## The STRING database

### Data flow from the experiment to the discovery

Damian Szklarczyk (UZH/SIB),







# MDM2

2024, Life Science Industry Meets Data Science







### © STRING CONSORTIUM 2023



SIB - Swiss Institute of Bioinformatics

CPR - Novo Nordisk Foundation Center Protein Research

EMBL - European Molecular Biology Laboratory



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ACCESS

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### STRING What is it?

- What? Access: **User Interface** 

  - API

### **Protein-protein interaction network / DB**

### **Functional Enrichment tool**

Data dumps

### Cytoscape / R packages



# STRING

### **Functional Associations Networks**

The linked proteins contribute to the same biological process.

Useful abstraction / very predictive at various tasks

Allows us to derive the predictions from multiple sources at various modalities

Pretty dense

Direct / Indirect / stable / transient

Non-directional



# **STRING** Physical (Co-complex) Networks

Proteins are part of the same physical complex.

Stable complexes / Transient interactions

The available data often does not define the complex structure

Curated knowledge / Text-mining / Experiments

Non-directional



# STRING Regulatory Networks

Protein A changes the activity / expression / stability of Protein B

Focus on directionality of the interaction

A regulates B

Postitive / Negative

Mode of regulation

Curated knowledge / Text-mining





### **Best prediction** performance for phenotype/disease associated genes on an independent benchmark

State of the Interactomes: an evaluation of molecular networks for generating biological insights.

S. Wright et al. Bioarxiv 2024

## STRING Users base

### 1 mln unique users / >8500 citations (yearly)

- **Survey:** 

  - 19% studnets
  - 6% industry

### 68% academia / hospitals

### 5% gov- and non-gov orgs





# **CC BY 4.0 ATTRIBUTION 4.0 INTERNATIONAL** Deed











Universität Zürich<sup>∪zH</sup>









- Gene neighborhood
- Gene fusions
- Phylogenetic profiles
- Experimentally validated
- Curated pathways
- **Co-expression**
- Text-mining

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datec





Gene neighborhood Gene fusions Phylogenetic profiles **Experimentally validated** Curated pathways **Co-expression** Text-mining



The STRING database in 2023: protein-protein association networks and functional enrichment analyses for any sequenced genome of interest.

D. Szklarczyk et al. NAR Db 2024





# All channels are weighted equal.

# **0.5** Experimental = **0.5** Text-mining



 $S = 1 - \prod_{i=1}^{n} \left( \frac{1 - p_i}{1 - p_r} \right)$ i=1  $\sum_{x}$  x

- Gene neighborhood
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### es dated



- Gene neighborhood
- Gene fusions
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- Text-mining



[click on the heatmap elements for details]

- Gene neighborhood
- Gene fusions
- Phylogenetic profiles
- Experimentally validated
- Curated pathways
- **Co-expression**



Relevant publications mentioning your query species (Escherichia coli K12):

PMID:20534632 The synthetic integron: an in vivo genetic shuffling device.
V Bikard D, Julie-Galau S, Cambray G, Mazel D
Nucleic Acids Res. 38(15):e153 2010.

### Abstract:

As the field of synthetic biology expands, strategies and tools for the rapid construction of new biochemical pathways will become increasingly valuable. Purely rational design of complex biological pathways is inherently limited by the current state of our knowledge. Selection of optimal arrangements of genetic elements from randomized libraries may well be a useful approach for successful engineering. Here, we propose the construction and optimization of metabolic pathways using the inherent gene shuffling activity of a natural bacterial site-specific recombination system, the integron. As a proof of principle, we constructed and optimized a functional tryptophan biosynthetic operon in Escherichia coli. The trpA ()-E genes along with 'regulatory' elements were delivered as individual recombination cassettes in a synthetic integron platform. Integrase-mediated recombination generated thousands of genetic combinations overnight. We were able to isolate a large number of arrangements displaying varying fitness and tryptophan production capacities. Several assemblages required as many as six recombination events and produced as much as 11-fold more tryptophan than the natural gene order in the same context. Excerpts from full text:

... ent integron cassettes and are abbreviations as follow. t, BioBrick terminator BBa\_B0015; p, BioBrick promoter BBa\_J23100 ('Materials and Methods' section); A, trpA (); B, trpB (); C, trpC (); D, trpD (); E, trpE (); Z, lacZalpha. The arrow means that the excised cassette was subsequently integrated at the attl site. The attC sites are numbered following their order in ...

