STRING

Protein Association Network Database

Paul Henry Flynn

Sections

Description

Features

Searching

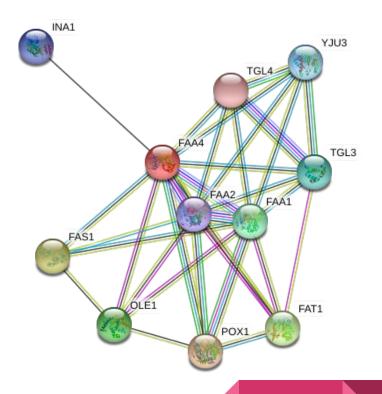
Results

Algorithms

Critiques

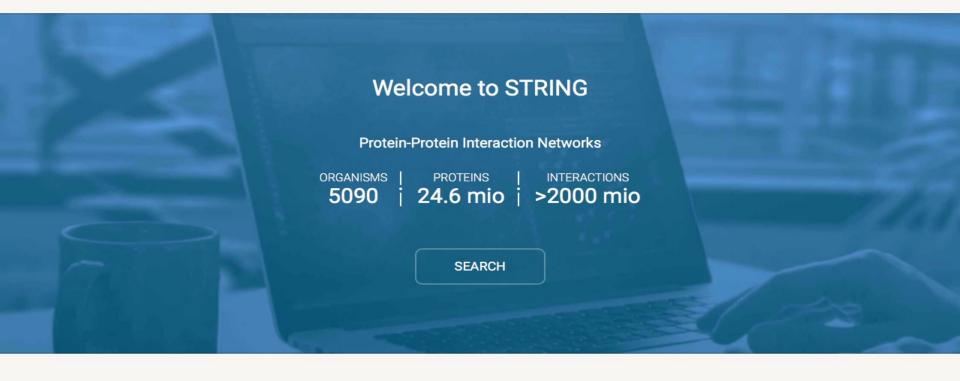
STRING

- Visual network view of protein associations
 - Models known and predicted associations for a particular group
- Interactions include direct, indirect
- Developers
 - Swiss Institute of Bioinformatics,
 Center for Protein Research,
 University of Zurich



Features









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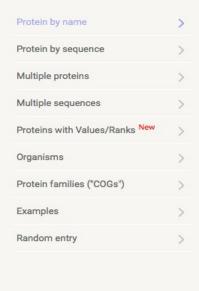
Licensing Partners
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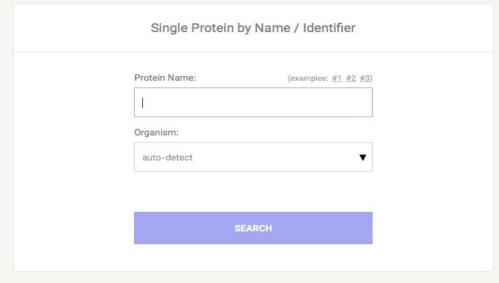
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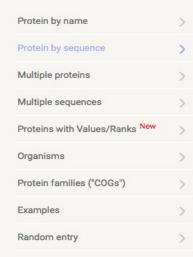
Software

Search

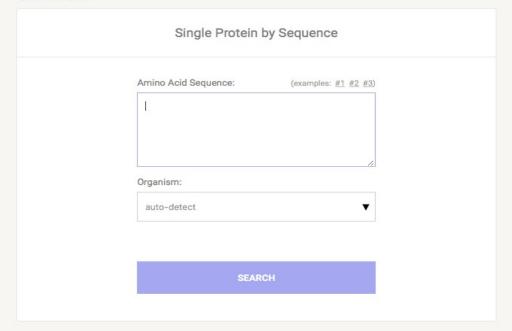
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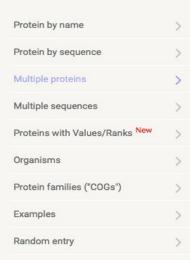
APIs

