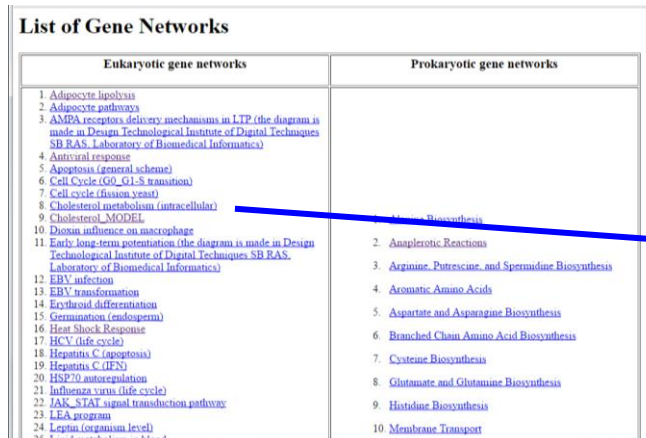
База GeneNet,
доступная для поиска
через систему SRS



Браузер базы GeneNet –
список видов организмов и
соответствующих им генов



Список диаграмм



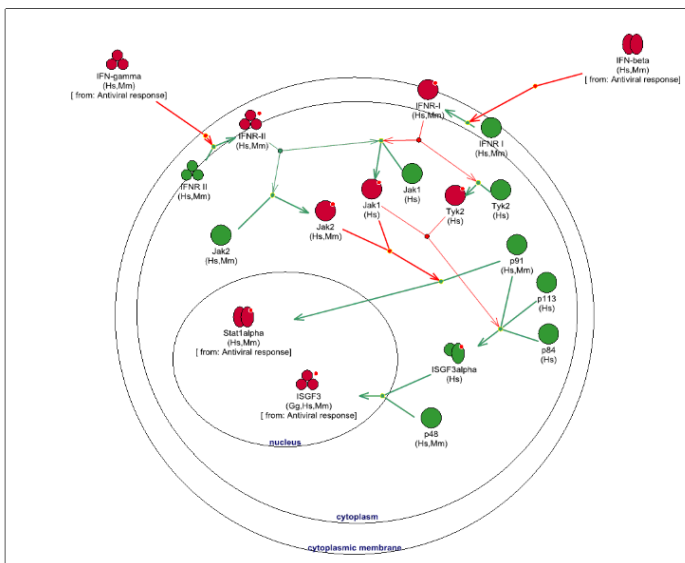
GeneNet: диаграмма, описывающая противовирусный ответ



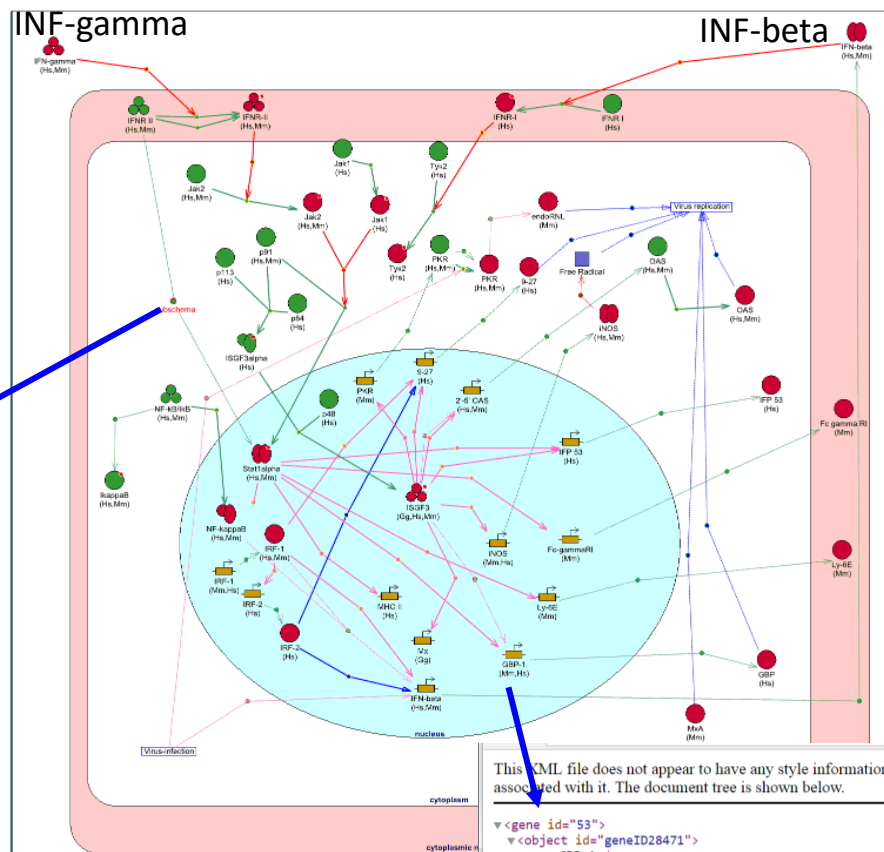
Гиперссылка на под схему

ЖАК/СТАТ сигнальный путь

JAK/STAT signal transduction pathway



Antiviral response



This XML file does not appear to have any style information associated with it. The document tree is shown below.

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<?xml version="1.0" encoding="UTF-8" standalone="no" ?>
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  <object id="53" ?>
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      <nm>guanylate-binding protein gene</nm>
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        <English>mouse</English>
      </os>
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        <ac>A00231</ac>
        <id>Mm:GBP1</id>
      </dbref>
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        <de>RAW 264.7 macrophage cell line</de>
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          <Latin>Mus musculus</Latin>
          <English>mouse</English>
        </os>
      </cell>
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        </journal>
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Информационное содержание интернет-доступной версии GeneNet



39 диаграмм
1006 генов
1766 белков
3634 связей
93 вида организмов

Тематические секции

Cell cycle
Lipid metabolism
Endocrine regulation
Erythrocyte maturation
Immune system
Plant genes networks
Stress response
Redox-regulation

KEGG: Kyoto Encyclopedia of Genes and Genomes

<http://www.genome.jp/kegg/>



KEGG ▾

Search

Help

[» Japanese](#)

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 Software

[KegTools](#)
[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](#) (January 1, 2017) for new and updated features.

New article

[KEGG: new perspectives on genomes, pathways, diseases and drugs](#)

Main entry point to the KEGG web service

[KEGG2](#) [KEGG Table of Contents](#) [\[Update notes\]](#)

Data-oriented entry points

KEGG PATHWAY [KEGG pathway maps](#)

KEGG BRITE [BRITE hierarchies and tables](#)

KEGG MODULE [KEGG modules](#)

KEGG ORTHOLOGY [KO functional orthologs](#)

KEGG GENOME [Genomes](#) [\[Release history\]](#)

KEGG GENES [Genes and proteins](#)

KEGG COMPOUND [Small molecules](#)

KEGG GLYCAN [Glycans](#)

KEGG REACTION [Biochemical reactions](#)

KEGG ENZYME [Enzyme nomenclature](#)

KEGG DISEASE [Human diseases](#)

KEGG DRUG [Drugs](#)

KEGG MEDICUS [Health information resource](#) [\[Drug labels search\]](#)

Organism-specific entry points

KEGG Organisms Enter org code(s) [hsa](#) [hsa](#) [eco](#)

Analysis tools

KEGG Mapper [KEGG PATHWAY/BRITE/MODULE mapping tools](#)

BlastKOALA [Genome annotation and KEGG mapping](#)

GhostKOALA [Metagenome annotation and KEGG mapping](#)

BLAST/FASTA [Sequence similarity search](#)

SIMCOMP [Chemical structure similarity search](#)

Subject-oriented entry points

[KEGG Cancer](#)

[KEGG Pathogen](#)

[KEGG Virus](#)

[KEGG Plant](#)

[KEGG Annotation](#)

[KEGG RModule](#)

[KEGG SeqData](#) *New!*



KEGG PATHWAY Database

Wiring diagrams of molecular interactions, reactions, and relations

[Menu](#) [PATHWAY](#) [BRITE](#) [MODULE](#) [KO](#) [GENOME](#) [GENES](#) [LIGAND](#) [DISEASE](#) [DRUG](#) [DBGET](#)

Select prefix

map

Organism

Enter keywords

Go

Help

[[New pathway maps](#) | [Update history](#)]

Pathway Maps

KEGG PATHWAY is a collection of manually drawn [pathway maps](#) representing our knowledge on the molecular interaction and reaction 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

and also on the structure relationships (KEGG drug structure maps) in:

7. Drug Development

Pathway Mapping

KEGG PATHWAY mapping is the process to map molecular datasets, especially large-scale datasets in genomics, transcriptomics, proteomics, and metabolomics, to the KEGG pathway maps for biological interpretation of higher-level systemic functions.

- [Search Pathway](#) - basic pathway mapping tool
- [Search&Color Pathway](#) - advanced pathway mapping tool
- [Color Pathway](#) - selected pathway map coloring tool

KEGG pathway: раздел , содержащий интегральные схемы (глобальные карты) метаболизма:

• [Color Pathway](#) - selected pathway map coloring tool

1. Metabolism

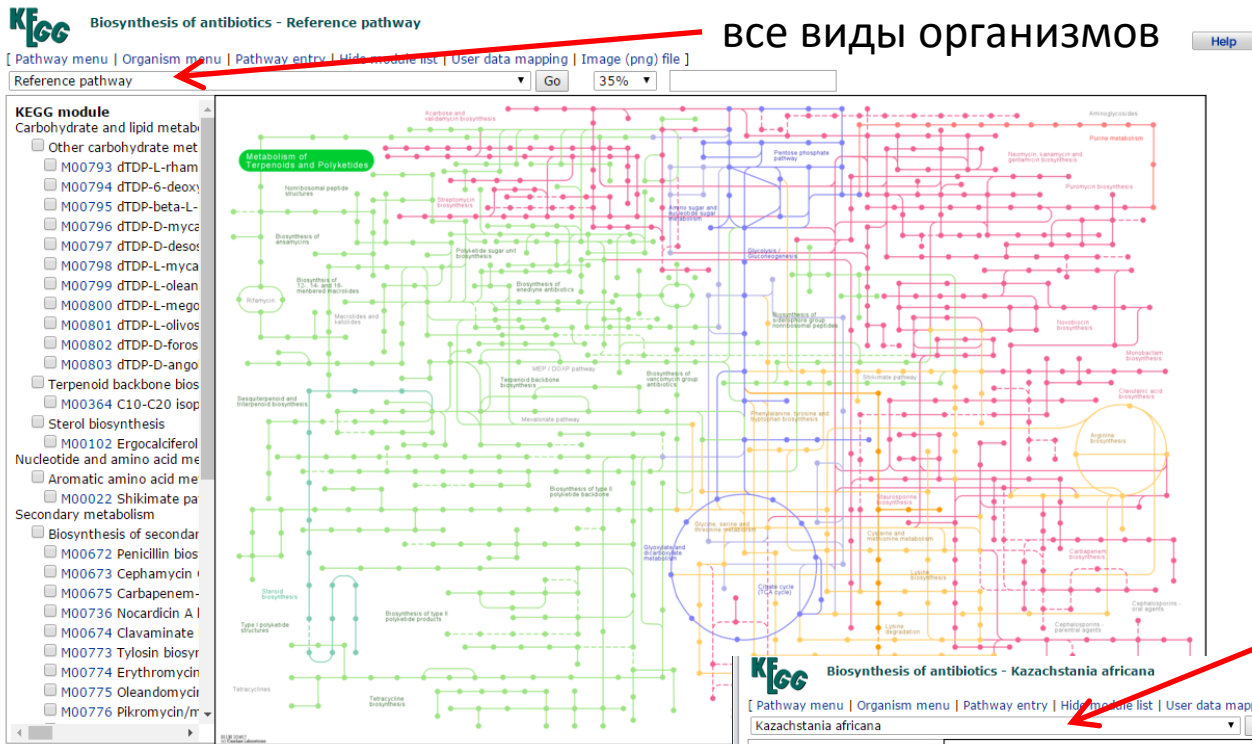
1.0 Global and overview maps

Metabolic pathways	[KEGG Atlas]	KEGG modules
Biosynthesis of secondary metabolites	[KEGG Atlas]	KEGG reaction modules
Microbial metabolism in diverse environments	[KEGG Atlas]	
Biosynthesis of antibiotics	[KEGG Atlas]	
Carbon metabolism	[KEGG Atlas]	
2-Oxocarboxylic acid metabolism	[KEGG Atlas]	
Fatty acid metabolism	[KEGG Atlas]	
Biosynthesis of amino acids	[KEGG Atlas]	
Degradation of aromatic compounds	[KEGG Atlas]	

1.1 Carbohydrate metabolism

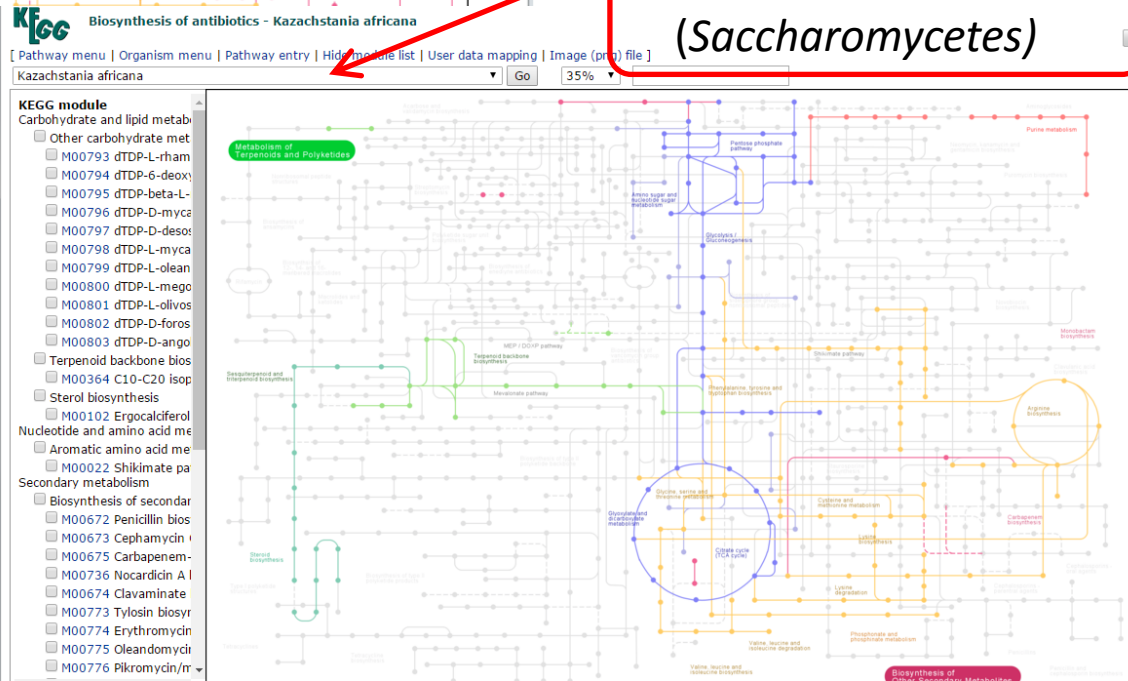
WP585_85198.png WP585_85198.owl WP585_85198 (1).gpml [Показать все](#)

KEGG: Интегральная схема биосинтеза антибиотиков (все виды организмов)

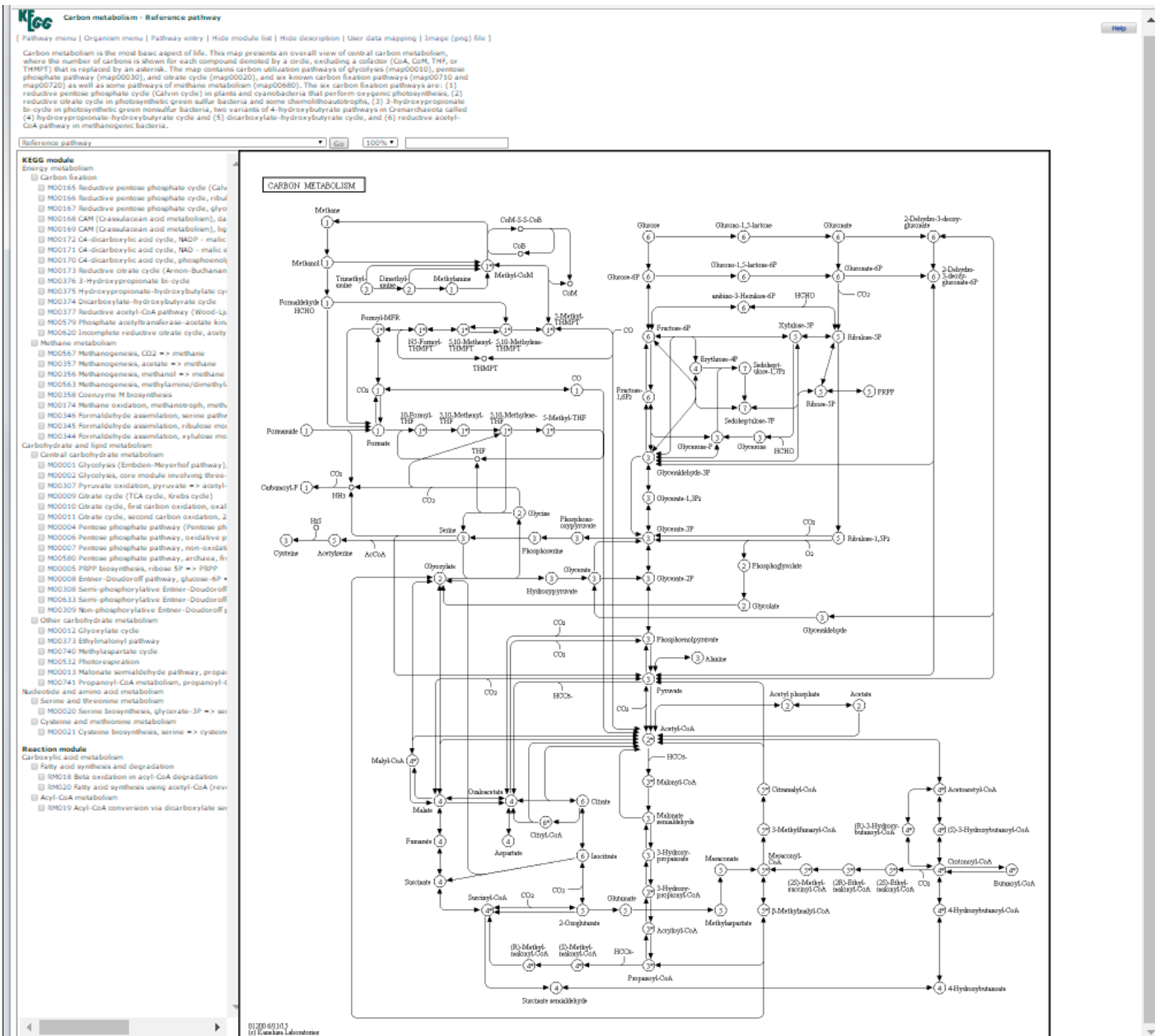


все виды организмов

Kazachstania Africana
(Saccharomycetes)