PMID:33514556 Microbiota control of maternal behavior regulates early postnatal growth of offspring. 🤝 Lee YM, Mu A, Wallace M, Gengatharan JM, Furst AJ, Bode L, Metallo CM, Ayres JS Sci Adv. 7(5) 2021.

### Abstract:

Maternal behavior is necessary for optimal development and growth of offspring. The intestinal microbiota has emerged as a critical regulator of growth and development in the early postnatal period life. Here, we describe the identification of an intestinal Escherichia coli strain that is pathogenic to the maternaloffspring system during the early postnatal stage of life and results in growth stunting of the offspring. However, rather than having a direct pathogenic effect on the infant, we found that this particular E. coli strain was pathogenic to the dams by interfering with the maturation of maternal behavior. This resulted in malnourishment of the pups and impaired insulin-like growth factor 1 (IGF-1) signaling, leading to the consequential stunted growth. Our work provides a new understanding of how the microbiota regulates postnatal growth and an additional variable that must be considered when studying the regulation of maternal behavior.

### Excerpts from full text:

... ecursor of serotonin, and gut microbes regulate tryptophan availability. We therefore directed our analyses toward genes associated with tryptophan metabolism (tnaA ()) and biosynthesis (trp operon). Analysis of the trp operon, by way of a multiple sequence alignment, revealed a concentrated number of amino acid substitutions in the region annotated as the bifunctional-fused indole-3-glycerol phosphate synthase/phosphoribosylanthranilate isomerase (
) (Fig. 5C and fig. S4). Furthermore, variant analysis identified a suite of misse [...] four strains, reported in parentheses as E. coli 06:H1 (ECN), E. coli 0157:H7 (EHEC), and E. coli 021:H21 (EC021) when compared with E. coli 016:H48 (MG1655): tryptophan synthase subunit alpha () (2, 3, and 1 variants), tryptophan synthase subunit beta (
) (2, 1, and 0 variants), fused indole-3-glycerol phosphate synthase/phosphoribosylanthranilate isomerase (
) (12, 10, and 4 variants), anthranilate synthase subunit TrpD (🗢) (1, 2, and 0 variants), and anthranilate synthase subunit TrpE (🔍) (5, 8, and 3 variants) (Fig. 5C, fig. S4, and data S1). Our analyses also included genes annotated as tryptophan transporters ...

PMID:26328893	XCluSim: a visual analytics tool for interactively comparing multiple clustering results of bioinformatics data.	D.
🔻 L'Yi S, Ko B, Shin l	D, Cho YJ, Lee J, Kim B, Seo J	
BMC Bioinformat	tics. 16 Suppl 11:S5 2015.	

### Abstract:

BACKGROUND: Though cluster analysis has become a routine analytic task for bioinformatics research, it is still arduous for researchers to assess the quality of a clustering result. To select the best clustering method and its parameters for a dataset, researchers have to run multiple clustering algorithms and compare them. However, such a comparison task with multiple clustering results is cognitively demanding and laborious. RESULTS: In this paper, we present XCluSim, a visual analytics tool that enables users to interactively compare multiple clustering results based on the Visual Information Seeking Mantra. We build a taxonomy for categorizing existing techniques of clustering results visualization in terms of the Gestalt principles of grouping. Using the taxonomy, we choose the most appropriate interactive visualizations for presenting individual clustering results from different types of clustering algorithms. The efficacy of XCluSim is shown through case studies with a bioinformatician. CONCLUSIONS: Compared to other relevant tools, XCluSim enables users to compare multiple clustering results in a more scalable manner. Moreover, XCluSim supports diverse clustering algorithms and dedicated visualizations and interactions for different types of clustering results, allowing more effective exploration of details on demand. Through case studies with a bioinformatics researcher, we received positive feedback on the functionalities of XCluSim, including its ability to help identify stably clustered items across multiple clustering results. Excerpts from full text:

... elations in pathways. However, he recognized two problems in the result. First of all, a cluster that had both Arg and Art regulons also contained a gene named tnaA () that was considered to be noise. This was because tnaA () showed a different expression pattern and was not highly related to other cluster members in biologi [...] was the most satisfying result for the dataset. Additionally, our participant gained insight by seeing a stable group in XCluSim. Genes in the trp operon (i.e. trpE (), trpD (), trpC (), trpB (), and trpA ()) were stably clustered together with yciF through the four different results (see the highlighted stable group in Figure 7A). Since yciF was assigned to a ...