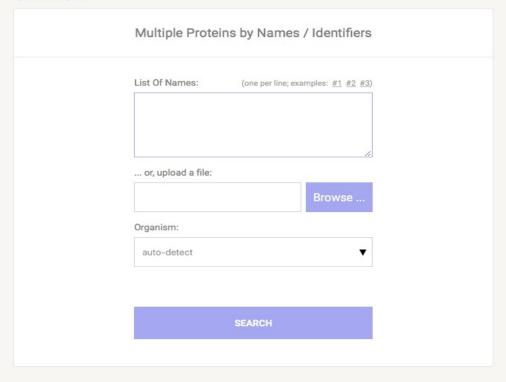
ACCESS

CREDITS

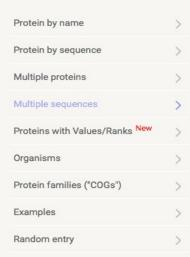
Datasources

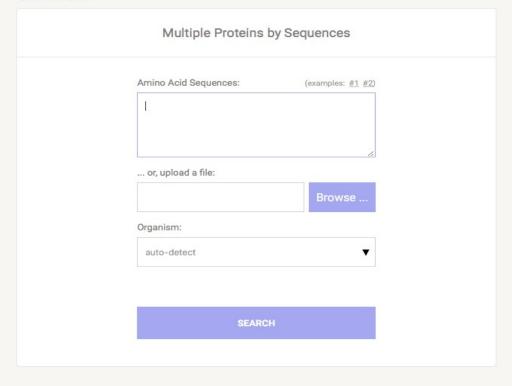














Protein by name	>
Protein by sequence	>
Multiple proteins	>
Multiple sequences	>
Proteins with Values/Ranks New	>
Organisms	>
Protein families ("COGs")	>
Examples	>
Random entry	>

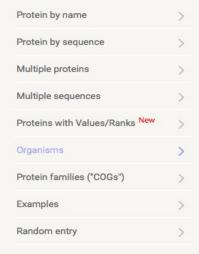
 tire experiment as a list of proteins - no cutoffs. otein, put a meaningful value for ranking (fold-change, log-pvalue, abundance,)
Proteins with Values: (one per line; examples: #1 #2 #3)
or, upload a file: Browse
Organism:
choose an organism ▼
SEARCH

Search

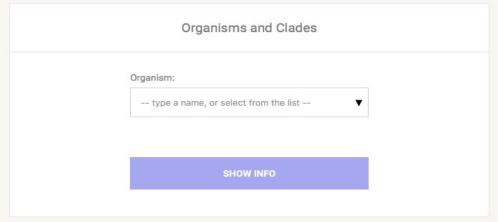
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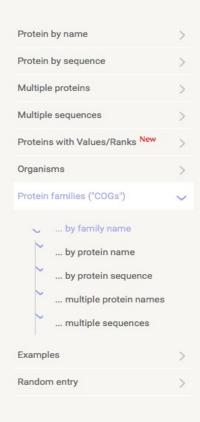
Statistics

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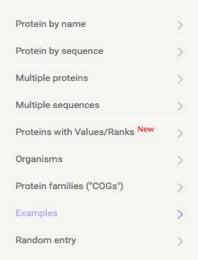
Help

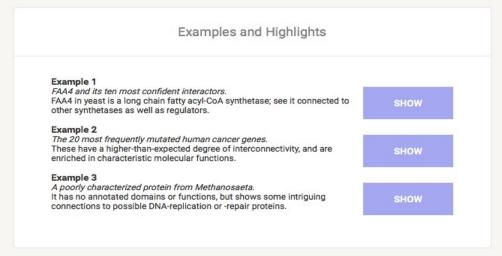
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Search Results



