

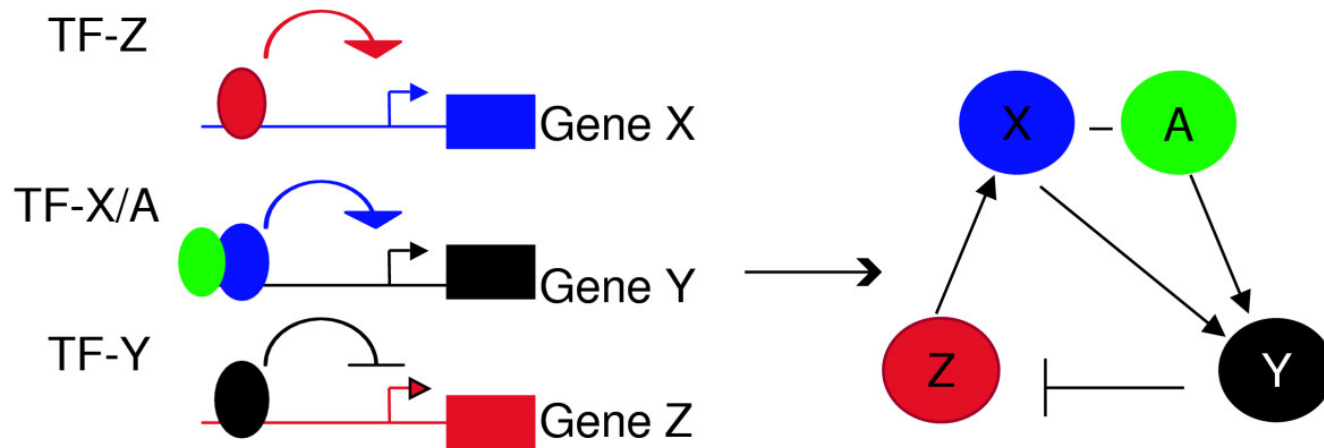
Лекция №4

1. Генные сети в эпоху
высокопроизводительного
секвенирования

2. Базы данных по генным сетям

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и теоретической генетики Игнатьева Е.В.

Транскрипционные регуляторные сети (Transcription regulatory networks)



Транскрипционные регуляторные сети содержат узлы, обозначающие 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 DNaseI в геноме и предсказание сайтов связывания транскрипционных факторов в районах ДНК, соответствующих сайтам чувствительности к DNaseI

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

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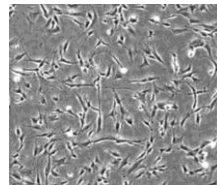
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Подход 2: Реконструкция транскрипционных регуляторных сетей (TRN) на основе исследования эффектов выключения генов с помощью siRNA (метод)

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

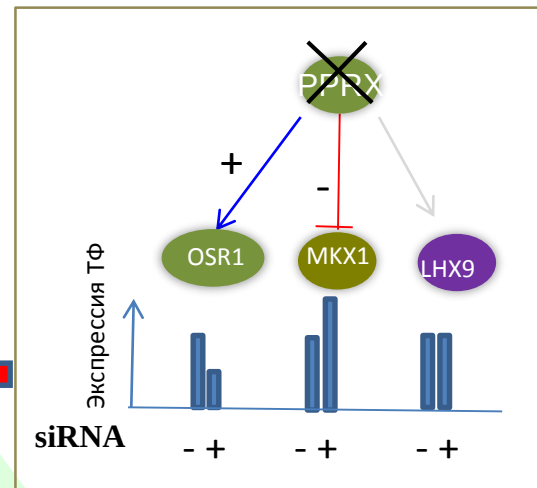


Список 18 транскрипционных факторов с повышенной экспрессией в фибробластах (fibroblast-enriched transcription factors)



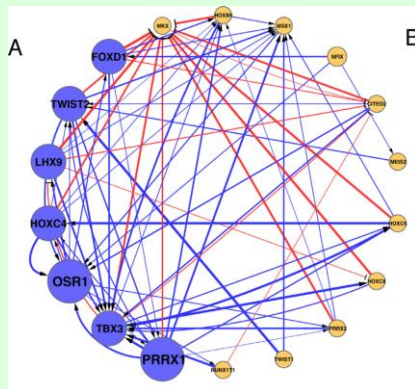
Эксперимент с поочередным выключением каждого из 18-ти ТФ с помощью siRNA

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

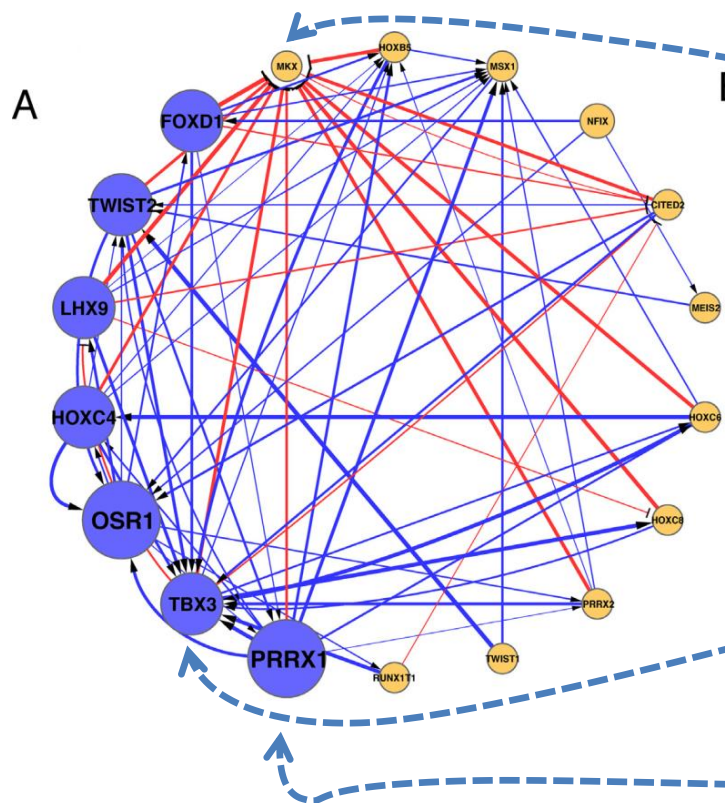
Фибробласт-специфичная сеть транскрипционной регуляции (TRN)



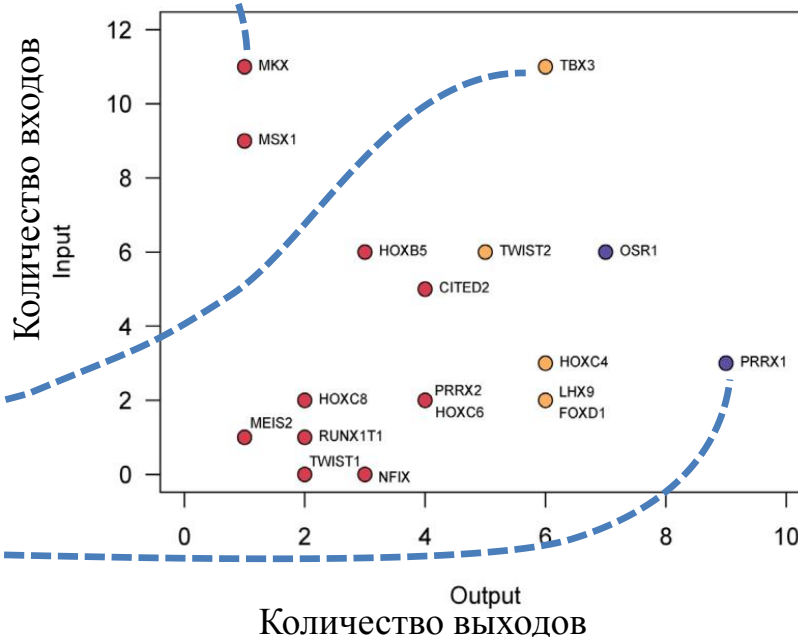
7 транскрипционных факторов с наибольшей значимостью + 11 других факторов

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

Фибробласт-специфичная сеть транскрипционной регуляции (TRN)



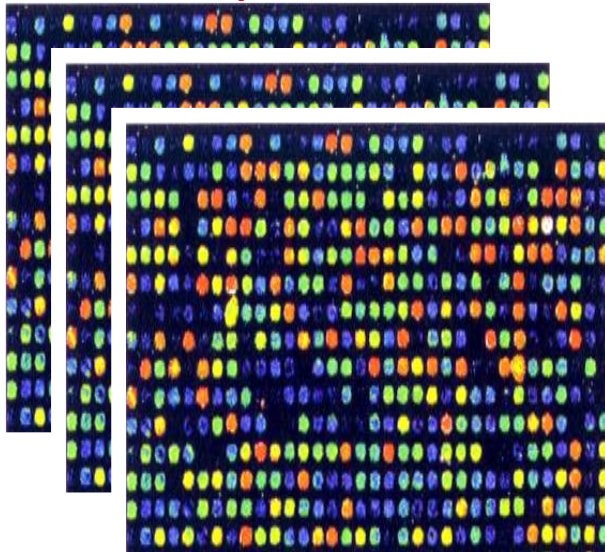
Характеристика узлов в сети по количеству входящих и выходящих регуляторных влияний



Задача в общем виде:

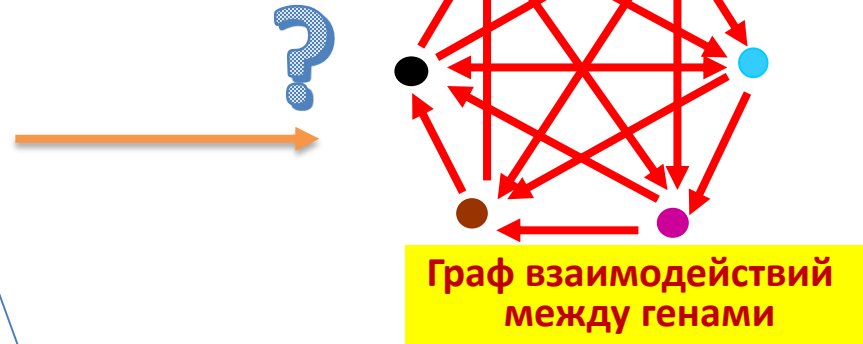
Реконструкция графов регуляторных генных сетей на основе данных по экспрессионным ДНК-чипам

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



$\Leftrightarrow$
 $\Leftrightarrow$

Надо построить:

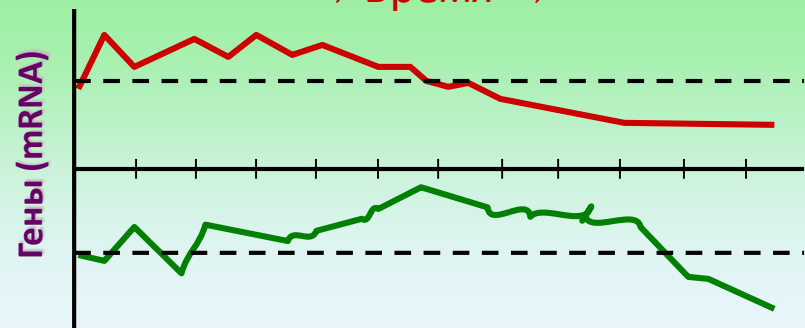


концентрация i -го гена
в j -й временной точке

→ 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

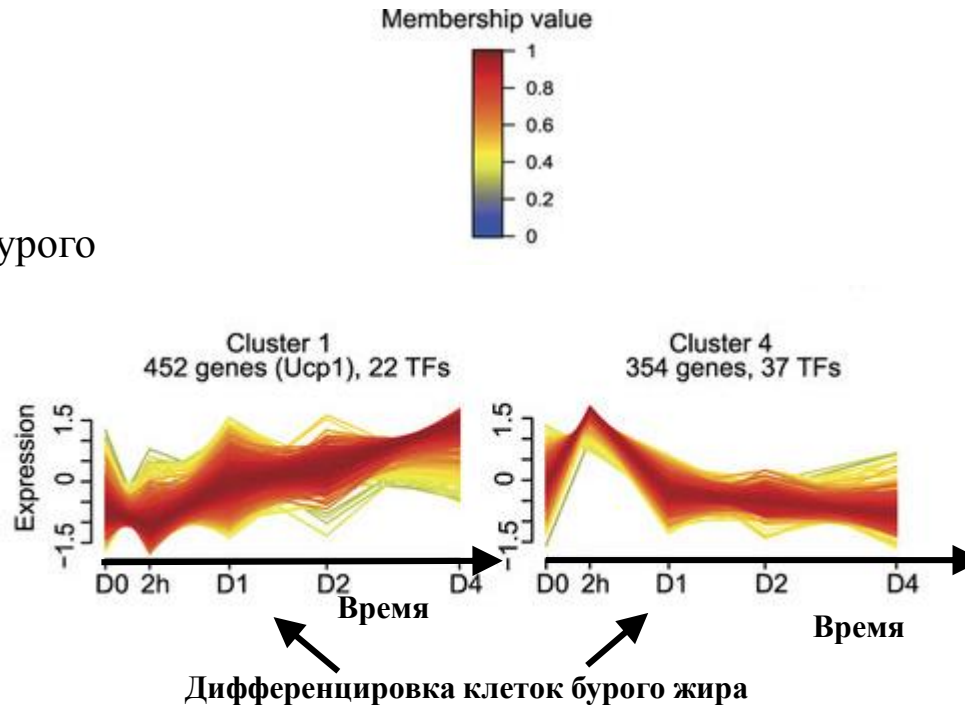
ГО термины:

Дифференцировка бурого
жира

Клеточный ответ на
инсулин

Биосинтез жирных
кислот

.....



ГО термины:

Морфогенез

эпителиальной трубки

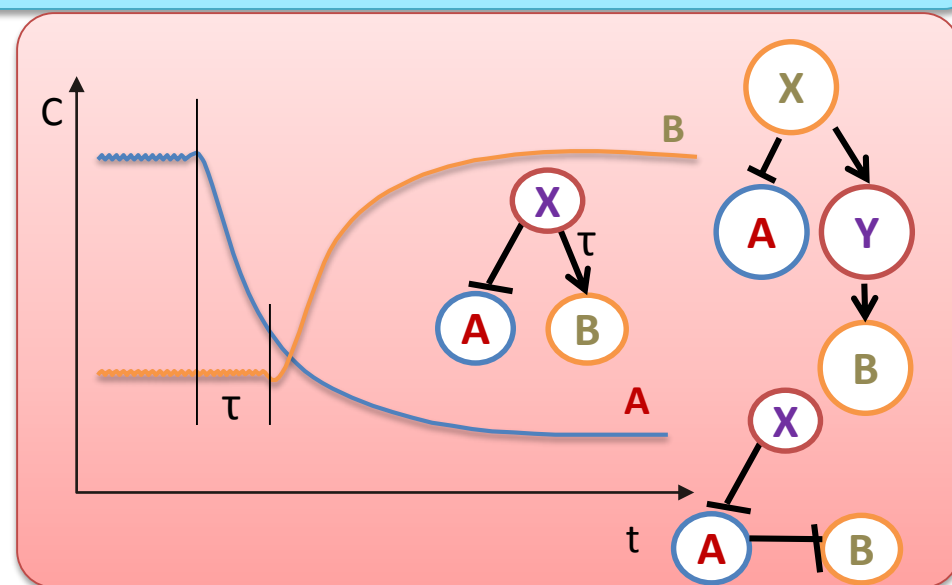
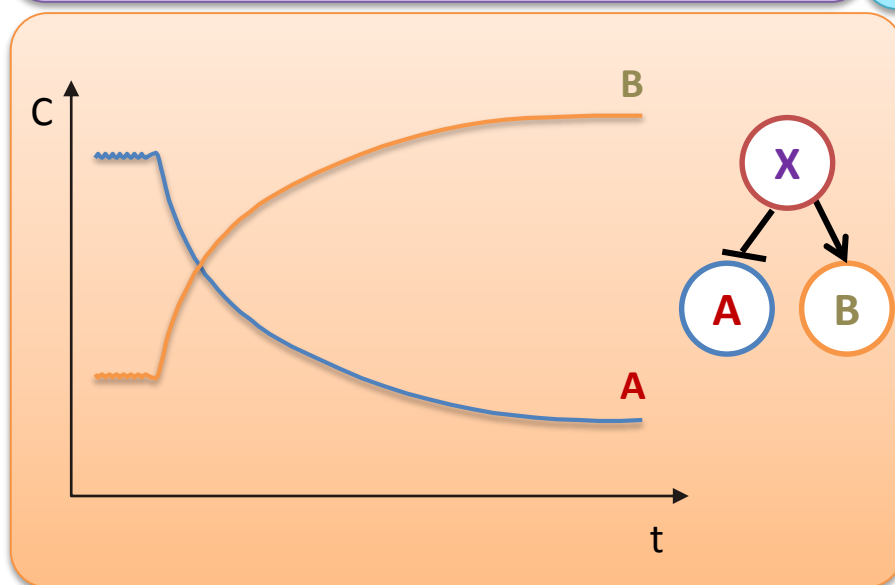
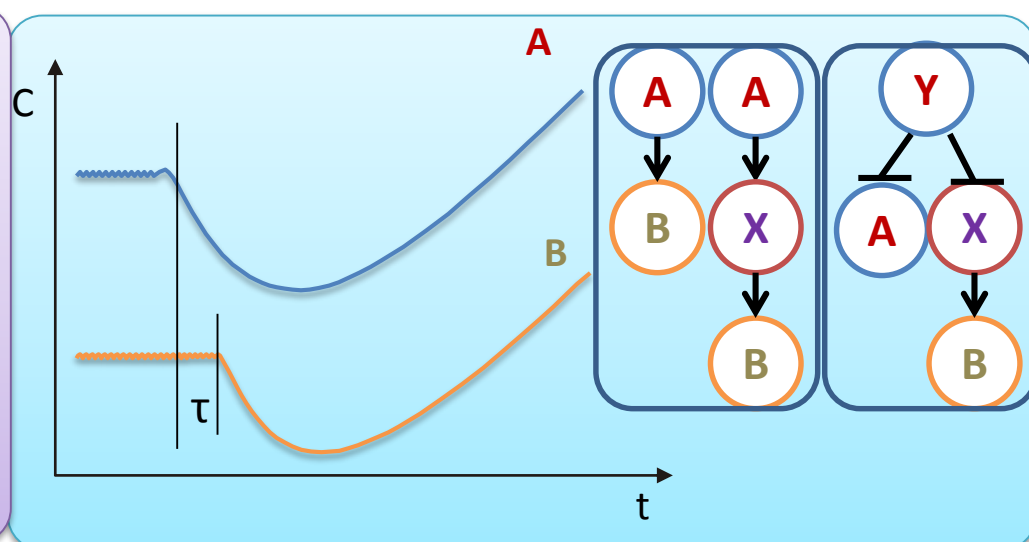
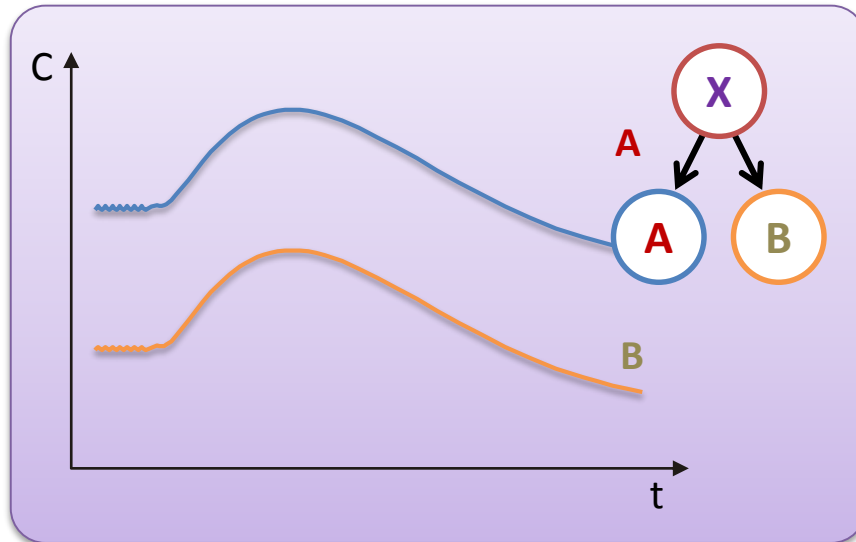
Пролиферация клеток

Дифференцировка

хондроцитов

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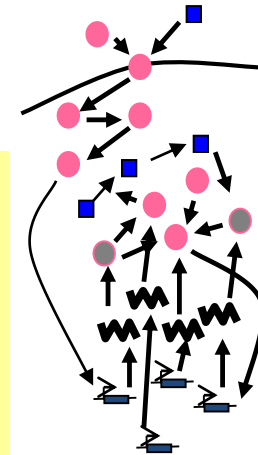
Построение гипотез о регуляторных взаимодействиях между генами основе данных по экспрессионным ДНК-чипам



Результаты неоднозначны, необходима экспериментальная проверка !!!!

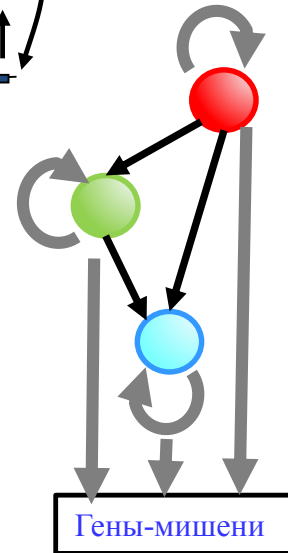
Генные сети, транскрипционные регуляторные сети- Что дальше ????

✓ **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, обозначающие два вида объектов:

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



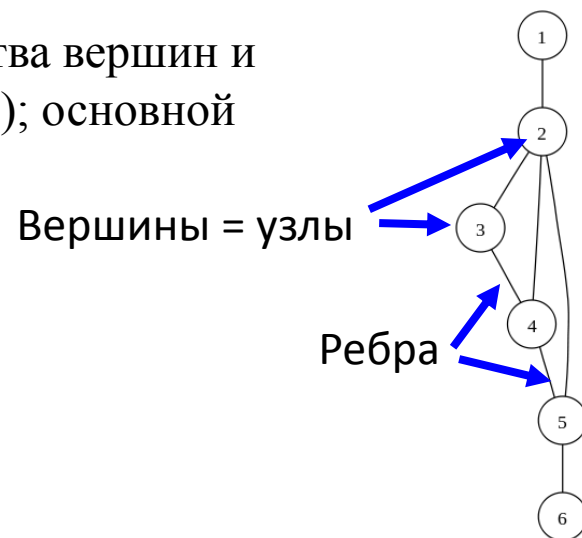
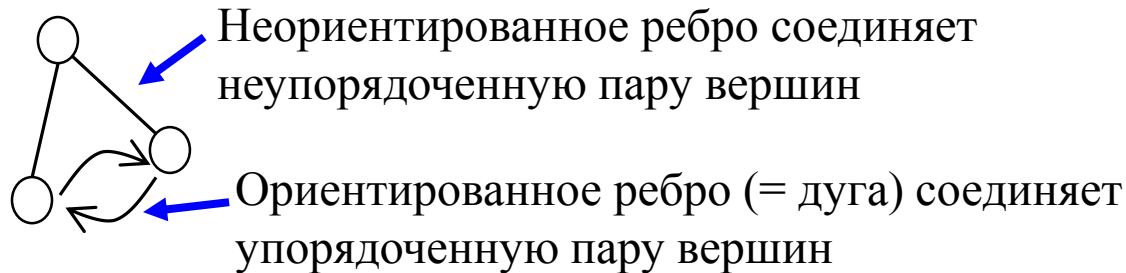
Сети взаимодействий между генами / белками

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

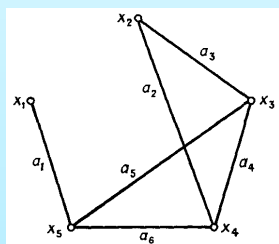
Граф (англ. *graph*) — совокупность непустого множества вершин и наборов пар вершин (связей между вершинами = ребер); основной объект изучения математической теории графов.

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



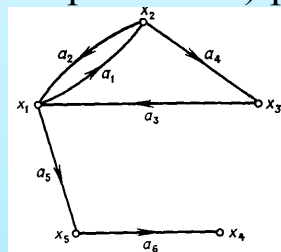
Классификация графов по типам входящих в них ребер

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



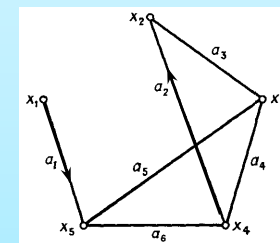
Пример неориентированного графа. x_1, x_2, x_3, x_4, x_5 — вершины графа. $a_1, a_2, a_3, a_4, a_5, a_6$ — ребра.

Оrientированный 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.

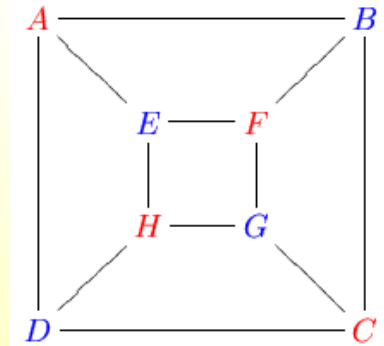


Пример смешанного графа. x_1, x_2, x_3, x_4, x_5 — вершины графа. a_1, a_2 — дуги. a_3, a_4, a_5, a_6 — ребра.