### Pub Med

### PubMed

### ub Med

## STRING **Textmining / Functional**





# STRING Blocklisting

### PMID:31212674

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### PMID:32670211

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### PMID:22380540

... of plant-associated bacteria amongst which many Pseudomonas spp.. Additionally, genes of the tryptophan biosynthesis gene cluster trp were present: trpD, trpG, trpE (O/O), trpC (O), trpF, trpD, trpB (O), trpA (O). Strain VI4.1 has also the ability to produce IAA via an additional nitrilase-driven pathway converting indole-3acetonitrile in IAA. The ability to produc ...







# STRING Blocklisting

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# **STRING** LLM - Regulatory / Physical Networks







R	ACTION
-	-
-	-
-	-
-	-



### Excerpts from full text:

representation of tyrosine synthesis displays th ...

... s associated with a local regulation and the local regulators define a functional "elementary module" (see details in the Discussion). For example, the enzymes TrpE (
), TrpG, TrpD (
), TrpF (
) TrpC (
), TrpA (
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) involved in the tryptophan synthesis together with the regulators TRAP, RtpA, the tryptophanspecific T-box and the tryptophan-rich peptid [...] al regulation and the local regulators define a functional "elementary module" (see details in the Discussion). For example, the enzymes TrpE (
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) involved in the tryptophan synthesis together with the regulators TRAP, RtpA, the tryptophan-specific T-box and the tryptophan-rich peptide leader Plead define an elementary module (see Additional file 5, Figure S26). Indeed the enzymatic complex TrpE ()+TrpG is regulated by TRAP at the genetic level, and by tryptophan at the enzymatic level. This elementary module definition is based on the mathematical de [...] amples of these ambiguities - glycine, proline and branched-chain amino acid syntheses - are presented below. Glycine is synthesized in one step from serine by GlyA (
) (see Additional file 5, Figure S13). The expression of glyA (
) is repressed by PurR, the global regulator involved in purine synthesis. Glycine is also requir [...] nscription involving the TRAP protein. TRAP binds to the nascent mRNA and prevents elongation of transcription. The translation of two genes of the trp operon (trpE () and trpD ()) is further modulated by TRAP (see below). tyrA and aroJ are also transcribed from an internal constitutive sigmaAdependent promoter. In our model, the co [...] regulon. The state "on" of TRAP, which is defined as the conditions that enable the binding on mRNA, is described by TRAP also modulates the translation of the trpE () and trpD () genes by binding to the complete trp-mRNA. The trpE () ribosome-binding site (RBS) is then sequestrated in a RNA secondary structure preventing ribosome bindi [...] he trpE () ribosome-binding site (RBS) is then sequestrated in a RNA secondary structure preventing ribosome binding and trpE () translation. The coding sequences of trpE () and trpD () overlap by 29 nucleotides thereby coupling the translation of these two genes. The translation of trpD () is also affected by the binding of TRAP to the trpE () [...] g and trpE () translation. The coding sequences of trpE (
) and trpD (
) overlap by 29 nucleotides thereby coupling the translation of these two genes. The translation of trpD (
) is also affected by the binding of TRAP to the trpE () RBS. In our graphic representation, a mechanism of translational regulation is modelled by a hexagon, which is bound (state "on") or not (state "off") to t [...] TRAP-dependent modulation of the transcription of all the genes involved in the synthesis of tryptophan; (iii) TRAP-dependent modulation of the translation of trpE () and trpD (); (iv) TRAP sequestration by RtpA; and (v) conditions of transcription and translation of RtpA. The graphic

# STRING **LLM Model RoBERTa-large-PM**

### Fine-tuned:

**POSITIVE:** ~1000 curated abstracts containing complex formation information

**NEGATIVE:** ~300 curated abstracts containing information genetic interactions.

Max F1 score over 11 epochs

Softmax activation function on a decision layer.

86.75% average precision, 82.05% average recall

# **RoBERTa-large-PM-M3-Voc**

### NLP-detected sentences suggesting physical associations:

Genes encoding components of a strong complex (e.g., trpA ())-trpB ()) are more likely to be cotranscribed than genes encoding noncomplex-forming proteins acting in the same pathway (e.g., trpE-trpD). [...]