Aspergillus nidulans

Blastomyces dermatitidis

There are several matches for 'FAA4'. <- BACK Please select one from the list below and press Continue to proceed. organism protein ■ Saccharomyces cerevisiae FAA4 - Long-chain-fatty-acid-CoA ligase 4; Long chain fatty acyl-CoA synthetase; activates fatty acids with a preference for C12:0-C16:0 chain lengths; role in the competitive import of long-chain fatty acids and sphingoid long-chain bases; role in stationary phase survival; localizes to lipid particles and the plasma membrane; role in sphingolipid-to-glycerolipid metabolism; forms cytoplasmic foci upon replication stress; faa1 faa4 double null complemented by any of human ACSBG1, ACSL1, 3, 4, 5, 6, SLC27A2, or 4; Belongs to the ATP-dependent AMP-binding enzyme family Homo sapiens MYH11 - Myosin-11; Muscle contraction; Belongs to the TRAFAC class myosin-kinesin ATPase superfamily. Myosin family [a.k.a. KIAA0866, NP 074035.1, ENSP00000484924, FAA4] Candida albicans FAA4 - annotation not available Scheffersomyces stipitis FAA4 - acyl-CoA synthetase (long-chain fatty acid CoA ligase) (fatty acid activator 2), activates imported fatty acids and provides substrates for N-myristoylation Wickerhamomyces ciferrii FAA4 - annotation not available Saccharomyces cerevisiae FAA1 - Long-chain-fatty-acid-CoA ligase 1; Long chain fatty acyl-CoA synthetase; activates fatty acids with a preference for C12:0-C16:0 chain lengths; role in the competitive import of long-chain fatty acids and sphingoid long-chain bases; accounts for most acyl-CoA synthetase activity; localizes to lipid particles and the plasma membrane; role in sphingolipid-to-glycerolipid metabolism; forms ER foci upon replication stress; faa1 faa4 double null complemented by any of human ACSBG1, ACSL1, 3, 4, 5. 6. SLC27A2, or 4 [a.k.a. YOR317W, 06136, Fatty acid activator 1] Schizosaccharomyces pombe Icf1 - Long-chain-fatty-acid-CoA ligase 1; Esterification, concomitant with transport, of exogenous long-chain fatty acids into metabolically active CoA thioesters for subsequent degradation or incorporation into phospholipids. It may supplement intracellular myristoyl-CoA pools from exogenous myristate. Preferentially acts on C12:0-C16:0 fatty acids with myristic and pentadecanic acid (C15:0) having the highest activities (By similarity). Appears to play a role in the maintenance of cell viability during stationary phase [a.k.a. SPBC18H10.02, NM_001021624, ACSL3, FAA4] Xenopus tropicalis myh11 - Myosin, heavy chain 11, smooth muscle; Belongs to the TRAFAC class myosin-kinesin ATPase superfamily. Myosin family [a.k.a. AAMC01009813, Myosin, heavy chain 11, smooth muscle, ENSXETG00000019650, faa4] Aspergillus flavus CADAFLAP00005791 - Fatty acid activator Faa4, putative [a.k.a. AFLA_044640, UPI00006784D1, XP_002377926] Aspergillus fumigatus CADAFUBP00002517 - Fatty acid activator Faa4, putative; AMP-binding enzyme (Fum16), putative [a.k.a. AFUA_2G09910,

AN6014.2 - Fatty acid activator Faa4, putative (AFU_orthologue; AFUA_2G09910) [a.k.a. ANIA_06014, 6.2.1.3, Q5B0B6_EMENI]

BDCG_02451 - Long-chain acyl-CoA synthetase; Fatty acid activator Faa4 [a.k.a. XP_002620768.1, GenelD:8501372,

6.2.1.3, CADAFUBT00002569]

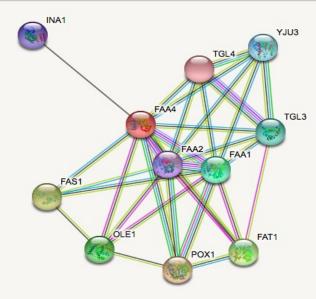
XM 002620722.11

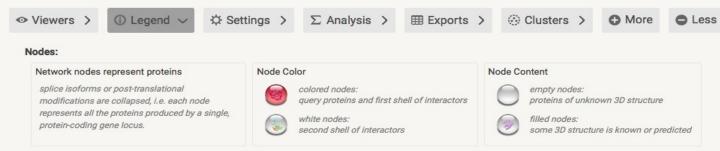
Others



Edges:

Edges represent protein-protein associations

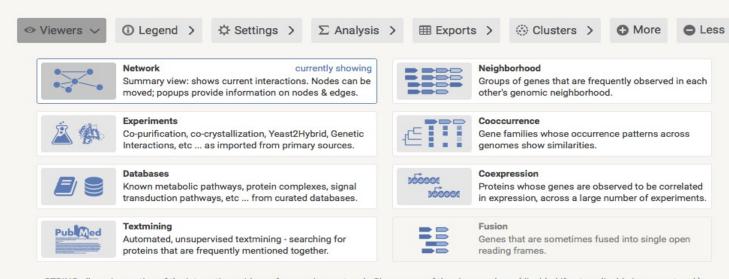




Known Interactions

Predicted Interactions

Result Options

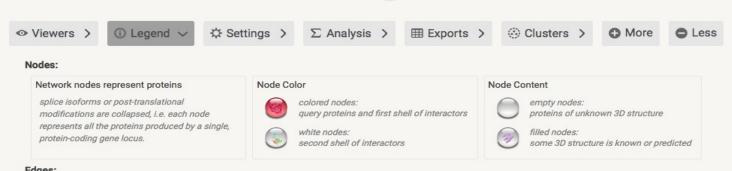


STRING allows inspection of the interaction evidence for any given network. Choose any of the viewers above (disabled if not applicable in your network).