Классификация графов по типам входящих в них ребер

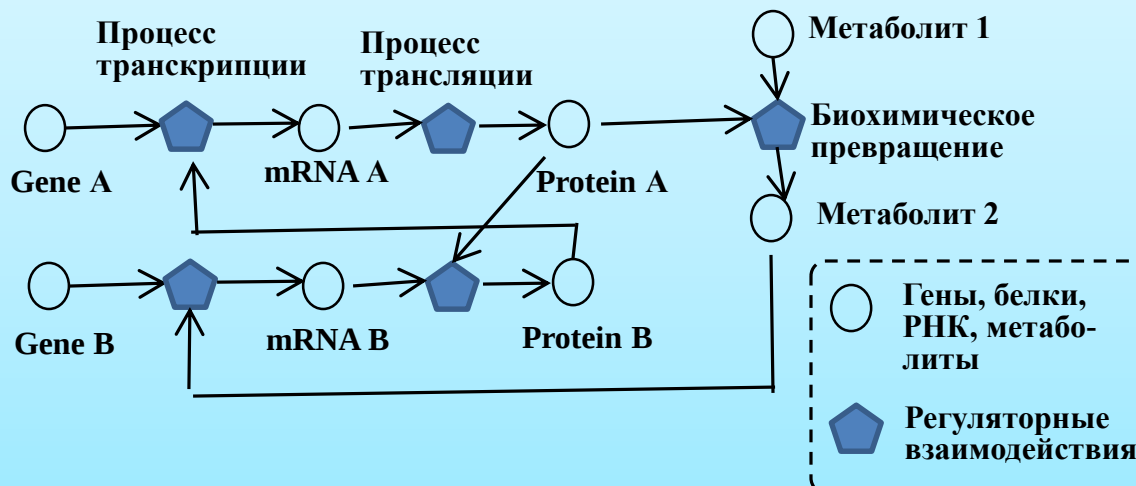
Граф называется двудольным, если его вершины можно разбить на два непересекающихся подмножества V_1 и V_2 так, что всякое ребро соединяет вершину из первого множества V_1 с вершиной из второго множества V_2 .

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 рёбер, соединяющих вершины одного и того же подмножества

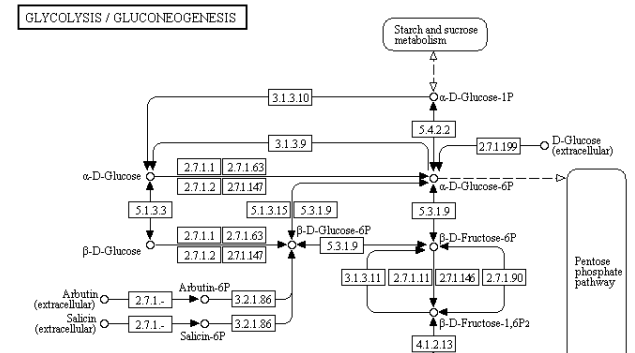


Пример двудольного графа. Первое множество вершин (**A, E, H, C**) и второе множество вершин (**E, B, D, G**).

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

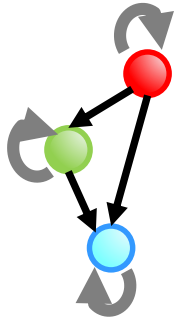
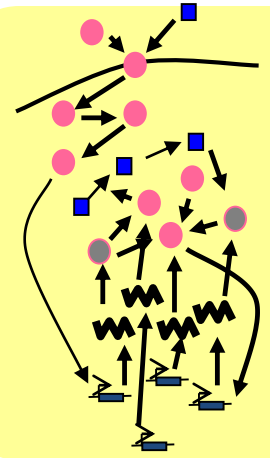


Представление данных о метаболическом пути в базе KEGG:
1-ый тип вершин – метаболиты
2-ой тип вершин – ферменты



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 : 1) гены, относящиеся к рассматриваемой системе; 2) транскрипционные факторы, регулирующие экспрессию генов. **Графическое обозначение двух типов вершин может быть одинаковым.**



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

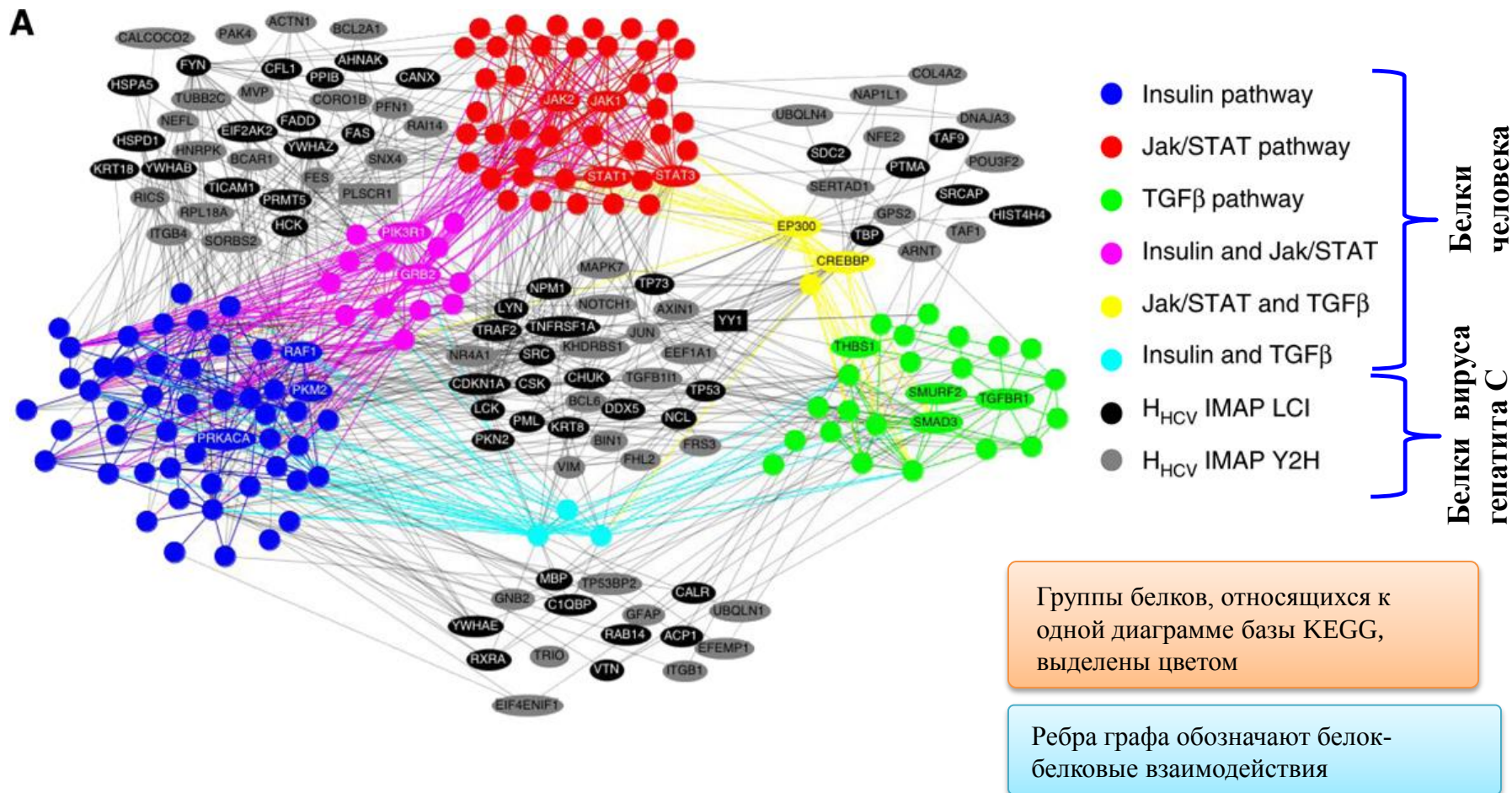
Коэкспрессию

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



Вершины графа (сферы) обозначают группы коэкспрессирующихся транскриптов. Радиус сфер пропорционален (числу транскриптов в каждой группе)⁻³

Ребра графа обозначают наличие корреляции ($r > 0.6$) между паттернами экспрессии транскриптов из двух соседних вершин.

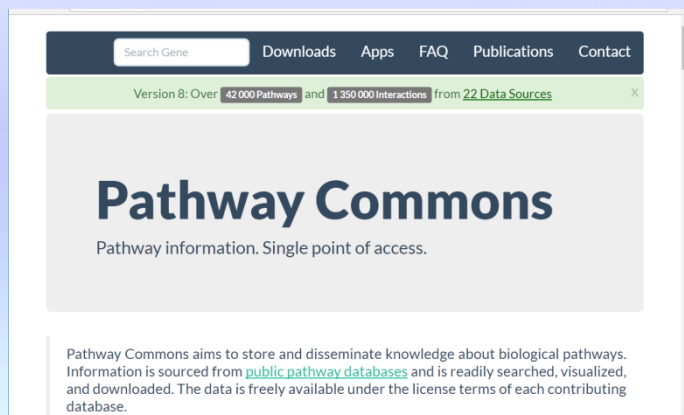
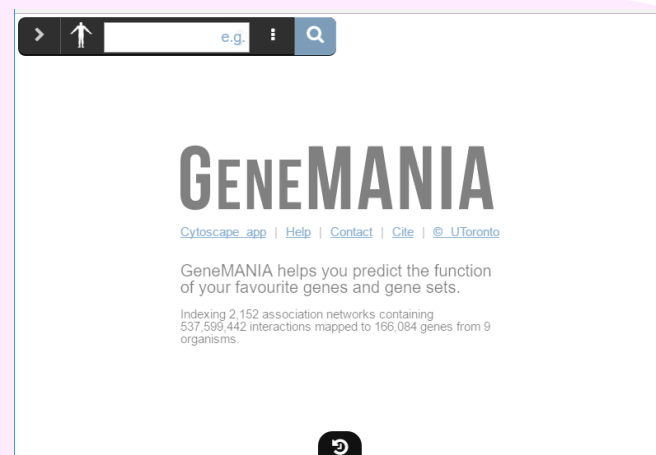
Как строить сети взаимодействий между генами / белками ??

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



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

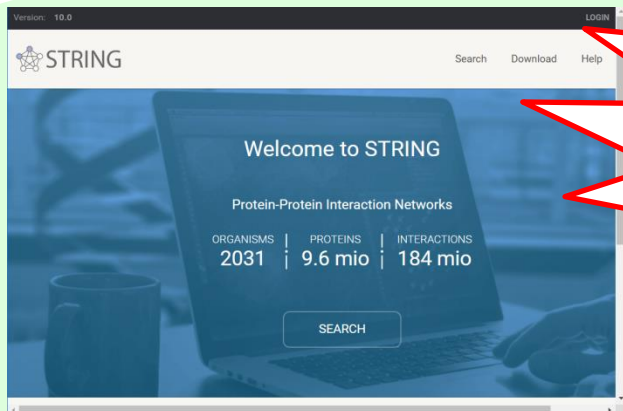
GeneMANIA
<http://genemania.org/>



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

Как строить сети взаимодействий между генами / белками ??

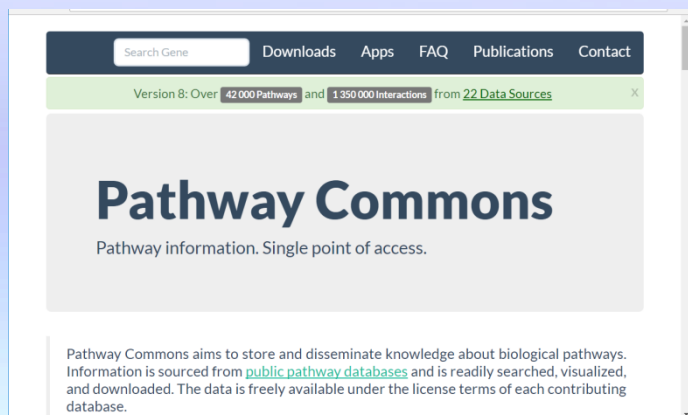
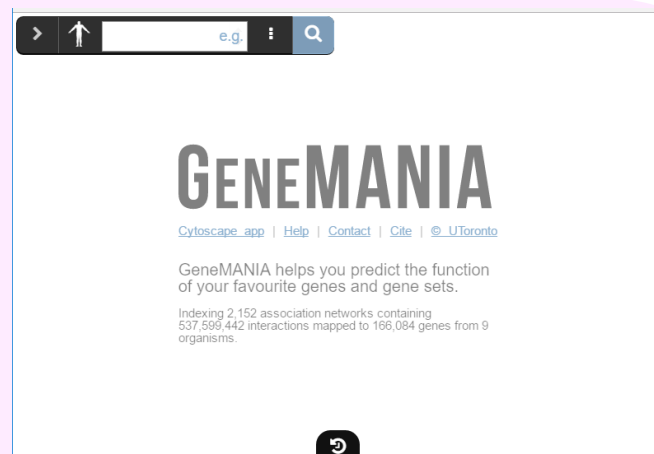
Интернет-доступные информационные компьютерные системы, позволяющие экстрагировать данные по связям различных типов между генами/белками



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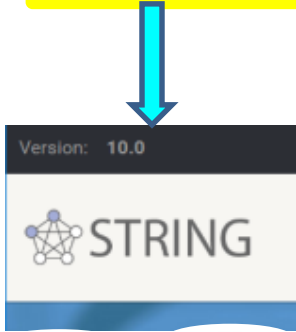


Pathway Commons - A Resource for Biological
Pathway Analysis

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

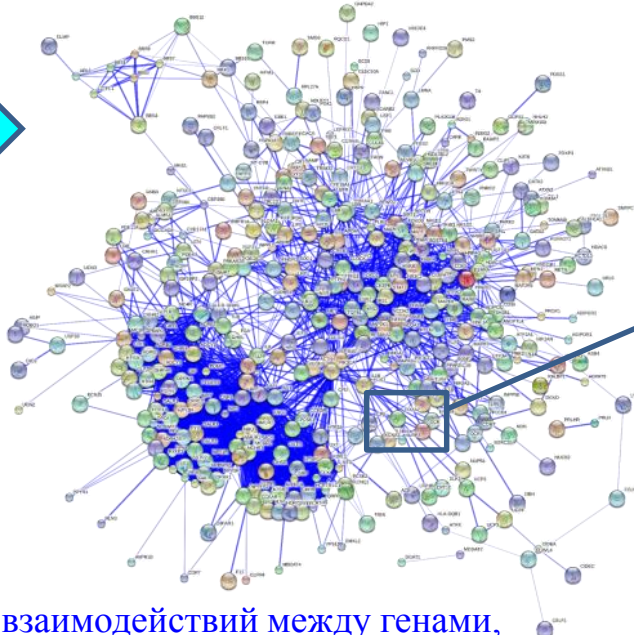
Сеть, реконструированная системой STRING, включает взаимодействия разных типов

Дано: список ~500 генов человека

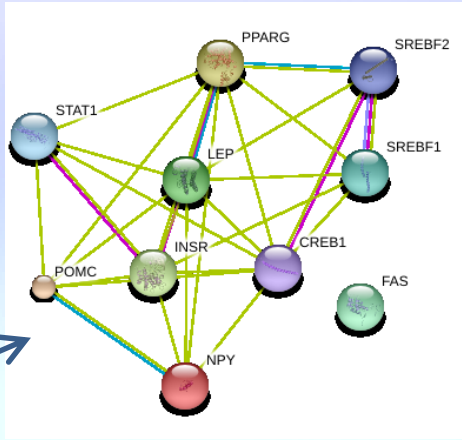


PPI Homology
Textmining

Базы данных взаимодействий
между генами



Фрагмент
сети



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

Условные обозначения

Known Interactions

- from curated databases
- experimentally determined

Predicted Interactions

- gene neighborhood
- gene fusions
- gene co-occurrence

Others

- textmining
- co-expression
- protein homology

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:

+ more proteins

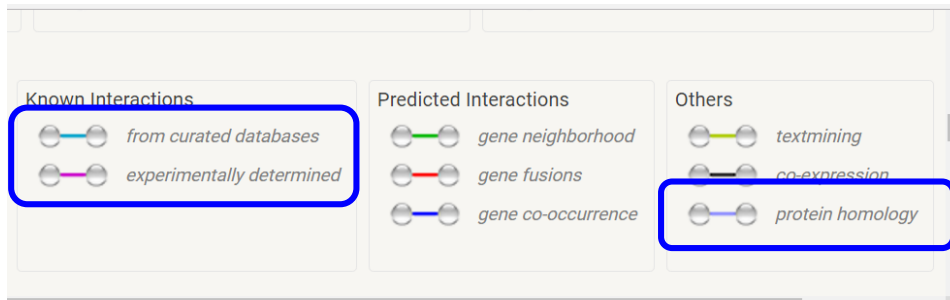
- less proteins

UPDATE SETTINGS

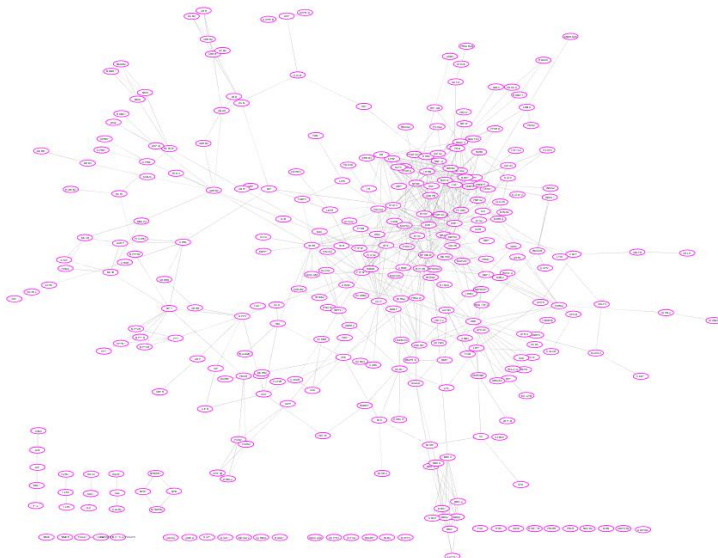
Какие новые знания можно получить, анализируя взаимодействия разных типов ???

ДАНО:

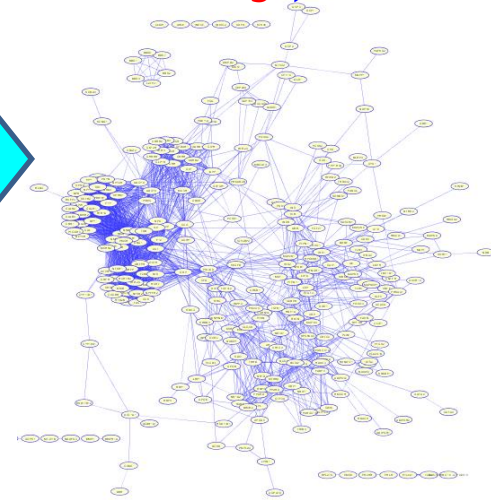
578 генов, участвующих в регуляции
пищевого поведения либо массы тела



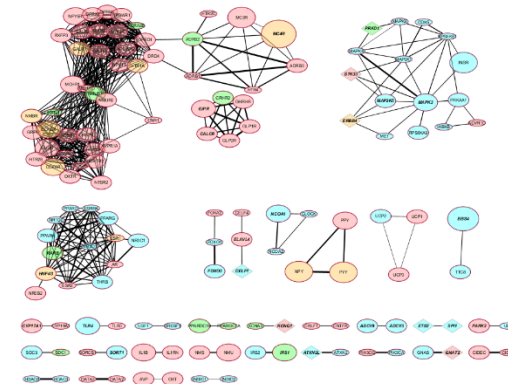
Подсеть белок-белковых взаимодействий
(тип связи *Experimental*)



Подсеть совместной встречаемости в
метаболических и сигнальных путях
(тип связи *Knowledge*)



Подсеть взаимодействий, отображающих
гомологию (тип связи *Homology*)



Методический вопрос:

Нужно ли (можно ли) рассматривать связи всех типов сразу или лучше по-отдельности ??

Рассмотрены три подсети:

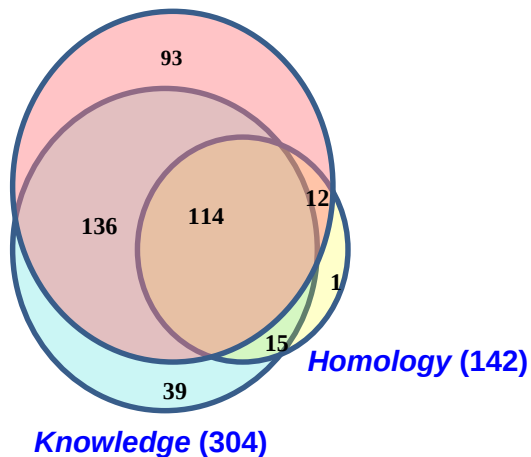
Подсеть белок-белковых взаимодействий (тип связи *Experimental*)

Подсеть совместной встречаемости в метаболических и сигнальных путях (тип связи *Knowledge*)

Подсеть взаимодействий, отображающих гомологию (тип связи *Homology*)

Количество генов, участвующих в сетях: 408

Experimental (355)



(А всего в запросе участвовало 578 генов)

Каждая сеть имела свои количественные характеристики

Тип сети	Кол-во генов, имеющих связи данного типа / доля генов от общего количества	Кол-во связей со скором > 0.4	Среднее число связей на ген
Experimental	355 (62%)	1243	4.28
Knowledge	304 (53%)	2397	15.87
Homology	142 (25%)	521	7.390
ВСЕГО	408 (~71%)		

Всего сетями было охвачено 71% генов

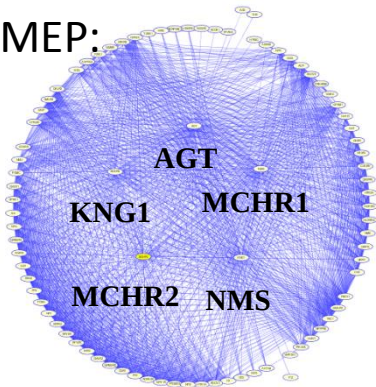
Каждая подсеть включала определенное количество уникальных генов, которые не присутствовали в других подсетях

Ни одна подсеть не включала все гены, участвовавшие в запросе

Продолжение Методический вопрос: Нужно ли рассматривать связи всех типов сразу или лучше по-отдельности ??

Для каждой сети были выделены «топовые гены», то есть гены, имеющие наибольшее количество связей

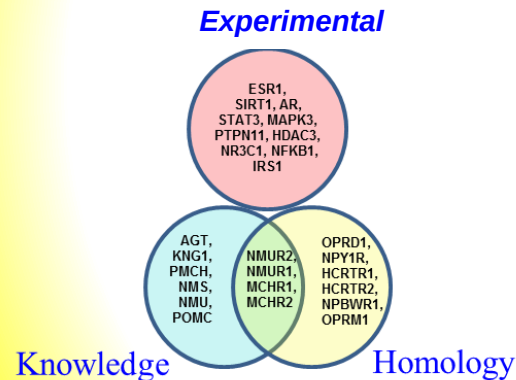
ПРИМЕР:



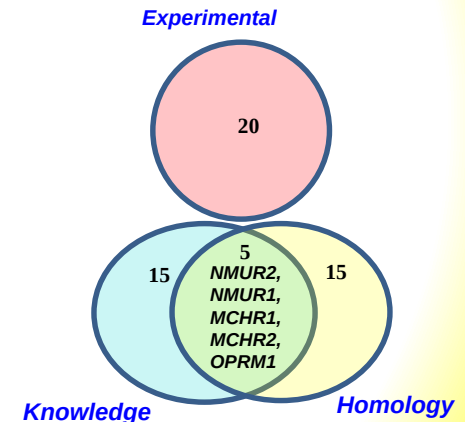
5 топовых генов в подсети **Knowledge**

Перекрывание списков генов, имеющих наибольшее количество связей в 3-х сетях

А) по 10-топовым генов



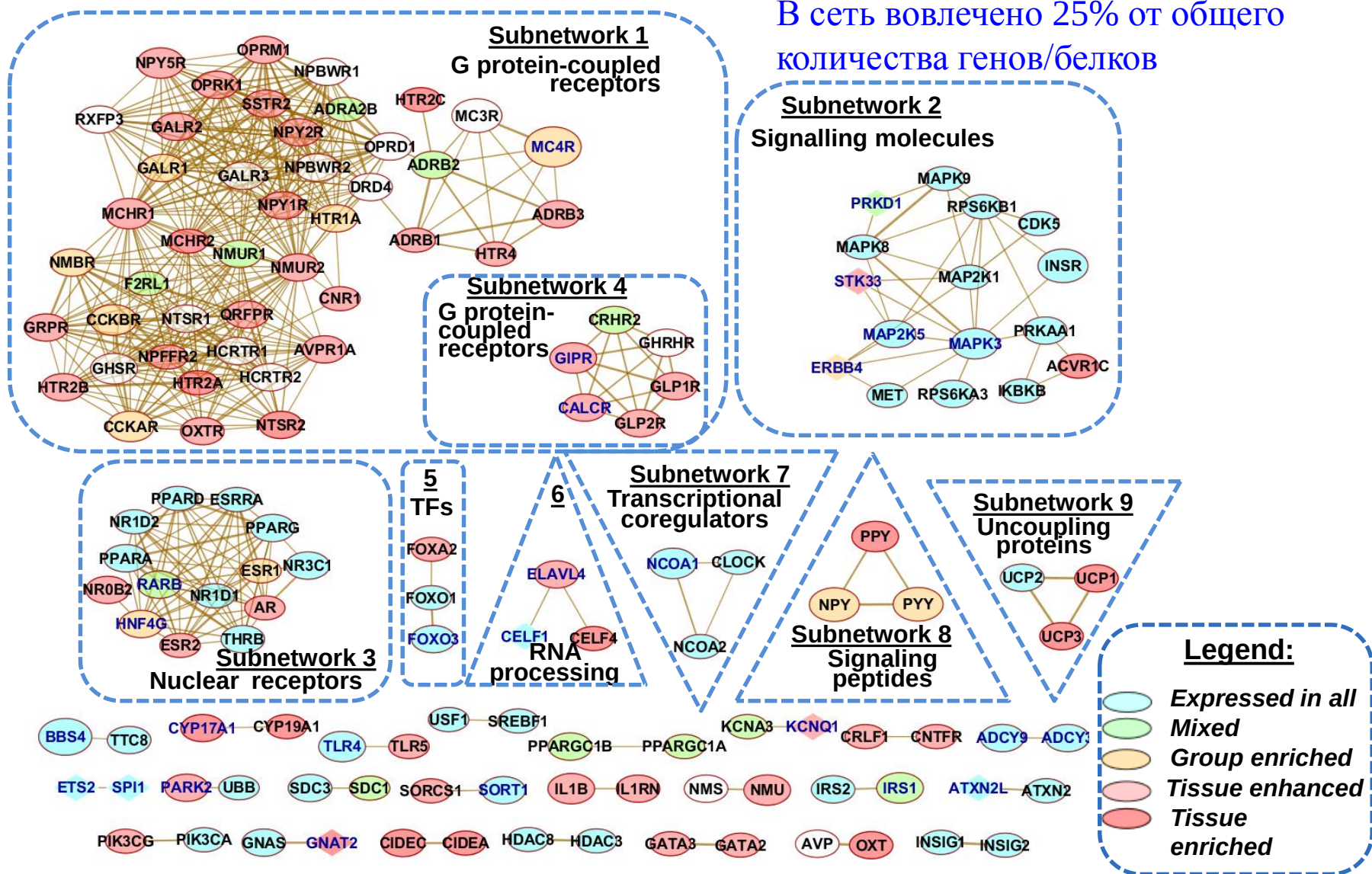
Б) по 20-топовым генов



Каждая сеть содержала уникальный набор «топовых» генов. При рассмотрении множеств 20-ти топовых генов одна из сетей (**Experimental**) характеризовалась набором 20-топовых генов, абсолютно не перекрывающимися с топовыми генами других двух сетей