### NLP-detected sentence suggesting physical associations:

Finally, tryptophan synthase (TS), also a tetrameric enzyme composed of two pairs of subunits (TS-alpha or TrpA ()) and TS-beta or TrpB ()), replaces the 0.675 glycerol phosphate side-chain of indole-3-glycerol-phosphate by the alanyl moiety of an l-serine (fig. [...]

### NLP-detected sentences suggesting physical associations:

Previous studies have indicated that in Chlamydia, TrpA () has lost its catalytic activity yet remains associated with TrpB () to support the beta reaction. [...] 0.490Tryptophan synthase is a bifunctional protein-protein complex consisting of two subunits: alpha, encoded by trpA (), and beta, encoded by trpB (). [...]

### NLP-detected sentence suggesting physical associations:

TrpS is comprised of two subunits, TrpA () (alpha-subunit) and TrpB () (beta-subunit) that function as a heterodimeric pair in an alphabetabetaalpha complex. [...]

### NLP-detected sentences suggesting physical associations:

It is a heterotetramer, where two alpha-subunits (TrpA (O)) interact with the beta-subunit (TrpB (O)) dimer to form an alphabetabeta lpha complex. [...] Bi-directional allosteric communication between TrpA () and TrpB () ensures that the generation of indole is coupled with its subsequent conversion to Ltryptophan. [...]

0.844

0.905

0.623

# **RoBERTa-large-PM-M3-Voc**

NLP-detected sentences suggest Genes encoding components of a COMDEX () trpB () are more likely to be cotranscribed than genes encoding noncomplex-forming proteins 0.844acting in the same pathway (e.g., trpe-trpp). [...]

### NLP-detected sentence suggesting physical associations:

Finally, tryptophan synthase (TS), also a tetrameric enzyme composed of two particles of two particles of the glycerol phosphate side-chain of indole-3-glycerol-phosphate by the alanyl moiety SUDUNITS of TrpA () and TS-beta or TrpB (), replaces the 0.675



### NLP-detected sentence suggesting physical associations: NLP-detected sentence suggesting physical associations: TrpS is comprised of two subunits, TrpA () (alpha-subunit) and TrpB () (beta-subunit) that funct ACC OC MCC phabetabetaalpha complex. [...]

NLP-detected sentences suggesting physical association in teraction of the subunit (TrpB (I)) dimer to form an alphabetabeta alpha complex. [...] Bi-directional allosteric communication between TrpA () and IrpB () ensures that the generation of indole is coupled with its subsequent conversion to Ltryptophan. [...]