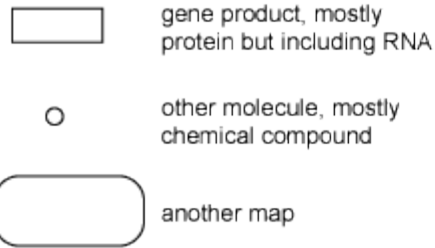


KEGG: Интегральная схема метаболизма углеводов (Carbon metabolism)

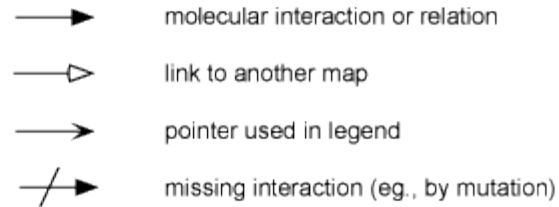


KEGG: условные обозначение

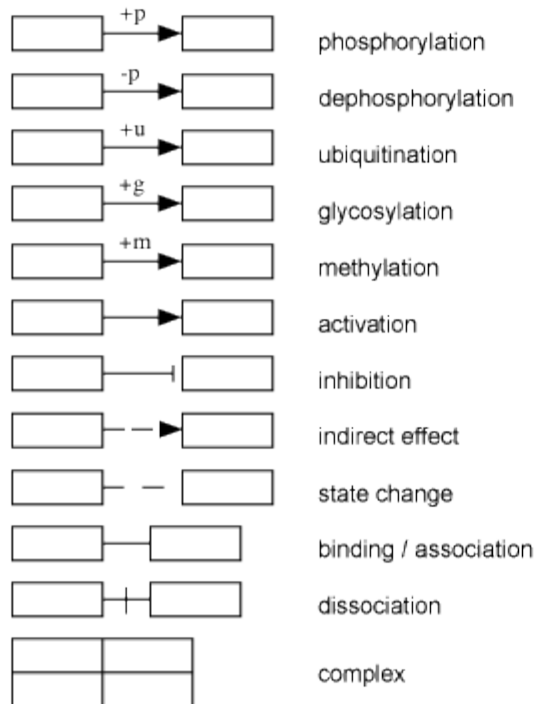
Objects



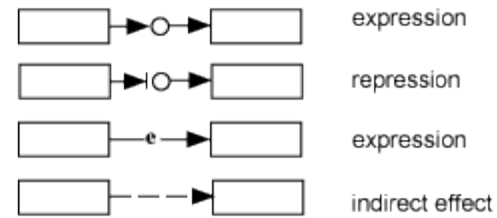
Arrows



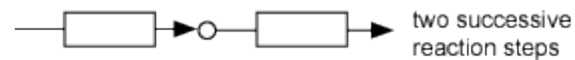
Protein-protein interactions



Gene expression relations



Enzyme-enzyme relations



KEGG: диаграмма Glycolysis / Gluconeogenesis



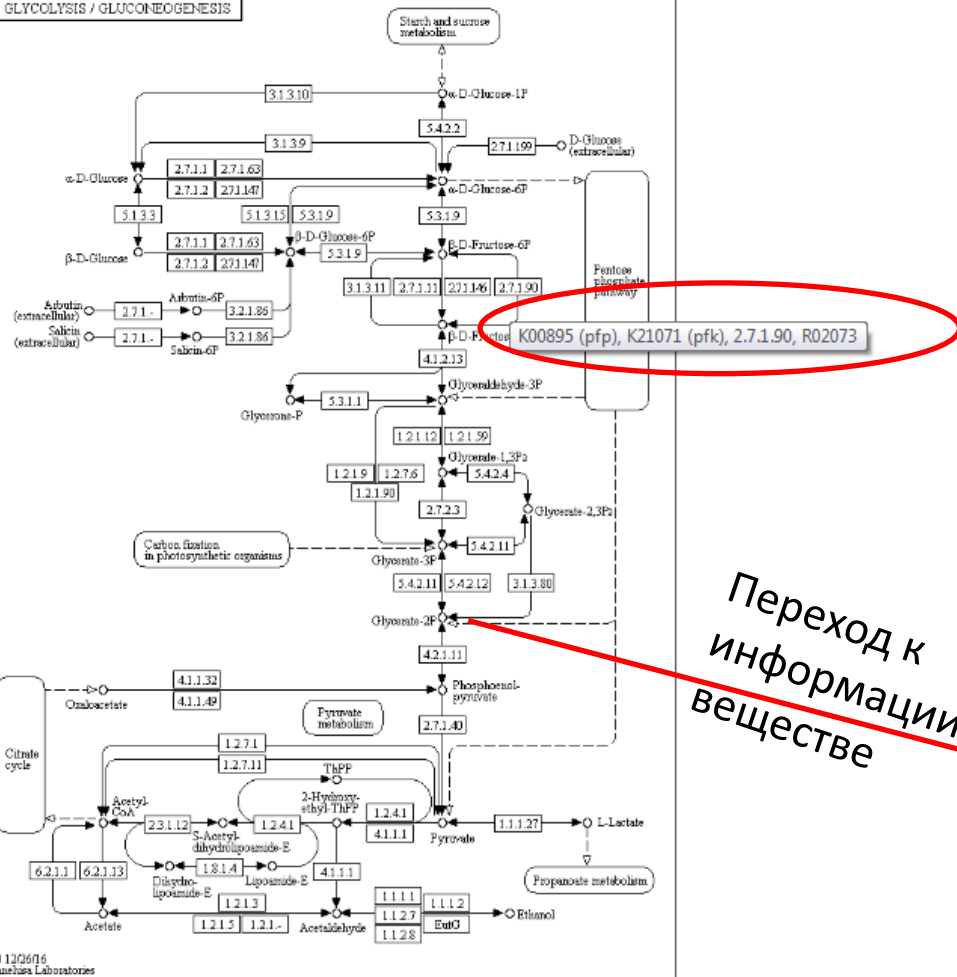
Glycolysis / Gluconeogenesis - Reference pathway

[Pathway menu | Organism menu | Pathway entry | Hide description | User data mapping]

Glycolysis is the process of converting glucose into pyruvate and generating small amounts of ATP (energy) and NADH (reducing power). It is a central pathway that produces important precursor metabolites: six-carbon compounds of glucose-6P and fructose-6P and three-carbon compounds of glyceraldehyde-3P, glyceralate-3P, phosphoenolpyruvate, and pyruvate [MD:M00001]. Acetyl-CoA, another important precursor metabolite, is produced by oxidative decarboxylation of pyruvate [MD:M00307]. When the enzyme genes of this pathway are examined in completely sequenced genomes, the reaction steps of three-carbon compounds from glyceraldehyde-3P to pyruvate form a conserved core module [MD:M00002], which is found in almost all organisms and which sometimes contains operon structures in bacterial genomes. Gluconeogenesis is a synthesis pathway of glucose from noncarbohydrate precursors. It is essentially a reversal of glycolysis with minor variations of alternative paths [MD:M00003].

Reference pathway [Go] 100%

GLYCOLYSIS / GLUCONEOGENESIS




ВХОД "Pyruvate"
Разделе базы
"KEGG Chemical Universe"

KEGG COMPOUND: C00022

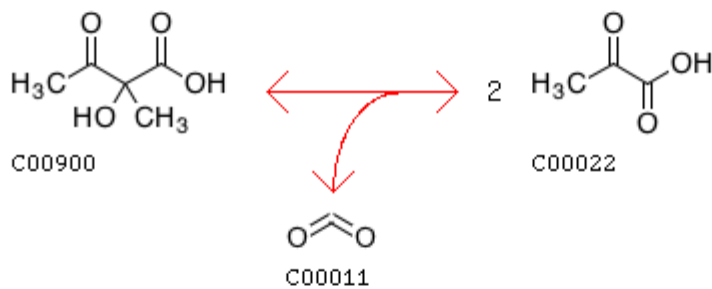
Entry	C00022	Compound
Name	Pyruvate; Pyruvic acid; 2-Oxopropanoate; 2-Oxopropanoic acid; Pyruvic acid	
Formula	C3H4O3	
Exact mass	88.016	
Mol weight	88.0621	
Structure		
Reaction	R00055 R00058 R00014 R00195 R00200 R00107 R00198 R00199 R00209 R00203 R00205 R00206 R00207 R00208 R00209 R00210 R00211 R00212 R00213 R00214 R00215 R00216 R00217 R00218 R00219 R00220 R00221 R00222 R00224 R00226 R00237 R00258 R00297 R00324 R00325 R00344 R00350 R00353 R00368 R00369 R00396 R00398 R00400 R00409 R00430 R00452 R00453 R00470 R00471 R00532 R00543 R00562 R00572 R00576 R00585 R00659 R00666 R00673 R00692 R00703 R00704 R00724 R00728 R00750 R00782 R00906 R00907 R00930 R00985 R00986 R01812 R01831 R01032 R01064 R01085 R01138 R01147 R01148 R01196 R01215 » show all	
Pathway	map00010 Glycolysis / Gluconeogenesis map00020 Citrate cycle (TCA cycle) map00030 Pentose phosphate pathway map00040 Pentose and glucuronate interconversions map00053 Ascorbate and aldarate metabolism	

Переход к информации о веществе

ВХОД “REACTION” В “KEGG REACTION”: Одна из реакций с участием вещества «Pyruvate»



REACTION: R00006

Entry	R00006	Reaction
Name	pyruvate:pyruvate acetaldehydetransferase (decarboxylating); 2-acetolactate pyruvate-lyase (carboxylating)	
Definition	2-Acetolactate + CO2 <=> 2 Pyruvate	
Equation	C00900 + C00011 <=> 2 C00022	
		
Comment	TPP-dependent enzymatic reaction (R00014+R03050)	
Reaction class	RC00106 C00022_C00900	
Enzyme	2.2.1.6	
Pathway	rn00770 Pantothenate and CoA biosynthesis	
Orthology	K01652 acetolactate synthase I/II/III large subunit [EC:2.2.1.6] K01653 acetolactate synthase I/III small subunit [EC:2.2.1.6]	

DBGET integrated database retrieval system

KEGG: схема сигнального пути , активируемого TNFa (TNF signaling pathway - Homo sapiens (human))

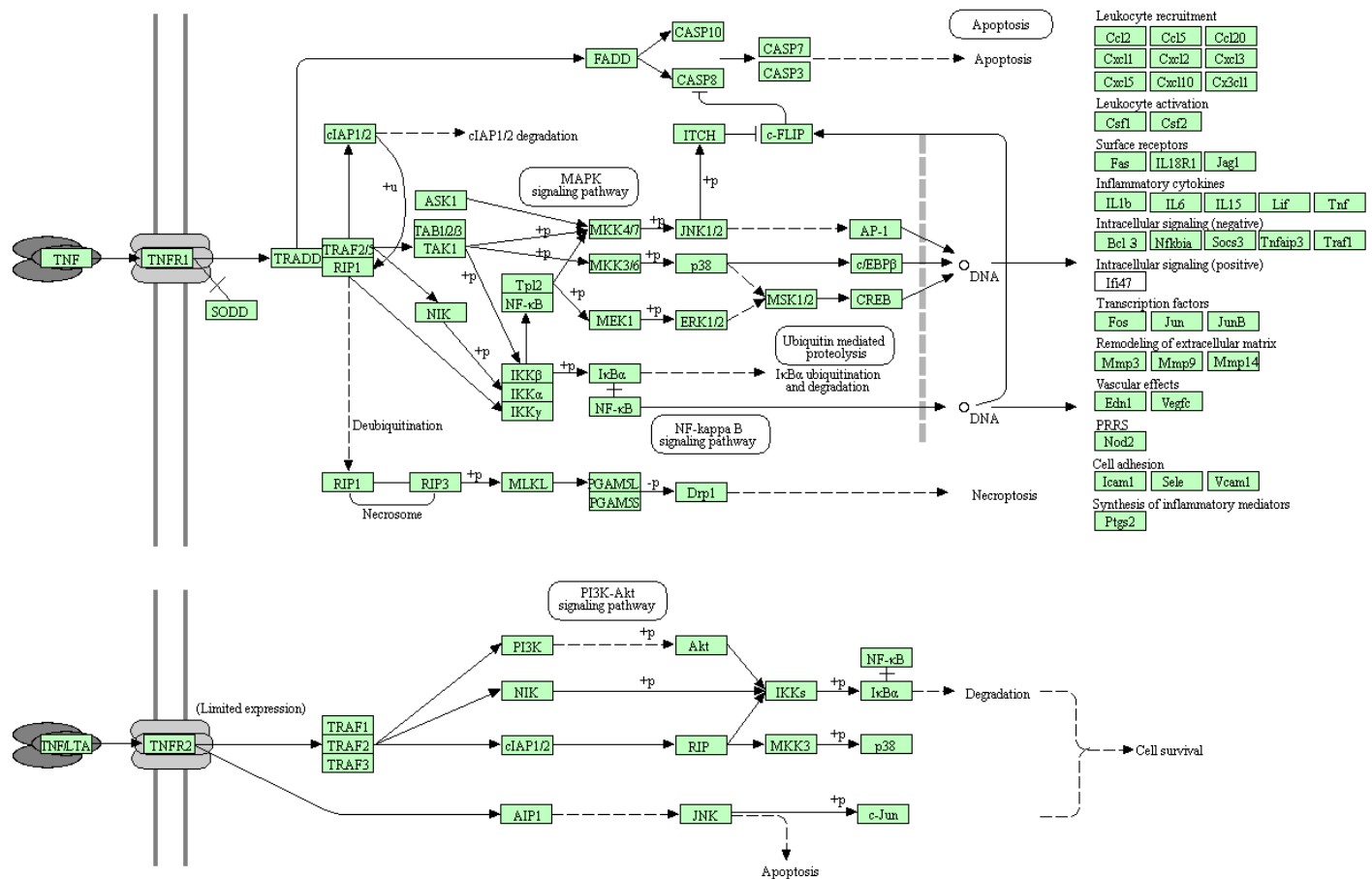


TNF signaling pathway - Homo sapiens (human)

Help

[[Pathway menu](#) | [Organism menu](#) | [Pathway entry](#) | [Download KGML](#) | [Hide description](#) | [User data mapping](#)]

TNF SIGNALING PATHWAY



KEGG: информация из раздела **Pathway entry** для сигнального пути , активируемого TNFa (TNF signaling pathway - Homo sapiens (human))