GO Permalink

Server load: low (10%) [HD]





textmining

co-expression

protein homology

Edges:



Long-chain-fatty-acid--CoA ligase 4; Long chain fatty acyl-CoA synthetase; activates fatty acids with a preference for C12-



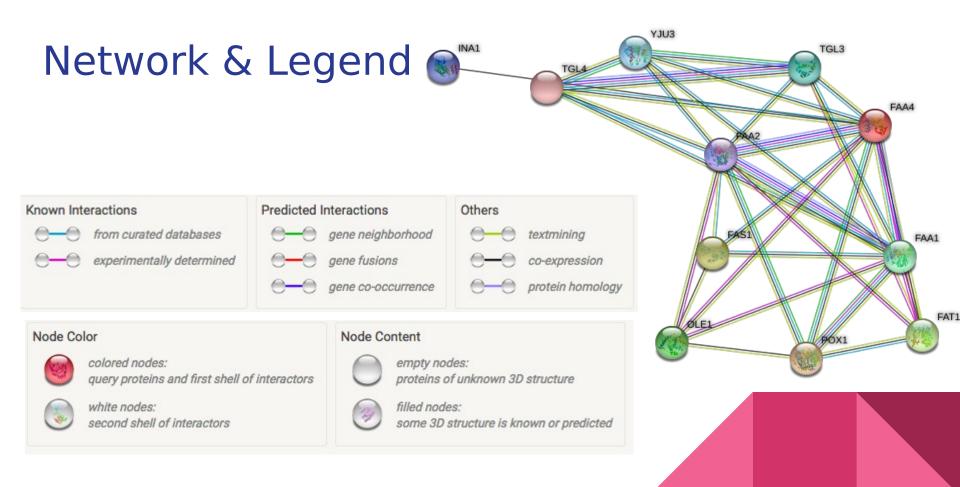
0-C16-0 chain lengths; role in the competitive import of long-chain fatty acids and sphingoid long-chain bases; role in FAA4 stationary phase survival; localizes to lipid particles and the plasma membrane; role in sphingolipid-to-glycerolipid metabolism; forms cytoplasmic foci upon replication stress; faa1 faa4 double null complemented by any of human ACSBG1, ACSL1, 3, 4, 5, 6, SLC27A2, or 4; Belongs to the ATP-dependent AMP-binding enzyme family (694 aa)

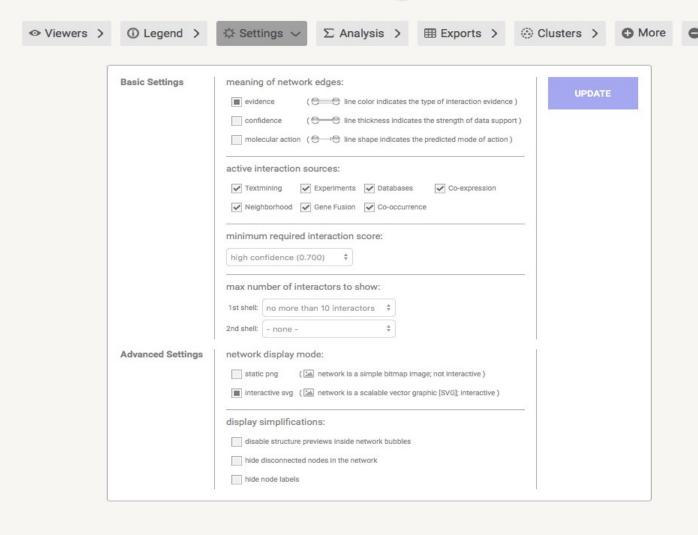
Predicted Functional Partners:

		-	 -	-		_	-,
⊜ POX1	Fatty-acyl coenzyme A oxidase; involved in the fatty acid beta-oxidation pathway; localized to the peroxisomal matrix (748		0		•	•	0.980
⊜ FAS1	Beta subunit of fatty acid synthetase; complex catalyzes the synthesis of long-chain saturated fatty acids; contains acetyltr			•	•	•	0.969
⊜ FAT1	Very long chain fatty acyl-CoA synthetase and fatty acid transporter, activates imported fatty acids with a preference for ve				-	•	0.955
OLE1	Acyl-CoA desaturase 1; Delta(9) fatty acid desaturase; required for monounsaturated fatty acid synthesis and for normal di		0		- 1	•	0.935
● FAA1	Long-chain-fatty-acidCoA ligase 1; Long chain fatty acyl-CoA synthetase; activates fatty acids with a preference for C12-0			• •	• (• •	0.923
● TGL3	Lipase 3; Bifunctional triacylglycerol lipase and LPE acyltransferase; major lipid particle-localized triacylglycerol (TAG) lipas		0			•	0.884
⊜ YJU3	Monoglyceride lipase (MGL); functional ortholog of mammalian MGL, localizes to lipid particles and membranes, also me				•		0.859
● INA1	Cell membrane protein YLR413W; Protein of unknown function; not an essential gene; YLR413W has a paralog, FAT3, that a		•				0.834
● FAA2	Long-chain-fatty-acidCoA ligase 2; Medium chain fatty acyl-CoA synthetase; activates imported fatty acids; accepts a wid			0 6	• (• •	0.819
€ TGI 4	Lipase 4: Multifunctional lipase/hydrolase/phospholipase; triacylglycerol lipase, steryl ester hydrolase, and Ca2+-independ.			-			0.819

Your Current Organism:

Saccharomyces cerevisiae







Network Stats

number of nodes: 11 expected number of edges: 10
number of edges: 32 PPI enrichment p-value: 4.49e-08
average node degree: 5.82 your network has significantly more interactions
avg. local clustering coefficient: 0.843 than expected (what does that mean?)

Functional enrichments in your network

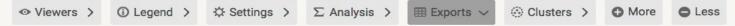
Note: some enrichments may be expected here (why?)

	Biological Process (GO)		
GO-term	description	count in gene set	false discovery rate
GO:0044255	cellular lipid metabolic process	10 of 280	2.85e-11
GO:0006631	fatty acid metabolic process	7 of 56	6.69e-11
GO:0001676	long-chain fatty acid metabolic process	4 of 7	4.38e-08
GO:0044539	long-chain fatty acid import into cell	3 of 3	1.49e-06
GO:0019433	triglyceride catabolic process	3 of 6	5.34e-06
			(more)

	Molecular Function (GO)		
GO-term	description	count in gene set	false discovery rate
GO:0015645	fatty acid ligase activity	4 of 5	3.70e-08
GO:0016405	CoA-ligase activity	4 of 8	7.24e-08
GO:0102391	decanoate-CoA ligase activity	3 of 4	1.72e-06
GO:0004467	long-chain fatty acid-CoA ligase activity	3 of 4	1.72e-06
GO:0031957	very long-chain fatty acid-CoA ligase activity	2 of 3	0.00022
			(more)

	Cellular Component (GC))	
GO-term	description	count in gene set	false discovery rate
GO:0005811	lipid droplet	7 of 55	9.84e-11
GO:0005777	peroxisome	3 of 83	0.0117
GO:0005886	plasma membrane	5 of 528	0.0181

GU:0005886	piasma memorane	5 01 528	0.0181
	Reference publications		
publication	(year) title	count in gene set	false discovery rate
PMID:23275493	(2013) Lipid droplets and peroxisomes: key players in cellul	10 of 148	3.93e-13
PMID:23139841	(2012) Neutral lipid metabolism influences phospholipid sy	7 of 28	8.31e-12
PMID:25461829	(2015) Overproduction and secretion of free fatty acids thr	6 of 11	1.15e-11
DMID-22245606	(2012) Metabolism and regulation of glycerolinide in the ve	9 of 134	1 150-11



Export your current network:

... as a bitmap image: download downloa

Browse interactions in tabular form:

<u>^node1</u>	node2	node1 accession	node2 accession	node1 annotation	node2 annotation	score
FAA1	FAA2	YOR317W	YER015W	Long-chain-fatty-acidCoA ligase 1; Long ch	Long-chain-fatty-acid-CoA ligase 2; Medium	0.822
FAA1	FAA4	YOR317W	YMR246W	Long-chain-fatty-acidCoA ligase 1; Long ch	Long-chain-fatty-acid-CoA ligase 4; Long ch	0.923
FAA1	FAS1	YOR317W	YKL182W	Long-chain-fatty-acidCoA ligase 1; Long ch	Beta subunit of fatty acid synthetase; compl	0.968
FAA1	FAT1	YOR317W	YBR041W	Long-chain-fatty-acidCoA ligase 1; Long ch	Very long chain fatty acyl-CoA synthetase an	0.974
FAA1	OLE1	YOR317W	YGL055W	Long-chain-fatty-acidCoA ligase 1; Long ch	Acyl-CoA desaturase 1; Delta(9) fatty acid d	0.915
FAA1	POX1	YOR317W	YGL205W	Long-chain-fatty-acidCoA ligase 1; Long ch	Fatty-acyl coenzyme A oxidase; involved in t	0.993
FAA1	TGL3	YOR317W	YMR313C	Long-chain-fatty-acidCoA ligase 1; Long ch	Lipase 3; Bifunctional triacylglycerol lipase a	0.884
FAA1	TGL4	YOR317W	YKR089C	Long-chain-fatty-acidCoA ligase 1; Long ch	Lipase 4; Multifunctional lipase/hydrolase/p	0.887
FAA1	YJU3	YOR317W	YKL094W	Long-chain-fatty-acidCoA ligase 1; Long ch	Monoglyceride lipase (MGL); functional orth	0.863
FAA2	FAA1	YER015W	YOR317W	Long-chain-fatty-acidCoA ligase 2; Medium	Long-chain-fatty-acid-CoA ligase 1; Long ch	0.822
FAA2	FAA4	YER015W	YMR246W	Long-chain-fatty-acidCoA ligase 2; Medium	Long-chain-fatty-acid-CoA ligase 4; Long ch	0.819
FAA2	FAS1	YER015W	YKL182W	Long-chain-fatty-acidCoA ligase 2; Medium	Beta subunit of fatty acid synthetase; compl	0.952
FAA2	FAT1	YER015W	YBR041W	Long-chain-fatty-acidCoA ligase 2; Medium	Very long chain fatty acyl-CoA synthetase an	0.893
FAA2	OLE1	YER015W	YGL055W	Long-chain-fatty-acidCoA ligase 2; Medium	Acyl-CoA desaturase 1; Delta(9) fatty acid d	0.817
FAA2	POX1	YER015W	YGL205W	Long-chain-fatty-acidCoA ligase 2; Medium	Fatty-acyl coenzyme A oxidase; involved in t	0.997
FAA2	TGL3	YER015W	YMR313C	Long-chain-fatty-acidCoA ligase 2; Medium	Lipase 3; Bifunctional triacylglycerol lipase a	0.719
FAA2	TGL4	YER015W	YKR089C	Long-chain-fatty-acidCoA ligase 2; Medium	Lipase 4; Multifunctional lipase/hydrolase/p	0.733
FAA2	YJU3	YER015W	YKL094W	Long-chain-fatty-acidCoA ligase 2; Medium	Monoglyceride lipase (MGL); functional orth	0.861
FAA4	FAA1	YMR246W	YOR317W	Long-chain-fatty-acidCoA ligase 4; Long ch	Long-chain-fatty-acid-CoA ligase 1; Long ch	0.923
FAA4	FAA2	YMR246W	YER015W	Long-chain-fatty-acidCoA ligase 4; Long ch	Long-chain-fatty-acid-CoA ligase 2; Medium	0.819
14 44 p	age 1 of	4 ▶▶ ▶Ⅱ				

Server load: low (10%) [HD]





network clustering	:	To be seen as a second
no clustering	(network is shown as it is)	APPLY
kmeans clustering	(network is clustered to a specified number of clusters)	
MCL clustering	(network is clustered to a specified "MCL inflation parameter")	

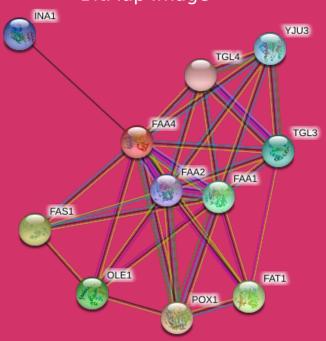
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Exports & Views