0.490

0.905

0.623

22       0.000       0         21       1.531       3         20       0.166       2         19       -0.600       1         18       -1.008       0         17       -0.524       -         16       -0.732       2         15       -0.732       2         14       -2.352       1         13       -3.934       -         12       -4.516       0         10       -1.618       0	0.000       0.000         3.358       4.568         2.214       3.321         1.099       1.568         0.586       0.588         -0.441       -1.07	0.000 6.362 8.529 5.060 1.735	0.000 2.490 1.309 0.626	0.000 5.186 6.305	0.000 9.769 31.516	0.000 9.920	0.000 9.712	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
21       1.531       2         20       0.166       2         19       -0.600       1         18       -1.008       0         17       -0.524       -         16       -0.732       2         15       -0.732       2         14       -2.352       1         13       -3.934       -         12       -4.516       0         10       -1.618       0	3.358       4.568         2.214       3.321         1.099       1.568         0.586       0.588         -0.441       -1.07	3       6.362         4       8.529         5       5.060         1       1.735	2.490 1.309 0.626	5.186 6.305	9.769	9.920	9.712	10 512	7 004	2 550					
20       0.166       2         19       -0.600       1         18       -1.008       0         17       -0.524       -         16       -0.422       -         16       -0.732       2         15       -1.702       1         14       -2.352       1         13       -3.934       -         12       -4.516       0         10       -1.618       0	2.214     3.321       1.099     1.568       0.586     0.588       -0.441     -1.07	8.529 5.060 1.735	1.309 0.626	6.305	31.516			10.515	1.224	3.558	0.717	0.392	0.453	0.432	0.357
19       -0.600       1         18       -1.008       0         17       -0.524       -         16       -0.422       -         16       -0.732       2         15       -1.702       1         14       -2.352       1         13       -3.934       -         12       -4.516       0         10       -1.618       0	1.099       1.568         0.586       0.588         -0.441       -1.07	3 5.060 3 1.735	0.626		51.510	34.723	30.925	39.330	12.245	0.316	0.337	0.307	0.248	0.253	0.290
18       -1.008 (0)         17       -0.524 -         16       -0.422 -         15       -0.732 2         14       -2.352 1         13       -3.934 -         12       -4.516 (0)         10       -1.618 (0)	0.586 0.588 -0.441 -1.07	3 1.735		1.849	25.754	39.092	50.523	69.007	7.805	-3.590	0.050	0.077	-0.109	-0.139	0.020
17       -0.524         16       -0.422         15       -0.732         14       -1.702         13       -3.934         12       -4.516         10       -1.618	-0.441 -1.07		0.354	1.537	19.917	36.754	46.165	77.417	7.517	-7.077	0.158	0.214	0.109	0.164	0.437
16       -0.422         15       -0.732         14       -1.702         13       -2.352         12       -4.516         11       -1.618	A 184	5-1.297	-0.280	-0.317	9.072	58.563	27.092	75.014	-0.713	-3.248	-0.170	0.086	0.310	0.155	0.159
15       -0.732       2         15       -1.702       1         14       -2.352       1         13       -3.934       -         12       -4.516       0         11       -1.618       0	-0.426 -0.45	1-0.341	-0.667	-1.011	2.003	74.995	8.566	65.026	-0.847	-2.921	-0.146	0.017	0.161	-0.123	-0.090
14       -1.702       1         13       -2.352       1         12       -3.934       -         11       -4.516       0         10       -1.618       0	2.142 1.444	0.787	0.078	-2.099	4.496	73.162	29.060	59.009	2.967	-1.683	0.104	-0.451	-0.003	0.040	-0.058
-2.352   -3.934 - -4.516 ( -1.618 ()	1.460 2.140	5 2.287	2.549	2.247	3.443	59.614	60.360	45.958	21.414	-1.110	-0.469	-0.144	-0.173	0.095	-0.116
12 12 -3.934 -4.516 0 -1.618 0	1.425 1.776	5 2.583	4.649	7.468	7.370	55.175	45.217	58.128	32.410	-1.677	-1.243	-1.132	-0.490	0.127	-0.339
-4.5160 -1.6180	-0.383 0.963	3.722	4.673	7.945	10.543	35.450	83.759	25.693	26.498	-2.475	-1.211	0.328	-0.527	0.006	-0.497
-1.618 0	0.183 1.168	3 4.041	7.488	11.607	17.723	24.354	63.085	-1.438	52.631	-3.128	-1.698	-2.574	-1.188	0.504	-0.522
	0.186 -0.05	4 1.196	2.787	8.131	12.668	41.058	76.323	32.737	16.954	-0.376	-3.265	0.575	0.160	0.121	0.091
4.031 2	2.401 3.598	6.297	7.255	10.582	5.686	-29.344	43.293	-6.746	27.116	-0.452	0.066	0.433	0.205	-0.453	-0.688
1.515 2	2.374 3.740	) 4.440	8.103	12.772	12.448	14.424	45.284	16.353	58.690	5.942	2.550	-0.851	0.088	-2.133	-1.190
<b>0</b> .693 2	2.635 1.580	5 1.492	7.467	3.035	15.279	-23.029	65.835	-40.806	42.841	10.222	3.888	3.987	0.170	-2.146	-2.589
0.778 2	2.096 1.154	2.103	6.557	3.309	9.712	-16.883	51.660	-25.789	46.193	3.134	2.661	6.421	0.591	-1.317	-4.095
0.866 -	-1.625 1.150	0.517	6.418	2.126	6.597	-33.233	38.380	28.862	29.817	0.475	-0.008	1.491	-0.498	-2.102	-0.315
3.104 1	1.721 2.600	0.827	3.370	-7.618	11.408	-33.038	49.387	-1.760	56.628	7.129	-2.601	2.540	0.537	-3.642	-3.424
4 1.023 -	-4.176 -2.73	4 -0.457	10.280	-10.089	-7.889	-37.395	44.649	2.696	65.498	15.834	1.335	7.550	0.307	-3.733	-0.545
3 -3.857 -	-0.795 -1.40	7 1.506	7.086	-1.291	-8.114	-50.828	65.311	-18.844	39.592	-3.819	2.623	-2.522	-0.387	-4.126	-0.715
2 -5.860 -	-1.289 -4.25	2 0.215	1.370	2.451	-0.682	-36.576	32.338	-20.239	10.954	-1.307	0.409	1.522	-4.939	-0.090	-1.412
-5.761 5	5.488 -4.73	5 12.372	7.468	15.919	-35.058	-32.376	47.344	-8.836	26.688	-12.632	-33.351	23.934	5.317	-3.435	-3.390
0 1.458 -	-2.533 -2.94	0 -1.930	6.293	9.087	-10.644	14.931	60.572	10.519	41.828	-0.500	0.248	-0.014	2.446	-0.614	0.794
mbeddings -2.905 (										0.000	0.210	0.011	2.440	-0.014	