PATHWAY: hsa04668

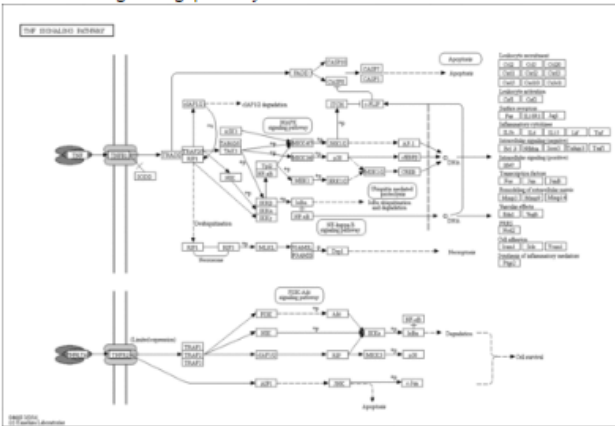
Help

Entry	hsa04668	Pathway
Name	TNF signaling pathway - Homo sapiens (human)	
Description	<p>Tumor necrosis factor (TNF), as a critical cytokine, can induce a wide range of intracellular signal pathways including apoptosis and cell survival as well as inflammation and immunity. Activated TNF is assembled to a homotrimer and binds to its receptors (TNFR1, TNFR2) resulting in the trimerization of TNFR1 or TNFR2. TNFR1 is expressed by nearly all cells and is the major receptor for TNF (also called TNF-alpha). In contrast, TNFR2 is expressed in limited cells such as CD4 and CD8 T lymphocytes, endothelial cells, microglia, oligodendrocytes, neuron subtypes, cardiac myocytes, thymocytes and human mesenchymal stem cells. It is the receptor for both TNF and LTA (also called TNF-beta). Upon binding of the ligand, TNFR mediates the association of some adaptor proteins such as TRADD or TRAF2, which in turn initiate recruitment of signal transducers. TNFR1 signaling induces activation of many genes, primarily controlled by two distinct pathways, NF-kappa B pathway and the MAPK cascade, or apoptosis and necroptosis. TNFR2 signaling activates NF-kappa B pathway including PI3K-dependent NF-kappa B pathway and JNK pathway leading to survival.</p>	

- All links**
- Pathway (1)
 - BioSystems (1)
 - Genome (1)
 - KEGG GENOME (1)
 - Gene (108)
 - KEGG GENES (108)
 - All databases (110)
- Download RDF

Class Environmental Information Processing; Signal transduction
[BRITE hierarchy](#)

Pathway map [hsa04668](#) TNF signaling pathway



[All organisms](#) [Ortholog table](#)

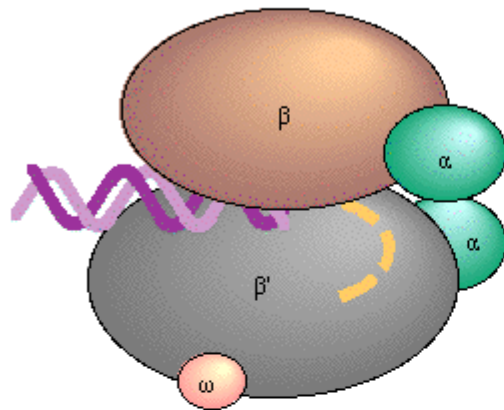
Other DBs BSID: 812256
GO: 0033209

Organism Homo sapiens (human) [GN:hsa]

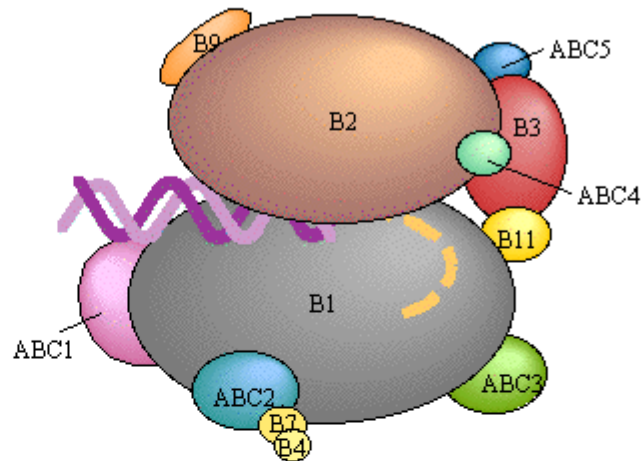
Gene	7124	TNF; tumor necrosis factor [KO:K03156]
	7132	TNFRSF1A; TNF receptor superfamily member 1A [KO:K03158]
	9530	BAG4; BCL2 associated athanogene 4 [KO:K09558]
	8717	TRADD; TNFRSF1A associated via death domain [KO:K03171]
	7186	TRAF2; TNF receptor associated factor 2 [KO:K03173]
	7188	TRAF5; TNF receptor associated factor 5 [KO:K09849]
	8737	RIPK1; receptor interacting serine/threonine kinase 1 [KO:K02861] [EC:2.7.11.1]
	329	BIRC2; baculoviral IAP repeat containing 2 [KO:K16060]
	330	BIRC3; baculoviral IAP repeat containing 3 [KO:K16060]
	6885	MAP3K7; mitogen-activated protein kinase kinase kinase 7 [KO:K04427] [EC:2.7.11.25]
	10454	TAB1; TGF-beta activated kinase 1 (MAP3K7) binding protein 1 [KO:K04403]

KEGG: диаграмма RNA polymerase из раздела 2.1 Transcription

RNA POLYMERASE

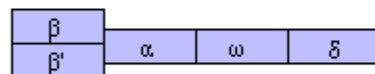


RNA polymerase (*Thermus aquaticus*)

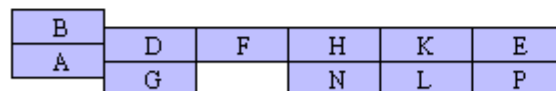


RNA polymerase II (*Saccharomyces cerevisiae*)

Bacterial

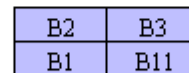


Archaeal

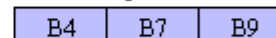


Eukaryotic Pol II

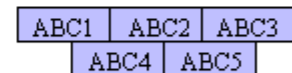
Core subunits



Pol II specific subunits

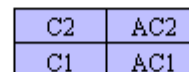


Pol I, II, and III common subunits

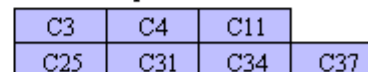


Eukaryotic Pol III

Core subunits

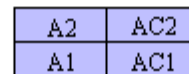


Pol III specific subunits

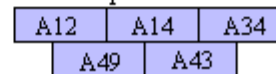


Eukaryotic Pol I

Core subunits



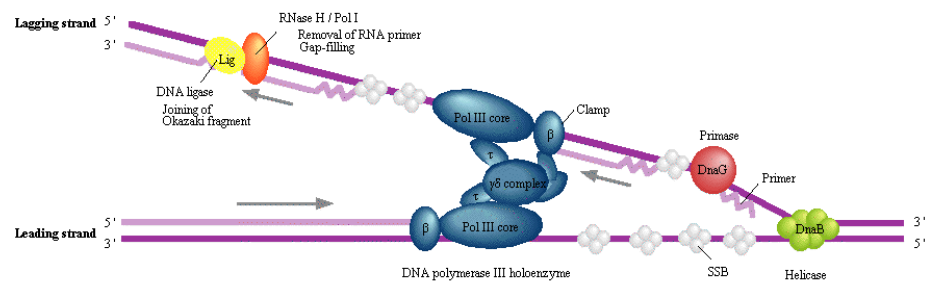
Pol I specific subunits



KEGG: диаграмма DNA replication из раздела 2.4 Replication and repair

DNA REPLICATION

Replication complex (Bacteria)



DNA polymerase III holoenzyme

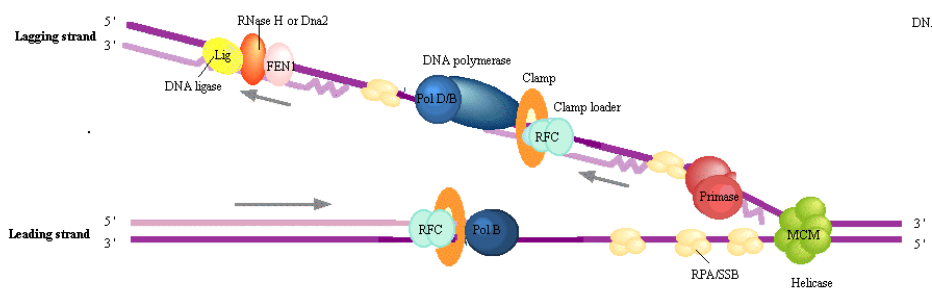
	β	
	ε	
	α	
	γ & τ	
Clamp	ψ	δ'
	β	χ

Pol III core
βδ complex

Helicase: DnaB
Primase: DnaG
SSB

RNaseH: RNaseHI, RNaseHII, RNaseHIII
DNA polymerase I: Dpol
DNA ligase: Lig

Replication complex (Archaea)



DNA polymerase B DNA polymerase D

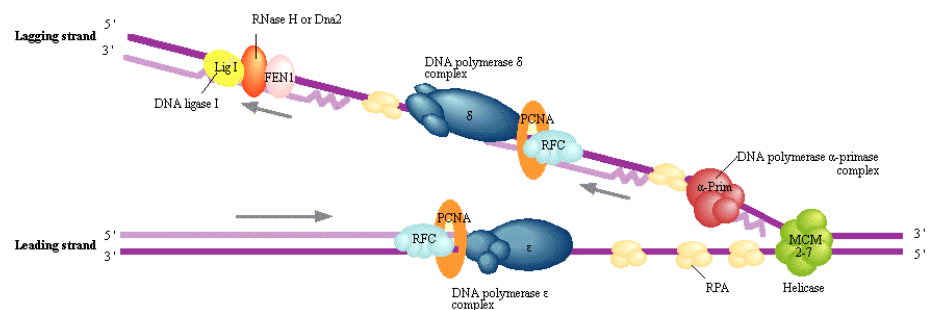
PoB	PolD1
	PolD2

Helicase: MCM
Primase: Pri1, Pri2
RFA/SSB: RFA

Clamp: PCNA
Clamp loader: RfcS, RfL
RNaseH: RNaseHI, RNaseHII

Helicase: Dna2
Primase: Fen1
DNA ligase: Lig

Replication complex (Eukaryotes)



DNA polymerase α-primase complex

α1	α2	Pri1	Pri2
----	----	------	------

DNA polymerase δ complex

δ1	δ2	δ3	δ4
----	----	----	----

DNA polymerase ε complex

ε1	ε2	ε3	ε4
----	----	----	----

MCM complex (helicase)

Mcm2	Mcm3	RFA
Mcm4	Mcm5	RFA1
Mcm6	Mcm7	RFA2/4
		RFA3

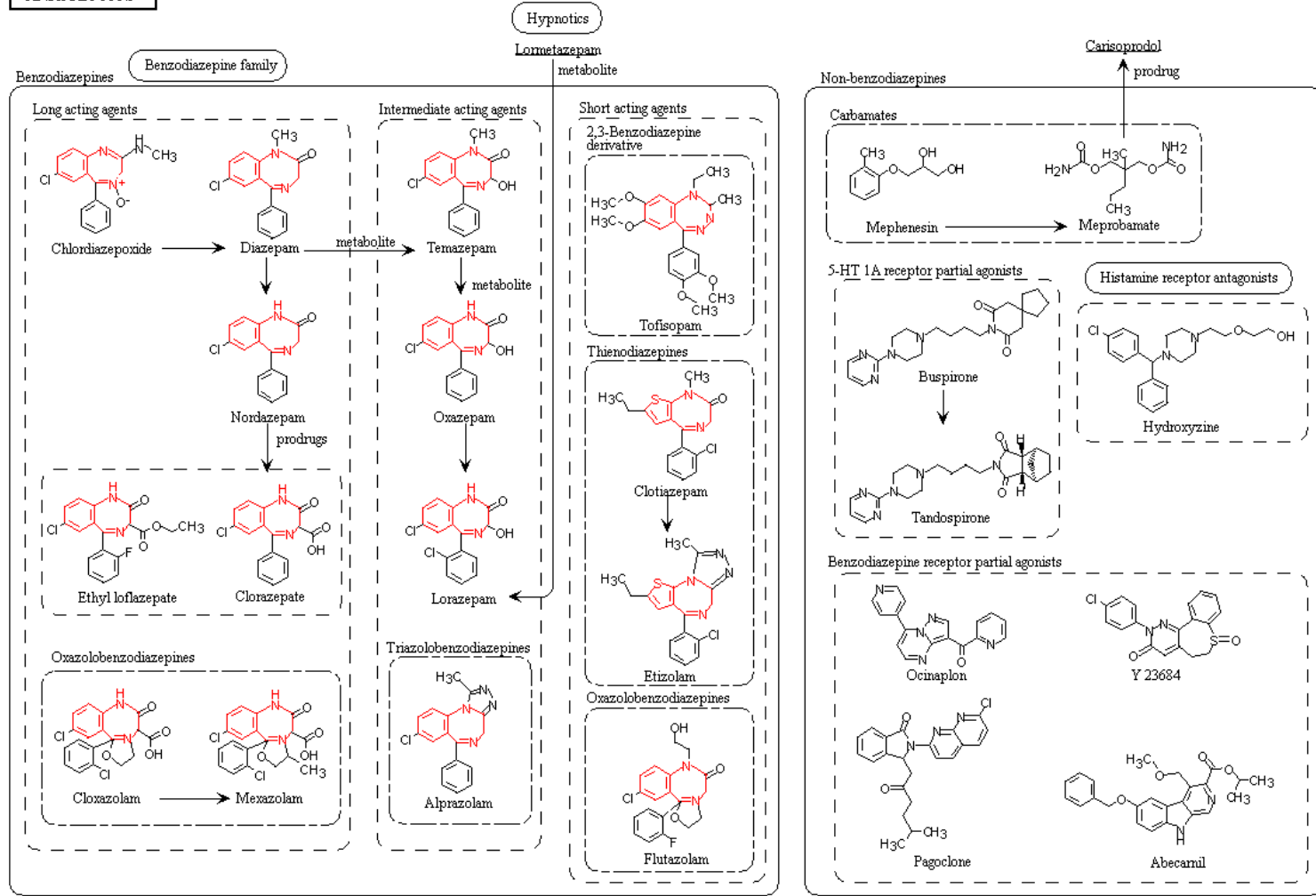
Clamp: PCNA
Clamp loader: RFC1, RFC2/4, RFC3/5

RNaseHI: RNaseHI
RNaseHII: RNaseHA, RNaseHB, RNaseHC

Helicase: Dna2
Primase: Fen1
DNA ligase: Lig1

KEGG: диаграмма Anxiolytics из раздела 7.3 Chronology: Nervous system agents

ANXIOLYTICS



07030 12/7/10
(c) Kanehisa Laboratories

Анксиолитики (= транквилизаторы): вещества, снимающие тревогу, страх, усталость

Manually drawn KEGG reference pathway maps

Category	Type	Number of maps ^a
Metabolism	Global map	4
	Overview map	5
	Regular map	160
	Chemical structure transformation map	9
Genetic information processing	Regular map	22
Environmental information processing	Regular map	38
Cellular processes	Regular map	24
Organismal systems	Regular map	78
Human diseases	Regular map	81
Drug development	Drug structure map	75

^aAs of 1 October 2016.

$\Sigma = 496$

Kanehisa M, Furumichi M, Tanabe M, Sato Y, Morishima K. KEGG: new perspectives on genomes, pathways, diseases and drugs. Nucleic Acids Res. 2017 Jan 4;45(D1):D353-D361.

А сколько видов представлено в базе KEGG pathway?

- Ответ зависит от того, какой вход (pathway) мы рассматриваем.

Alzheimer's disease - Homo sapiens (human)

Alzheimer's disease (AD) is a chronic disorder that slowly destroys neurons and causes serious cognitive disability. It is associated with senile plaques and neurofibrillary tangles (NFTs). Amyloid-beta (A β), a major component of senile plaques, is produced by the amyloid precursor protein (APP). The extracellular A β oligomers may activate caspases, leading to cell death. Alternatively, intracellular A β may contribute to pathology by facilitating phosphorylation, disrupting mitochondrial function, and triggering calcium dysregulation. To date, genetic studies have identified four genes that may be linked to autosomal dominant or familial early onset AD (FAD). These four genes include: amyloid precursor protein (APP), presenilin 1 (PS1), presenilin 2 (PS2), and apolipoprotein E (ApoE). All mutations associated with APP and PS1/2 can lead to an increase in the production of A β peptides, specifically the more amyloidogenic form, A β 42. A linked PS1 mutation downregulates the unfolded protein response and leads to vulnerability to ER stress.

Reference pathway
Reference pathway (KO)
-----< Set personalized menu >-----
-----< Sort below by alphabet >-----

- Homo sapiens (human)
- Homo sapiens (human) + Disease/drug
- Pan troglodytes (chimpanzee)
- Pan paniscus (bonobo)
- Gorilla gorilla gorilla (western lowland gorilla)
- Pongo abelii (Sumatran orangutan)
- Nomascus leucogenys (northern white-cheeked gibbon)
- Macaca mulatta (rhesus monkey)
- Macaca fascicularis (crab-eating macaque)
- Chlorocebus sabaeus (green monkey)
- Rhinopithecus roxellana (golden snub-nosed monkey)
- Callithrix jacchus (white-tufted-ear marmoset)
- Saimiri boliviensis boliviensis (Bolivian squirrel monkey)
- Mus musculus (mouse)
- Rattus norvegicus (rat)
- Cricetulus griseus (Chinese hamster)
- Nannospalax qalili (Upper Galilee mountain blind mole rat)

Secretase
DAMDD7
Secretase
BACE
Secretase
RTN3/4
Secretase
N2 PSEN
STN APH-1
Secretase

Apoptosis
APP processing
Decreased energy production?