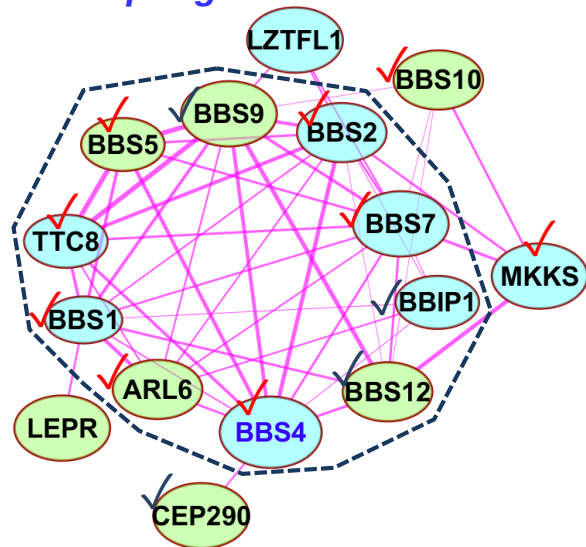
**ВЫВОД: Все рассмотренные основные характеристики сетей различны
Сети получились совсем разные !!!!**

Анализ подсетей разных типов характеризует набор генов с разных сторон: Подсеть Homology содержит несколько несвязных подсетей

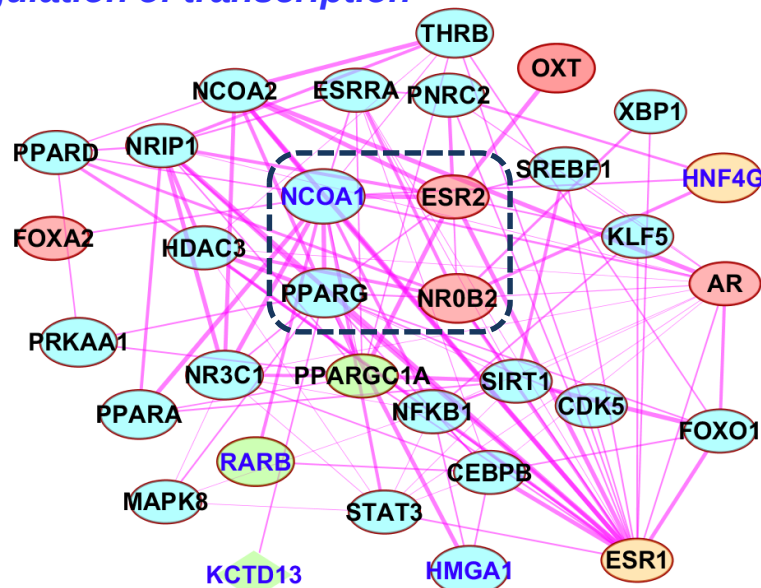


Анализ подсетей разных типов характеризует набор генов с разных сторон: Выявление кластеров в подсети Experimental (белок-белковые взаимодействия)

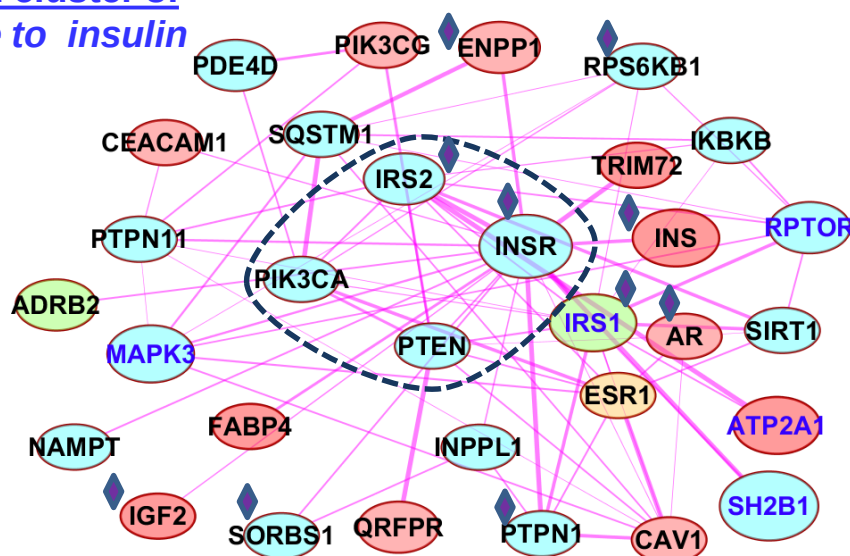
Extended cluster 1:
cilium morphogenesis



Extended cluster 2:
regulation of transcription



Extended cluster 3:
response to insulin stimulus

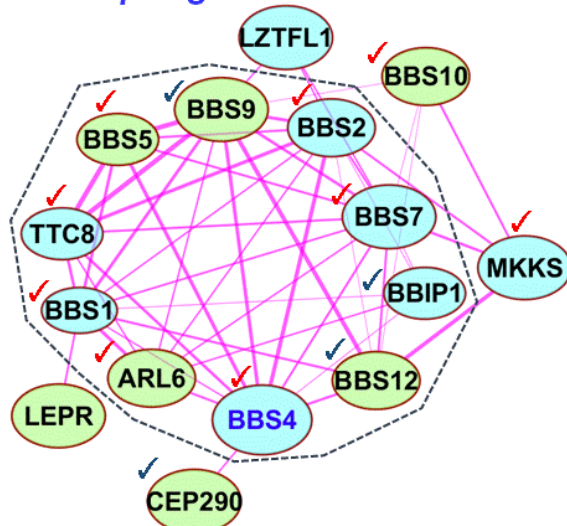


Legend:

- Expressed in all
- Mixed
- Group enriched
- Tissue enhanced
- Tissue enriched

Биологическая функция белков из кластера 1

Extended cluster 1: *cilium morphogenesis*



Гены, связанные с синдромом Барде — Бидля (Bardet-Biedl syndrome 1): BBS1, BBS7, BBS12, BBS4, BBS9, BBS2, ARL6
Кодируют структурные белки ресничек.

Внутриклеточный транспорт по микротрубочкам, участвуют
развитии и во внутриклеточной передаче сигналов от
рецепторов на мембране:

InsR - insulin receptor;

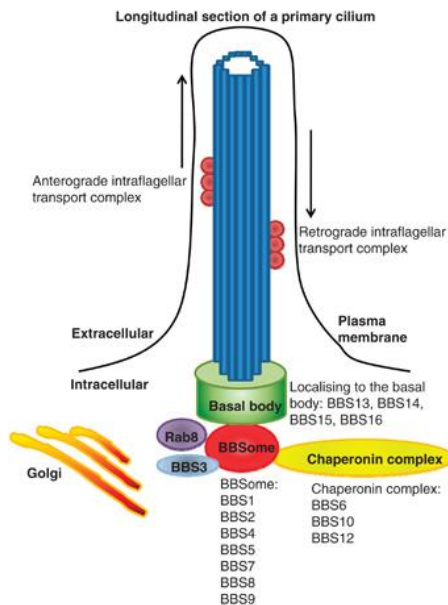
IGFR - insulin growth factor receptor;;

LepR - leptin receptor;

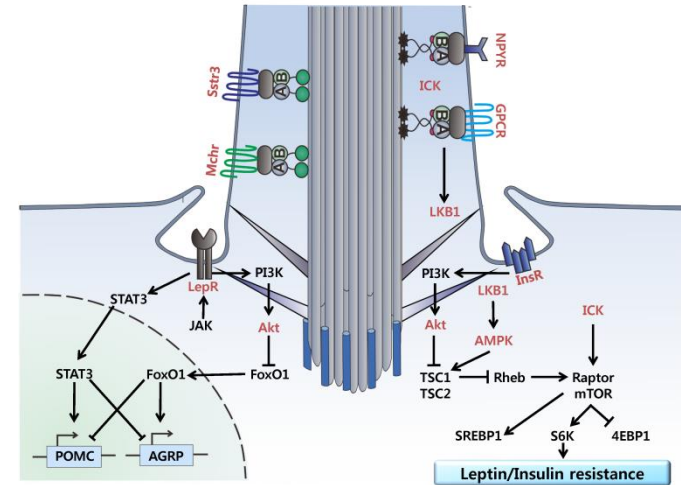
MCHR - melanin-concentrating hormone receptor ;

NPYR - neuropeptide Y receptor

Активируют сигнальные пути (Hedgehog, Notch, Wnt, mTOR
and PDGFRalpha)



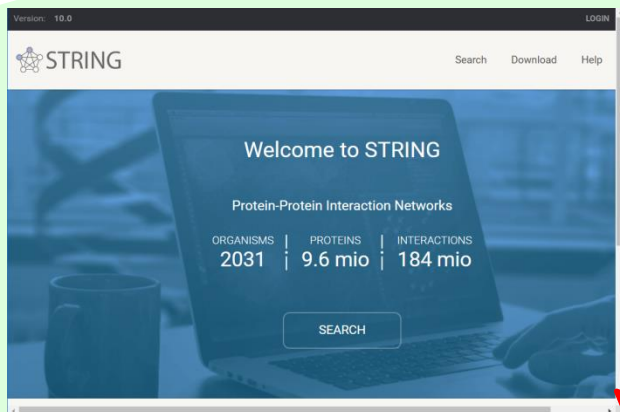
Forsythe E., Beales P.L. Bardet-Biedl syndrome.
Eur J Hum Genet. 2013 Jan;21(1):8-13.



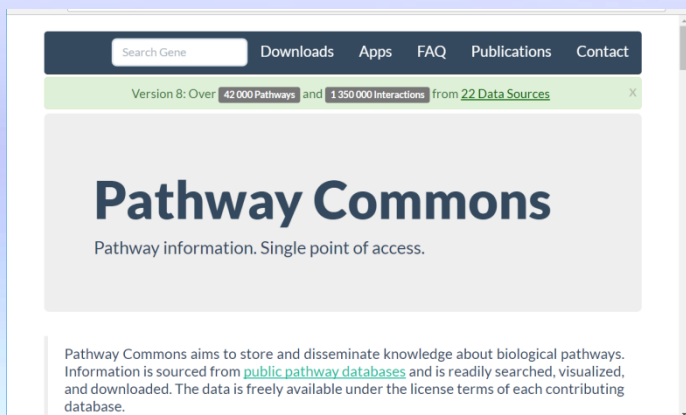
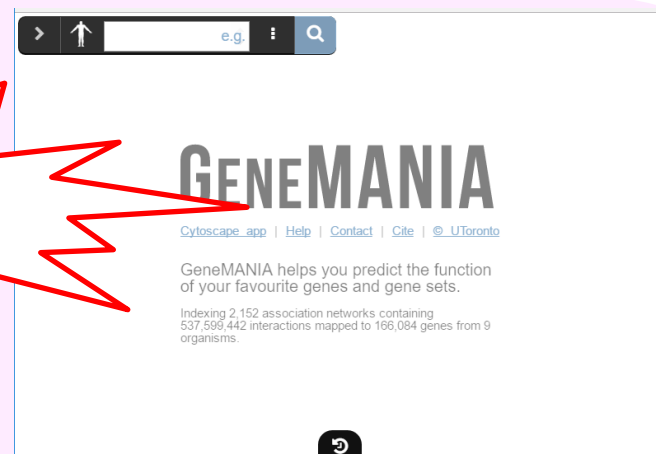
Lee H. et al., Primary cilia in energy balance
signaling and metabolic
disorder *BMB Rep.* 2015;48(12): 647-654

Как строить сети взаимодействий между генами / белками ??

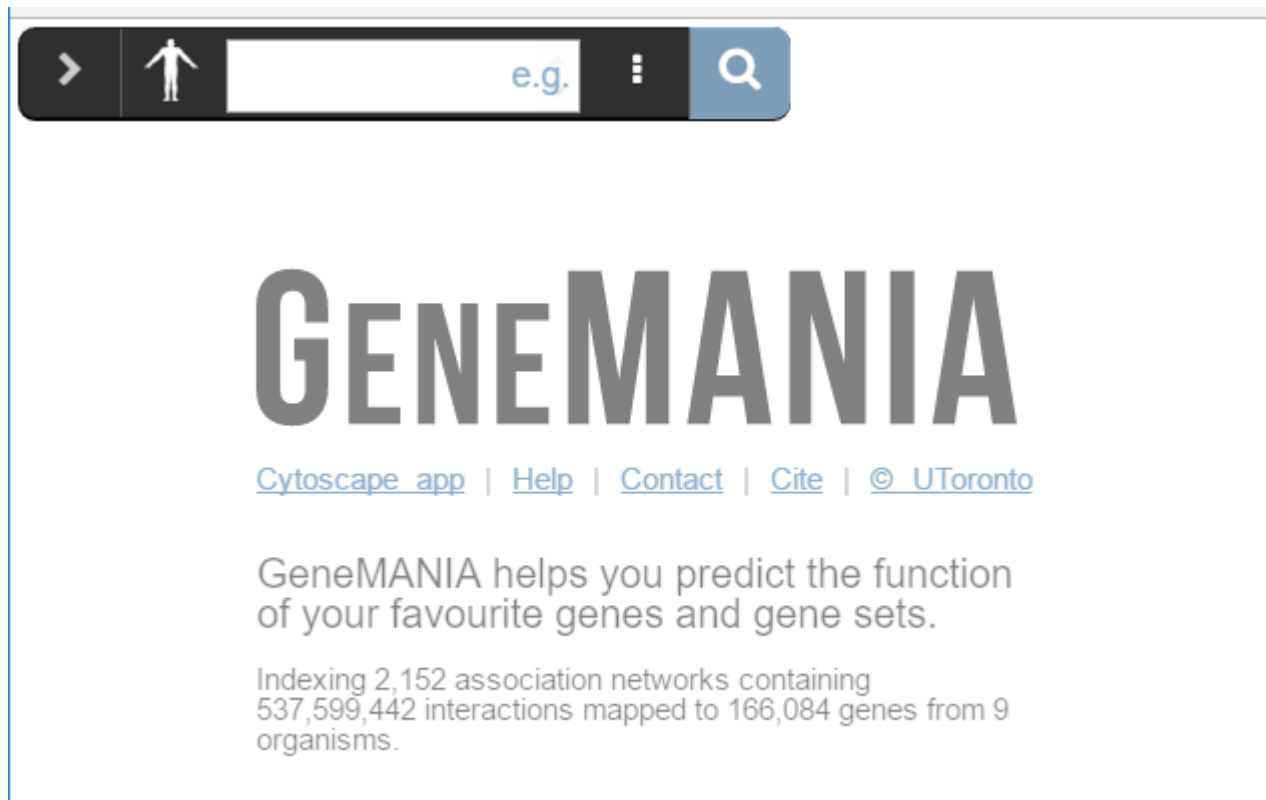
Интернет-доступные информационные компьютерные системы, позволяющие экстрагировать данные по связям различных типов между генами/белками



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

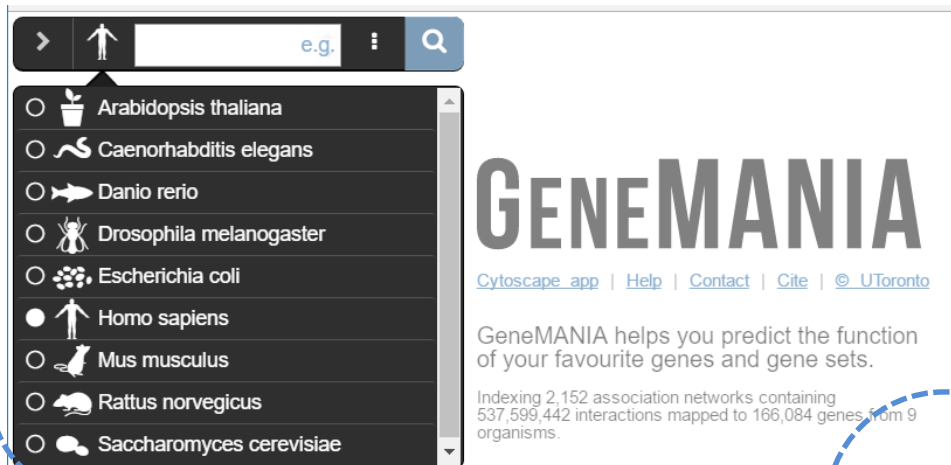


Pathway Commons - A Resource for Biological Pathway Analysis
<http://www.pathwaycommons.org/>

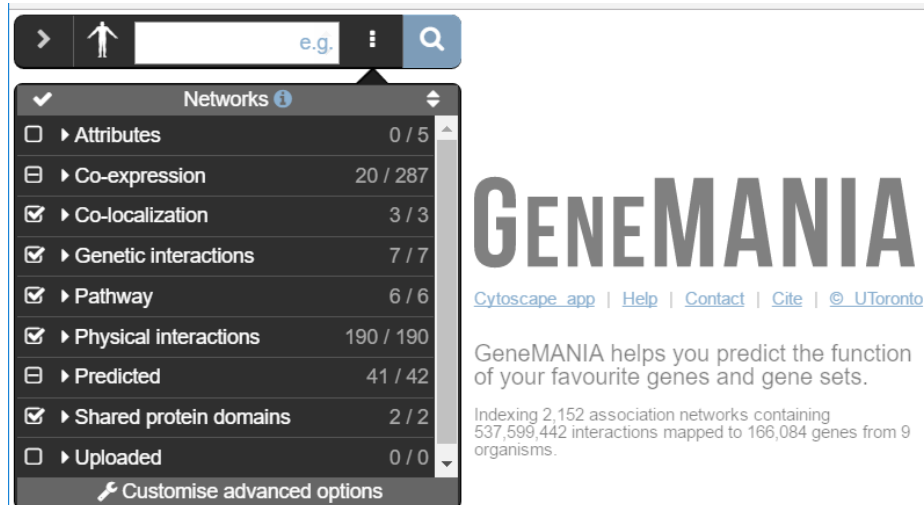


Ресурс, позволяющий определять функциональность генов и наборов генов. Имеет две реализации: Интернет-доступную, а также как плагин системы Cytoscape

Ресурс, позволяет работать с 9-ю видами организмов



А также выбирать (комбинировать) данные различных типов:

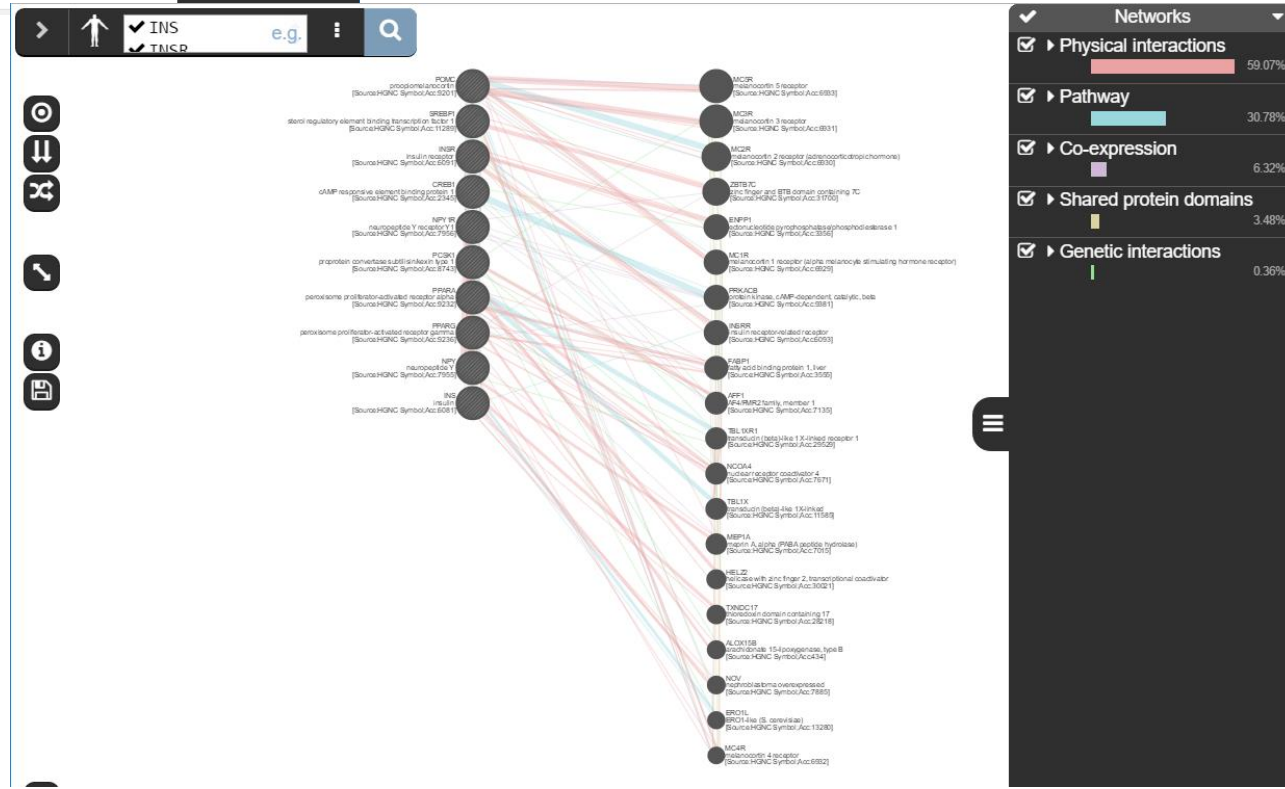
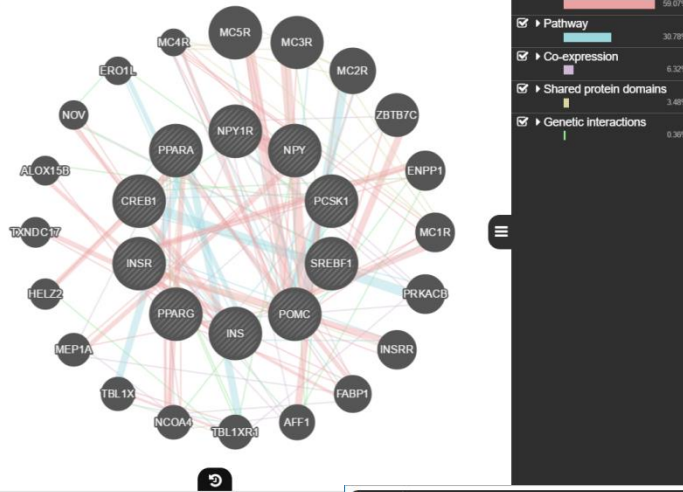


Результат тестового запроса к GeneMania

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

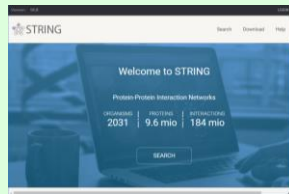
Два способа
представления
полученного
результата



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)

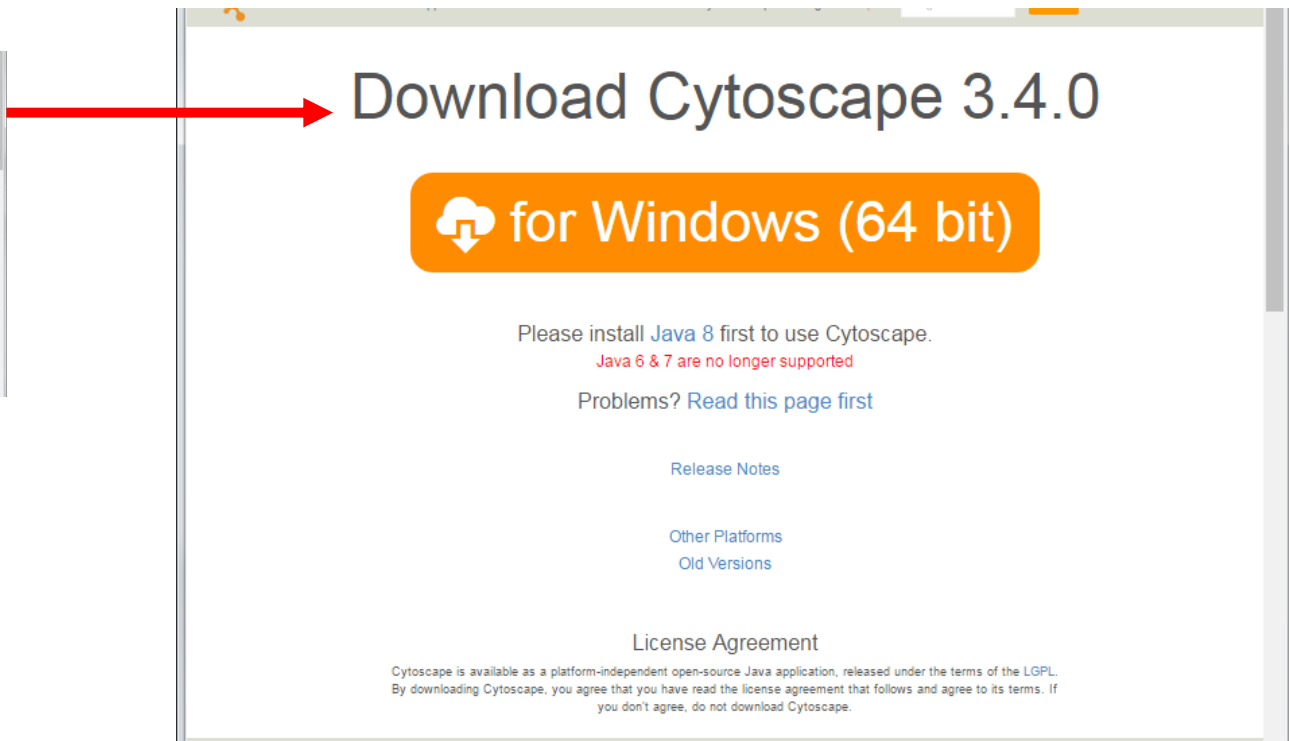
Общий комплексный сетевой анализ (General Complex Network Analysis)