23	ĠThe Ġformatio	n Ġof Ġ	a Ġstable	Ġtetrameric	Ġ	[unused1]		[unused1]	Ġcomplex		Ġwhich	Ġrequired	Ġthe	Ġdimerization	Ġdomain
22	0.000 0.000	0.000 0.00	0 0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
21	1.531 3.358	4.568 6.36	2 2.490	5.186	9.769	9.920	9.712	10.513	7.224	3.558	0.717	0.392	0.453	0.432	0.357
20	0.166 2.214	3.321 8.52	9 1.309	6.305	31.516	34.723	30.925	39.330	12.245	0.316	0.337	0.307	0.248	0.253	0.290
19	-0.600 1.099	1.568 5.06	0 0.626	1.849	25.754	39.092	50.523	69.007	7.805	-3.590	0.050	0.077	-0.109	-0.139	0.020
18	-1.008 0.586	0.588 1.73	5 0.354	1.537	19.917	36.754	46.165	77.417	7.517	-7.077	0.158	0.214	0.109	0.164	0.437
17	-0.524 -0.441	-1.075 -1.2	97 -0.280	-0.317	9.072	58.563	27.092	75.014	-0.713	-3.248	-0.170	0.086	0.310	0.155	0.159
16	-0.422 -0.426	-0.451 -0.3	41 -0.667	-1.011	2.003	74.995	8.566	65.026	-0.847	-2.921	-0.146	0.017	0.161	-0.123	-0.090
15	-0.732 2.142	1.444 0.78	7 0.078	-2.099	4.496	73.162	29.060	59.009	2.967	-1.683	0.104	-0.451	-0.003	0.040	-0.058
14	-1.702 1.460	2.146 2.28	7 2.549	2.247	3.443	59.614	60.360	45.958	21.414	-1.110	-0.469	-0.144	-0.173	0.095	-0.116
13	-2.352 1.425	1.776 2.58	3 4.649	7.468	7.370	55.175	45.217	58.128	32.410	-1.677	-1.243	-1.132	-0.490	0.127	-0.339
12	-3.934 -0.383	0.963 3.72	2 4.673	7.945	10.543	35.450	83.759	25.693	26.498	-2.475	-1.211	0.328	-0.527	0.006	-0.497
11	-4.5160.183	1.168 4.04	1 7.488	11.607	17.723	24.354	63.085	-1.438	52.631	-3.128	-1.698	-2.574	-1.188	0.504	-0.522
10	-1.618 0.186	-0.054 1.19	6 2.787	8.131	12.668	41.058	76.323	32.737	16.954	-0.376	-3.265	0.575	0.160	0.121	0.091
9	4.031 2.401	3.598 6.29	7 7.255	10.582	5.686	-29.344	43.293	-6.746	27.116	-0.452	0.066	0.433	0.205	-0.453	-0.688
8	1.515 2.374	3.740 4.44	0 8.103	12.772	12.448	14.424	45.284	16.353	58.690	5.942	2.550	-0.851	0.088	-2.133	-1.190
7	0.693 2.635	1.586 1.49	2 7.467	3.035	15.279	-23.029	65.835	-40.806	42.841	10.222	3.888	3.987	0.170	-2.146	-2.589
6	0.778 2.096	1.154 2.10	3 6.557	3.309	9.712	-16.883	51.660	-25.789	46.193	3.134	2.661	6.421	0.591	-1.317	-4.095
5	0.866 -1.625	1.156 0.51	7 6.418	2.126	6.597	-33.233	38.380	28.862	29.817	0.475	-0.008	1.491	-0.498	-2.102	-0.315
3	3.104 1.721	2.600 0.82	7 3.370	-7.618	11.408	-33.038	49.387	-1.760	56.628	7.129	-2.601	2.540	0.537	-3.642	-3.424
4	1.023 -4.176	-2.734 -0.4	57 10.280	-10.089	-7.889	-37.395	44.649	2.696	65.498	15.834	1.335	7.550	0.307	-3.733	-0.545
5	-3.857 -0.795	-1.407 1.50	6 7.086	-1.291	-8.114	-50.828	65.311	-18.844	39.592	-3.819	2.623	-2.522	-0.387	-4.126	-0.715
2	-5.860 -1.289	-4.252 0.21	5 1.370	2.451	-0.682	-36.576	32.338	-20.239	10.954	-1.307	0.409	1.522	-4.939	-0.090	-1.412
1	-5.761 5.488	-4.735 12.3	72 7.468	15.919	-35.058	-32.376	47.344	-8.836	26.688	-12.632	-33.351	23.934	5.317	-3.435	-3.390
0	1.458 -2.533	-2.940 -1.9	30 6.293	9.087	-10.644	14.931	60.572	10.519	41.828	-0.500	0.248	-0.014	2.446	-0.614	0.794
embeddin	gs -2.905 0.707	4.800 5.77	3 5.332	-1.487	0.904	-0.386	7.242	6.091	11.238	16.226	-1.650	1.032	-2.435	0.429	0.244