Oxidative Phosphorylation
Mitochondrial c

ABAD
Ca²⁺ overload
Bad

IDE
NEP
LPL
ApoE
LRP
Fas/TNFR
FADD
CASP8
Bid

Degradation
Amyloid β (A β)
AICD
Oligomeric, intracellular A β
A β aggregation

42 вида организмов

Metabolic pathways - Reference pathway

[Pathway menu | Organism menu | Pathway entry | Hide module list | User data mapping | Image (png) file]

Alligator mississippiensis (American alligator) 35%

- Myotis davidii
- Pteropus alecto (black flying fox)
- Loxodonta africana (African savanna elephant)
- Monodelphis domestica (opossum)
- Sarcophilus harrisii (Tasmanian devil)
- Ornithorhynchus anatinus (platypus)
- Gallus gallus (chicken)
- Meleagris gallopavo (turkey)
- Coturnix japonica (Japanese quail)
- Anas platyrhynchos (mallard)
- Taeniopygia guttata (zebra finch)
- Geospiza fortis (medium ground-finch)
- Ficedula albicollis (collared flycatcher)
- Pseudopodoces humilis (Tibetan ground-tit)
- Corvus comix (hooded crow)
- Falco peregrinus (peregrine falcon)
- Falco cherrug (Saker falcon)
- Columba livia (rock pigeon)
- Apteryx australis mantelli (brown kiwi)
- Alligator sinensis (Chinese alligator)
- Alligator mississippiensis (American alligator)

Carbohydrate Metabolism
Lipid Metabolism
Metabolism of Terpenoids and Polyketides

> 1000 видов организмов

KEGG ORTHOLOGY

KO (KEGG ORTHOLOGY) Database
Linking genomes to pathways by ortholog annotation

Menu PATHWAY BRITE MODULE KO Annotation ENZYME RModule BlastKOALA

Search KO for

KO Database of Molecular Functions

In KEGG, molecular-level functions are stored in the **KO (KEGG Orthology)** database and associated with ortholog groups in order to enable extension of experimental evidence in a specific organism to other organisms. Genome annotation in KEGG is ortholog annotation, assigning KO identifiers (K numbers) to individual genes in the GENES database. No updates are made to original data, such as gene names and descriptions given by RefSeq or GenBank, even if they are inconsistent with the KO assignment.

Major efforts have been initiated to associate each KO entry with experimental evidence of functionally characterized sequence data, now shown in the SEQUENCE subfield of the REFERENCE field. Furthermore, the genome-based collection of KEGG GENES has been expanded to allow individual protein data to be included in the addendum category. Eventually the KO database will cover all knowledge on functionally characterized protein sequences (see also KEGG Enzyme).

KEGG Mapping by the KO System

In general KO grouping of functional orthologs is defined in the context of KEGG molecular networks (KEGG pathway maps, BRITE hierarchies and KEGG modules), which are in fact represented as networks of nodes identified by K numbers. The relationships between KOs and corresponding molecular networks are represented in the following KO system.

[KEGG Orthology \(KO\)](#)

Enter K numbers (Example) K00161 K00162 K00163 K00627 K00382

K00161

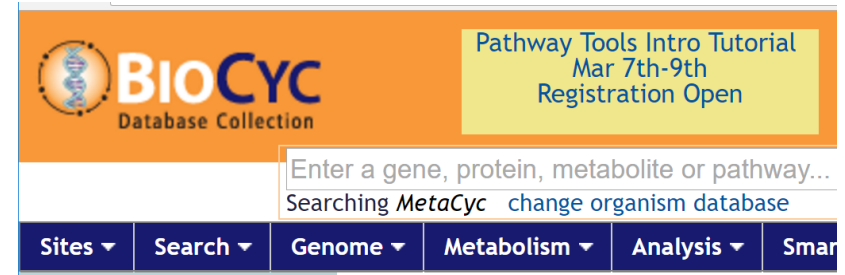
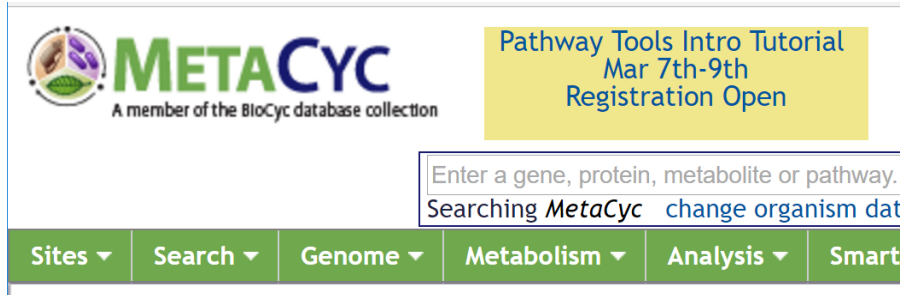
Гены всех видов сгруппированы в группы ортологов. Каждая группа имеет индивидуальный идентификатор (вида K00161), через который можно вести поиск как по генам, так и по разделу KEGG Pathway

Ortholog table

All ▾

Grp	Genus	Organism	K00161 (PDHA)[4084]
E.Ani	Homo	hsa	5161 5160
E.Ani	Pan	ptr	471255 465525
E.Ani	Pan	pps	100984797 100993455
E.Ani	Gorilla	ggo	101128322 101125835
E.Ani	Pongo	pon	100174745 100443483
E.Ani	Nomascus	nle	100587584 100595000
E.Ani	Macaca	mcc	709359 100423990
E.Ani	Macaca	mcf	102125852 102140136
E.Ani	Chlorocebus	csab	103231682 103235992
E.Ani	Rhinopithecus	rro	104679850 104682411
E.Ani	Callithrix	cjc	100403644 100400144
E.Ani	Saimiri	sbq	101051150 101046119
E.Ani	Mus	mmu	18597 18598
E.Ani	Rattus	rno	117098 29554
E.Ani	Cricetulus	cge	100774853 100772790
E.Ani	Nannospalax	ngi	103728085 103736226 103741428
E.Ani	Heterocephalus	hgl	101716937 101710793
E.Ani	Oryctolagus	ocu	100350273 100357349
E.Ani	Tupaia	tup	102502588 102496416
E.Ani	Canis	cfa	480858
E.Ani	Ailuropoda	aml	100471829 100467550
E.Ani	Ursus	umr	103668166 103677911
E.Ani	Felis	fca	101080765 101081627
E.Ani	Panthera	ptg	102963682 102968217

Семейство баз данных MetaCyc – BioCyc: метаболические пути



MetaCyc содержит более **2400** метаболических путей **из >46 000 публикаций** для **2816** видов организмов

BioCyc - Коллекция **9390** организм-специфичных Pathway/Genome Databases (PGDBs), каждая из которых содержит полный геном и **предсказанные** метаболические сети данного организма (включая описание метаболитов, ферменты, реакции, метаболические пути, предсказанные опероны, транспортные системы и фильтры, позволяющие получать информацию о метаболических путях)

Общий формат представления данных, поисковые системы, средства анализа

Базы развиваются с 2005 года (BioCyc) и 2001 года (MetaCyc)

Caspi R, et al., The MetaCyc database of metabolic pathways and enzymes and the BioCyc collection of Pathway/Genome Databases. Nucleic Acids Res. 2014;42:D459-71

Caspi R et al., The MetaCyc database of metabolic pathways and enzymes and the BioCyc collection of pathway/genome databases. Nucleic Acids Res. 2016;44(D1):D471-80.

MetaCyc: список видов, для которых имеется 20 и более метаболических путей с экспериментально подтвержденными данными

Bacteria		Eukarya		Archaea	
<i>Escherichia coli</i>	329	<i>Arabidopsis thaliana</i>	335	<i>Methanocaldococcus jannaschii</i>	29
<i>Pseudomonas aeruginosa</i>	71	<i>Homo sapiens</i>	264	<i>Methanosarcina barkeri</i>	22
<i>Bacillus subtilis</i>	62	<i>Saccharomyces cerevisiae</i>	188	<i>Sulfolobus solfataricus</i>	21
<i>Pseudomonas putida</i>	51	<i>Rattus norvegicus</i>	83		
<i>Salmonella typhimurium</i>	41	<i>Glycine max</i>	62		
<i>Pseudomonas fluorescens</i>	32	<i>Solanum lycopersicum</i>	55		
<i>Mycobacterium tuberculosis</i>	31	<i>Pisum sativum</i>	55		
<i>Klebsiella pneumoniae</i>	29	<i>Mus musculus</i>	54		
<i>Synechocystis sp. PCC 6803</i>	27	<i>Zea mays</i>	48		
<i>Enterobacter aerogenes</i>	26	<i>Nicotiana tabacum</i>	46		
<i>Agrobacterium tumefaciens</i>	24	<i>Oryza sativa</i>	46		
		<i>Solanum tuberosum</i>	43		
		<i>Catharanthus roseus</i>	30		
		<i>Spinacia oleraca</i>	29		
		<i>Hordeum vulgare</i>	27		
		<i>Triticum aestivum</i>	25		
		<i>Bos taurus</i>	23		
		<i>Petunia x hybrida</i>	21		
		<i>Sus scrofa</i>	20		

Информационное содержание базы HumanCyc


<https://humancyc.org/humancyc/release-notes.shtml>

The screenshot shows the HumanCyc website interface. At the top, there is a navigation bar with the HumanCyc logo and a member of the BioCyc database collection. A yellow banner announces a 'Pathway Tools Intro Tutorial' from March 7th-9th with registration open. Below this is a search bar with a text input field containing 'Enter a gene, protein, metabolite or pathway...', a 'Quick Search' button, and a 'Gene Search' button. A red navigation bar contains menu items: Sites, Search, Genome, Metabolism, Analysis, SmartTables, and Help. The main heading is 'HumanCyc Release Notes History'. Below it is a table titled 'HumanCyc Statistics' with columns for the years 2016, 2015, 2014, 2013, and a 'Description' column. The 'Pathways' row is highlighted with a red border, and a blue arrow points from it to the text 'KEGG Pathway – 496 pathways' at the bottom of the image.

	2016	2015	2014	2013	Description
Pathways	307	289	288	293	Number of metabolic and signaling pathways, excluding super-pathways
Reactions	2640	2619	2611	2582	Number of reactions
Genes	20792	20791	20801	20892	Number of genes
Polypeptides	20512	20469	20480	20629	Number of polypeptides
Protein complexes	474	456	456	341	Number of protein complexes
Enzymes	3636	3250	3260	3765	Number of enzymes
Transporters	393	466	470	451	Number of transporters
Chemical compounds	1841	1798	1798	1657	Number of chemical compounds
Citations	41455	40753	40687	40551	Number of citations to the scientific literature


KEGG Pathway – 496 pathways

HumanCyc - Pathway: superoxide radicals degradation


 Please take 3 minute BioCyc survey Welcome: Elena Ignatieva | Logout | Help | My preferences

Enter a gene, protein, metabolite or pathway...
Searching *Homo sapiens* [change organism database](#)

Sites ▾ Search ▾ Genome ▾ Metabolism ▾ Analysis ▾ SmartTables ▾ Help ▾



Homo sapiens Pathway: superoxide radicals degradation



superoxide dismutase: SOD1
superoxide dismutase: SOD2
superoxide dismutase: SOD3
1.15.1.1

catalase: CAT
1.11.1.6/1.11.1.21

4 superoxide + 4 H⁺ → 2 hydrogen peroxide + 2 oxygen

2 hydrogen peroxide → oxygen + 2 H₂O

Compound: H₂O
Synonyms: H₂O, hydrogen oxide, water

If an enzyme name is shown in bold, there is experimental evidence for this

Synonyms: removal of superoxide radicals

Superclasses: [Detoxification](#) → [Reactive Oxygen Species Degradation](#)

Pathway Summary from MetaCyc:

General Background

All organisms living in an aerobic environment are exposed to reactive oxygen species (ROS) that are formed through metabolic processes and various environmental stresses such as drought, air pollutants, UV light and high light intensities, chilling temperatures and external chemicals [Van99, Alscher02]. For example, active oxygen species are produced during the β-oxidation of fatty acids or as a result of photorespiration in photosynthetic organisms [Frugoli96]. ROS such as superoxide and hydroxyl radicals as well as hydrogen peroxide can cause significant damage to proteins, nucleic acids and cell organelles.

Most of the aerobic organisms have developed defense systems to face oxidative stress and to scavenge oxidative radicals in the form of enzymes that can detoxify ROS, such as superoxide dismutase (SOD) and hydroperoxidase (CAT) [Beyer87]. For example, *Arabidopsis thaliana*, a member of the mustard family (oilseed plants), stores energy reserves preliminary as lipids that undergo β-oxidation during germination. The hydrogen peroxide that is produced during this metabolic process is detoxified by catalase. Another form of ROS, superoxide radicals, are by-products of aerobic electron transfer chains, and are disposed of by the action of superoxide dismutase. Since ROS can be found in any compartment of the eukaryotic cell, organisms have developed small gene families encoding for several SOD and CAT enzymes that operate in the various cell compartments [Kliebenstein98, McClung97].

About This Pathway

SODs represent the first line of defense against ROS, converting superoxide radicals to hydrogen peroxide and water. SODs are

<https://humancyc.org/compound?orgid=HUMAN&id=WATER>; iron-dependent, manganese-dependent and copper/zinc-dependent SODs, subcellular location. In plants, FeSODs are located in chloroplasts and are

HumanCyc - Pathway: superoxide radicals degradation (продолжение)

About This Pathway

show operations ▲

SODs represent the first line of defense against ROS, converting [superoxide](#) radicals to [hydrogen peroxide](#) and water. SODs are differentiated with regard to their metal cofactor. There are iron-dependent, manganese-dependent and copper/zinc-dependent SODs, which differ not only in their metal cofactor but also in their subcellular location. In plants, FeSODs are located in chloroplasts and are regarded the most ancient SOD group. MnSODs are found in the mitochondrion and the peroxisome and are structurally very similar to FeSODs. The last group, the Cu-ZnSODs operates in chloroplasts, the cytosol and even the extracellular space. They are structurally very different from the other two SOD groups because of the different electrical properties of copper in comparison to iron or manganese, which resulted in a major structural change in the protein [Alscher02].

To date seven SODs have been identified in *Arabidopsis thaliana*, three of them iron-dependent, three having copper as metal cofactor and one manganese-dependent SOD [Hindges92, Van90, Kliebenstein98]. It has been demonstrated that a copper-chaperone (AtCCS, At1g12520) is crucial for the activation of all three Cu/Zn-dependent SODs in this organism. The SOD holoenzyme usually constitutes either a homodimer or a homotetramer. However, the exact composition of the SODs in Arabidopsis is currently not known and remains to be verified (here displayed as polypeptides).

Catalase is second in the defense line against active oxygen, converting [hydrogen peroxide](#) into water and oxygen. Three genes encoding subunits of catalase and at least 6 catalase isoenzymes have been identified in Arabidopsis so far [Zhong94, McClung97, Frugoli96, Zhong96]. Besides their implication in detoxifying ROS, catalases are thought to play a role in the signal transduction pathway in plants leading to the development of SAR (systemic acquired resistance) [Jones94]. The functional protein of catalase is a tetramer but the question whether it exists as homo- or heterotetramer of different subunits remains to be investigated.

Superpathways: [reactive oxygen species degradation](#)

Locations of Mapped Genes:



Pathway Evidence Glyph:



This organism is in the expected taxonomic range for this pathway.

Key to pathway glyph edge colors: ●

■ An enzyme catalyzing this reaction is present in this organism

■ The reaction is unique to this pathway in MetaCyc

Credits:

Created in MetaCyc 07-Dec-1994 by Riley M , Marine Biological Laboratory
Reviewed in MetaCyc 30-Nov-2006 by Foerster H , The Arabidopsis Information Resource
Revised in MetaCyc 20-Feb-2009 by Caspi R , SRI International
Imported from MetaCyc 01-Nov-2016 by Caspi R , SRI International

References

Alscher02: Alscher RG, Erturk N, Heath LS (2002). "Role of superoxide dismutases (SODs) in controlling oxidative stress in plants." J Exp Bot 53(372):1331-41. PMID: 11997379

Beyer87: Beyer WF Jr, Fridovich I (1987). "Catalases-with and without heme." In MG Simic, KA Taylor, JF Ward, C Von Sonntag, eds, Oxygen Radicals in Biology and Medicine. Plenum, New York, 651-661.

HumanCyc – Pathway: superoxide radicals degradation – информация о ферменте SOD


gene **SOD1** enzyme **superoxide dismutase [Cu-Zn]** show operations
Homo sapiens Add to SmartTable

Synonyms IPOA, ALS1, ALS, superoxide dismutase 1, soluble (amyotrophic lateral sclerosis 1 (adult)), Cu/Zn superoxide dismutase, Superoxide dismutase-1, soluble

Accession IDs	HS06899 (HumanCyc) P00441 (UniProt)	Length	8905 bp
		Map Position	[29,692,513 -> 29,701,417] (61.86 centisomes) on Chromosome 21 View in Genome Browser
		Location	cytosol

Reaction **2 superoxide + 2 H⁺ → hydrogen peroxide + oxygen**

Pathways [superoxide radicals degradation](#)
[reactive oxygen species degradation](#)

Evidence  Assay of protein purified to homogeneity from a heterologous host [Kajihara88]

Summary | GO Terms (8) | Essentiality | Reactions (1) | Protein Features | Gene Context | References | Show All

Summary

Superoxide dismutases are metalloproteins which destroy radicals normally produced within cells that are toxic to biological systems. They catalyze the dismutation of superoxide to oxygen and hydrogen peroxide [Kajihara88].