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



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/>)



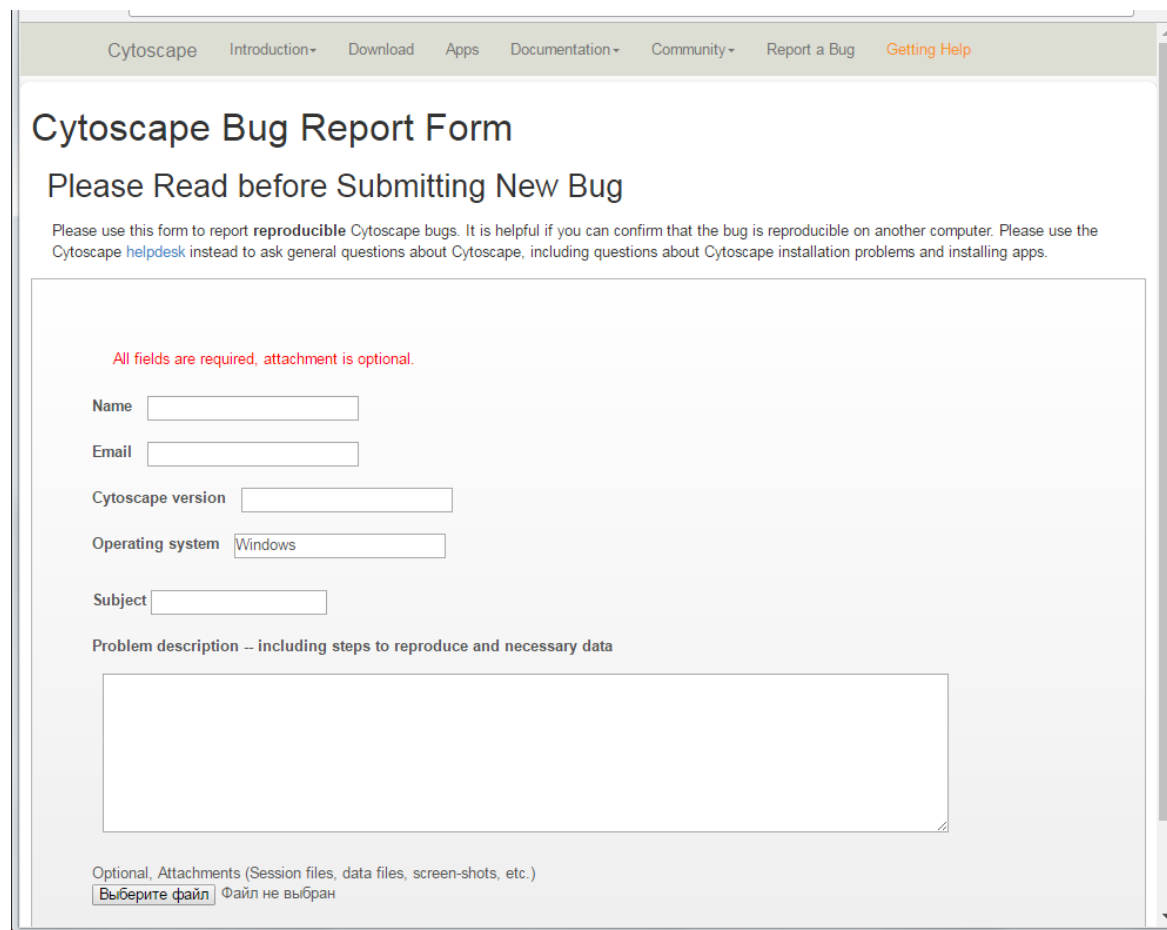
- *Cytoscape* - компьютерная программа (система), (компьютерная платформа), (пакет программ) **с открытым исходным кодом**, это позволяет компьютерным специалистам всего мира участвовать в развитии *Cytoscape*.
- Функционирует отлаженная система отслеживания ошибок.
- Большое количество возможностей 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 bar with links: 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 explains that the form is for reproducible bugs and that the Cytoscape helpdesk should be used 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, with a note to include steps to reproduce and necessary data. At the bottom, there is a section for optional attachments, showing 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**

Cytoscape App Store Submit an App Search the App Store Sign In

All Apps

Categories

- 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
- core app

more »

Newest Releases Get Started with the App Store »

- ReNE** Regulatory Network Enhancing Plugin - ReNE allows users to
- EClerialize**
- CytoMCS** Computes the maximum common edge subgraph for multiple large
- ClueGO** Creates and visualizes a functionally grouped network of
- CluePedia** CluePedia: A ClueGO plugin for pathway insights using integrated
- PCM** Assemble Predicted Clusters For better Proteins Cluster Detection

more newest releases »

Top Downloaded Apps

- ClueGO** Creates and visualizes a functionally grouped network of
- BiNGO** Calculates overrepresented GO terms in the network and display
- GeneMANIA** Imports interaction networks from public databases from a list of
- CluePedia** CluePedia: A ClueGO plugin for pathway insights using integrated
- AgilentLiteratureSearch** Mines scientific literature to find publications related to search terms
- MCODE** Clusters a given network based on topology to find densely connected

more top downloads »

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 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/s12918-016-0313-3. 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

 CrossMark

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*†}, Yuri Georgievich Matushkin¹, Konstantin Vladimirovich Gunbin¹ and Dmitry Arkadievich Afonnikov^{1,2}

From The International Conference on Bioinformatics of Genome Regulation and Structure (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



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)

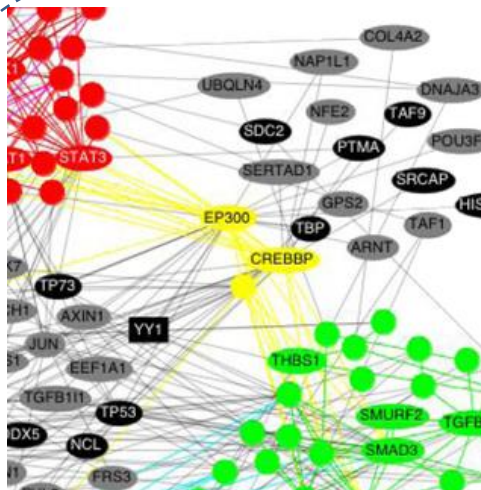
Nested network format (NNF or .nnf format)

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



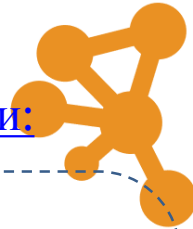
Условные обозначения

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)

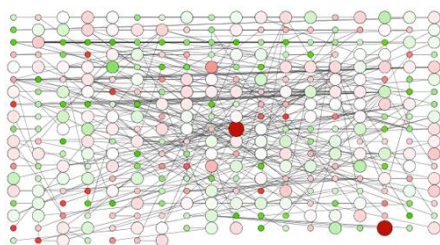


В области молекулярной биологии, системной биологии, геномики и протеомики:

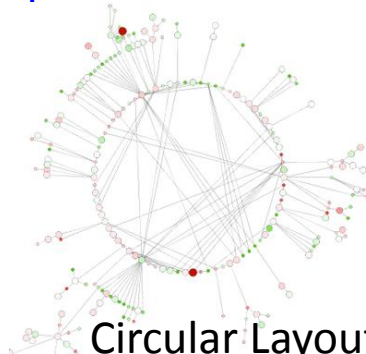
Визуализация информации в различных режимах



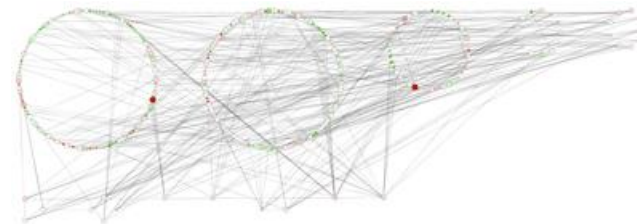
Organic Layout



Grid Layout

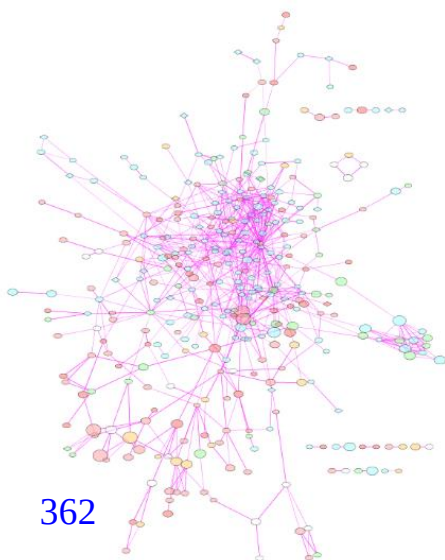


Circular Layout



GroupAttributesLayout

Анализировать и моделировать на основе плагинов



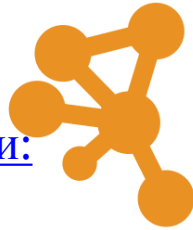
Число вершин 362



Кластеризация
с помощью
программы
MCODE
(плагин Cytoscape)

Results Panel		
MCODE Result 1		
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 Edges: 13

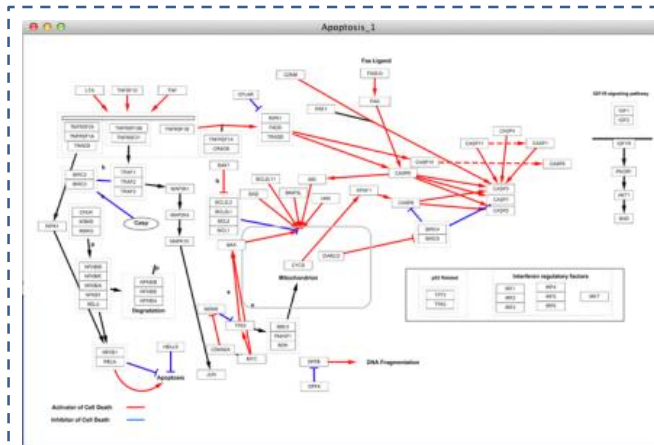
Возможности Cytoscape (продолжение)



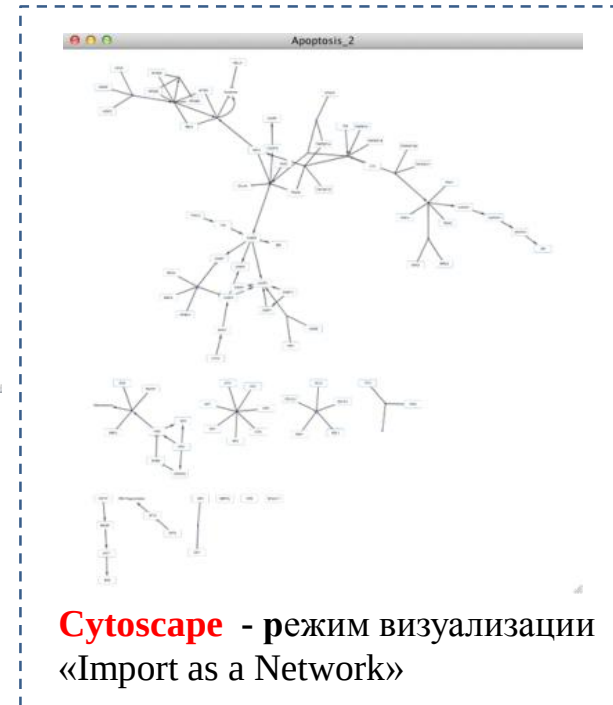
В области молекулярной биологии, системной биологии, геномики и протеомики:

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

Диаграмма
Апоптозис из
WikiPathways

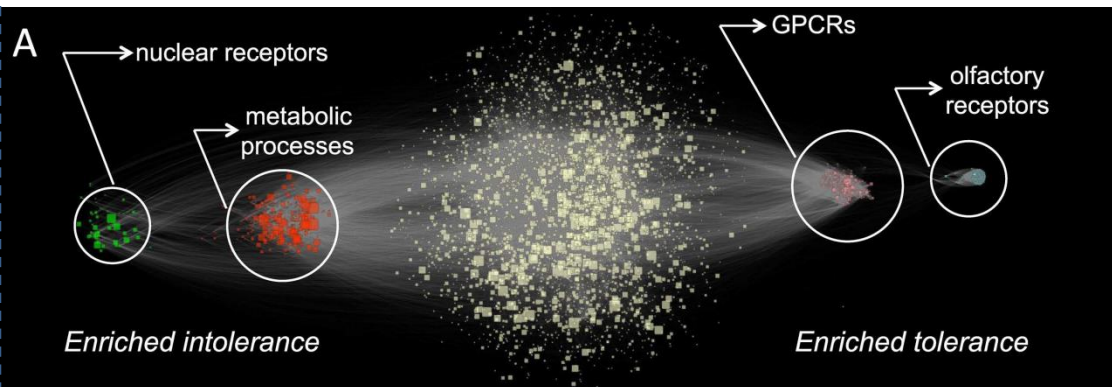


Cytoscape - режим
визуализации «By default»

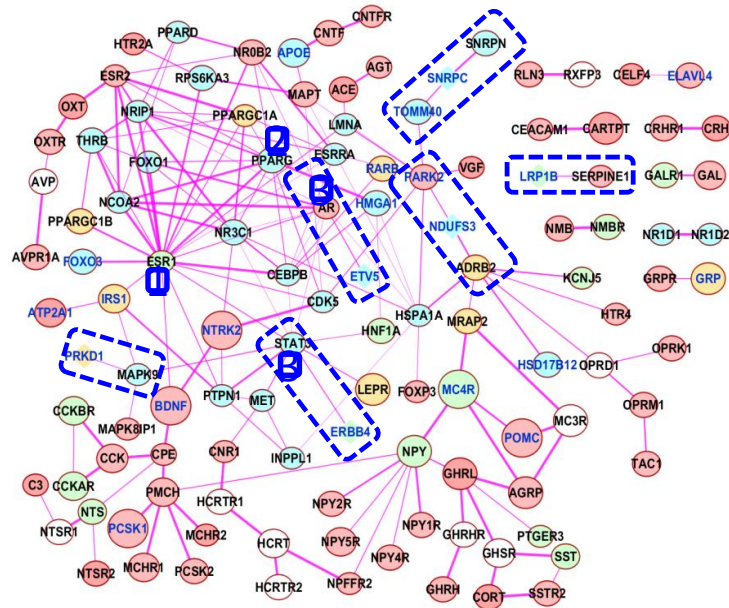


Cytoscape - режим визуализации
«Import as a Network»

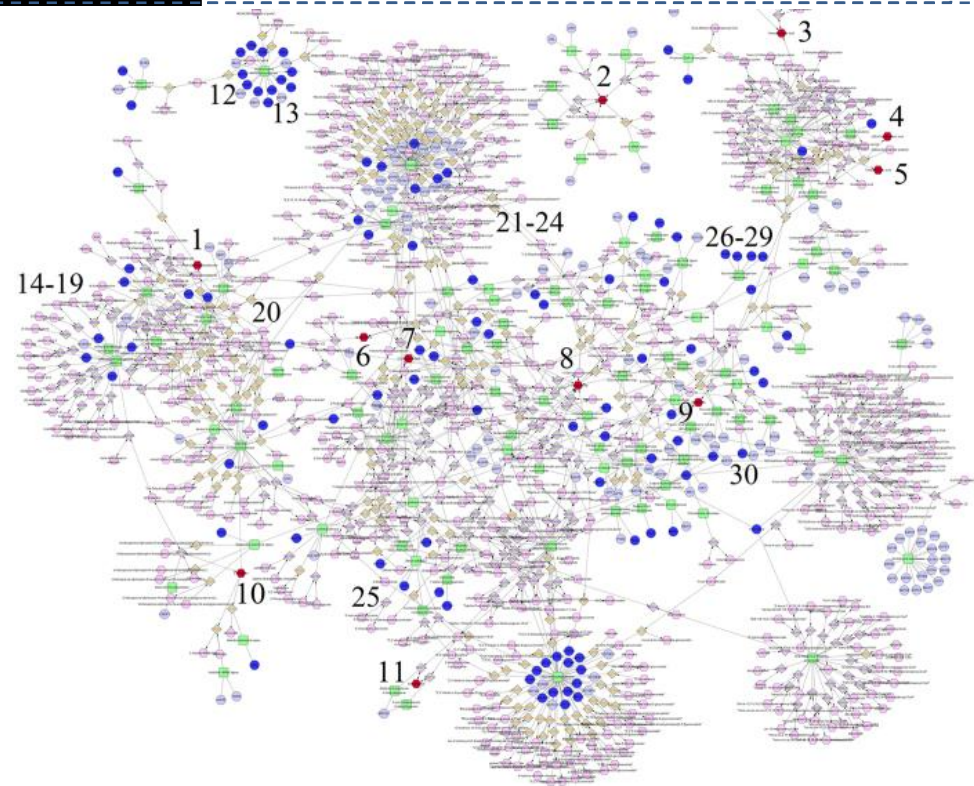
Примеры визуализации данных с помощью Cytoscape



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.

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

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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](#)

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[Nucleotide Sequence Databases](#)
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[Protein-protein interactions](#)
[Signalling pathways](#)
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[CGDB](#)
[CR. Cistrome](#)
[KBDock](#)
[NetworkKIN](#)
[P2CS](#)
[pathDIP](#)
[PepCyber:P~Pep](#)
[PhosphoAt](#)
[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](#)

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[Category/Paper List](#)
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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) BioCarta [https://cgap.nci.nih.gov/Pathways/BioCarta Pathways](https://cgap.nci.nih.gov/Pathways/BioCarta_Pathways)
- 6) WikiPathways <http://www.wikipathways.org/index.php/WikiPathways>
- 7) Signor <http://signor.uniroma2.it/>
- 8) SPIKE <http://www.cs.tau.ac.il/~spike/>

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,
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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, 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 ORACLE9i; (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 modeling 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 5254 relationships between gene network units, and 552 kinetic constants. Information distributed between 16 inter-linked tables was obtained by annotating 1980 journal publications. SRS release of the GeneNet database, the graphical viewer and the modeling section are available at <http://www.mgs.bionet.nsc.ru/mgs/gnw/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 specialized 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

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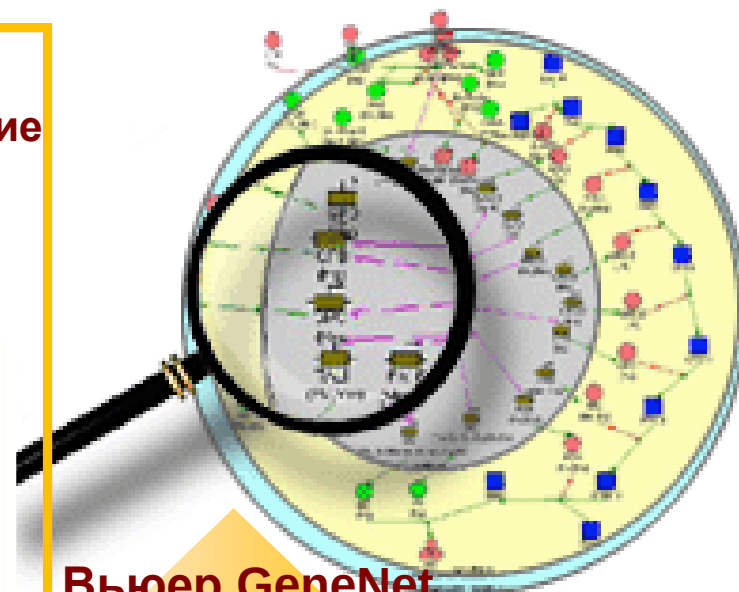
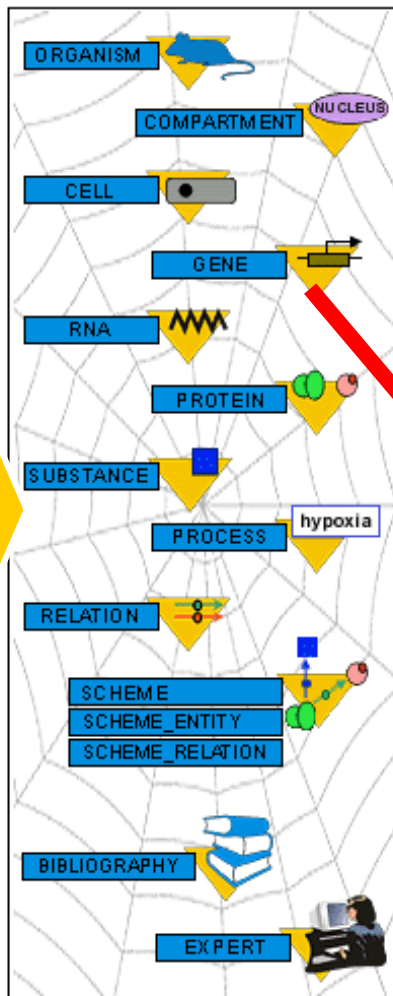
Технология GeneNet: основные модули, которыми пользуются разработчики базы

Статьи из журналов с описанием экспериментов



Графический редактор GeneEd для внесения новой информации

База данных (текстовое описание объектов, связей, диаграмм)

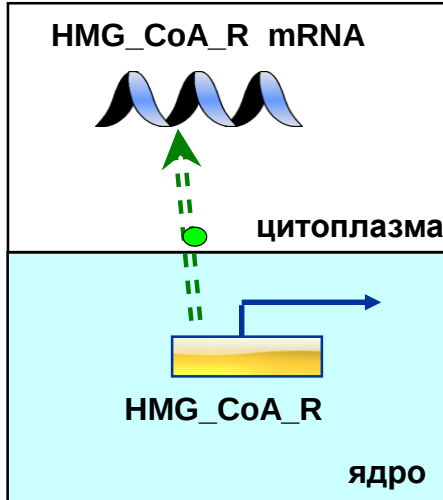


Вьюер GeneNet = редактор GeneEd, у которого отключена опция редактирования

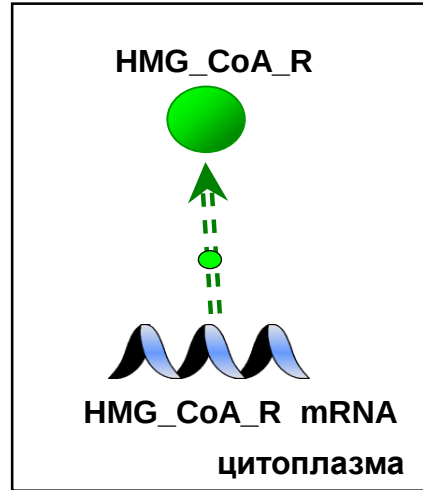
Доступ к информации через поисковую систему SRS

GeneNet: примеры графического изображения элементарных процессов (повторение)