BitMap Image



string_protein_sequences.fa-2.txt >

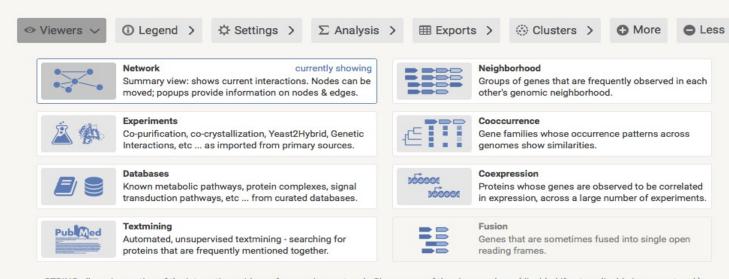
>FAT1 4932.YBR041W Very long chain fatty acyl—CoA synthetase and fatty acid transporter; activates imported fatty acids with a preference for very long lengths (C20—C26); has a separate function in the transport of long chain fatty acids MSPIQVVVFALSRIFLLLFRLIKLIITPIQKSLGYLFGNYFDELDRKYRYKEDWYIIPYFLKSVFCYIIDVRRHRFQNWYLFIKQ VQQNGDHLAISYTRPMAEKGEFQLETFTYIETYNIVLRLSHILHFDYNVQAGDYVAIDCTNKPLFVFLWLSLWNIGAIPAFLNYN TKGTPLVHSLKISNITQVFIDPDASNPIRESEEEIKNALPDVKLNYLEEQDLMHELLNSQSPEFLQQDNVRTPLGLTDFKPSMLI YTSGTTGLPKSAIMSWRKSSVGCQVFGHVLHMTNESTVFTAMPLFHSTAALLGACAILSHGGCLALSHKFSASTFWKQVYLTGAT HIQYYGEVCRYLLHTPISKYEKMHKVKVAYGNGLRPDIWQDFRKRFNIEVIGEFYAATEAPFATTTFQKGDFGIGACRNYGTIIQ WFLSFQQTLVRMDPNDDSVIYRNSKGFCEVAPVGEPGEMLMRIFFPKKPETSFQGYLGNAKETKSKVVRDVFRRGDAWYRCGDLL KADEYGLWYFLDRMGDTFRWKSENVSTTEVEDQLTASNKEQYAQVLVVGIKVPKYEGRAGFAVIKLTDNSLDITAKTKLLNDSLS RLNLPSYAMPLFVKFVDEIKMTDNHKILKKVYREQKLPKGLDGNDTIFWLKNYKRYEVLTAADWEAIDAQTIKL

>FAA2 4932.YER015W Long-chain-fatty-acid--CoA ligase 2; Medium chain fatty acyl-CoA synthetase; activates imported fatty acids; accepts a wide range of fatty acid chain lengths with a preference for medium chains, C9:0-C13:0; localized to the peroxisome; comparative analysis suggests that a mitochondrially targeted form may result from translation starting at a non-canonical codon upstream of the annotated start codon

MAAPDYALTDLIESDPRFESLKTRLAGYTKGSDEYIEELYSQLPLTSYPRYKTFLKKQAVAISNPDNEAGFSSIYRSSLSSENLV SCVDKNLRTAYDHFMFSARRWPQRDCLGSRPIDKATGTWEETFRFESYSTVSKRCHNIGSGILSLVNTKRKRPLEANDFVVAILS HNNPEWILTDLACQAYSLTNTALYETLGPNTSEYILNLTEAPILIFAKSNMYHVLKMVPDMKFVNTLVCMDELTHDELRMLNESL LPVKCNSLNEKITFFSLEQVEQVGCFNKIPAIPPTPDSLYTISFTSGTTGLPKGVEMSHRNIASGIAFAFSTFRIPPDKRNQQLY DMCFLPLAHIFERMVIAYDLAIGFGIGFLHKPDPTVVEDLKILKPYAVALVPRILTRFEAGIKNALDKSTVQRNVANTILDSKS ARFTARGGPDKSIMNFLVYHRVLIDKIRDSLGLSNNSFIITGSAPISKDTLLFLRSALDIGIRQGYGLTETFAGVCLSEPFEKDV GSCGAIGISAECRLKSVPEMGYHADKDLKGELQIRGPQVFERYFKNPNETSKAVDQDGWFSTGDVAFIDGKGRISVIDRVKNFFK LAHGEYIAPEKIENIYLSSCPYITQIFVFGDPLKTFLVGIVGVOVDAAQPILAAKHPEVKTWTKEVLVENLNRNKKLRKEFLNKI NKCTDGLQGFEKLHNIKVGLEPLTLEDDVVTPTFKIKRAKASKFFKDTLDQLYAEGSLVKTEKL