Superoxide dismutases are classified according to the metal ion, Zn, Mn or Cu, which are a required cofactor for enzymic activity. There are three known superoxide dismutases in humans, [superoxide dismutase \[Cu-Zn\]](#), [superoxide dismutase \[Mn\]](#) and [extracellular superoxide dismutase \[Cu-Zn\]](#). Human [superoxide dismutase \[Cu-Zn\]](#) is a non-disulfide linked homodimer which binds one Cu and one Zn per subunit and is found primarily in the cytosol [Banci98][Arnesano04].

Human [superoxide dismutase \[Cu-Zn\]](#) is succinylated and succinylation decreases enzyme activity. NAD-dependent deacetylase sirtuin-5 binds to [superoxide dismutase \[Cu-Zn\]](#), desuccinylating and activating the enzyme. Mutations of the [superoxide dismutase \[Cu-Zn\]](#) succinylation site inhibits the growth of lung tumor cells, revealing a role for succinylation and desuccinylation of this enzyme in the growth of certain tumors [Lin13].

Mutations in the *SOD1* gene give rise to familial amyotrophic lateral sclerosis (ALS) also known as Lou Gehrig's disease [Hart98][Nakano94]. Familial amyotrophic lateral sclerosis is a neurodegenerative disorder affecting upper motor neurons in the brain and lower motor neurons in the brain stem and spinal cord, resulting in fatal paralysis.


Experiments *in vitro* have shown that the loss of zinc from [superoxide dismutase \[Cu-Zn\]](#) induces apoptosis in cultured motor neurons mediated by nitric oxide. Both familial and sporadic ALS may involve an oxidative mechanism requiring nitric oxide [Estevez99].

Additional Citations: [Levanon85, Sherman83]

Subunit Composition [SOD1]₂

Gene-Reaction Schematic

Expand/Contract the Schematic connections: Expand?



Credits:
Created 09-Jun-2014 by SRI International

Unification Links

Ensembl	ENSG00000142168
Entrez	AA805661, AA805662, AA859492, AA859626, AA859627, AAC41773, AAH01034, CAA25915, CAA25916, CAA25917, CAA25918, CAA25919, CAA26182, CAA64520
Entrez-gene	6647
Entrez-Nucleotide	BC001034, K00065, L44139, X02317
GeneCards	SOD1
MOPEd	P00441
OMIM	105400, 147450, 158700
PDB	1AZV, 1BA9, 1MFM, 1SOS, 1SPD
RefSeq	NM_000454, NP_000445
UCSC Human Genome	NM_000454
UniGene	75428
UniProt	P00441

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Page generated by Pathway Tools version 20.5 (software by SRI International) on Sun Mar 5, 2017, BIOCYC17B.
HumanCyc version 20.5.

Data type	Number (Release 20.1)
Genes	4505
Gene products covered by a mini-review	3884
Gene products with GO terms with EXP evidence	3350
Enzymes	1567
Metabolic reactions	1913
Compounds	2699
Transporters	282
Transport reactions	485
Transported substrates	338
Transcription factors	204
Regulatory interactions	6399

EcoCyc : статистика по данным, относящимся к регуляции транскрипции

Data type	Total	New
Transcription Unit	3553	95
Promoter	3841	73
Terminator	283	31
Transcription Factor	205	14
Transcription Factor Binding Site	2836	199
Regulatory Interaction	3374	183

Представление данных в EcoCyc: результат поиска по названию гена aceB



Please take 3 minute BioCyc survey

LOGIN | Why Login? | Create New Account

Enter a gene, protein, metabolite or pathway... Quick Search Gene Search

Searching *Escherichia coli* K-12 substr. MG1655 (EcoCyc) change organism database

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show operations

gene enzyme
aceB **malate synthase A**



Escherichia coli K-12 substr. MG1655

Synonym mas

Accession IDs	EG10023 (EcoCyc) b4014 ECK4006 P08997 (UniProt)	Length	1602 bp / 533 aa
		Map Position	[4,215,478 -> 4,217,079] (90.82 centisomes, 327°) View in Genome Browser
		Location	cytosol

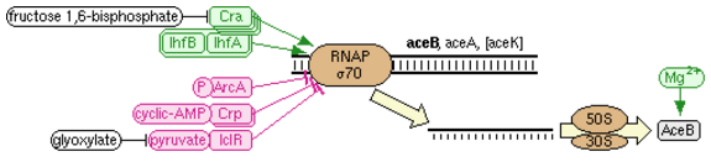
Reaction $\text{acetyl-CoA} + \text{glyoxylate} + \text{H}_2\text{O} \rightarrow (\text{S})\text{-malate} + \text{coenzyme A} + \text{H}^+$

Pathway [glyoxylate cycle](#)

Evidence  Assay of protein purified to homogeneity from its native host [Lohman08]
 Assay of unpurified protein expressed in its native host [Chung88]

Summary GO Terms (7) Essentiality Reactions (1) Protein Features Operons References Show All

Regulation Summary Diagram



Summary

There are two isozymes of malate synthase in *E. coli* [Falmagne65, Molina94]. Malate synthase A encoded by the *aceB* gene is a key enzyme in the [glyoxylate cycle](#). It metabolizes glyoxylate formed in the dissimilation of acetate. The relatively more studied isozyme malate synthase G encoded by the *glcB* gene is responsible for almost all of the malate synthase activity in cells metabolizing glyoxylate formed during growth on glycolate [Molina94].

Malate synthase A catalyzes the irreversible condensation of [acetyl-CoA](#) with [glyoxylate](#) to produce (*S*)-malate and [coenzyme A](#). The formation of (*S*)-malate is a key reaction in the [glyoxylate cycle](#). This cycle is similar to the TCA cycle (see [TCA cycle 1 \(prokaryotic\)](#)) but it bypasses the TCA cycle reactions that lead to a loss of CO₂, thus providing TCA cycle intermediates for cell carbon biosynthesis (see [superpathway of glyoxylate bypass and TCA](#)). The glyoxylate cycle has been extensively studied in connection with growth on acetate which is used in the synthesis of these biosynthetic precursors.

E. coli malate synthase A has been structurally characterized [Lohman08]. Its encoding gene *aceB* is located in the *aceBAK* operon which is

Unification Links

ASAP	ABE-0013125
CGSC	1051
EchoBASE	EB0022
EcoGene	EG10023
EcolWiki	b4014
ModBase	P08997
QU-Microarray	b4014
PortEco	aceB
PR	PRO_000022037

Представление данных в EcoCyc: результат поиска по названию гена aceB (продолжение)

lacks the α/β domain found in isoform G. However when substrate is bound, the two active sites are nearly identical and inhibitors bind with similar affinities [Lohman08].

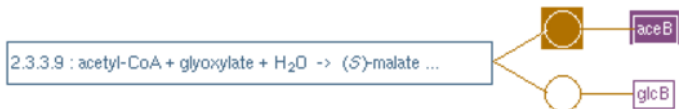
A series of vectors inducibly expressing paired-terminus antisense RNAs was constructed to silence central carbon metabolism in host *E. coli* K-12 MG1655. A vector that silenced *aceB* mRNA at 98% efficacy resulted in a defect in carbon catabolite repression [Nakashima14].

Review: [Cortay89]

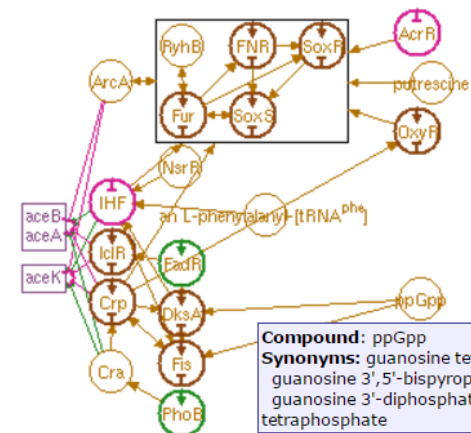
Additional Citations: [Byrne88, Byrne88a, LaPorte85]

Molecular Weight of Polypeptide 60.274 kD (from nucleotide sequence)

Gene-Reaction Schematic



Genetic Regulation Schematic



Relationship Links

InterPro: In-Family	IPR001465, IPR006252, IPR011076, IPR019830
Panther: In-Family	PTHR21631:SF1
PDB: Structure	3CUZ, 3CV1, 3CV2
Pfam: In-Family	PF01274
Prosite: In-Family	PS00510

Регуляторная геновая сеть !!!!

History:

10/20/97 Gene b4014 from Blattner lab Genbank (v. M52) entry merged into EcoCyc gene EG10023; confirmed by SwissProt match.

Credits:

Last-Curated 08-Jan-2016 by Fulcher C, SRI International

[Report Errors or Provide Feedback](#)

Page generated by Pathway Tools version 20.5 (software by SRI International) on Sun Mar 5, 2017, BIOCYC17A.

EcoCyc version 20.5.



BioCyc: скачать данные можно, только купив лицензию

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We provide two types of downloadable materials for the BioCyc databases and Pathway Tools software.

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- Pathway Tools [attribute-value](#) format
- Pathway Tools [tabular](#) format
- [SBML](#) format
- Gene Ontology annotations (EcoCyc only): [\[Download from GO Web site\]](#)

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БАЗА ДАННЫХ REACTOME – метаболические, сигнальные пути, схемы процессов

<http://www.reactome.org/>



Данные находятся в
открытом доступе !!

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Download Data

Reactome provides [open-source](#) and [open-data](#). We have continuously supported the major open-data standards, including [BioPAX](#), [PSI-MITAB](#), [SBML](#) and [SBGN](#) export formats. The Reactome data and source code continues to be publicly accessible under the terms of a Creative Commons Attribution 3.0 Unported License.

The Reactome website can be installed locally on Debian or Ubuntu Linux. This [shell script](#) will automate the Reactome local installation. More [detailed instructions](#) for local installation of Reactome database and website are also available. The website code can be downloaded as [reactome.tar.gz](#).

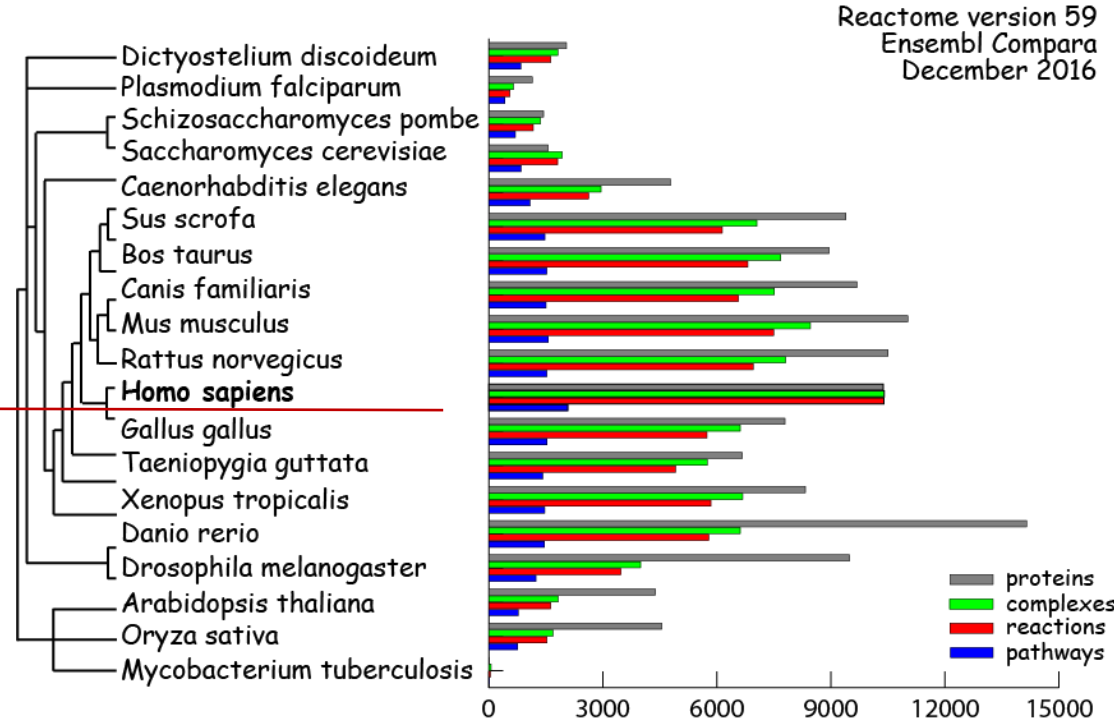
GitHub Repository is accessible [here](#).

For those of you requiring access to legacy data, you can download this from the [Reactome archive](#). Otherwise, access to our most recent data release can be found below.

Reactome provides [open-source](#) and [open-data](#). We have continuously supported the major open-data standards, including [BioPAX](#), [PSI-MITAB](#), [SBML](#) and [SBGN](#) export formats. The Reactome data and source code continues to be publicly accessible under the terms of a Creative Commons Attribution 3.0 Unported License.

БАЗА ДАННЫХ REACTOME(Version 59): статистика

Species	PROTEINS	COMPLE- XES	REAC- TIONS	PATHWAYS
D. discoideum	2042	1815	1631	841
P. falciparum	1144	648	555	424
S. pombe	1440	1362	1167	695
S. cerevisiae	1558	1932	1810	850
C. elegans	4780	2954	2627	1084
S. scrofa	9394	7050	6141	1473
B. taurus	8951	7684	6813	1526
C. familiaris	9683	7514	6566	1504
M. musculus	11020	8459	7491	1568
R. norvegicus	10506	7810	6957	1528
*H. sapiens	10374	10399	10391	2080
G. gallus	7790	6615	5737	1533
T. guttata	6666	5746	4915	1419
X. tropicalis	8328	6677	5841	1468
D. rerio	14148	6617	5784	1467
D. melanogaster	9487	3996	3472	1239
A. thaliana	4381	1821	1624	772
O. sativa	4550	1690	1530	761
M. tuberculosis	13	58	40	12



 19 видов организмов

БАЗА ДАННЫХ REACTOME: интерфейс

Иерархический список разделов (диаграмм)

The screenshot displays the Reactome database interface for Homo sapiens. On the left, an 'Event Hierarchy' lists various biological processes, with 'Chromatin organization' and 'Chromatin modifying enzymes' highlighted. The main area shows a detailed diagram of the 'Chromatin modifying enzymes' pathway. A 'Diagram key' legend is overlaid on the right, defining symbols for entities (Small molecule, Protein, Complex(es), Set(s), Genome encoded entity, Encapsulated Pathway) and reaction types (Transition/Process, Association/Binding, Dissociation, Omitted, Uncertain). Below the legend, 'Reaction Attributes' are defined, including Stoichiometry, Catalysis, Positive/Negative Regulation, Set to member link, Wild Type, and Disease-associated. A table below the legend lists 'Chemical Compounds (16)' and 'Proteins (241)'. A search bar at the top indicates 'Pathways for: Homo sapiens'.

Event Hierarchy:

- Cell Cycle
- Cell-Cell communication
- Cellular responses to stress
- Chromatin organization**
- Chromatin modifying enzymes**
- Circadian Clock
- Developmental Biology
- Disease
- DNA Repair
- DNA Replication
- Extracellular matrix organization
- Gene Expression
- Hemostasis
- Immune System
- Mitophagy
- Metabolism
- Metabolism of proteins
- Muscle contraction
- Neuronal System
- Organelle biogenesis and maintenance
- Programmed Cell Death
- Reproduction
- Signal Transduction
- Transmembrane transport of small molecules
- Vesicle-mediated transport
- Membrane Trafficking
- Binding and Uptake of Ligands by Scavenger Receptors

Diagram key

- Small molecule
- Protein
- Complex(es)
- Set(s)
- Genome encoded entity
- Encapsulated Pathway

Reaction Types:

- Transition/Process
- Association/Binding
- Dissociation
- Omitted
- Uncertain

Reaction Attributes:

- Stoichiometry
- Catalysis
- Positive Regulation
- Negative Regulation
- Set to member link
- Wild Type
- Disease-associated

Chemical Compounds (16)

Proteins (241)

Условные обозначения

БАЗА ДАННЫХ REACTOME:

фрагмент диаграммы, представляющей реакции гликолиза

REACTOME 3.2
Pathways for: Homo sapiens

Analysis: [Bar Chart Icon] Tour: [Crosshair Icon] Layout: [Grid Icon]

Event Hierarchy:
- Circadian Clock
- Developmental Biology
- Disease
- DNA Repair
- DNA Replication
- Extracellular matrix organization
- Gene Expression
- Hemostasis
- Immune System
- Mitophagy
- **Metabolism**
- **Metabolism of carbohydrates**
- Digestion of dietary carbohydrate
- CHIA hydrolyses chitin
- CHIT1 hydrolyses CHIT to 3xADGP
- Hexose transport
- **Glucose metabolism**
- **Glycolysis**
- **HK1,2,3,GCK phosphorylate Glc to form G6P**
- alpha-D-glucose 6-phosphate <=> D-fructose 6-p
- Dephosphorylation of phosphoPFKFB1 by PP2A-ABdeltaC complex
- D-fructose 6-phosphate + ATP => D-fructose 2,6-
- D-fructose 6-phosphate + ATP => D-fructose 1,6-
- D-fructose 1,6-bisphosphate <=> dihydroxyaceto
- dihydroxyacetone phosphate <=> D-glyceraldehy
- D-glyceraldehyde 3-phosphate + orthophosphate
- 1,3-bisphospho-D-glycerate + ADP <=> 3-phospho

endoplasmic reticulum lumen

SLC37A4

glucokinase and hexokinases

PKA catalytic subunit

PP2A-ABdeltaC complex

phosphoPFKFB1 dimer

PFKFB dimers

PGM1:Mg2+, PGM2:Mg2+

SLC2A5


Description | Molecules 8/438 | Structures | Expression | Analysis | Downloads

Metabolism of carbohydrates | Species: Homo sapiens | Download

Chemical Compounds (4/140) +

Proteins (4/297) +

DNA/RNA (0/1) +



BETA
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Pathways for the People

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We want your feedback! A quick survey to help us focus development and renew funding.
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Welcome to WikiPathways BETA

WikiPathways is a database of biological pathways maintained by and for the scientific community.