<b>ĠThe Ġformat</b>	ion Ġof	Ġa	Ġstable	Ġtetrameric	Ġ	[unused1]	-	[unused1]	Ġcomplex	,	Ġwhich	Ġrequired	Ġthe	Ġdimerization	Ġd
0.000 0.000	0.000 (	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.0
1.531 3.358	4.568	5.362	2.490	5.186	9.769	9.920	9.712	10.513	7.224	3.558	0.717	0.392	0.453	0.432	0.3
0.166 2.214	3.321 8	8.529	1.309	6.305	31.516	34.723	30.925	39.330	12.245	0.316	0.337	0.307	0.248	0.253	0.2
-0.600 1.099	1.568	5.060	0.626	1.849	25.754	39.092	50.523	69.007	7.805	-3.590	0.050	0.077	-0.109	-0.139	0.0
-1.008 0.586	0.588 1	1.735	0.354	1.537	19.917	36.754	46.165	77.417	7.517	-7.077	0.158	0.214	0.109	0.164	0.4
-0.524 -0.441	-1.075 -	1.297	-0.280	-0.317	9.072	58.563	27.092	75.014	-0.713	-3.248	-0.170	0.086	0.310	0.155	0.1
-0.422 -0.426	-0.451 -	0.341	-0.667	-1.011	2.003	74.995	8.566	65.026	-0.847	-2.921	-0.146	0.017	0.161	-0.123	-0.
-0.732 2.142	1.444 (	0.787	0.078	-2.099	4.496	73.162	29.060	59.009	2.967	-1.683	0.104	-0.451	-0.003	0.040	-0.
-1.702 1.460	2.146 2	2.287	2.549	2.247	3.443	59.614	60.360	45.958	21.414	-1.110	-0.469	-0.144	-0.173	0.095	-0.
-2.352 1.425	1.776 2	2.583	4.649	7.468	7.370	55.175	45.217	58.128	32.410	-1.677	-1.243	-1.132	-0.490	0.127	-0
-3.934 -0.383	0.963	3.722	4.673	7.945	10.543	35.450	83.759	25.693	26.498	-2.475	-1.211	0.328	-0.527	0.006	-0
-4.516 0.183	1.168 4	4.041	7.488	11.607	17.723	24.354	63.085	-1.438	52.631	-3.128	-1.698	-2.574	-1.188	0.504	-0
-1.618 0.186	-0.054	1.196	2.787	8.131	12.668	41.058	76.323	32.737	16.954	-0.376	-3.265	0.575	0.160	0.121	0.
4.031 2.401	3.598 6	5.297	7.255	10.582	5.686	-29.344	43.293	-6.746	27.116	-0.452	0.066	0.433	0.205	-0.453	-0
1.515 2.374	3.740 4	4.440	8.103	12.772	12.448	14.424	45.284	16.353	58.690	5.942	2.550	-0.851	0.088	-2.133	-1
0.693 2.635	1.586	1.492	7.467	3.035	15.279	-23.029	65.835	-40.806	42.841	10.222	3.888	3.987	0.170	-2.146	-2
0.778 2.096	1.154 2	2.103	6.557	3.309	9.712	-16.883	51.660	-25.789	46.193	3.134	2.661	6.421	0.591	-1.317	-4
0.866 -1.625	1.156 (	0.517	6.418	2.126	6.597	-33.233	38.380	28.862	29.817	0.475	-0.008	1.491	-0.498	-2.102	-0
3.104 1.721	2.600 0	0.827	3.370	-7.618	11.408	-33.038	49.387	-1.760	56.628	7.129	-2.601	2.540	0.537	-3.642	-3
1.023 -4.176	-2.734 -	0.457	10.280	-10.089	-7.889	-37.395	44.649	2.696	65.498	15.834	1.335	7.550	0.307	-3.733	-0
-3.857 <mark>-0.795</mark>	-1.407	1.506	7.086	-1.291	-8.114	-50.828	65.311	-18.844	39.592	-3.819	2.623	-2.522	-0.387	-4.126	-0
-5.860 -1.289	-4.252 (	0.215	1.370	2.451	-0.682	-36.576	32.338	-20.239	10.954	-1.307	0.409	1.522	-4.939	-0.090	-1
-5.761 <mark>5.488</mark>	-4.735	12.372	7.468	15.919	-35.058	-32.376	47.344	-8.836	26.688	-12.632	-33.351	23.934	5.317	-3.435	-3
1.458 -2.533	-2.940 -	1.930	6.293	9.087	-10.644	14.931	60.572	10.519	41.828	-0.500	0.248	-0.014	2.446	-0.614	0.
-2.905 0.707	4.800 5	5.773	5.332	-1.487	0.904	-0.386	7.242	6.091	11.238	16.226	-1.650	1.032	-2.435	0.429	0.