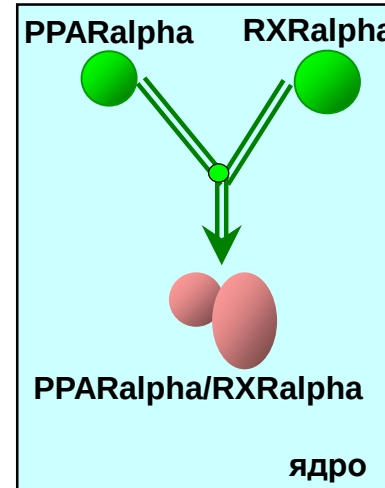
Транскрипция



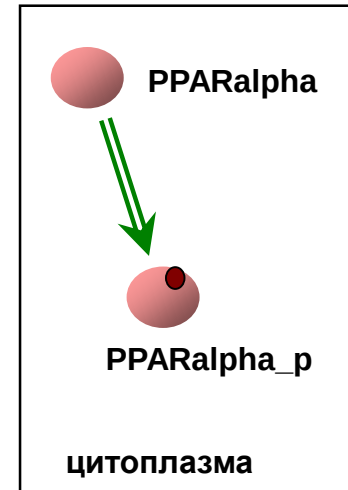
Трансляция



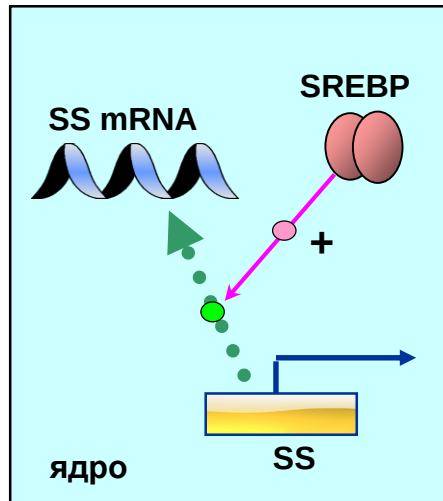
Мультимеризация
белка



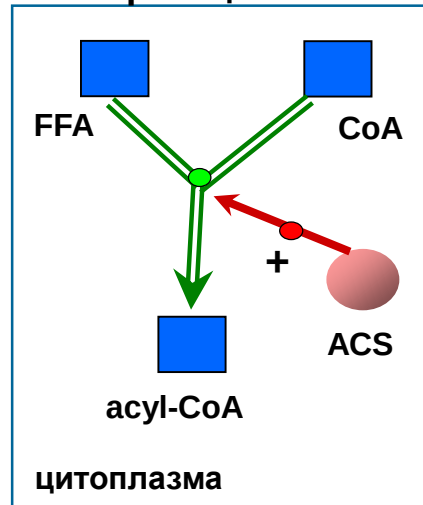
Фосфорилирование
белка



Активация
транскрипции



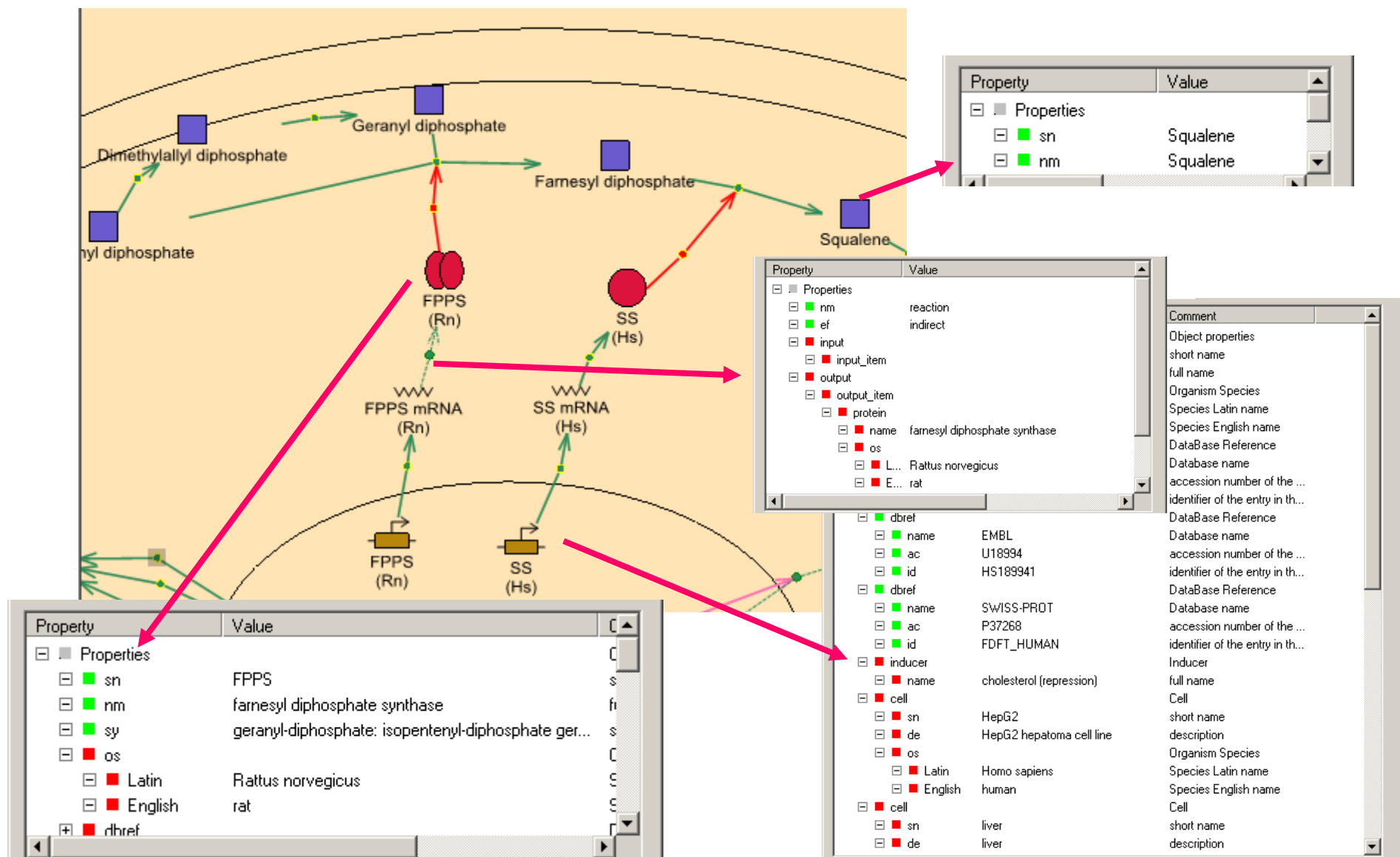
Ферментативная
реакция

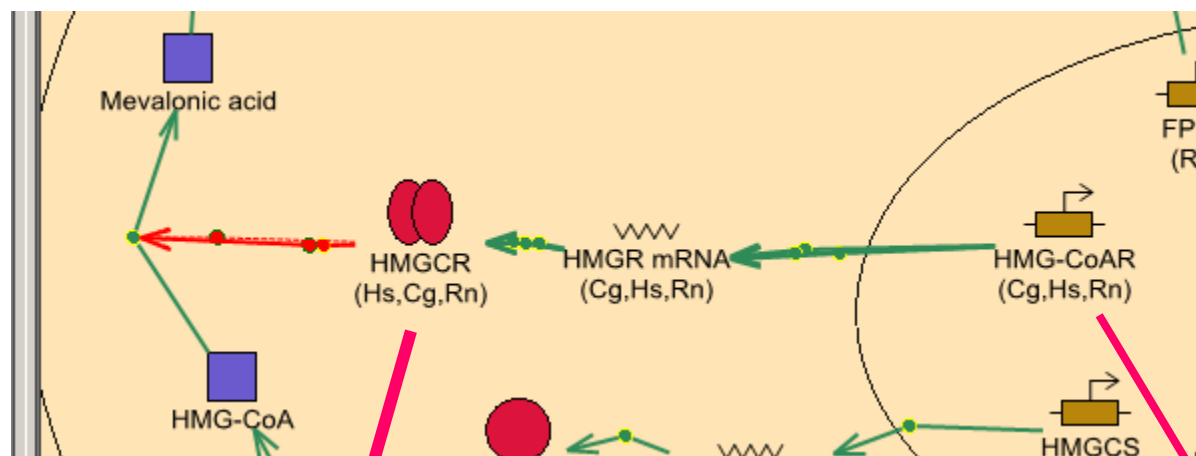


Условные обозначения:



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





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

Cgl	: HMG-CoAR : HMG-CoA reductase gene
Hsl	: HMG-CoAR : HMG-CoA reductase gene
Rnl	: 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://wwwmgs.bionet.nsc.ru/mgs/gnw/genenet/>

 **Gene Networks**¹

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

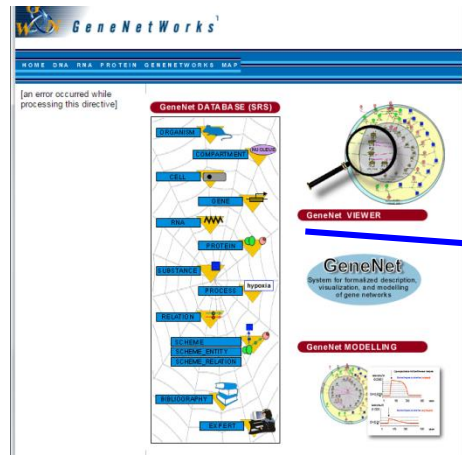
- [Versions info](#)
- [Information contents](#)
- [GeneNet functional sections](#)

2017_02.htm ^

Показать все ×

Интернет-доступная версия GeneNet: основные модули

База GeneNet,
доступная для поиска
через систему SRS



GeneNet SRS search results for GN_GENE.

Name	Short Name	Type	No. of Keys	No. of Entries	Indexing Date	Status
Identifier	id	index	1006	1006	03-Nov-2015	ok
IC code	ic	index	1005	1006	03-Nov-2015	ok
EntryInfo	DI	index	433	4440	03-Nov-2015	ok
Species	DS	index	166	2012	03-Nov-2015	ok
ShortName	SN	index	775	1006	03-Nov-2015	ok
FullName	NM	index	788	1008	03-Nov-2015	ok
Organism	SY	index	578	767	03-Nov-2015	ok
CellTissueLink	SL	index	280	958	03-Nov-2015	ok
Chromosome	CI	index	124	202	03-Nov-2015	ok
Inducer_Represor	RE	index	170	540	03-Nov-2015	ok
ProteinTissueLink	PN	index	9	9	03-Nov-2015	ok
DatabaseLink	DB	index	11	886	03-Nov-2015	ok
Reference	RE	index	897	1205	03-Nov-2015	ok
Comments	CC	show	0	0		not indexed

Браузер базы GeneNet –
список видов организмов и
соответствующих им генов

GeneNet Browser: Browse genes by species.

Latin name	English name
<i>Anolis carolinensis</i>	anole
<i>Apis mellifera</i>	honey bee
<i>Arabidopsis thaliana</i>	thale cress
<i>Bos taurus</i>	cow
<i>Brassica oleracea</i>	broccoli
<i>Brassica napus</i>	oilseed rape
<i>Chlamydomonas reinhardtii</i>	green alga
<i>Drosophila melanogaster</i>	fruit fly
<i>Escherichia coli</i>	bacterium
<i>Gallus gallus</i>	chicken
<i>Homo sapiens</i>	human
<i>Mus musculus</i>	mouse
<i>Nicotiana glauca</i>	tobacco
<i>Plasmodium falciparum</i>	malaria parasite
<i>Rattus norvegicus</i>	rat
<i>Saccharomyces cerevisiae</i>	baker's yeast
<i>Salmonella enterica</i>	salmonella
<i>Strawberry</i>	strawberry
<i>Taraxacum officinale</i>	dandelion
<i>Xenopus laevis</i>	clayton frog
<i>Zebrafish</i>	zebrafish

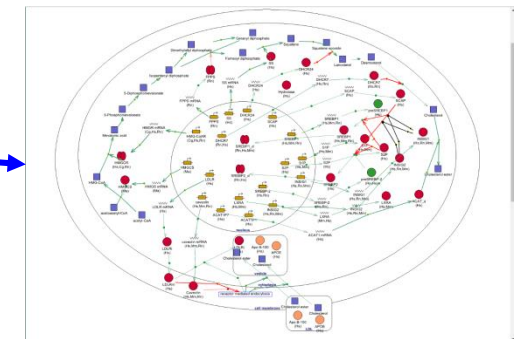
GeneNet SRS search results for GN_GENE.

Name	Short Name	Type	No. of Keys	No. of Entries	Indexing Date	Status
Identifier	id	index	1006	1006	03-Nov-2015	ok
IC code	ic	index	1005	1006	03-Nov-2015	ok
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Inducer_Represor	RE	index	170	540	03-Nov-2015	ok
ProteinTissueLink	PN	index	9	9	03-Nov-2015	ok
DatabaseLink	DB	index	11	886	03-Nov-2015	ok
Reference	RE	index	897	1205	03-Nov-2015	ok
Comments	CC	show	0	0		not indexed

Список диаграмм

List of Gene Networks

Eukaryotic gene networks	Prokaryotic gene networks
1. Adipocyte lipolysis	1. Anaplerotic Reactions
2. Adipocyte pathways	2. Arginine, Putrescine, and Spermidine Biosynthesis
3. AMPA receptors delivery mechanisms in LTP (the diagram is made in Design Technological Institute of Digital Techniques SB RAS, Laboratory of Biomedical Informatics)	3. Aromatic Amino Acids
4. Antiviral response	4. Aspartate and Asparagine Biosynthesis
5. Apoptosis (general scheme)	5. Branched Chain Amino Acid Biosynthesis
6. Cell Cycle (G0, G1-S transition)	6. Cysteine Biosynthesis
7. Cell cycle (fission yeast)	7. Glutamate and Glutamine Biosynthesis
8. Cholesterol metabolism (intracellular)	8. Histidine Biosynthesis
9. Cholesterol MODEL	9. Membrane Transport
10. Dioxin influence on macrophage	
11. Early long-term potentiation (the diagram is made in Design Technological Institute of Digital Techniques SB RAS, Laboratory of Biomedical Informatics)	
12. EBV infection	
13. EBV transformation	
14. Erythroid differentiation	
15. Germination (endospore)	
16. Heat Shock Response	
17. HCV (life cycle)	
18. Hepatitis C (apoptosis)	
19. Hepatitis C (IFN)	
20. HSP70 autoregulation	
21. Influenza virus (life cycle)	
22. IAK STAT signal transduction pathway	
23. LEA program	
24. Lysine (organism level)	



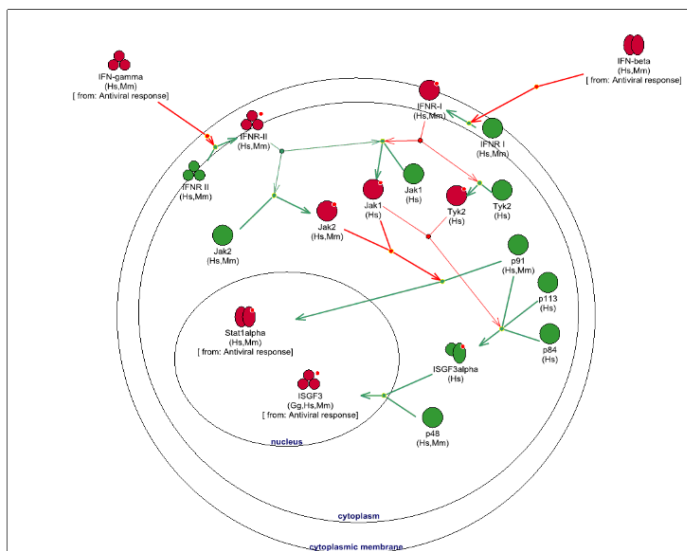
GeneNet: диаграмма, описывающая противовирусный ответ