Find Pathways

Search

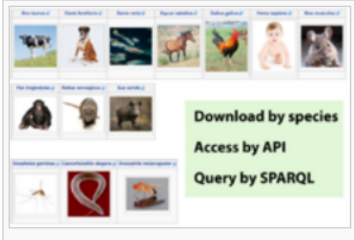
Browse



Browse by species and category

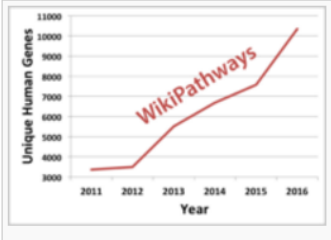
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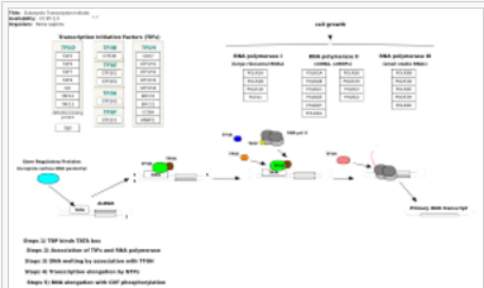
Growth



Year	Unique Human Genes
2011	~3500
2012	~4000
2013	~6000
2014	~7000
2015	~8000
2016	~10000

Today's Featured Pathway

Eukaryotic Transcription Initiation (Homo sapiens)

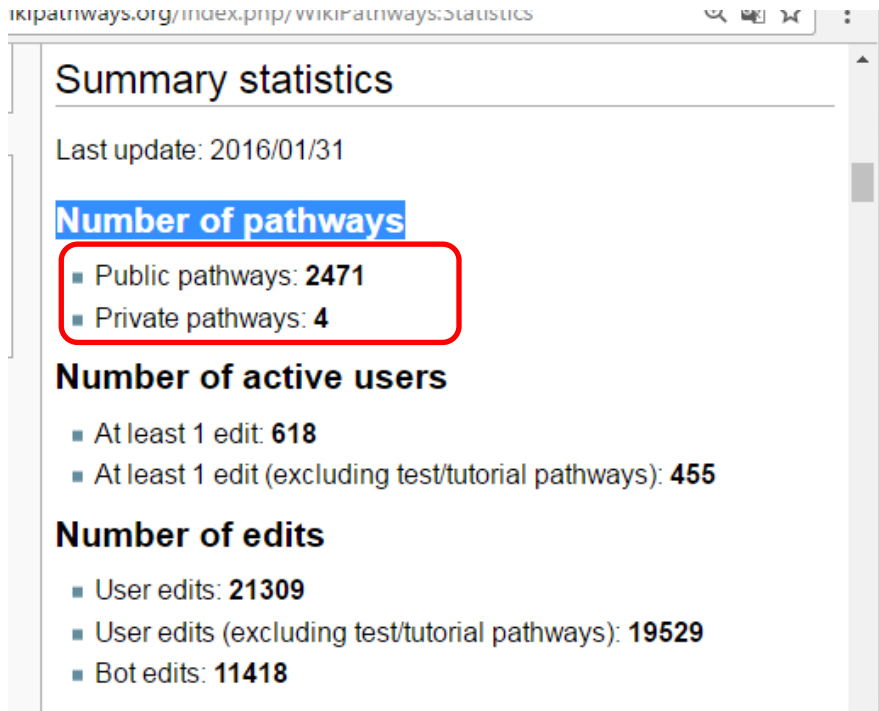


Eukaryotic Transcription Initiation

Updates

- February 2017 Release:** 56 edits by 8 contributors this month
- February 2: Rett syndrome pathway is now live at [Wikipedia](#)
- January 2017 Release:** 25 new human pathways with 181 new genes
- December 22: Blog post about our [translation of mouse pathways](#)
- December 2016 Release:** 201 edits by 15 contributors this month
- November 11: [Enrichment analysis of single-cell dataset on differentiation](#)
- November 2016 Release:** 143 new human genes

Статистика базы WikiPathways



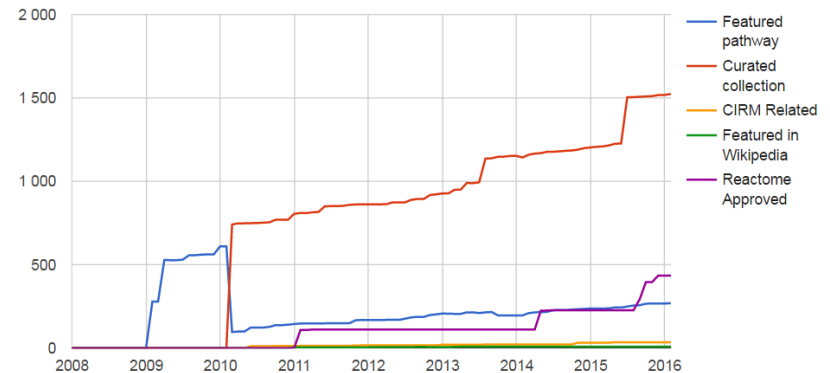
Kutmon M, Riutta A, Nunes N, Hanspers K, Willighagen EL, Bohler A, Mélius J, Waagmeester A, Sinha SR, Miller R, Coort SL, Cirillo E, Smeets B, Evelo CT, Pico AR. **WikiPathways: capturing the full diversity of pathway knowledge** *Nucl. Acids Res.*, 44, D488-D494 (2016)

Pico AR, Kelder T, van Iersel MP, Hanspers K, Conklin BR, Evelo C. (2008) WikiPathways: Pathway Editing for the People. *PLoS Biol* 6(7)

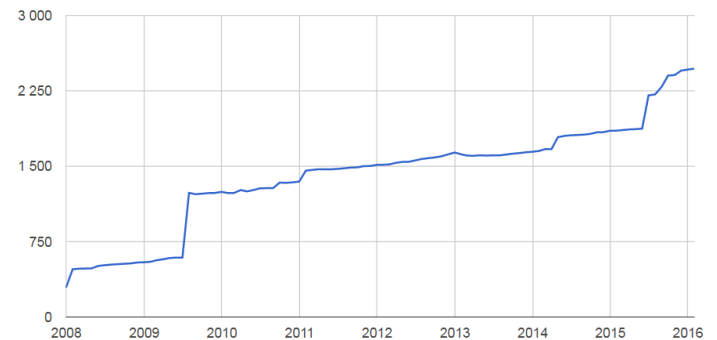
Неуклонный рост базы по годам

Pathways per collection

The size of different pathways collections over time.



Show pathway counts for



25 видов организмов базы WikiPathways








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Versioned Releases
Each month we release an updated set of pathways in various data and image formats. These pathways have been reviewed and tagged as created, and are considered ready for analysis and data overlays.

Current version: 20170210 (10 February 2017) <#>







Vertebrates

Bos taurus #	Canis familiaris #	Danio rerio #	Equus caballus #	Gallus gallus #	Homo sapiens #	Mus musculus #
						



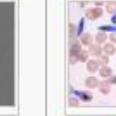
Invertebrates

Pan troglodytes #	Rattus norvegicus #	Sus scrofa #
		




Plants

Arabidopsis thaliana #	Hordeum vulgare #	Oryza sativa #	Populus trichocarpa #	Solanum lycopersicum #	Zea mays #
					

Eukaryotic microorganisms

Gibberella zeae #	Saccharomyces cerevisiae #	Plasmodium falciparum #
		

Bacteria

Bacillus subtilis #	E. coli #	Mycobacterium tuberculosis #
		

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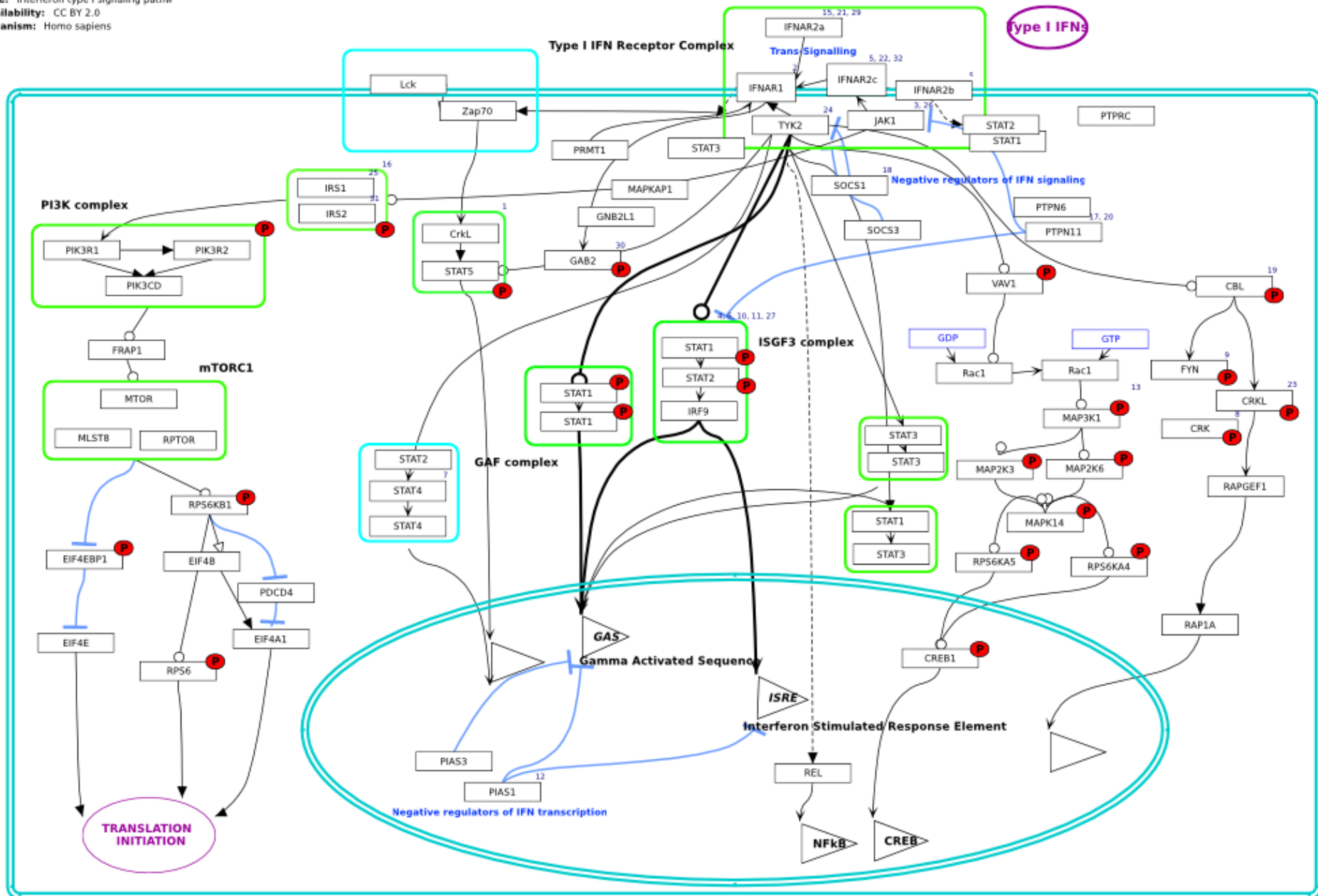
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Пример представления данных в базе WikiPathways: Диаграмма «Interferon type I signaling pathways (Homo sapiens)»

Title: Interferon type I signaling pathw
Availability: CC BY 2.0
Organism: Homo sapiens



Все данные диаграмм WikiPathways можно скачать !!!!! (Первый способ)

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Multiple formats and methods

Выбор вида организма

Архивный файл всех диаграмм одного вида организма (gpm1 формат)

Имя	Размер	Сжат	Тип	Изменён	CRC32
Папка с файл...					
Hs_4-hydroxytamoxifen,_Dexamethasone,_and_Retinoic_Acids_Regulation_of...	26 521	3 845	Файл "GPML"	13.10.2016 ...	BF8AD...
Hs_ACE_Inhibitor_Pathway_WP554_84372.gpml	37 697	5 343	Файл "GPML"	17.02.2016 ...	0728A...
Hs_Acetylcholine_Synthesis_WP528_79855.gpml	17 076	3 113	Файл "GPML"	04.05.2015 ...	1A63E...
Hs_Adipogenesis_WP236_80209.gpml	68 570	8 125	Файл "GPML"	22.05.2015 ...	B4C92...
Hs_Aflatoxin_B1_metabolism_WP699_70509.gpml	31 383	4 309	Файл "GPML"	04.05.2015 ...	DF49A...
Hs_AGE-RAGE_pathway_WP2324_89798.gpml	143 216	23 741	Файл "GPML"	06.10.2016 ...	6AAA3...
Hs_Alanine_and_aspartate_metabolism_WP106_91240.gpml	67 203	8 879	Файл "GPML"	21.01.2017 ...	85824...
Hs_Allograft_Rejection_WP2328_90020.gpml	160 876	20 090	Файл "GPML"	08.10.2016 ...	C9F45C...
Hs_Alpha_6_Beta_4_signaling_pathway_WP244_85199.gpml	74 687	9 742	Файл "GPML"	25.04.2016 ...	64D85...
Hs_Alzheimers_Disease_WP2059_87372.gpml	144 549	16 630	Файл "GPML"	22.07.2016 ...	C66543...
Hs_Amino_acid_conjugation_of_benzoic_acid_WP521_88588.gpml	9 727	1 726	Файл "GPML"	11.08.2016 ...	CF347B...
Hs_Amino_acid_conjugation_WP715_63154.gpml	5 556	1 132	Файл "GPML"	04.05.2015 ...	DDBB9...
Hs_Amino_Acid_metabolism_WP3925_90737.gpml	201 780	25 954	Файл "GPML"	13.12.2016 ...	32E4C9...
Hs_AMP-activated_Protein_Kinase_(AMPK)_Signaling_WP1403_90259.gpml	79 507	12 713	Файл "GPML"	27.10.2016 ...	73E441...
Hs_Amplification_and_Expansion_of_Oncogenic_Pathways_as_Metastatic_Trait...	22 371	4 143	Файл "GPML"	13.10.2016 ...	947498...
Hs_Amyotrophic_lateral_sclerosis_(ALS)_WP2447_85186.gpml	63 458	10 080	Файл "GPML"	23.04.2016 ...	314524...
Hs_Androgen_receptor_signaling_pathway_WP138_79958.gpml	105 471	16 748	Файл "GPML"	04.05.2015 ...	B374D...
Hs_Angiogenesis_WP1539_88983.gpml	47 789	6 560	Файл "GPML"	18.08.2016 ...	2A716...
Hs_Angiopoietin_Like_Protein_8_Regulatory_Pathway_WP3915_90629.gpml	183 173	25 164	Файл "GPML"	02.12.2016 ...	BBDDF...
Hs_ApoE_and_miR-146_in_inflammation_and_atherosclerosis_WP3926_90739...	16 810	3 236	Файл "GPML"	13.12.2016 ...	F98AC...
Hs_Apoptosis_Modulation_and_Signaling_WP1772_91293.gpml	90 928	9 952	Файл "GPML"	23.01.2017 ...	9ED92...
Hs_Apoptosis_Modulation_by_HSP70_WP384_67054.gpml	34 491	4 874	Файл "GPML"	27.04.2015 ...	B15FE...
Hs_Apoptosis_WP254_88977.gpml	74 141	9 805	Файл "GPML"	18.08.2016 ...	A06A1...
Hs_Apoptosis-related_network_due_to_altered_Notch3_in_ovarian_cancer_WP...	46 898	5 207	Файл "GPML"	04.05.2015 ...	EB991E...
Hs_Arachidonate_Epoxygenase_-_Epoxide_Hydrolase_WP678_71506.gpml	38 335	5 169	Файл "GPML"	04.05.2015 ...	2C7AD...
Hs_Arrhythmogenic_Right_Ventricular_Cardiomyopathy_WP2118_71265.gpml	97 314	9 064	Файл "GPML"	04.05.2015 ...	C856B...
Hs_Aryl_Hydrocarbon_Receptor_Pathway_WP2873_88902.gpml	92 983	10 444	Файл "GPML"	17.08.2016 ...	5AF732...
Hs_Aryl_Hydrocarbon_Receptor_WP2586_89793.gpml	158 322	19 370	Файл "GPML"	06.10.2016 ...	F4D3EF...
Hs_Arylamine_metabolism_WP694_89536.gpml	18 479	2 823	Файл "GPML"	16.09.2016 ...	4EA6D...
Hs_Association_Between_Physico-Chemical_Features_and_Toxicity_Associated...	62 386	8 420	Файл "GPML"	13.10.2016 ...	D6733...
Hs_ATM_Signaling_Network_in_Development_and_Disease_WP3878_89745.g...	42 186	5 966	Файл "GPML"	29.09.2016 ...	B48E87...
Hs_ATM_Signaling_Pathway_WP2516_90247.gpml	295 343	34 278	Файл "GPML"	26.10.2016 ...	0FAF71...