>OLE1 4932.YGL055W Acyl-CoA desaturase 1; Delta(9) fatty acid desaturase; required for monounsaturated fatty acid synthesis and for normal distribution of mitochondria

MPTSGTTIELIDDQFPKDDSASSGIVDEVDLTEANILATGLNKKAPRIVNGFGSLMGSKEMVSVEFDKKGNEKKSNLDRLLEKDN



STRING allows inspection of the interaction evidence for any given network. Choose any of the viewers above (disabled if not applicable in your network).

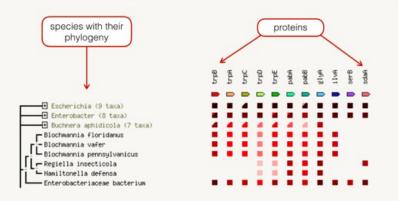
GO Permalink

Server load: low (10%) [HD]



Co-expression trpB 🛑 trpA 🗁 🔳 trpC 🗆 🔳 🔳 trpD 🗁 🔳 🔳 trpE - - - pabA 🗁 pabB 🗪 glyA 🗀 ilvA serB 🗪 sdaA 🗪 trpB trpC trpC trpE pabh pabh glyA ilvA serB

Co-occurrence



Experiments

protein-protein interaction (dip)

Detected by biochemical and biophysical assays

Databases

annotated pathway (KEGG)

Name: Biosynthesis of amino acids

• trp8 • trp0 • trpE • glyA • ilvA • ser8 • sdaA

[... and 109 other proteins]

Text mining

Investigation of the adaptation of Lactococcus lactis to isoleucine starvation integrating dynamic transcriptome and proteome information.

**Pub Med Diversaire C, Redon E, Gitton C, Loubière P, Monnet V, Cocaign-Bousquet M

**Microb Cell Fact. 10 Suppl 1:S18 (2011).

**TrpB, trpB ** trpC ** trpD ** trpE ** pabB ** SdaA, sdaA ** GlyA, glyA ** pabA ** IlvA, ilvA ** SerB, serB ...

Methods & Algorithms

Sourcing

STRING is a database of known and predicted protein-protein interactions. The interactions include direct (physical) and indirect (functional) associations; they stem from computational prediction, from knowledge transfer between organisms, and from interactions aggregated from other (primary) databases.

Data Sources

Interactions in STRING are derived from five main sources:



Genomic Context Predictions



High-throughput Lab Experiments



(Conserved) Co-Expression



Automated Textmining



Previous Knowledge in Databases

Coverage

The STRING database currently covers 9'643'763 proteins from 2'031 organisms.

Algorithm: Interaction Scoring

- Scores assigned to protein-protein interactions
 - Calculated by integrating probabilities from various sources
 - Corrects for probability of random observation of interaction
 - Indicate confidence, not strength or specificity
 - \bigcirc 0.5 = Half of all interactions erroneous
- 'Transfer' Score
 - Not originally observed in organism desired
 - Normal score adapted based on homology

- low confidence 0.15 (or better),
- medium confidence 0.4,
- high confidence 0.7,
- highest confidence 0.9.

Experiments using STRING

- 1.) Researching protein-networks in the context of early immune system establishment
- 2.) Highly connected proteins have stable steady-state distribution of gene expression
- 3.) Searching for candidate genes involved in the immune response to gluten
- 4.) Identifying candidates for unknown enzyme in a pathway
- 5.) Using STRING to narrow the search space for two-locus epistatis
- 6.) Using STRING to show network connectivity
- 7.) STRING as a general purpose database
- 8.) STRING to guide experiments
- 9.) Prioritizing functional assignments in RNAi screens using interaction network data

Critiques

Critiques

- First time user What is STRING?
 - About Content
- Powerful and Versatile tool
 - Text-mining
 - Several views of information
 - In-House view of gathered data
- EMBL's IntAct
 - Provides links on Associations
 - Not visual
- 6 Databases Reduced Selection
- High Quality User Manual necessary?

Thank You