Гиперссылка на
подсхему

JAK/STAT сигнальный путь

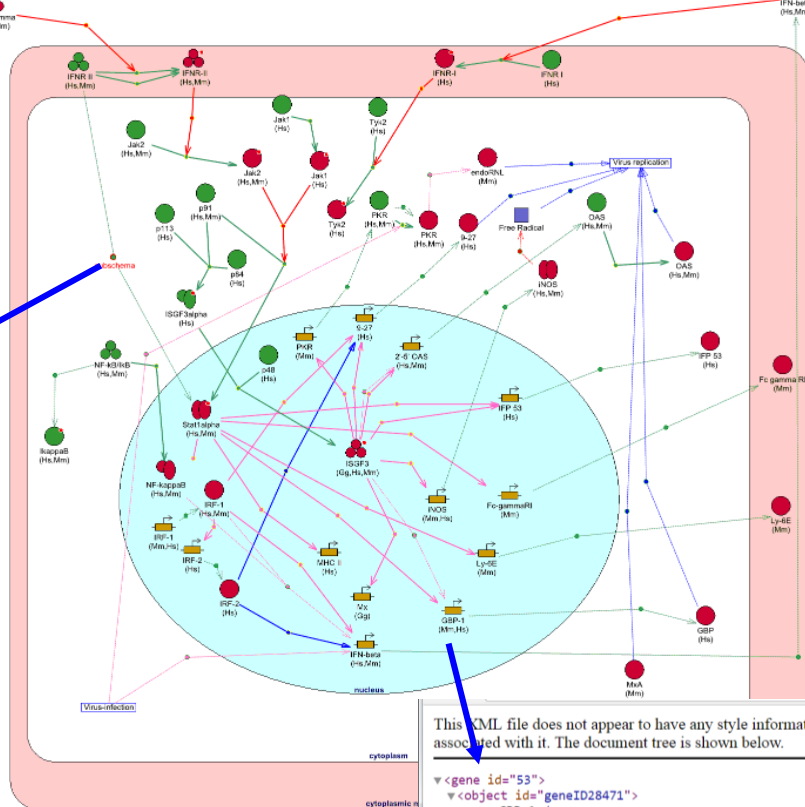
JAK/STAT signal transduction pathway



Antiviral response

INF-gamma

INF-beta



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        <English>mouse</English>
      </os>
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    </object>
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      <de>RAW 264.7 macrophage cell line</de>
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        <English>mouse</English>
      </os>
    </cell>
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      <authors>Nicolet C.M. and Paulnock D.M.</authors>
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      </journal>
    </ref>
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</document>
```

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 ▼

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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

Enter keywords

[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:

геленвен форте купить x SquirrelMail x WikiPathways: building x Interferon type I signalin x KEGG PATHWAY Databa x

← → ↻ ⓘ www.genome.jp/kegg/pathway.html#drug 🔍 📁 ☆ ⋮

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

1. Metabolism

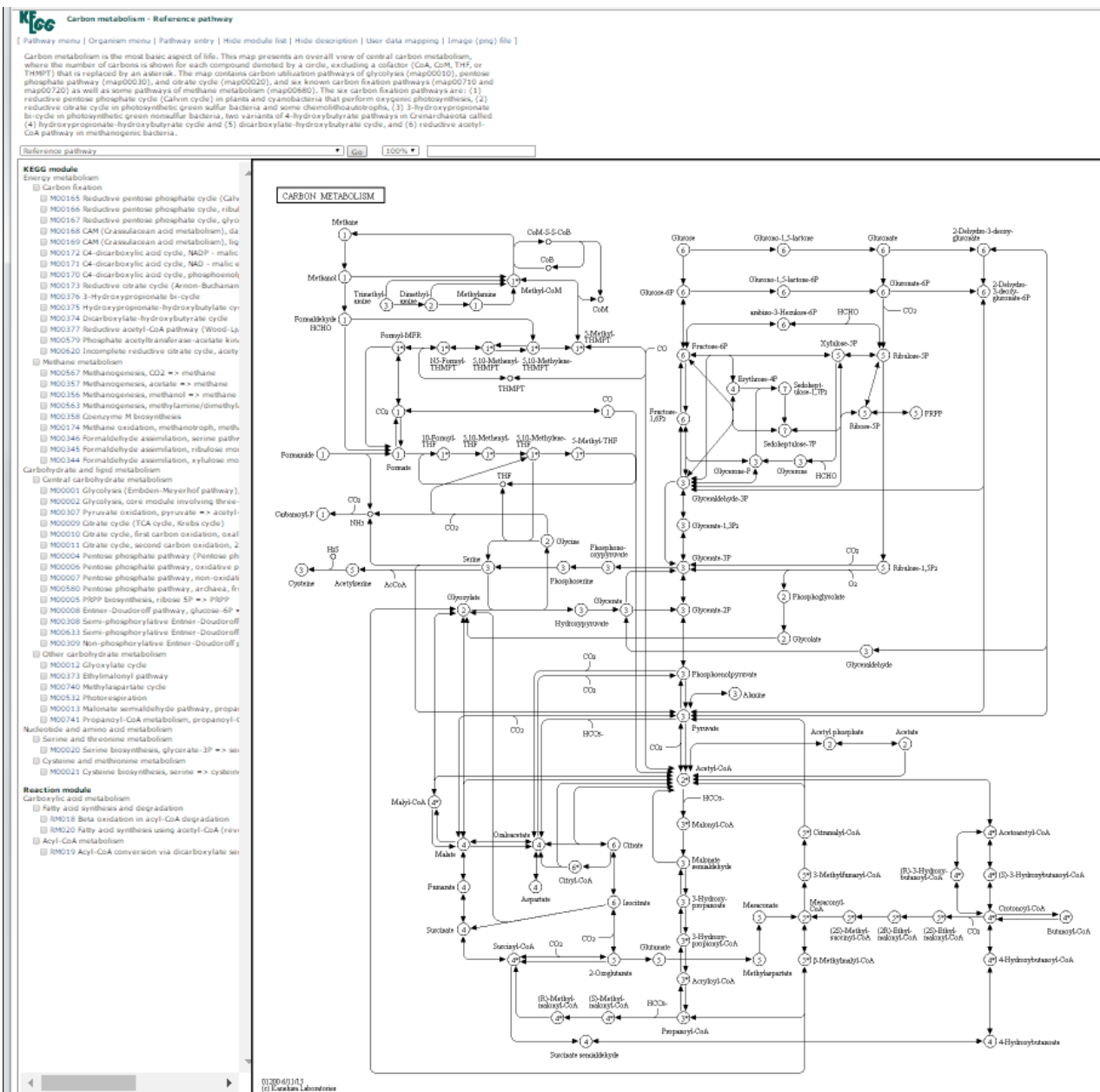
1.0 Global and overview maps

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

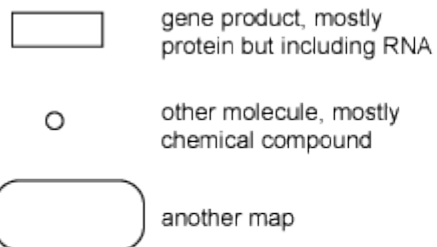
WP585_85198.png ^ WP585_85198.owl ^ WP585_85198 (1).gpml ^ Показать все x

KEGG: Интегральная схема метаболизма углеводов (Carbon metabolism)

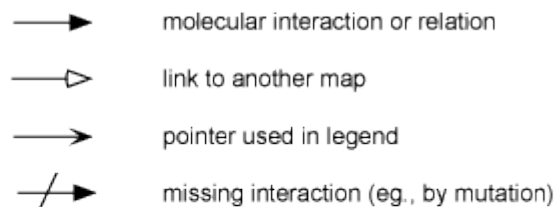


KEGG: условные обозначение

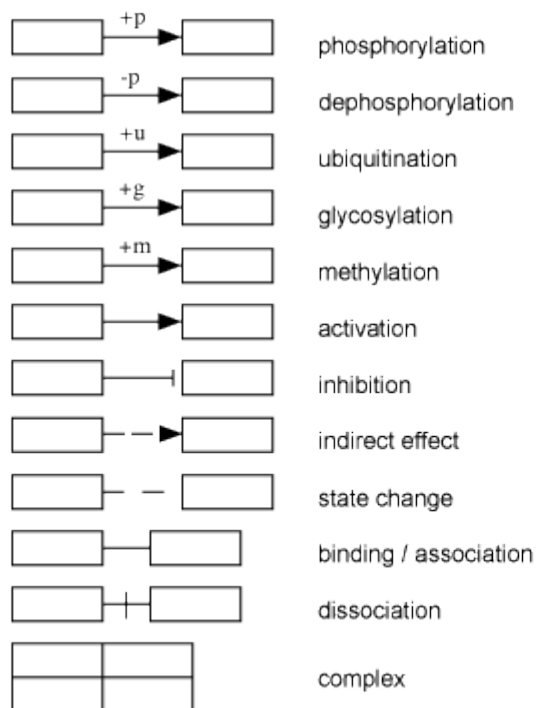
Objects



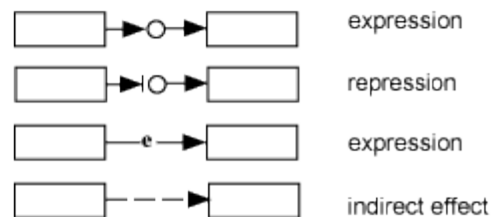
Arrows



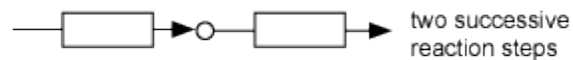
Protein-protein interactions



Gene expression relations



Enzyme-enzyme relations



KEGG: диаграмма Glycolysis / Gluconeogenesis

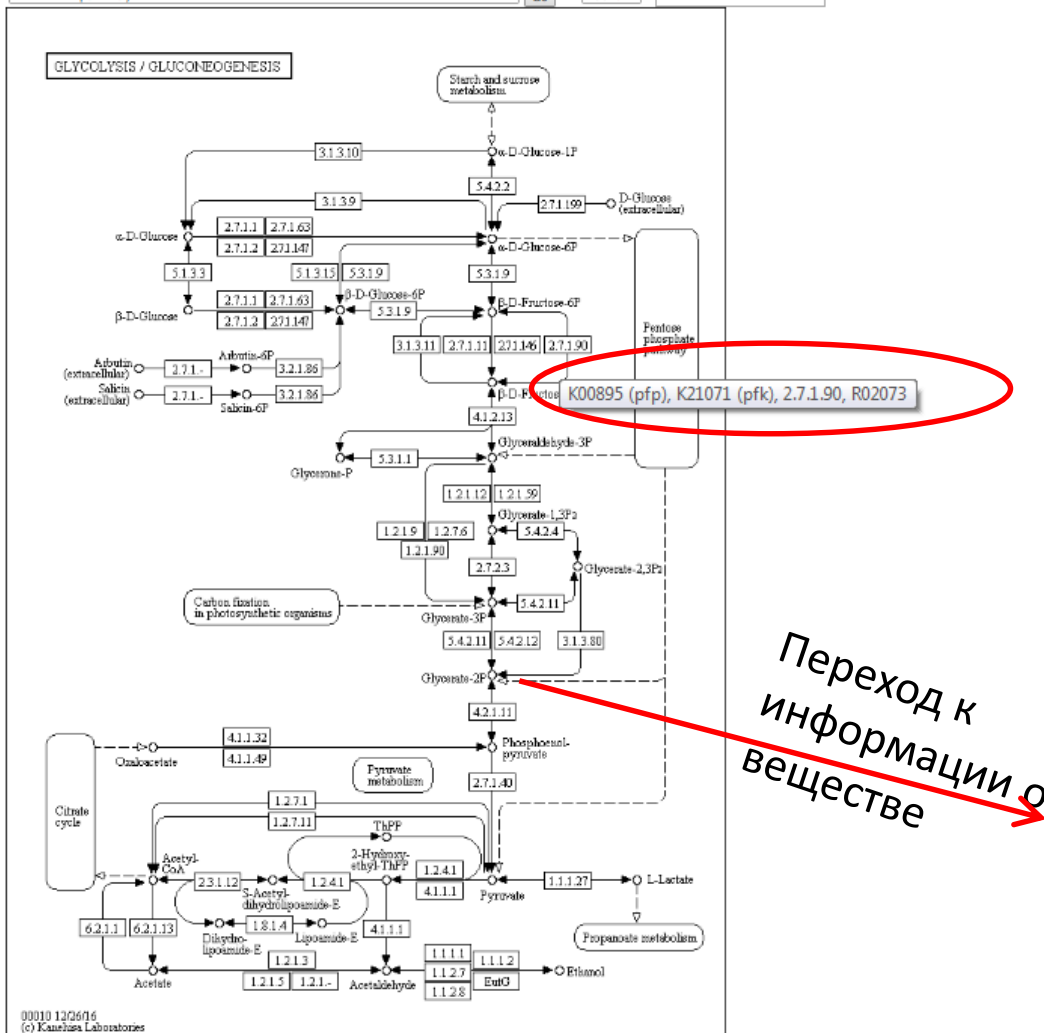


Glycolysis / Gluconeogenesis - Reference pathway

[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%



ВХОД "Pyruvate"
Разделе базы
"KEGG Chemical Universe"

KEGG COMPOUND: C00022 [Help](#)

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	R00005 R00008 R00014 R00195 R00205 R00197 R00198 R00199 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 R01012 R01031 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	

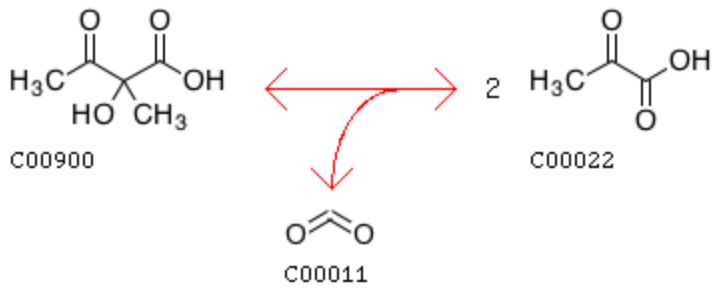
Переход к
информации о
веществе

ВХОД "REACTION" в "KEGG REACTION": Одна из реакций с участием вещества «Pyruvate»



REACTION: R00006

Help

Entry	R00006
Name	pyruvate:pyruvate acetaldehydetransferase (decarboxylating); 2-acetolactate pyruvate-lyase (carboxylating)
Definition	2-Acetolactate + CO ₂ <=> 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 TNFα (TNF signaling pathway - Homo sapiens (human))

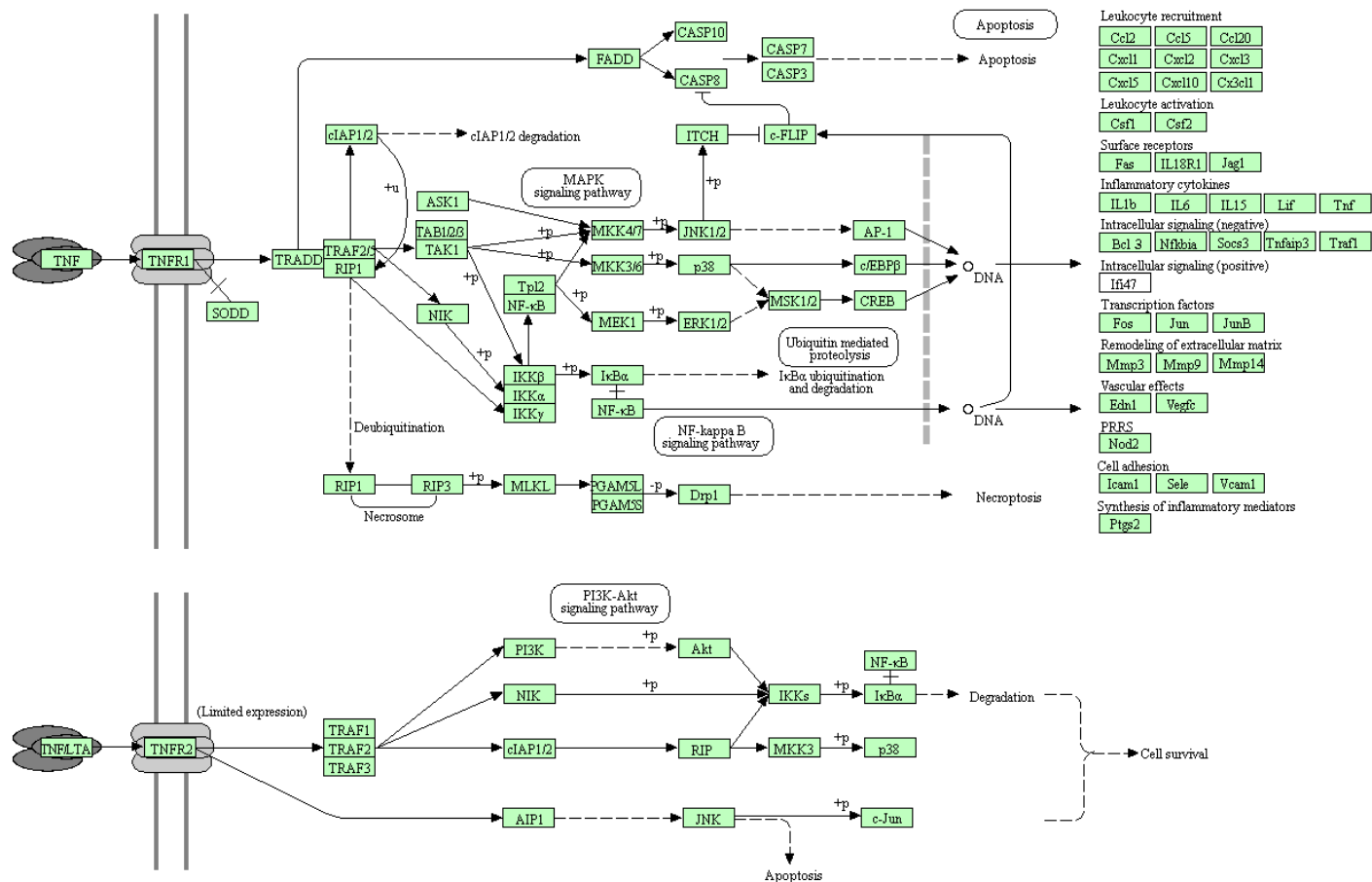


TNF signaling pathway - Homo sapiens (human)

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 TNFα
(**TNF signaling pathway - Homo
sapiens (human)**)

PATHWAY: hsa04668

[Help](#)

Entry	hsa04668	Pathway
Name	TNF signaling pathway - Homo sapiens (human)	
Description	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.	
Class	Environmental Information Processing; Signal transduction	

[BRITE hierarchy](#)

Pathway map hsa04668 TNF signaling pathway

The diagram illustrates the TNF signaling pathway. TNF (tumor necrosis factor) binds to its receptors, TNFR1 and TNFR2. TNFR1 signaling leads to the activation of NF-κB via the IKK complex (IKKα, IKKβ, NEMO) and the MAPK cascade (JNK, p38, ERK). TNFR2 signaling also involves NF-κB and MAPK. Both pathways lead to the transcription of target genes. The diagram also shows the involvement of other molecules like TRADD, TRAF1, TRAF2, and RIPK1.

[All organisms](#)

[Ortholog table](#)

Other DBS	BSID: 812256 GO: 0033209
-----------	---

Organism Homo sapiens (human) [GN:*hsa*]

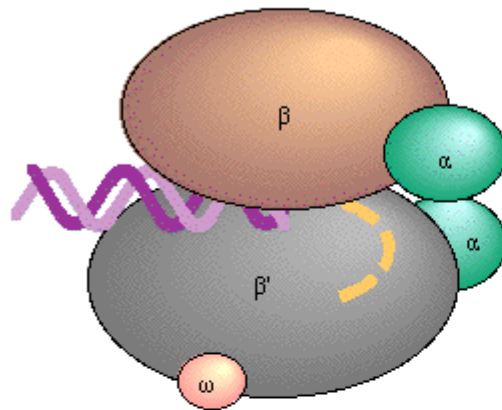
Gene	7124 TNF; tumor necrosis factor [KO:K03156] 7132 TNFRSF1A; TNF receptor superfamily member 1A [KO:K03158] 9530 BAG4; BCL2 associated athanogene 4 [KO:K09558] 8717 TRADD; TNFRSF1A associated via death domain [KO:K03171] 7186 TRAF2; TNF receptor associated factor 2 [KO:K03173] [EC:2.3.2.27] 7188 TRAF5; 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]
------	---

All links

[Pathway \(1\)](#)
[BioSystems \(1\)](#)
[Genome \(1\)](#)
[KEGG GENOME \(1\)](#)
[Gene \(108\)](#)
[KEGG GENES \(108\)](#)
[All databases \(110\)](#)
[Download RDF](#)

KEGG: диаграмма RNA polymerase из раздела 2.1 Transcription

RNA POLYMERASE



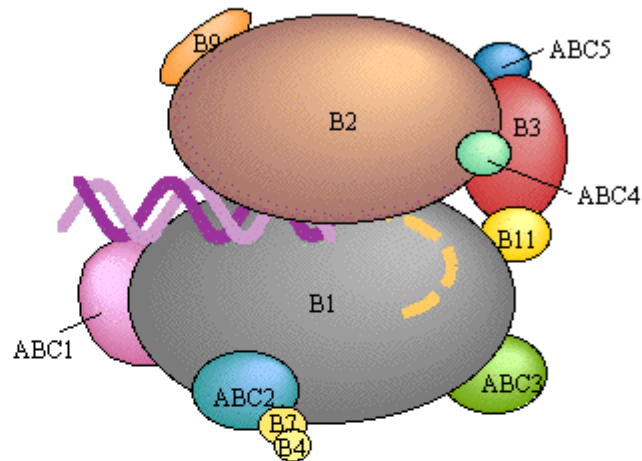
RNA polymerase (*Thermus aquaticus*)

Bacterial

β	α	ω	δ
β'			

Archaeal

B	D	F	H	K	E
A	G		N	L	P



RNA polymerase II (*Saccharomyces cerevisiae*)

Eukaryotic Pol II

Core subunits

B2	B3
B1	B11

Pol II specific subunits

B4	B7	B9
----	----	----

Pol I, II, and III common subunits

ABC1	ABC2	ABC3
ABC4	ABC5	

Eukaryotic Pol III

Core subunits

C2	AC2
C1	AC1

Pol III specific subunits

C3	C4	C11
C25	C31	C34
		C37

Eukaryotic Pol I

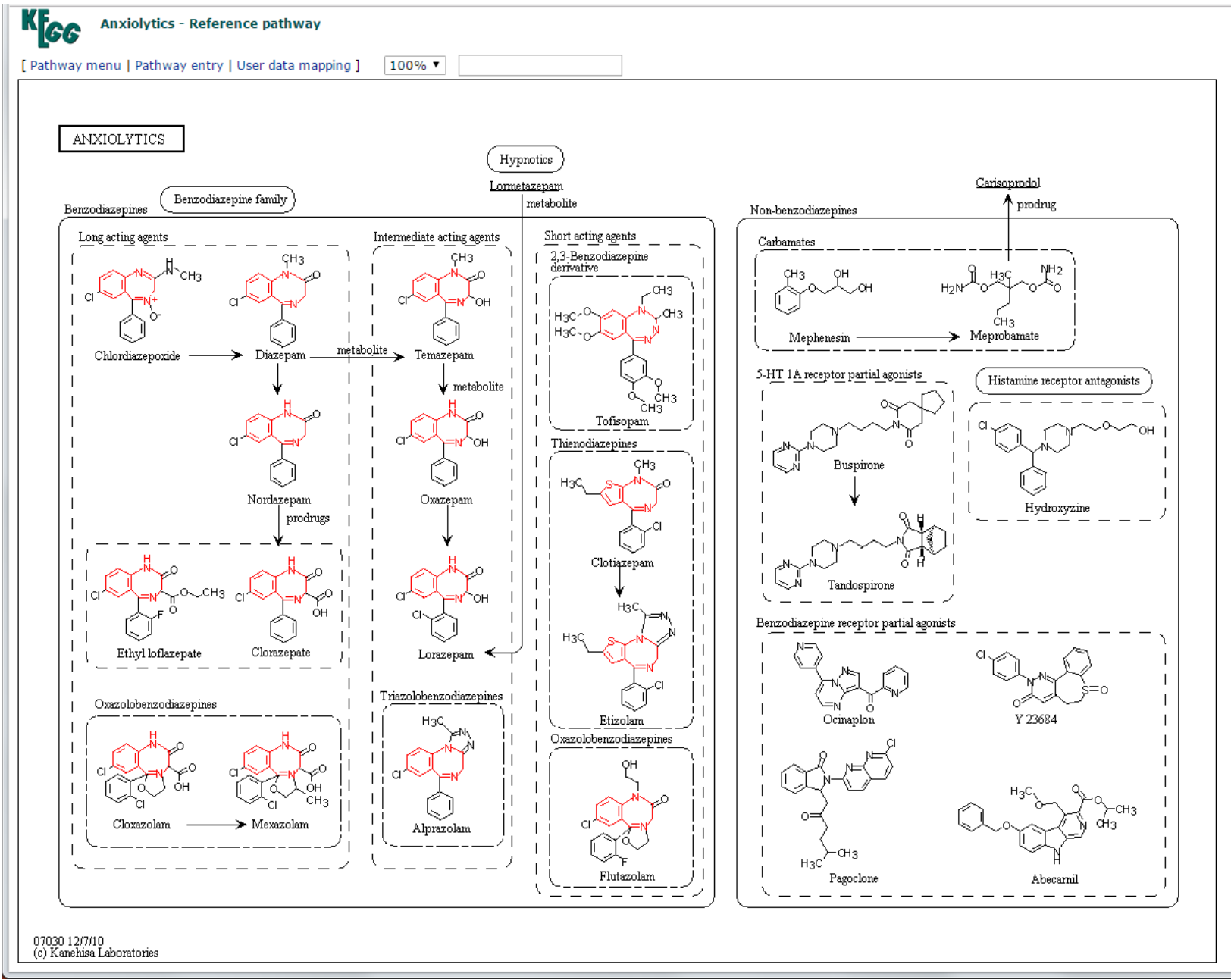
Core subunits

A2	AC2
A1	AC1

Pol I specific subunits

A12	A14	A34
A49	A43	

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



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

Manually drawn KEGG reference pathway maps

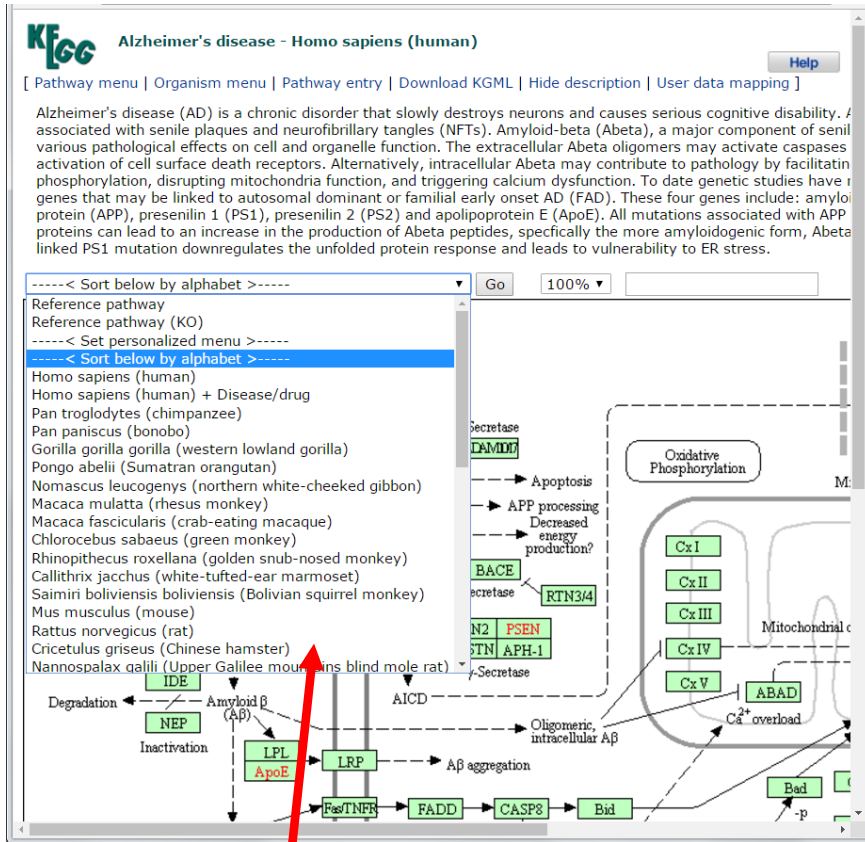
Category	Type	Number of maps ^a
Metabolism	Global map	4
	Overview map	5
	Regular map	160
	Chemical structure transformation map	9
Genetic information processing	Regular map	22
Environmental information processing	Regular map	38
Cellular processes	Regular map	24
Organismal systems	Regular map	78
Human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

^aAs of 1 October 2016.

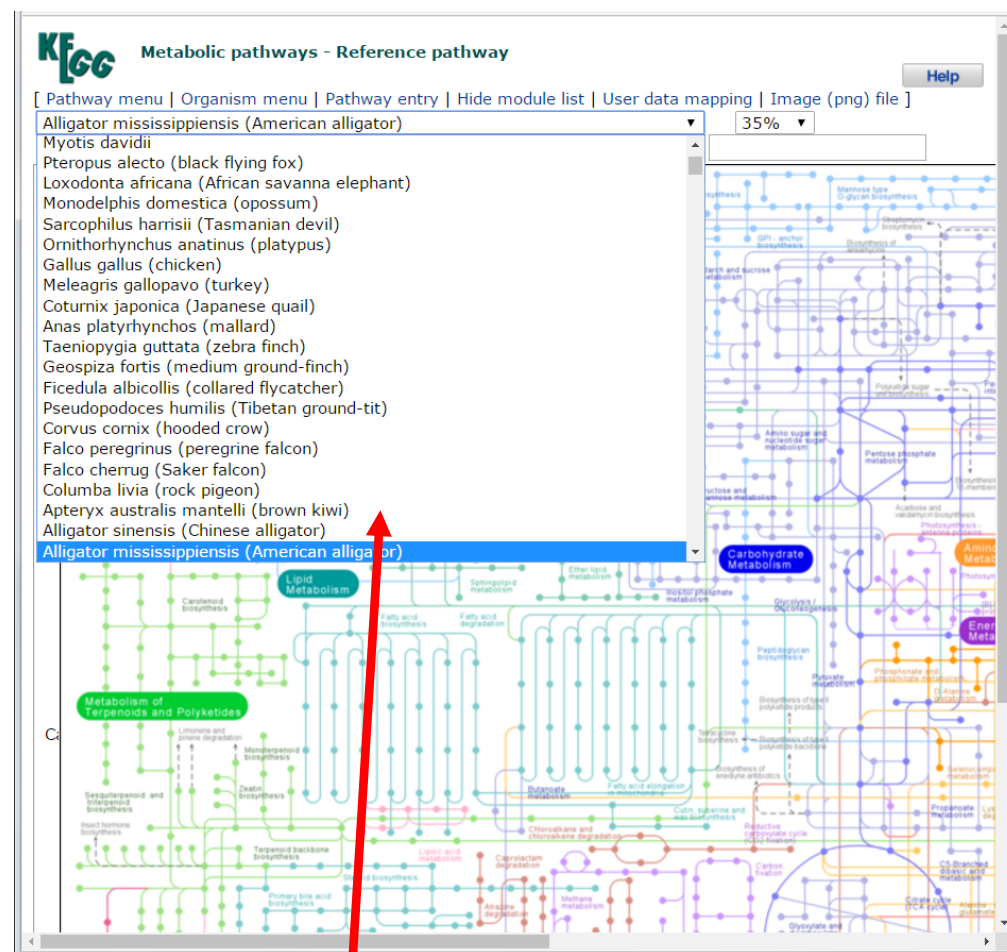
$\Sigma = 496$

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.

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



42 вида організмів



> 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 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.

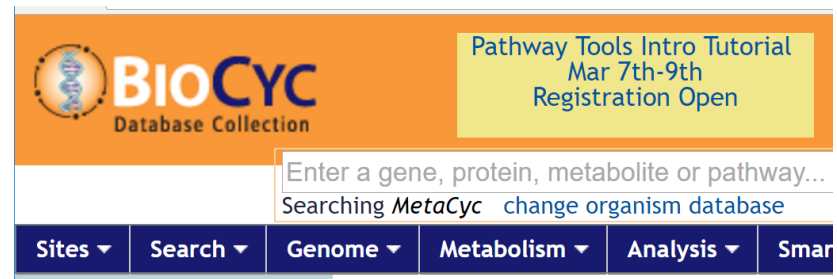
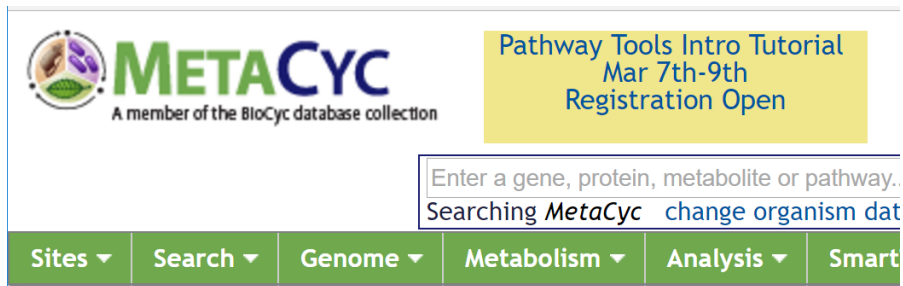
[KEGG Orthology \(KO\)](#)

Enter K numbers (Example) K00161 K00162 K00163 K00627 K00382

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



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

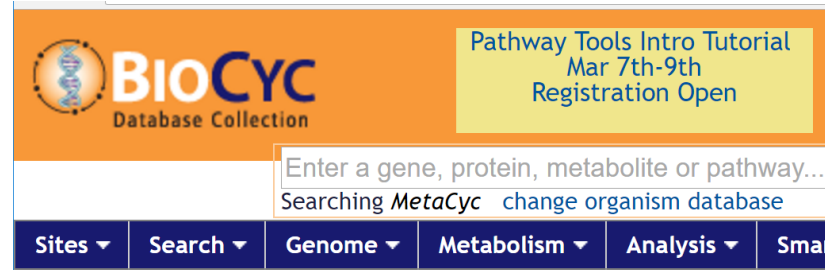
Базы развиваются с 2005 года (BioCyc) и 2001 года (MetaCyc)

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.

Информационное содержание базы данных BioCyc

<https://biocyc.org/>



9390 организм-специфичных Pathway/Genome Databases (PGDBs),
Три уровня достоверности данных:

Tier 1 PGDBs - ручной способ наполнения :

[EcoCyc](#), - база по *Escherichia coli* K-12.

[MetaCyc](#), - экспериментально исследованные ферменты и метаболитические пути 2,740 видов организмов

[AraCyc](#)

[HumanCyc](#)

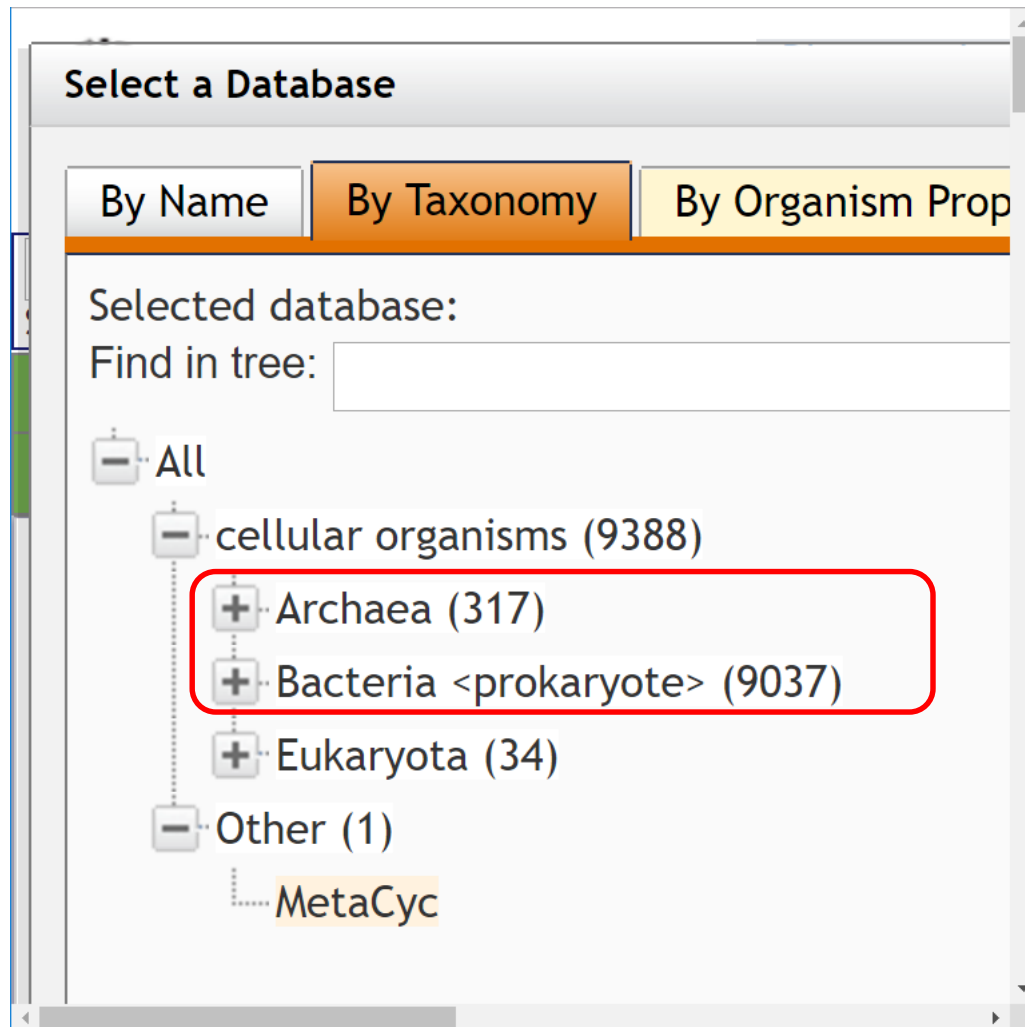
[LeishCyc](#) (*Leishmania major*)

[YeastCyc](#)

Tier 2 содержит 42 PGDBs. Данные сгенерированы программой PathoLogic и подвергнуты неглубокой ручной проверке.

Tier 3 содержит 7,625 PGDBs. Данные сгенерированы программой PathoLogic и не подвергались ручной проверке совсем.

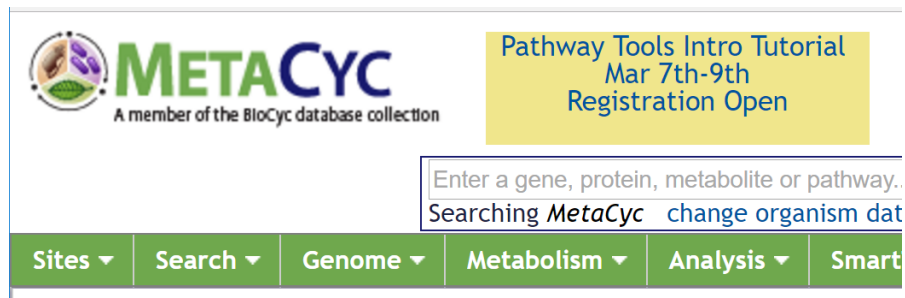
Виды организмов, представленные в базе BioCyc



Наибольшее количество информации относится к прокариотам

Информационное содержание базы данных MetaCyc

<https://metacyc.org/>



MetaCyc содержит
более 2490 метаболических путей
из > 46 000 публикаций
для 2816 видов организмов

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 oleracea</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>

Screenshot of the HumanCyc website showing the release notes history.

The browser window displays the URL <https://humancyc.org/humancyc/release-notes.shtml>. The page header includes the HumanCyc logo, a member of the BioCyc database collection, and a yellow banner for the Pathway Tools Intro Tutorial (Mar 7th-9th, Registration Open). Navigation links include LOGIN, Why Login?, and Create New Account.

The search bar contains the text "Enter a gene, protein, metabolite or pathway..." and "Quick Search" and "Gene Search" buttons. Below the search bar, it indicates "Searching *Homo sapiens* change organism database".

The main navigation menu includes: Sites, Search, Genome, Metabolism, Analysis, SmartTables, and Help.

HumanCyc Release Notes History

HumanCyc Statistics

	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

HumanCyc – возможности поиска и пролистывания информации



Pathway Tools Intro Tutorial
Mar 7th-9th
Registration Open

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

Hum

Search Genes, Proteins or RNAs

Search Compounds

Search Reactions

Search Pathways

Search Growth Media

Advanced Search

Cross Organism Search

BLAST Search

Google Search of this Site

Polypeptides

Protein complexes

Enzymes

Transporters

Chemical compounds

Citations