Всего: 25 661 938 байт в 379 файлах

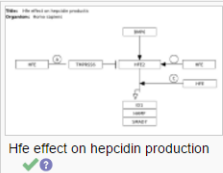
Данные диаграмм WikiPathways можно все скачать !!!!! (Второй способ)

special

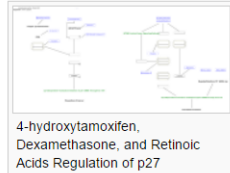
Log in / create account

Browse pathways

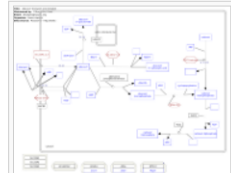
Species: Homo sapiens Collection: All Tags View: Thumbnail Mode



Hfe effect on hepcidin production



4-hydroxytamoxifen, Dexamethasone, and Retinoic Acids Regulation of p27 Expression



Abacavir transport and metabolism

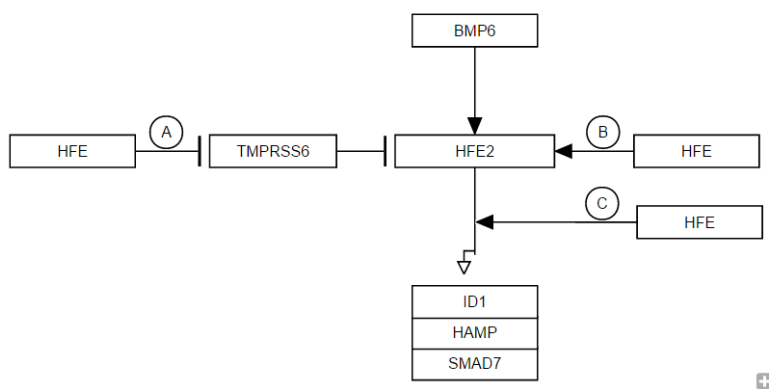
pathway discussion view source

Hfe effect on hepcidin production (Homo sapiens)

Kristina Hanspers

Search for...

Title: Hfe effect on hepcidin production
Organism: Homo sapiens



Download

- PathMeio (.gpm)
- Scalable Vector Graphics (.svg)
- Gene list (.txt)
- Biopax level 3 (.owl)
- Eu Gene (.pwl)
- Png image (.png)
- Acrobat (.pdf)

Description

Hfe, the mouse equivalent of the human hemochromatosis gene, is known to promote expression of hepcidin, a gene product that inhibits iron absorption. Evidence obtained from gene testing on mice seems to indicate that Hfe inhibits Tmprss6, which acts with the cycle(Hfe could be acting on the interaction at points A,B, or C). Hfe, as well as Tmprss6, are involved in the regulation of hepcidin production. Evidence obtained from gene testing on mice seems to indicate that Hfe inhibits Tmprss6, which acts with the cycle(Hfe could be acting on the interaction at points A,B, or C). Hfe, as well as Tmprss6, are involved in the regulation of hepcidin production.

Скачиваем каждую диаграмму поотдельности в форматах:

- gpm1,
- svg,
- txt,
- owl,
- pwl,
- png,
- pdf

PECYPC Signor

http://signor.uniroma2.it/

Signor 2.0
The SIGNaling Network Open Resource

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Feedback

Homo sapiens Mus musculus Rattus norvegicus

type entity here...

all connect

Search tips:
To search a single entity type its name or ID into the search bar.
For a multi-protein search type their Uniprot IDs separated by one of the following delimiters: comma(,), semi-colon(;), space.

About SIGNOR

Latest publication: [Abstract](#) | [Article](#)

SIGNOR, the **SIGNaling Network Open Resource**, organizes and stores in a structured format signaling information published in the scientific literature.

The captured information is stored as binary causative relationships between biological entities and can be represented graphically as activity flow.

The entire network can be freely downloaded and used to support logic modeling or to interpret high content datasets.
The core of this project is a collection of more than 11000 manually-annotated causal relationships between proteins that participate in

PATHWAY BROWSER

Selected organism: **Homo sapiens**

To view a pathway select it from the drop-down menu.

Select Pathway below

Select Disease below

Select Tumor below

NEWS

30-03-2016

Sacco et al "Deep Proteomics of Breast Cancer Cells Reveals that Metformin Reverses Signaling Networks Away from a Pro-growth State" Cell systems 2, 3, p159–171, 23 March 2016 use the SIGNOR network to interpret phospho-proteomics data

SignaLink UniProt PubChem menta PhosphoSitePlus elixir MINT

База данных по сигнальным путям трех видов организмов (человек , мышь, крыса). Данные взяты из научных публикаций

Статистика данных в базе Signor

<http://signor.uniroma2.it/statistics.php>

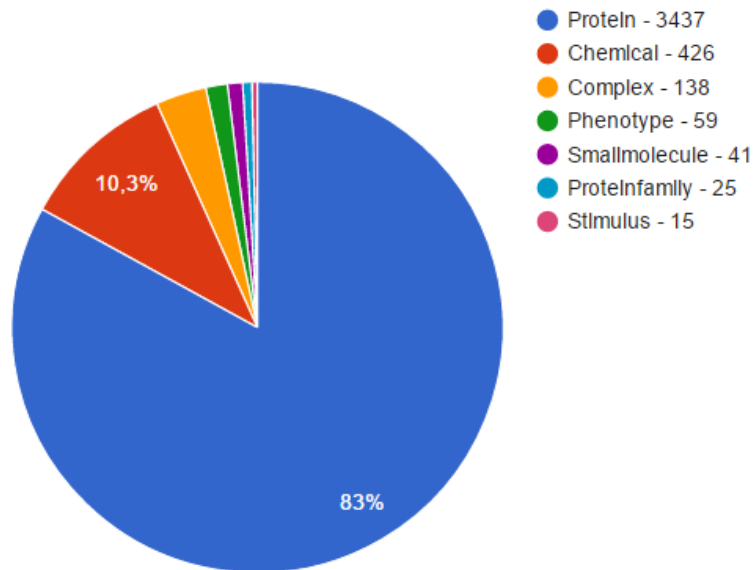


The SIGNaling Network Open Resource

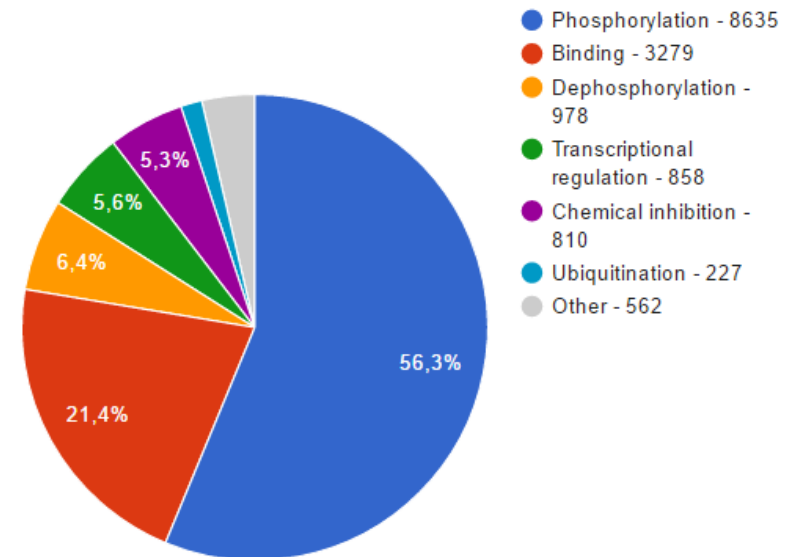
HOME USER GUIDE STATISTICS CURATION CONTACT DOWNLOADS SEARCH

16246 curated relations - 6295 curated publications

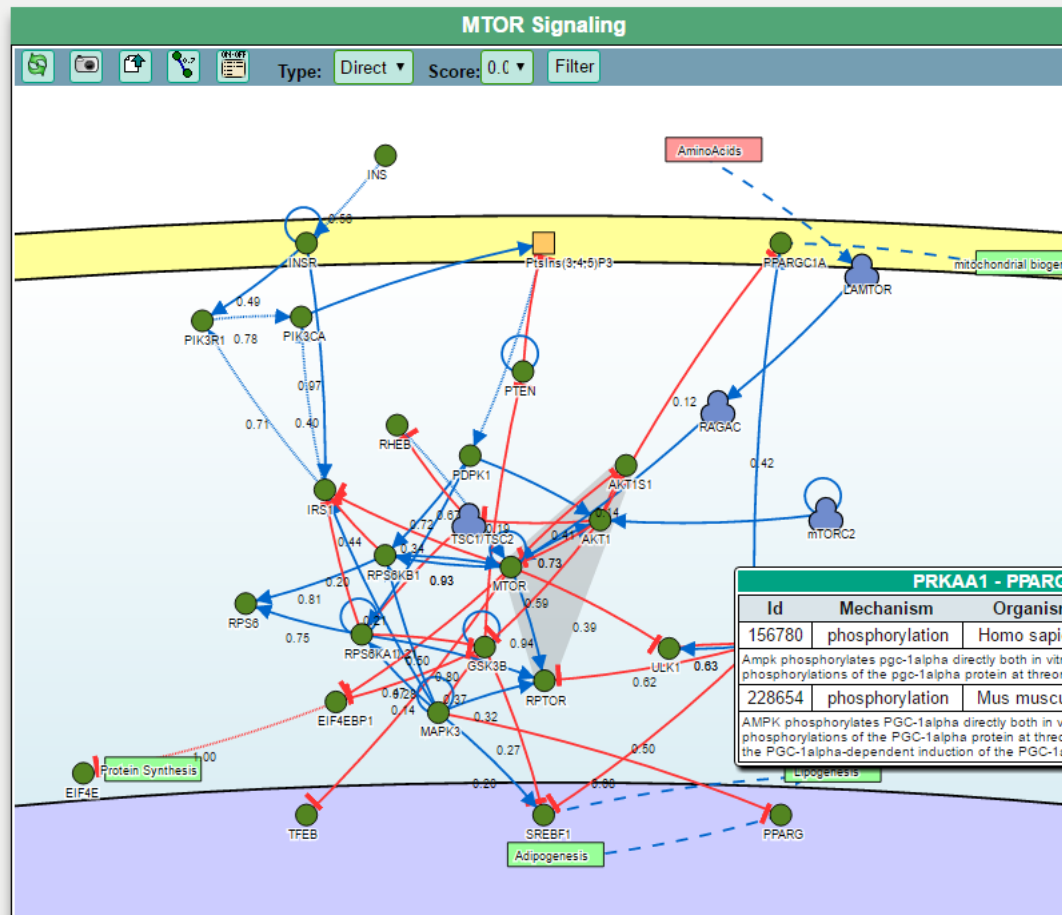
Entity types



Mechanisms



Ресурс Signor : представление данных по mTOR сигнальному пути



Pathway ID: SIGNOR-MTOR

Description: The mammalian target of rapamycin (mTOR) signaling pathway couples energy and nutrient abundance to cellular growth. mTOR is serine/threonine kinase acting in two complexes (mTORC1 and mTORC2) which exert their actions by regulating other important kinases, such as S6K and Akt. In particular, mTORC1 integrates multiple signals reflecting nutrients' availability or deprivation promoting cellular growth or catabolic processes respectively.

37 Seed Entities

Name Primary ID

Organism:

Add Entity

Adipogenesis SIGNOR-PH26

AKT1 P31749

AKT1S1 Q96B36

AminoAcids SIGNOR-ST5

EIF4E P06730

EIF4EBP1 Q13541

GSK3B P49841

HIF1AN Q9NWT6

INS P01308

MITOCHONDRIAL BIOGENESIS P06213

MTOR P35568

PPARGC1A SIGNOR-C26

RAGAC SIGNOR-PH30

RPTOR P27361

TFEB SIGNOR-PH32

ULK1 P42345

mTORC2 SIGNOR-C2

PDPK1 O15530

PIK3CA P42336

PIK3R1 P27986

PPARG P37231

PPARGC1A Q9UBK2

PRKAA1 Q13131

PRKAG1 P54619

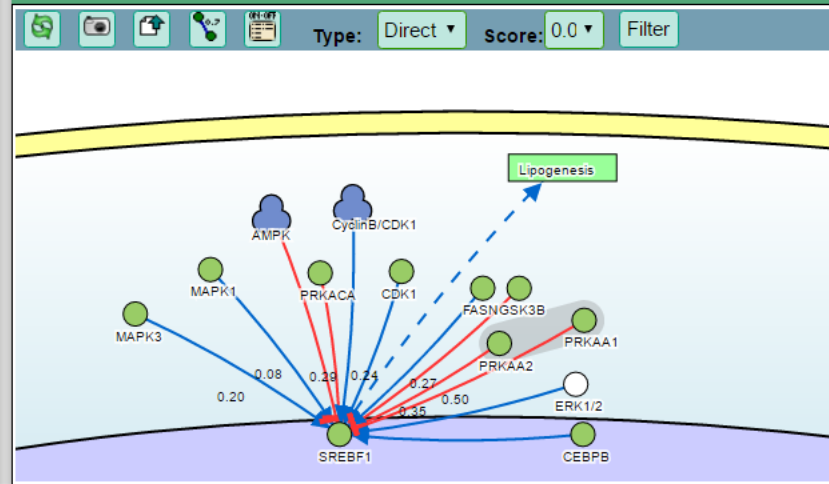
Ресурс Signor : представление данных о путях активации фактора SREBP1

Summary

Name	SREBF1 View Modifications
Full Name	Sterol regulatory element-binding protein 1
Synonyms	SREBP-1, Class D basic helix-loop-helix protein 1, bHLHd1, Sterol regulatory element-binding transcription factor 1 BHLHD1, SREBP1
Primary ID	P36956
Links	- -
Type	protein
Relations	26

Viewer

[Expand](#)



Search Tools

Refine search:

- by mechanism

- by effect

- by organism:

Modifications Tables

Relations

	REGULATOR	MECHANISM	TARGET	SCORE
+	<u>MAPK3</u>	up-regulates activity → phosphorylation	<u>SREBF1</u>	0.20
Publications: 1		Organism: Homo Sapiens		
Pathways: MTOR Signaling				
+	<u>MAPK1</u>	up-regulates → phosphorylation	<u>SREBF1</u>	0.08
Publications: 1		Organism: Homo Sapiens		

Ресурс Signor : данные можно скачать



The SIGNaling Network Open Resource

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Available Downloads

[Whole database data](#) [view](#)

[SIGNOR entity data](#) [view](#)

[Pathway-related data](#) [view](#)




[Phosphorylation data](#) [view](#)

[Download by relation id](#) [view](#)

[Download by entity or list of entities](#) [view](#)

Download All Data

Select Organism:

-  Homo sapiens
-  Mus musculus
-  Rattus norvegicus

Select a format below to download all data from the database:

- file csv
- file xls (slower)

Download SIGNOR entity data

SIGNOR Complexes:

SIGNOR Protein Families:

PECYPC SPIKE

<http://www.cs.tau.ac.il/~spike/>



Signaling Pathway Integrated Knowledge Engine

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SPIKE is a database of highly curated human signaling pathways with an associated interactive software tool.

Users can view and download individual pathway maps and browse the entire database from this website, or launch a map viewer tool that allows dynamic visualization of the database and save networks in XGMML format that can be viewed in all generic XGMML viewers.

Browsing and downloading the database does not require registration or login.