otes History

HumanCyc

Release Notes for HumanCyc Version 20.5

Released on ?, 2016

Since the last release we have added 25 new pathways to HumanCyc. A main effort focused on glycosylation pathways, describing the biosynthesis of the ABH histo-blood group antigens, the Lewis histo-blood group antigens, and several types of glycosphingolipids, including all common gangliosides. HumanCyc was also updated by propagation of new data from MetaCyc.

New Pathways

- anthranilate degradation IV (aerobic)
- arachidonate biosynthesis III (metazoa)
- arachidonate biosynthesis IV (8-deaturase)
- biosynthesis of ABH and Lewis epitopes from type 1 precursor disaccharide
- biosynthesis of ABH and Lewis epitopes from type 2 precursor disaccharide
- cardenolide biosynthesis
- docosahexaenoate biosynthesis III (mammals)
- gala-series glycosphingolipids biosynthesis
- ganglio-series glycosphingolipids biosynthesis
- globo-series glycosphingolipids biosynthesis
- i antigen and I antigen biosynthesis
- lacto-series glycosphingolipids biosynthesis
- methionine salvage cycle III
- N-end rule pathway I (eukaryotic)
- neolacto-series glycosphingolipids biosynthesis
- pentose phosphate pathway (oxidative branch) I
- plasmalogen biosynthesis
- plasmalogen degradation
- protein S-nitrosylation and denitrosylation
- protein ubiquitylation
- S-methyl-5-thio-α-D-ribose 1-phosphate degradation
- superoxide radicals degradation
- tRNA splicing II
- UDP-α-D-glucuronate biosynthesis (from UDP-glucose)

New Superpathways

- superpathway of glycosphingolipids biosynthesis

Release Notes for HumanCyc Version 18.1

Released on Jun 23, 2014

Since the last release we have added six new pathways to HumanCyc. These include a novel threonine degradation pathway in humans, an alternate lysine degradation pathway via pipecolate, carnosine and homocarnosine biosynthesis, fructose 2,6-bisphosphate metabolism and hydrogen sulfide biosynthesis. We also revised 10 existing pathways in HumanCyc, which include ubiquinol 10, taurine, asparagine and coenzyme A biosynthesis; glycine betaine, purines, beta alanine, asparagine and valine degradation; and the superpathway of choline degradation to serine. HumanCyc was also updated by propagation of new data from MetaCyc.

New Pathways

- threonine degradation
- hydrogen sulfide biosynthesis (trans-sulfuration)
- lysine degradation II (pipecolate pathway)
- fructose 2,6-bisphosphate synthesis/dephosphorylation
- homocarnosine degradation
- carnosine degradation

Revised pathways:

HumanCyc - Pathway: superoxide radicals degradation

**HUMANCyc**
A member of the BioCyc database collection

Please take 3 minute BioCyc survey

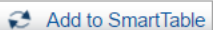
Welcome: Elena Ignatieva | Logout | Help | My preferences

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

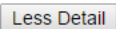
Quick SearchGene Search

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

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

catalase: **CAT**
1.11.1.6/1.11.1.21

2 hydrogen peroxide → 2 H₂O + oxygen

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

Compound: H₂O
Synonyms: H₂O, hydrogen oxide, water

<https://humancyc.org/compound?orgid=HUMAN&id=WATER>

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
Homo sapiens

enzyme
superoxide dismutase [Cu-Zn]

show operations

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?](#)

1.15.1.1 : 2 superoxide + 2 H⁺ -> hydrogen peroxide + ... +



Credits:

Created 09-Jun-2014 by SRI International

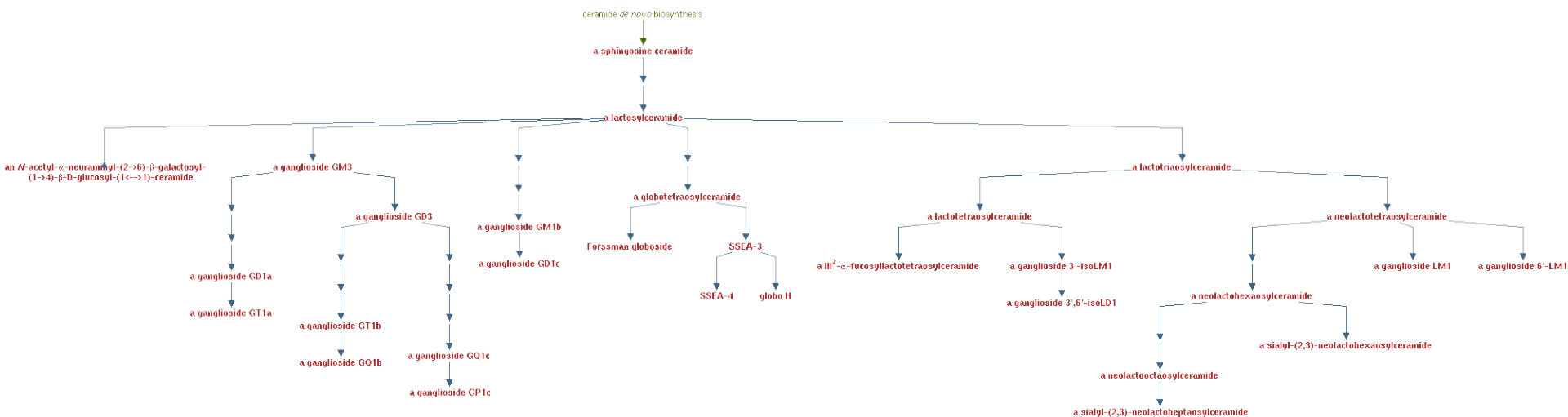
Unification Links

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
QMIM	105400, 147450, 158700
PDB	1AZV, 1BA9, 1NFM, 1SOS, 1SPD
RefSeq	NM_000454, NP_000445
UCSC Human Genome	NM_000454
UniGene	75428
UniProt	P00441

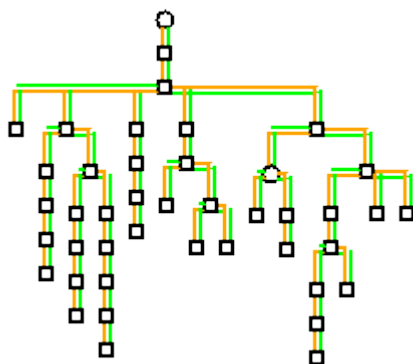
Report Errors or Provide Feedback

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

HumanCyc : Pathway: super pathway of glycosphingolipids biosynthesis



Pathway Evidence Glyph:



Key to Pathway Evidence Glyph

Edge Colors:

- An enzyme catalyzing this reaction is present in this organism
- No enzyme catalyzing this reaction has been identified in this organism
- An enzyme catalyzing this reaction was identified in this organism by the Pathway Hole Filler
- The reaction is an orphan, meaning no enzyme catalyzing this reaction has been sequenced in any organism
- The reaction has been designated a key reaction of this pathway
- The reaction and any enzyme that catalyzes it (if one has been identified) is unique to this pathway
- Represents spontaneous reactions, or lines that do not represent reactions (e.g. in polymerization pathways)

Node Shapes:

- Amino Acids
- Carbohydrates
- Proteins
- Purines
- Pyrimidines
- Cofactors
- tRNAs
- Other
- (Any filled shape) Phosphorylated

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

ЕсоСус : 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...
Searching *Escherichia coli* K-12 substr. MG1655 (EcoCyc) [change organism database](#)

Quick SearchGene Search

SitesSearchGenomeMetabolismAnalysisSmartTablesHelp

show operations

gene
aceB
Escherichia coli K-12 substr. MG1655

enzyme
malate synthase A

log in to add to SmartTable.

Synonymmas

Accession IDsEG10023 (EcoCyc)
b4014
ECK4006
P08997 (UniProt)

Length1602 bp / 533 aa

Map Position[4,215,478 -> 4,217,079] (90.82 centisomes, 327°)
View in Genome Browser

Locationcytosol

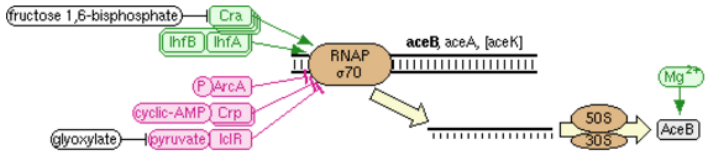
Reactionacetyl-CoA + glyoxylate + H₂O → (S)-malate + coenzyme A + H⁺

Pathwayglyoxylate cycle

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

SummaryGO Terms (7)EssentialityReactions (1)Protein FeaturesOperonsReferencesShow 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 I (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
EcoliWiki	b4014
ModBase	P08997
QU-Microarray	b4014
PortEco	aceB
PR	PRO_000022037

Представление данных в EcoСус: 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].

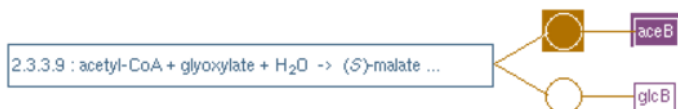
A series of vectors inducibly expressing paired-terminus antisense RNAs was constructed to silence central carbon metabolism in host *E. coli* K-12 MG1655. A vector that silenced *aceB* mRNA at 98% efficacy resulted in a defect in carbon catabolite repression [Nakashima14].

Review: [Cortay89]

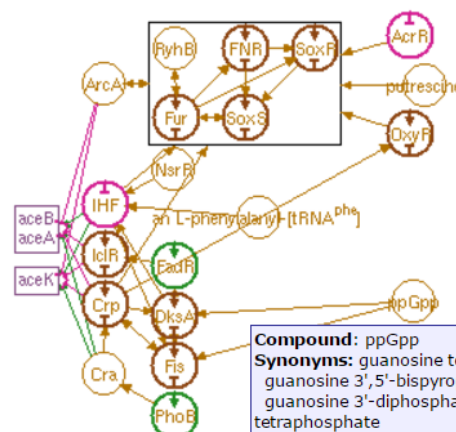
Additional Citations: [Byrne88, Byrne88a, LaPorte85]

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
генная 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](#)

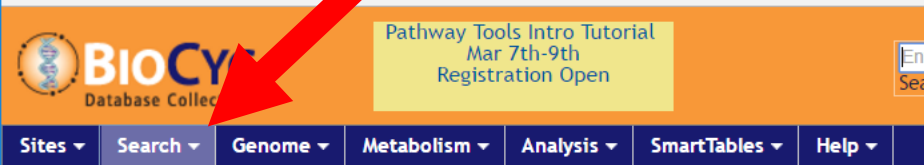
Page generated by Pathway Tools version 20.5 (software by SRI International) on Sun Mar 5, 2017, BIOCYC17A.

EcoCyc version 20.5.

<https://ecocyc.org/compound?orgid=ECOLI&id=GUANOSINE-5DP-3DP>

BioCyc: возможности для поиска и анализа данных

Самостоятельное изучение !!!!



- Search Genes, Proteins or RNAs
- Search Compounds
- Search Reactions
- Search Pathways
- Search DNA or mRNA Sites
- Search Growth Media
- Advanced Search
- Cross Organism Search
- BLAST Search
- Sequence Pattern Search
- Google Search of this Site



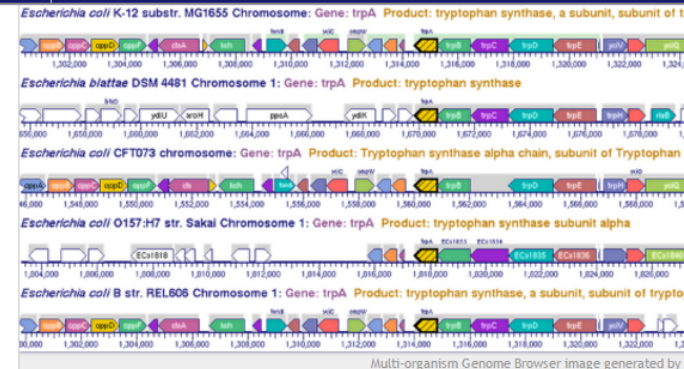
BioCyc Data

Subscriptions are now re
information on obtaining
transition to subscription
subscription if your instit
right corner of this page or appears here.

BioCyc is a collection of 9390 Pathway/Genome Databases (PGDBs), plus software tools for understanding their data.

Getting Started

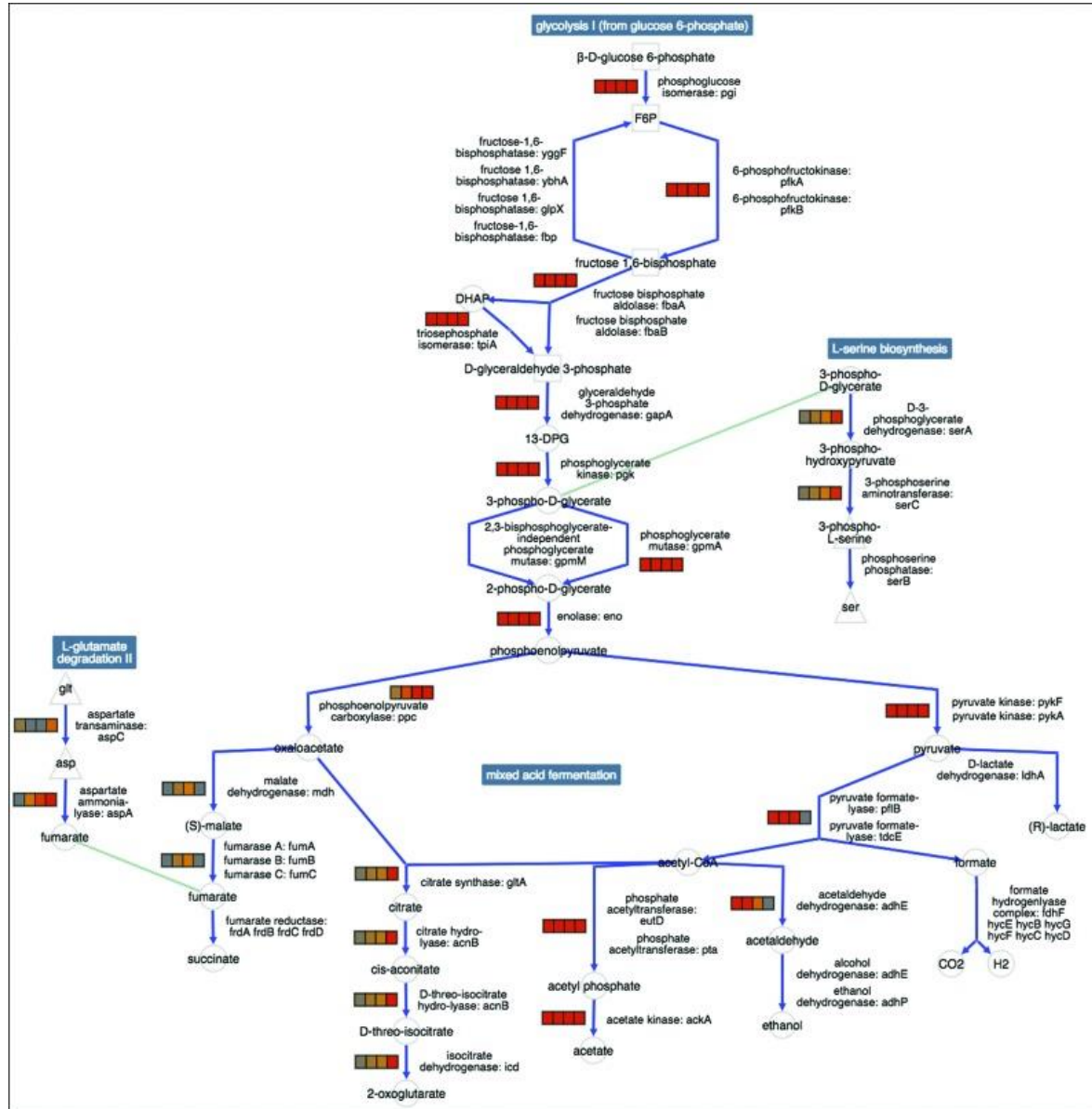
- Cellular Overview
- Run Metabolic Model
- Dead-end Metabolites
- Chokepoint Reactions
- Metabolic Route Search
- Metabolite Translation Service
- Pathway Collages
- Browse Pathway Ontology
- Browse Enzyme Commission Ontology
- Browse Compound Ontology
- Generate Metabolic Map Poster



Comparative Genome Analysis

Multiple comparative analysis tools are available in this website.

BioСус: одна из новых возможностей – конструирование супердиаграммы из выбранного набора диаграмм. (Pathway Collage tool)



BioCyc: скачать данные можно, купив лицензию

DOWNLOAD BIOCYC DATABASES AND PATHWAY TOOLS SOFTWARE

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

Note that the BioCyc web-based SmartTables facility can save you significant time in answering large-scale data analysis questions, and is significantly easier to use than is downloading and parsing BioCyc files. See the SmartTables menu.

Download BioCyc Data Files

We provide the BioCyc databases (such as [EcoCyc](#) and [MetaCyc](#)) as collections of data files in several alternative formats including the following.

Due to BioCyc moving to a subscription model in 2016, access to BioCyc DBs other than EcoCyc or MetaCyc requires [purchase of a subscription](#) (with the exception that older versions of BioCyc are freely available).

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

[Click here](#) for an exact listing of files provided and their formats.

Programmatic Access to BioCyc Data