Map Topics

- Cell cycle progress and check points
- DNA damage response
- Programmed cell death related processes
- Stress-activated transcription factors
- Mitogen-activated protein kinase pathways
- Immune response signaling
- HEarSpike: hearing related pathways

28 сигнальных путей

[1] R. Elkon, R. Vesterman, N. Amit, J. Assa, I. Ulitsky, G. Steinfeld, R. Blechman, Y. Shiloh, R. Shamir. "SPIKE – a database, visualization and analysis tool of cellular signaling pathways". BMC Bioinformatics 9:110 (2008)

[2] Arnon Paz, Zippora Brownstein, Yaara Ber, Shani Bialik, Eyal David, Dorit Sagir, Igor Ulitsky, Ran Elkon, Adi Kimchi, Karen B. Avraham, Yosef Shiloh and Ron Shamir "SPIKE: a database of highly curated human signaling pathways". Nucleic Acids Research, 2011, Vol. 39, Database issue

News (January 2012)

Maps Updates:

Updated Map: Apoptosis Anti-Apoptosis (Jan12)

Updated Map: p53 (Jan12)

Updated Map: ATM (Jan12)

New Map: Ras signaling (Jan12)

New Map: WNT signaling (Nov11)

Updated Map: Autophagy (Aug11)

Updated Map: NFkB Signaling Network (Jun11)

Updated Map: MAPK signaling (Jun11)

Updated Map: Mismatch repair (Jun11)

Updated Map: Base excision and single strand break repair (Jun11)

Updated Map: Repair of Interstrand Crosslinks (May11)

Updated Map: Nucleotide excision repair (Apr11)

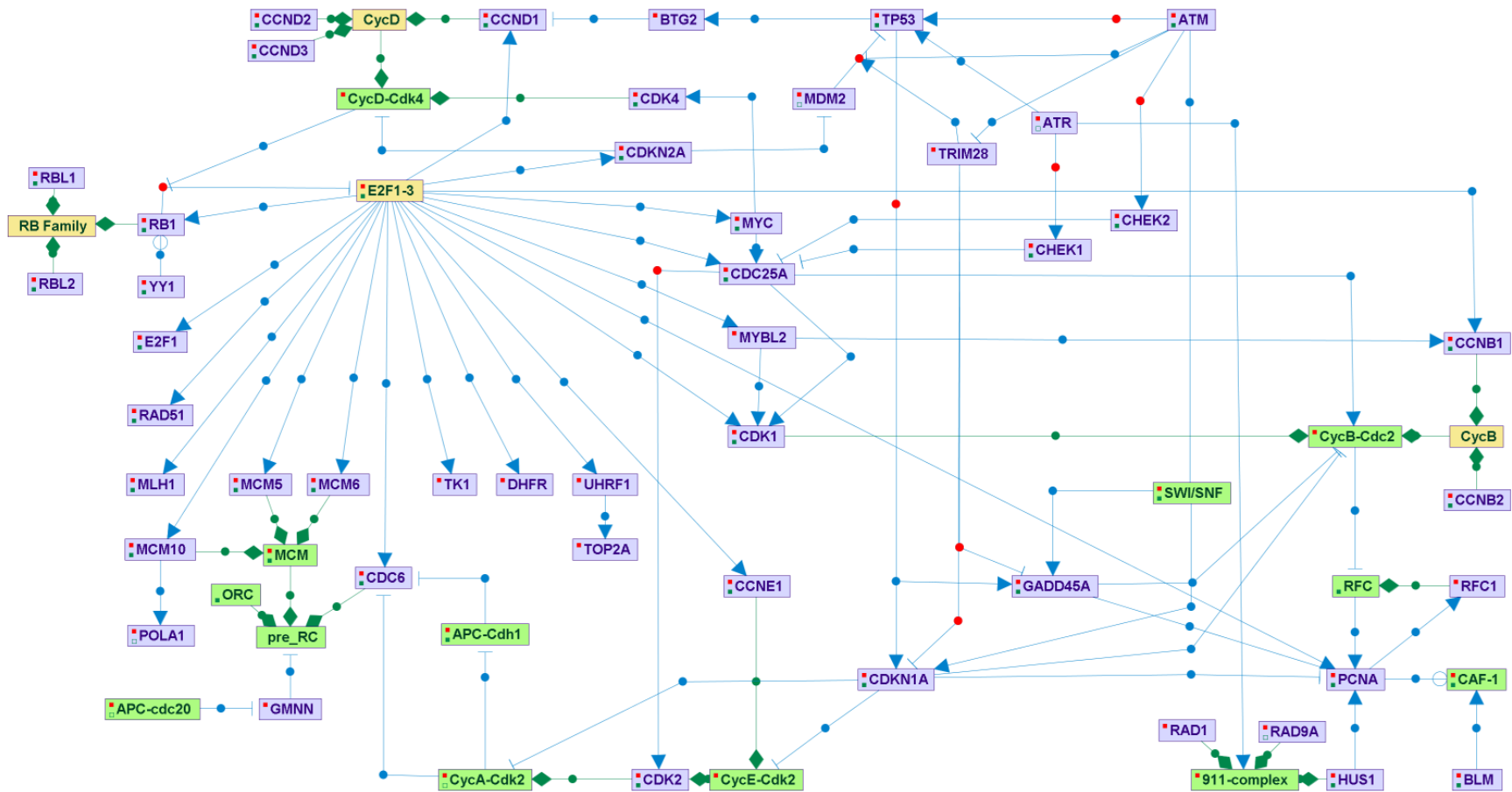
see the Maps section

Designed by Spike Team.

База SPIKE: Представление данных о процессе «DNA damage induced G1-S checkpoint (spike00003)»



Signaling Pathway Integrated Knowledge Engine





SPIKE

Signaling Pathway Integrated Knowledge Engine

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Spike database in XML format

- [SPIKE DB](#)

Spike database in other formats

The Spike database is available for download in the following formats:

- [BioPax](#)
 - [Sif](#)
-

ИНФОРМАЦИОННЫЙ РЕСУРС BIO CARTA

https://cgap.nci.nih.gov/Pathways/BioCarta_Pathways

National Cancer Institute | U.S. National Institutes of Health | www.cancer.gov

CANCER GENOME ANATOMY PROJECT

CGAP How To | Genes | Chromosomes | Tissues | SAGE Genie | RNAi | Pathways | Tools

Pathways

Pathway information provided by BioCarta
(See Terms and Conditions of use)
For information on sources of Pathway diagrams, see Biocarta Pathways HowTo

A B C D E F G H I K L M N O P R S T U V W Y ?

A

- Acetylation and Deacetylation of RelA in The Nucleus **H M**
- Actions of Nitric Oxide in the Heart **H**
- Activation of cAMP-dependent protein kinase, PKA **H M**
- Activation of Csk by cAMP-dependent Protein Kinase Inhibits Signaling through the T Cell Receptor **H M**
- Activation of PKC through G protein coupled receptor **H M**
- Activation of Src by Protein-tyrosine phosphatase alpha **H M**
- Acute Myocardial Infarction **H**
- Adhesion and Diapedesis of Granulocytes **H**
- Adhesion and Diapedesis of Lymphocytes **H**
- Adhesion Molecules on Lymphocyte **H M**
- ADP-Ribosylation Factor **H M**
- Agrin in Postsynaptic Differentiation **H M**
- Ahr Signal Transduction Pathway **H M**

Боле 300 диаграмм

БАЗА НЕ ОБНОВЛЯЕТСЯ:

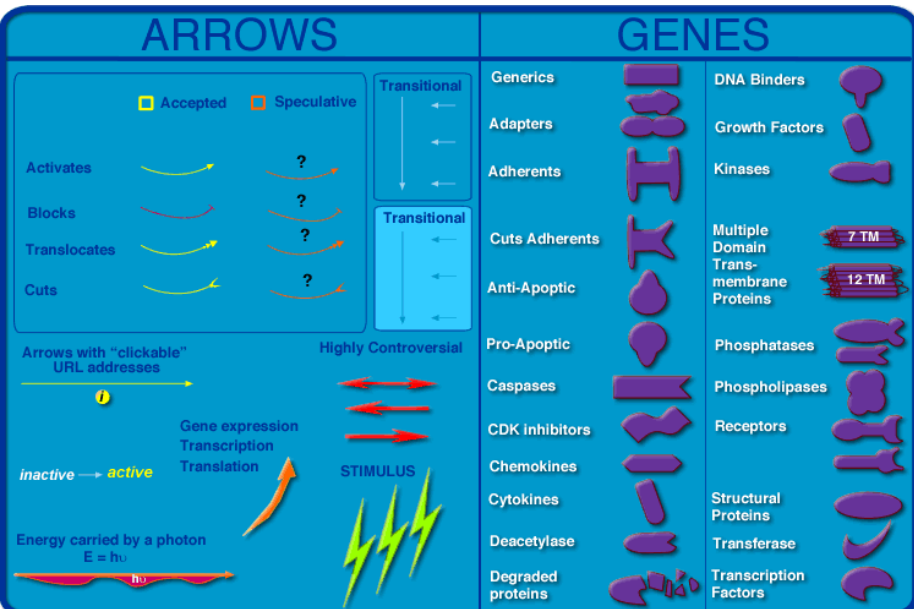
BioCarta had not been updating its pathways. The information provided might have been outdated. As a result, we have discontinued offering pathway information online. You may view our pathway figures at http://cgap.nci.nih.gov/Pathways/BioCarta_Pathways.

<http://www.biocarta.com/>

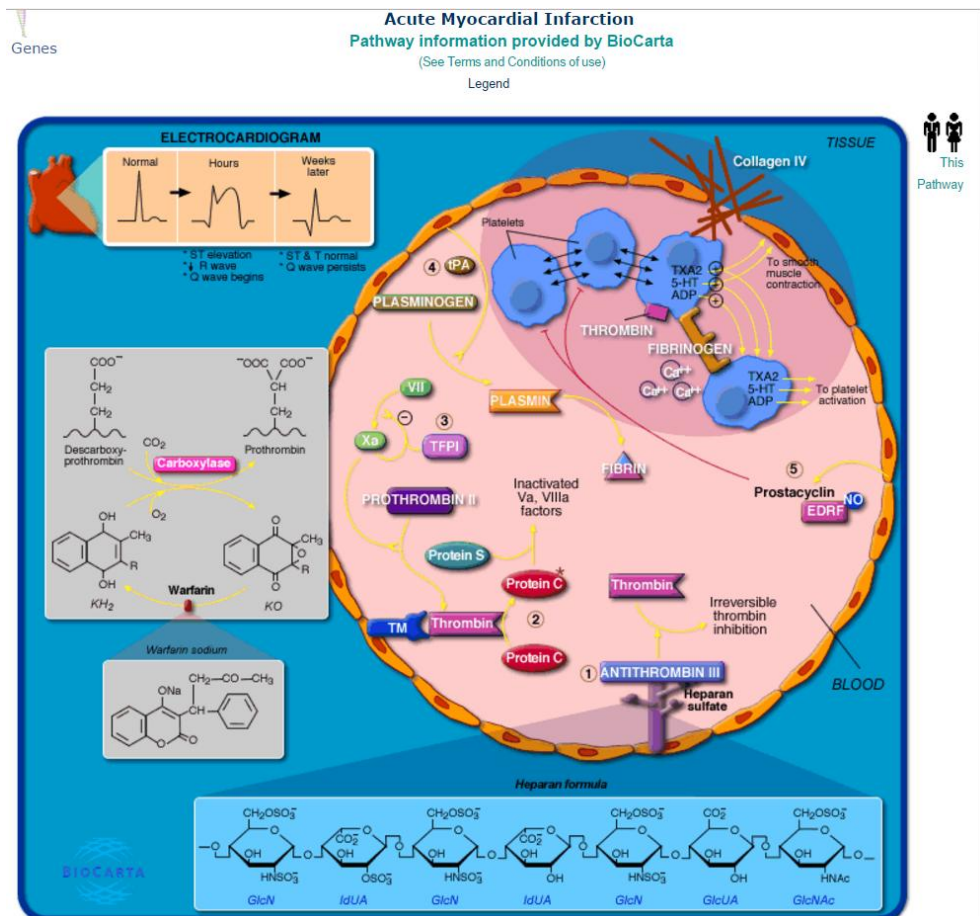
ИНФОРМАЦИОННЫЙ РЕСУРС ВЮСАРТА

Содержит схемы метаболических либо сигнальных путей, а также схемы процессов

Условные обозначения



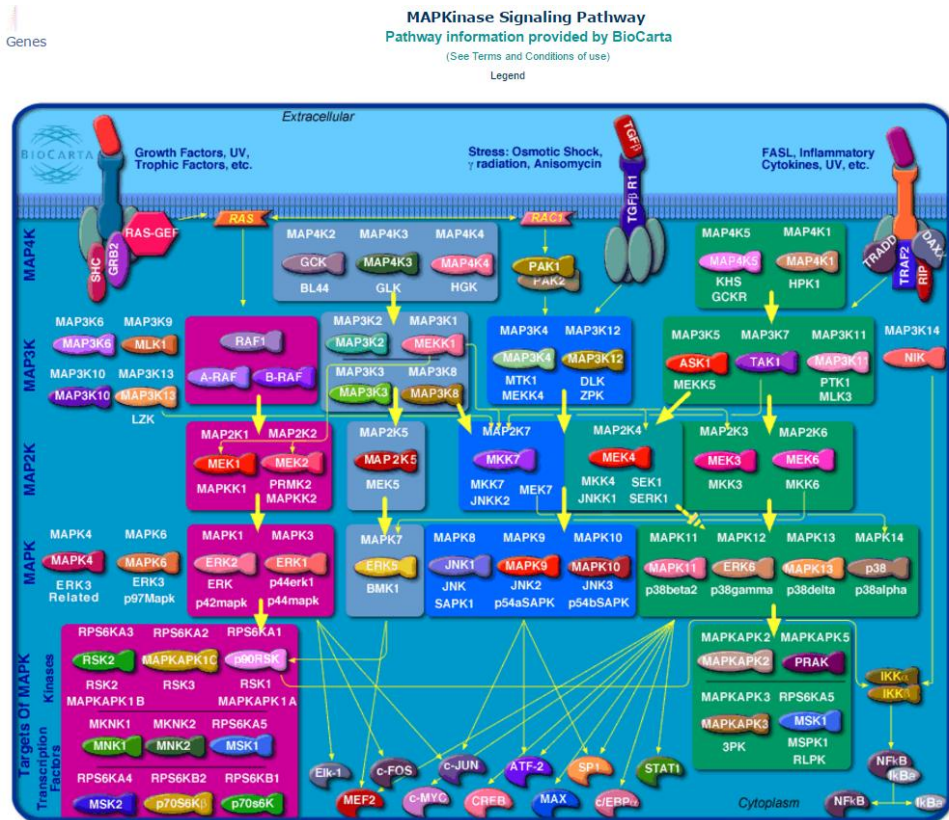
Acute Myocardial Infarction



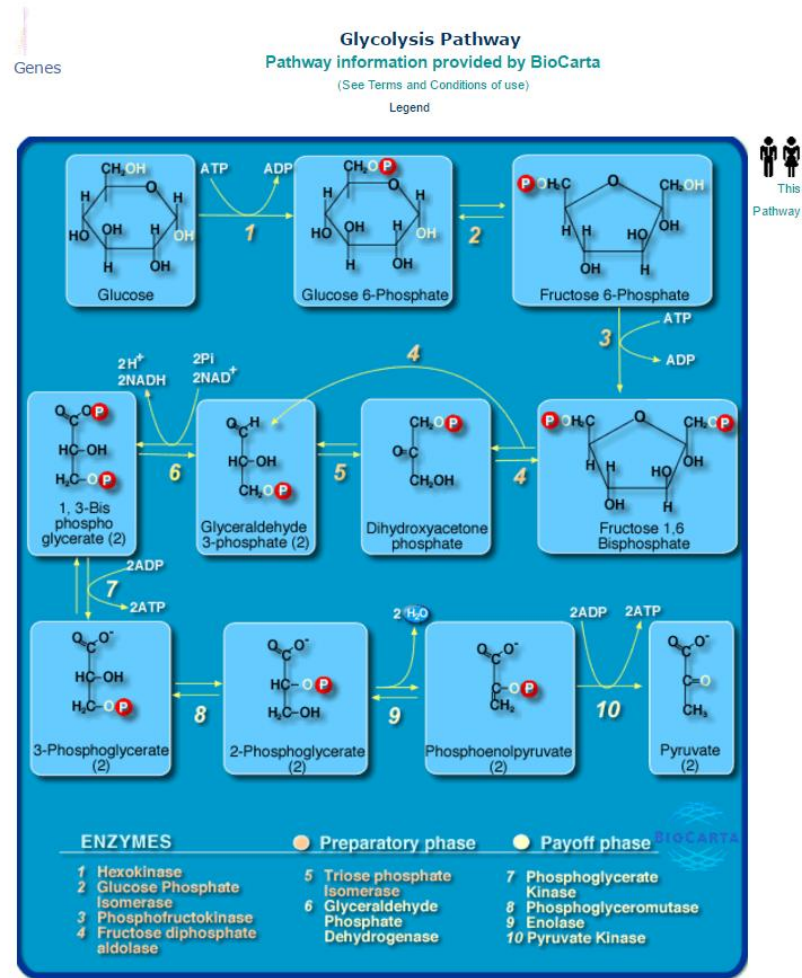
ИНФОРМАЦИОННЫЙ РЕСУРС ВIOСARTА (продолжение)

Содержит схемы метаболических либо сигнальных путей, а также схемы процессов

MAPKinase Signaling Pathway



Glycolysis Pathway



ПОВТОРЕНИЕ: В лекции № 4 были рассмотрены базы данных по генным сетям, а также по метаболическим и сигнальным путям:

- 1) GeneNet – ИЦиГ СО РАН , г.Новосибирск
<http://wwwmgs.bionet.nsc.ru/mgs/gnw/genenet/>
- 2) KEGG Kyoto encyclopedia of genes and genomes:
integrated suite of databases on genes, proteins, and metabolic pathways
<http://www.genome.ad.jp/kegg>
- 3) MetaCyc Metabolic Database <http://metacyc.org/>
+ BioCyc (Database Collection) <https://biocyc.org/>
- 4) Reactome <http://www.reactome.org/>
- 5) WikiPathways <http://www.wikipathways.org/index.php/WikiPathways>
- 7) Signor <http://signor.uniroma2.it/>
- 8) SPIKE <http://www.cs.tau.ac.il/~spike/>
- 9) BioCarta https://cgap.nci.nih.gov/Pathways/BioCarta_Pathways

СПАСИБО ЗА ВНИМАНИЕ !