We provide several APIs for accessing BioCyc data.

БАЗА ДАННЫХ REACTOME

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

Download Data

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](#).

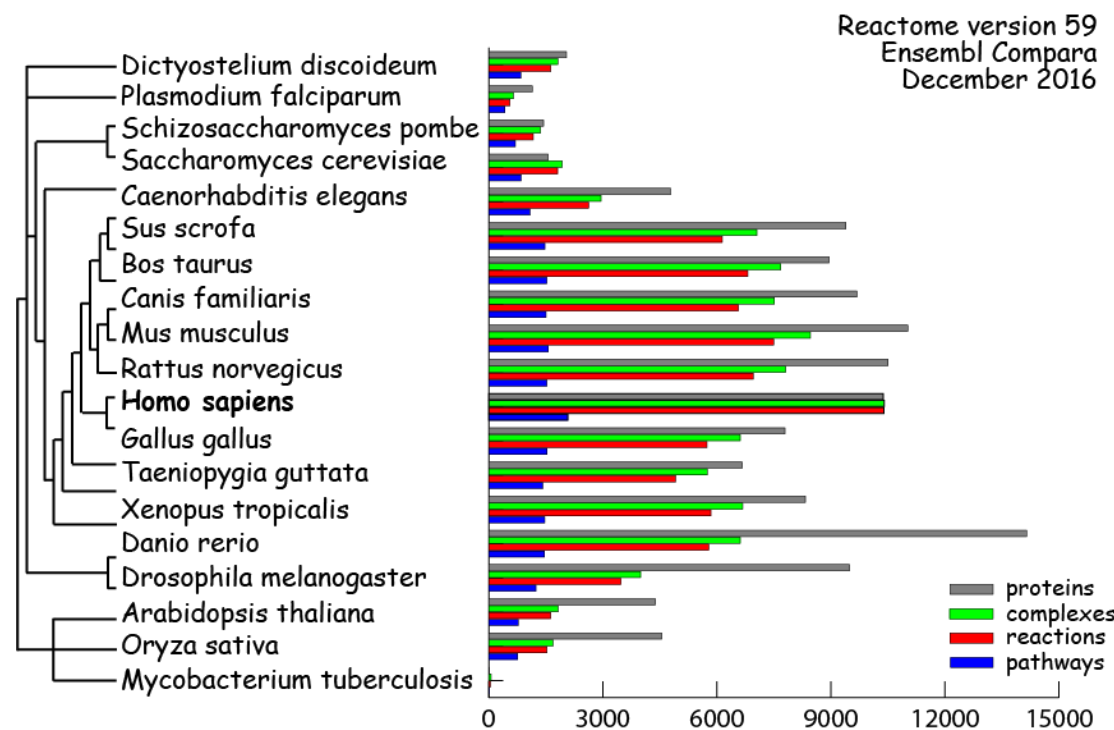
GitHub Repository is accessible [here](#).

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



БАЗА ДАННЫХ REACTOME

Иерархический список
разделов (диаграмм)

The screenshot displays the Reactome database interface. On the left, a hierarchical list of biological processes is shown, with 'Chromatin organization' and 'Chromatin modifying enzymes' highlighted. On the right, a detailed pathway diagram is displayed, showing a complex network of reactions and entities. A 'Diagram key' pop-up window is visible, providing a legend for the diagram's components. The key includes symbols for Small molecule, Protein, Complex(es), Set(s), Genome encoded entity, and Encapsulated Pathway. It also defines Reaction Types (Transition/Process, Association/Binding, Dissociation, Omitted, Uncertain) and Reaction Attributes (Stoichiometry, Catalysis, Positive Regulation, Negative Regulation, Set to member link, Wild Type, Disease-associated).

Reactome 3.2

Pathways for: Homo sapiens

Tour: [Icon]

Layout: [Icon]

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

Description

Molecules

Chromatin modifying enzymes

Chemical Compounds (16)

Proteins (241)

Условные обозначения

ИНФОРМАЦИОННЫЙ РЕСУРС BIOCARТА

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

Pathways 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

Более 300 диаграмм

БАЗА НЕ ОБНОВЛЯЕТСЯ:

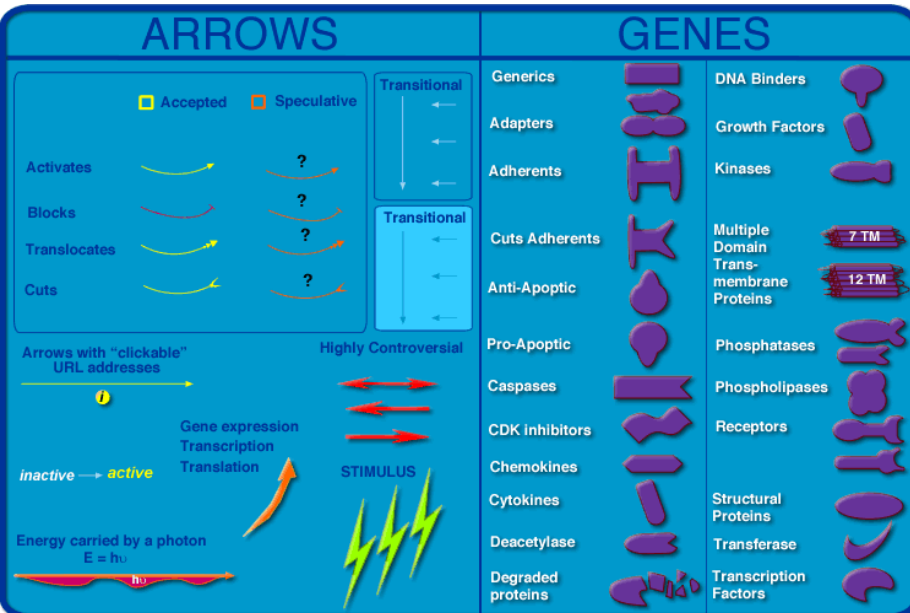
BioCarta had not been updating its pathways. The information provided might have been outdated. As a result, we have discontinued offering pathway information online. You may view our pathway figures at http://cgap.nci.nih.gov/Pathways/BioCarta_Pathways.

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

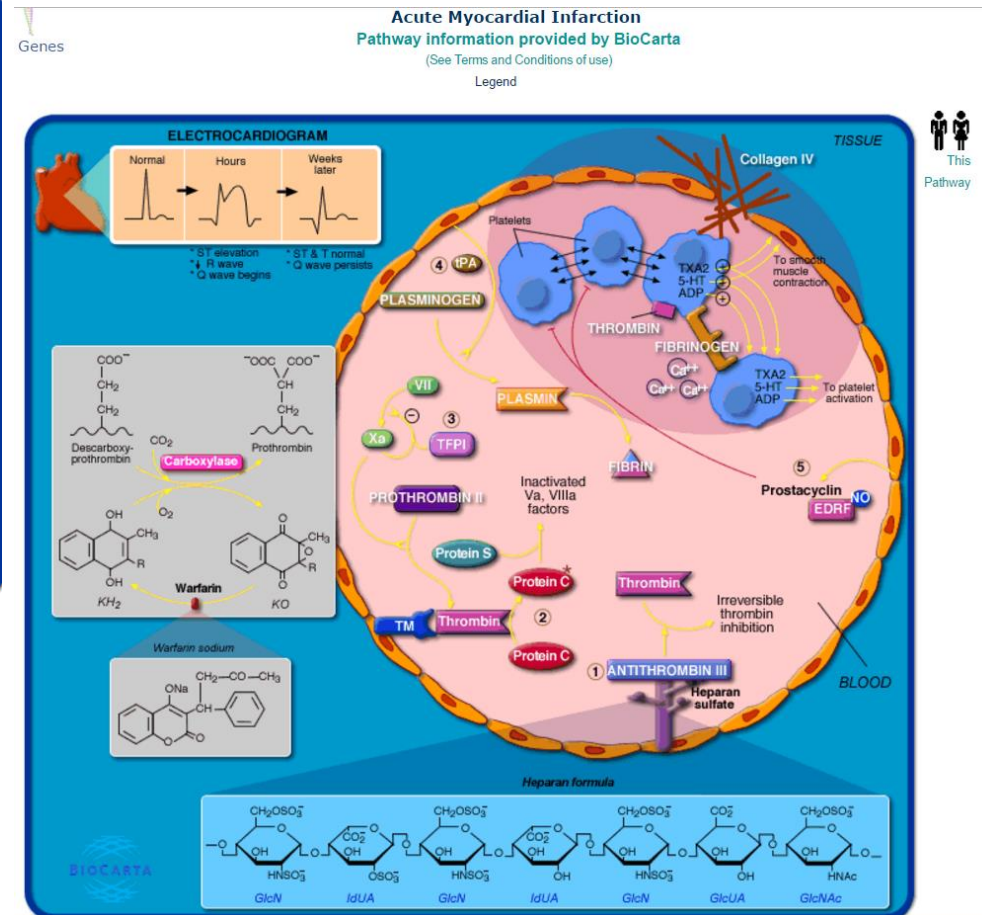
ИНФОРМАЦИОННЫЙ РЕСУРС BIOARTA

Содержит схемы метаболических либо сигнальных путей, а также схемы процессов

Условные обозначения



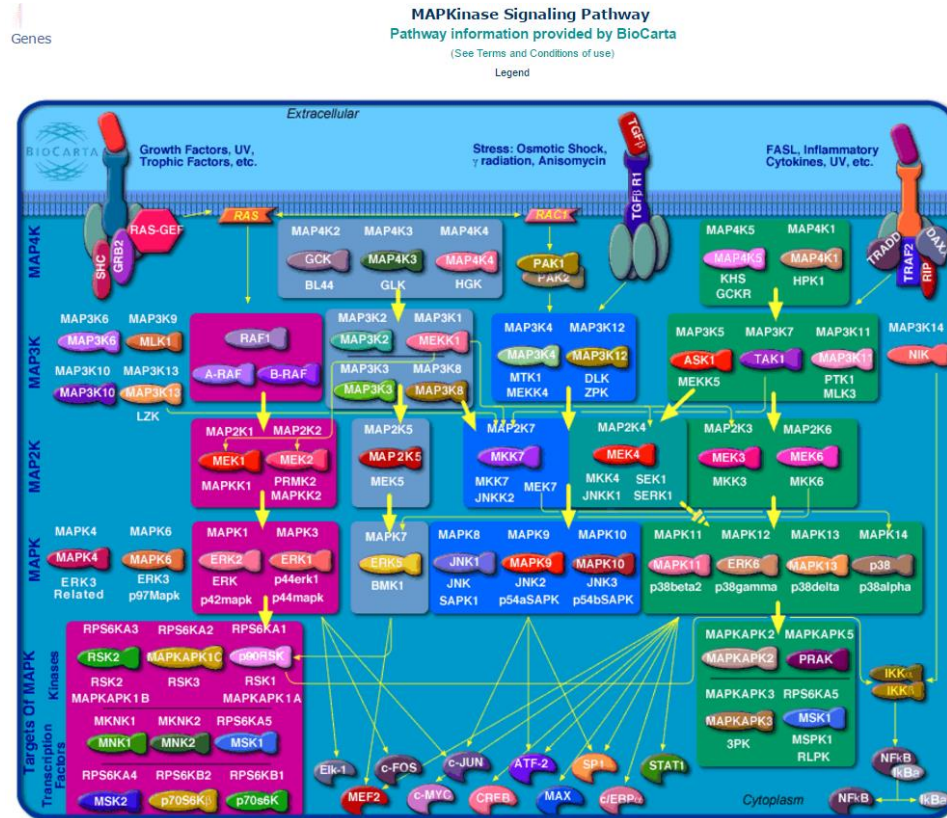
Acute Myocardial Infarction



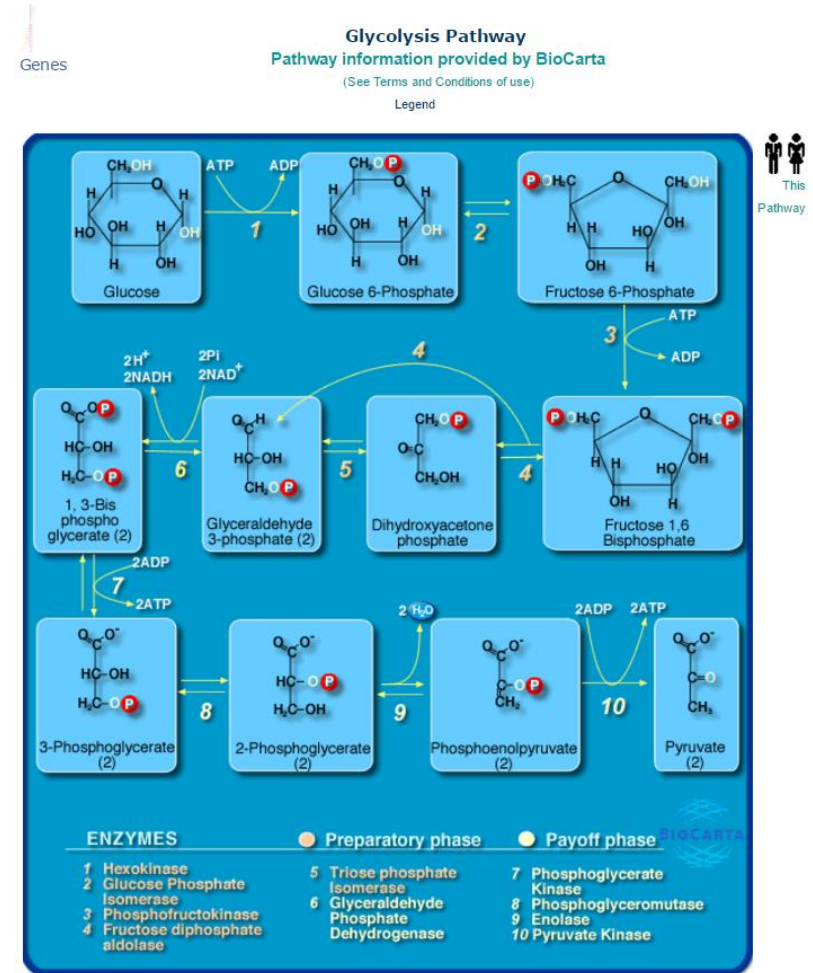
ИНФОРМАЦИОННЫЙ РЕСУРС BIOCARТА (продолжение)

Содержит схемы метаболических либо сигнальных путей, а также схемы процессов

MAPKinase Signaling Pathway



Glycolysis Pathway





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We want your feedback! A quick survey to help us focus development and renew funding.
<https://www.surveymonkey.com/r/wikipathways>

Welcome to WikiPathways BETA

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

Find Pathways

Search

Search

Browse

Browse pathways



Browse by species and category

You can search by:

- Pathway name (*Apoptosis*)
- Gene or protein name (*p53*)
- Any page content (*cancer*)

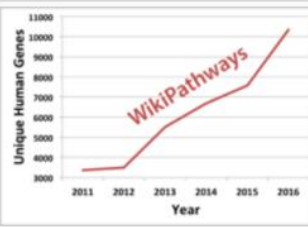
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Access by API
Query by SPARQL

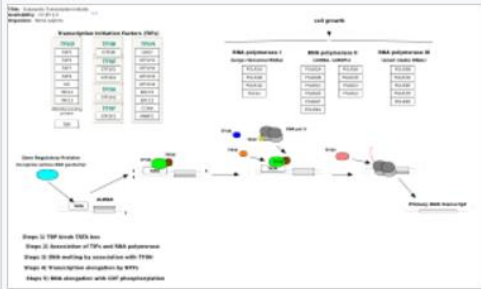
Growth



Year	Unique Human Genes
2011	~3000
2012	~4000
2013	~6000
2014	~7500
2015	~9000
2016	~11000

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

Неуклонный рост базы по годам

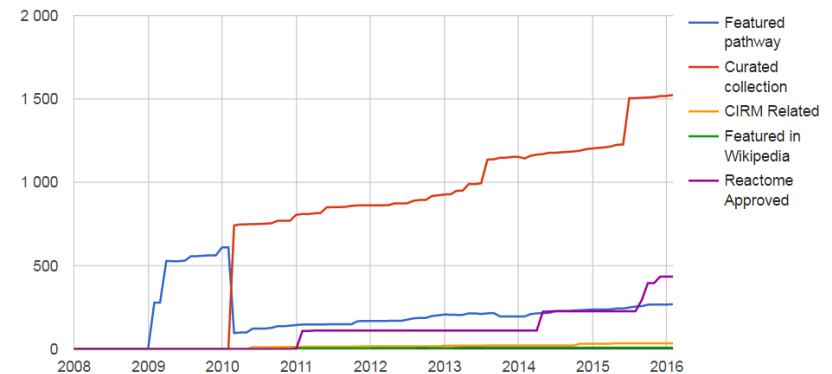


Kutmon M, Riutta A, Nunes N, Hanspers K, Willighagen EL, Bohler A, Mélius J, Waagmeester A, Sinha SR, Miller R, Coort SL, Cirillo E, Smeets B, Evelo CT, Pico AR. **WikiPathways: capturing the full diversity of pathway knowledge** *Nucl. Acids Res.*, 44, D488-D494 (2016)

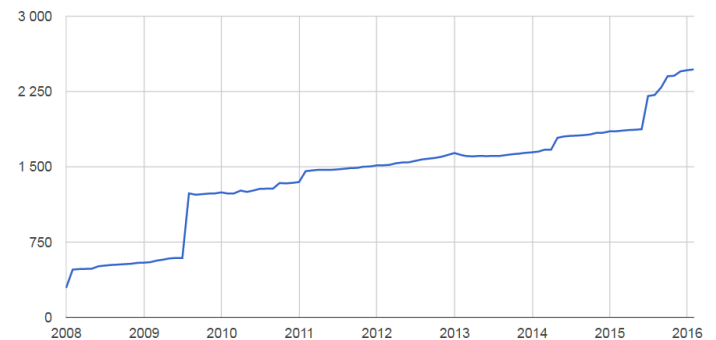
Pico AR, Kelder T, van Iersel MP, Hanspers K, Conklin BR, Evelo C. (2008) WikiPathways: Pathway Editing for the People. *PLoS Biol* 6(7)

Pathways per collection

The size of different pathways collections over time.



Show pathway counts for



25 видов организмов базы WikiPathways



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toolbox

- What links here
- Related changes
- Upload file
- Portable version
- Permanent link

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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 curated, 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
						
Pan troglodytes	Rattus norvegicus	Sus scrofa				
						

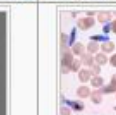
Invertebrates

Anopheles gambiae	Caenorhabditis elegans	Drosophila melanogaster
		

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
		

Все данные диаграмм WikiPathways можно скачать !!!!!

(Первый способ)

Get Pathways

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Multiple formats and methods

Выбор вида организма

Архивный файл всех диаграмм одного вида организма (gpml 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_Arhythmicogenic_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 !!!!!

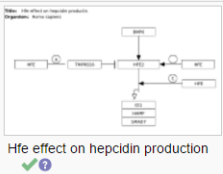
(Второй способ)

special

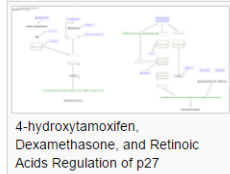
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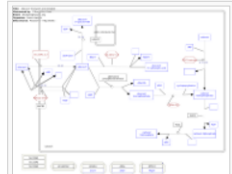
Species: Homo sapiens Collection: All Tags View: Thumbnail Mode



Hfe effect on hepcidin production



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



Abacavir transport and metabolism

Скачиваем каждую диаграмму поотдельности в форматах:

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

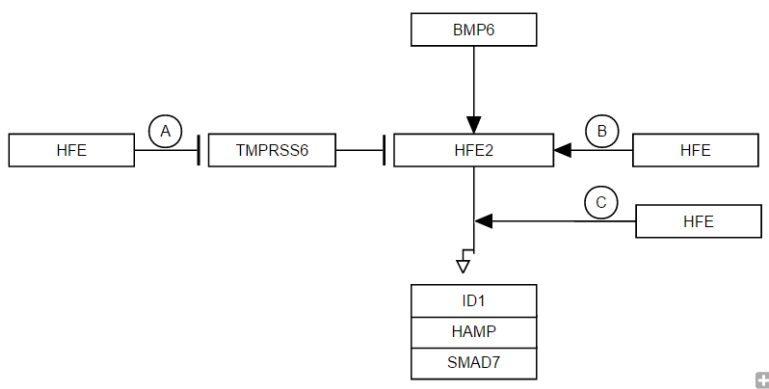
pathway discussion view source

Hfe effect on hepcidin production (Homo sapiens)

Kristina Hanspers

Search for...

Title: Hfe effect on hepcidin production
Organism: Homo sapiens



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- PathMio (.gpm1)
- 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. Hfe acts with the cycle (Hfe could be acting on the interaction at points A.B, or C). Hfe, as well as Tmprss6, controls. Evidence obtained from gene testing as well as some seems to indicate that Hfe inhibits Tmprss6.

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

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

Enzymes and enzyme nomenclature
Metabolic pathways ←

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- [BioCarta Pathways](#)
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- [CeCaFDB](#)
- [ClusterMine360](#)
- [EAWAG-BBD](#)
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- [HMDB - The Human Metabolome Database](#)
- [iPAVS](#)
- [KaPPA-View](#)
- [KEGG - Kyoto Encyclopedia of Genes and Genomes](#)
- [KEGG LIGAND Database](#)
- [LAMP](#)
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Protein-protein interactions
Signalling pathways
Human and other Vertebrate Genomes
Human Genes and Diseases

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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 Rewires 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 mentha 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>

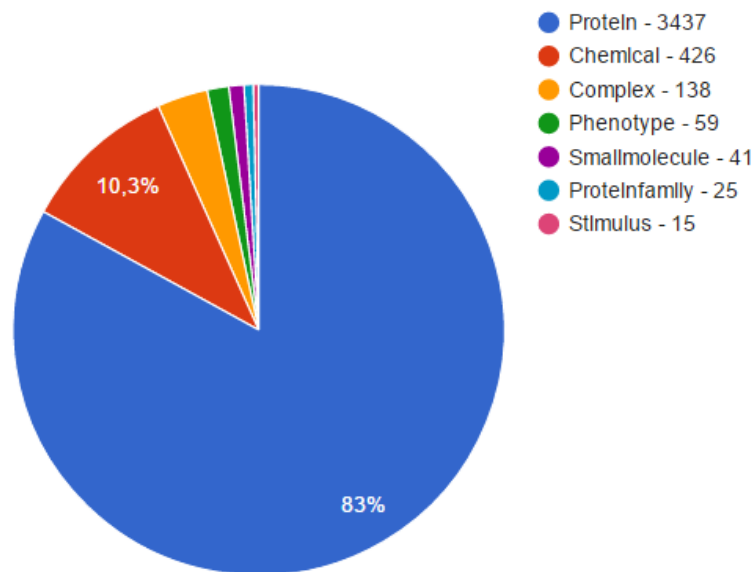


The SIGnaling Network Open Resource

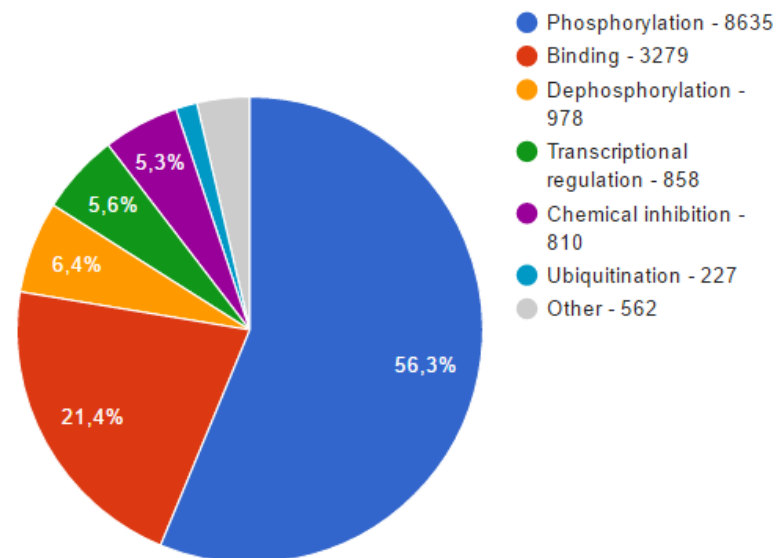
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16246 curated relations - 6295 curated publications

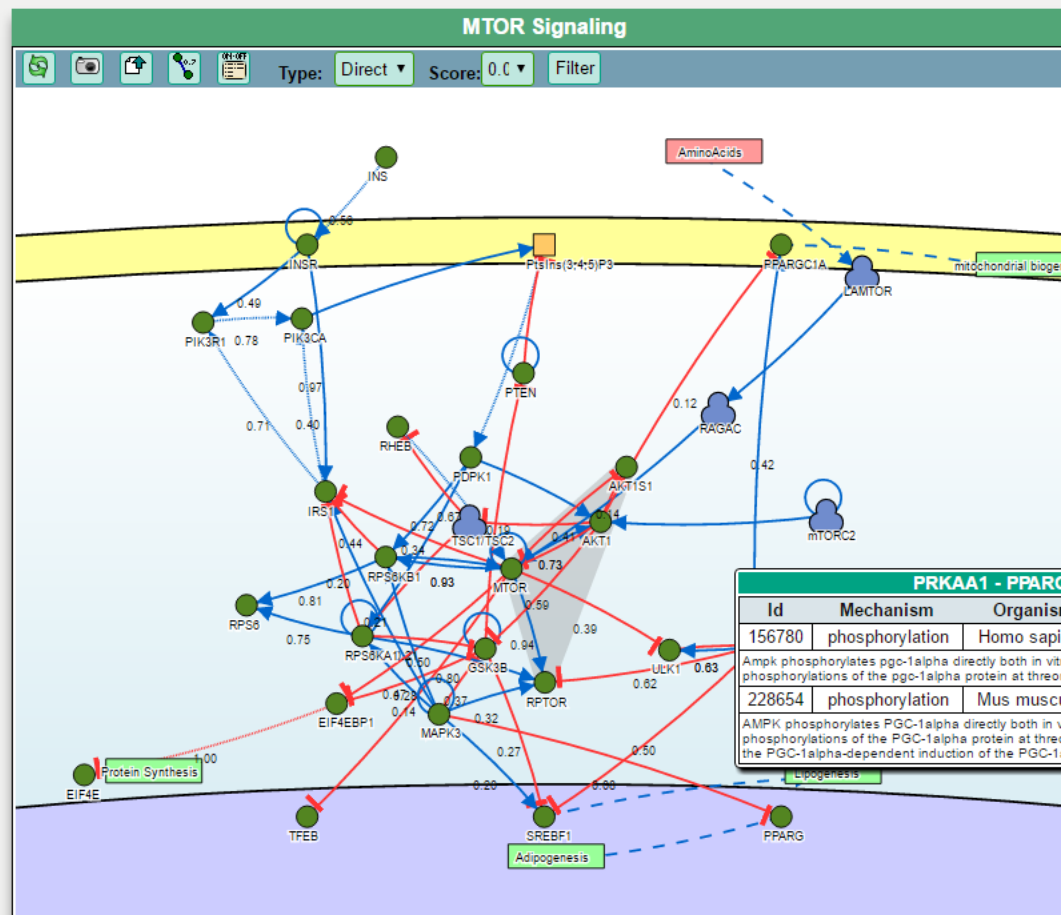
Entity types



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 P42345

mTORC2 SIGNOR-C2

PDPK1 O15530

PIK3CA P42336

PIK3R1 P27986

PPARG P37231

PPARGC1A Q9UBK2

PRKAA1 Q13131

PRKAG1 P54619

Protein Synthesis

TFEB

Adipogenesis

Lipogenesis

Ресурс Signor : представление данных о путях активации фактора SREBP1

**Signor**_{2.0} The SIGnaling Network Open Resource

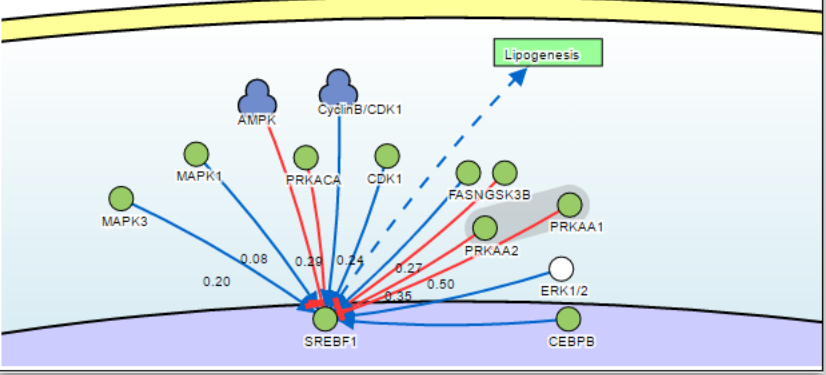
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Summary

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

Type: Score:



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: <u>MTOR Signaling</u>				
+	<u>MAPK1</u>	up-regulates → phosphorylation	<u>SREBF1</u>	0.08
Publications: 1 Organism: Homo Sapiens				

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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](#)

Download SIGNOR entity data

SIGNOR Complexes:

[Download complex data](#)

SIGNOR Protein Families:

[Download protein family data](#)

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

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)

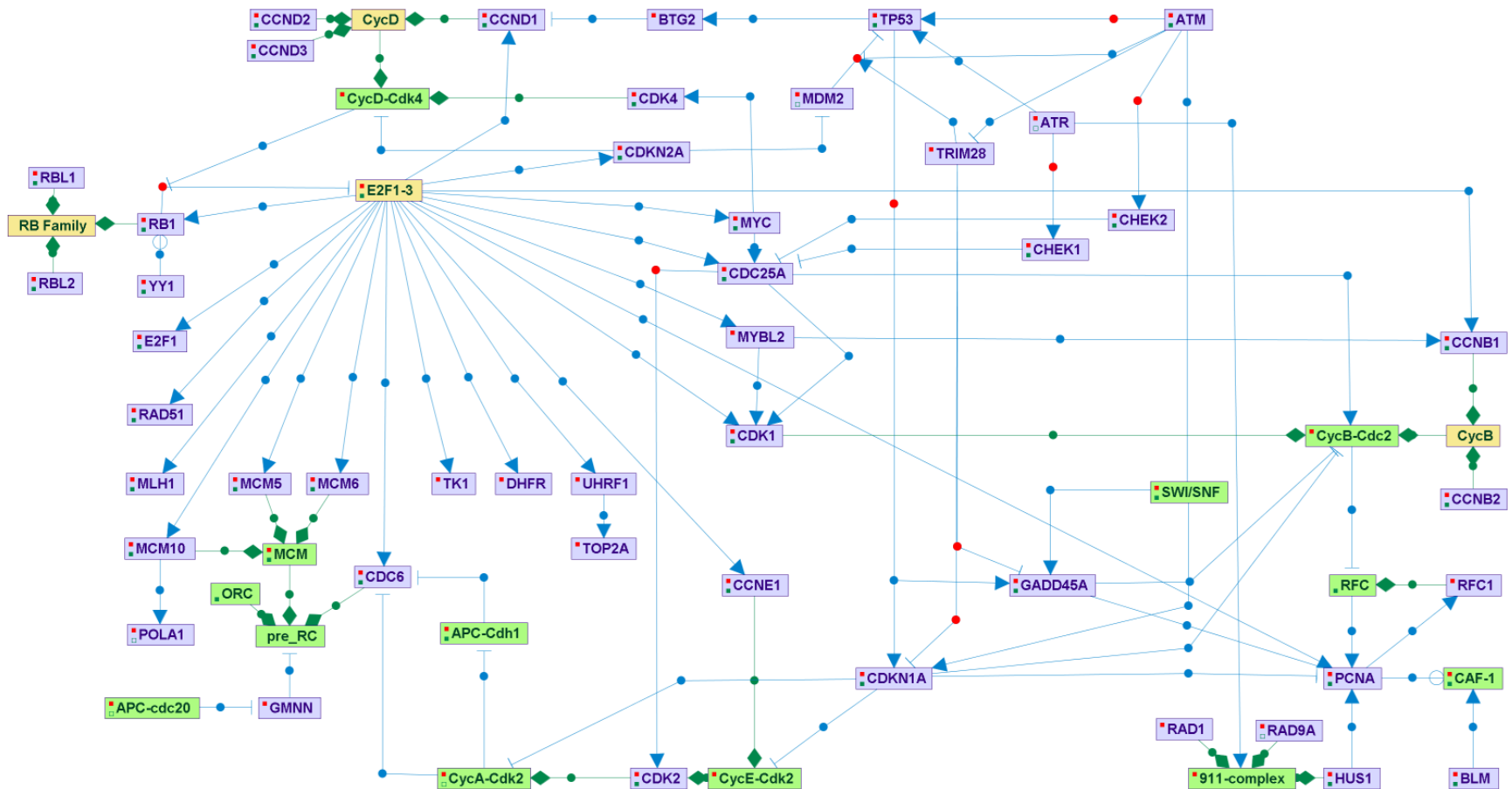
see the Maps section

[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

Designed by Spike Team.

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



Ресурс SPIKE : данные можно скачать



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](#)

Designed by Spike Team.

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://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) BioCarta [https://cgap.nci.nih.gov/Pathways/BioCarta Pathways](https://cgap.nci.nih.gov/Pathways/BioCarta_Pathways)
- 6) WikiPathways <http://www.wikipathways.org/index.php/WikiPathways>
- 7) Signor <http://signor.uniroma2.it/>
- 8) SPIKE <http://www.cs.tau.ac.il/~spike/>

СПАСИБО ЗА ВНИМАНИЕ !