23	<b>ĠThe Ġformation</b>	Ġof	Ġa	Ġstable	Ġtetrameric	Ġ	[unused1]		[unused1]	Ġcomplex		Ġwhich	Ġrequired	Ġthe	Ġdimerization	Ġdomain
23	0.000 0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
21	1.531 3.358	4.568	6.362	2.490	5.186	9.769	9.920	9.712	10.513	7.224	3.558	0.717	0.392	0.453	0.432	0.357
20	0.166 2.214	3.321	8.529	1.309	6.305	31.516	34.723	30 <b>.92</b>	5 39.330	12.245	0.316	0.337	0.307	0.248	0.253	0.290
19	-0.600 1.099	1.568	5.060	0.626	1.849	25.754	39.092	50.52	3 69.007	7.805	-3.590	0.050	0.077	-0.109	-0.139	0.020
18	-1.008 0.586	0.588	1.735	0.354	1.537	19.917	36.754	46.16	<mark>5</mark> 77.417	7.517	-7.077	0.158	0.214	0.109	0.164	0.437
17	-0.524 -0.441	-1.075	5-1.297	-0.280	-0.317	9.072	58.563	27.09	2 75.014	0.713	-3.248	-0.170	0.086	0.310	0.155	0.159
16	-0.422 -0.426	-0.451	-0.341	-0.667	-1.011	2.003	74.995	8.566	65.026	0.847	-2.921	-0.146	0.017	0.161	-0.123	-0.090
15	-0.732 2.142	1.444	0.787	0.078	-2.099	4.496	73.162	29.06	0 59.009	2.967	-1.683	0.104	-0.451	-0.003	0.040	-0.058
14	-1.702 1.460	2.146	2.287	2.549	2.247	3.443	59.614	60.36	0 45.958	21.414	-1.110	-0.469	-0.144	-0.173	0.095	-0.116
13	-2.352 1.425	1.776	2.583	4.649	7.468	7.370	55.175	4 <b>5.2</b> 1	7 58.128	32.410	-1.677	-1.243	-1.132	-0.490	0.127	-0.339
12	-3.934 -0.383	0.963	3.722	4.673	7.945	10.543	35.450	83.75	<mark>9</mark> 25.693	26.498	-2.475	-1.211	0.328	-0.527	0.006	-0.497
11	-4.516 0.183	1.168	4.041	7.488	11.607	17.723	24.354	63.08	5 -1.438	52.631	-3.128	-1.698	-2.574	-1.188	0.504	-0.522
10	-1.618 0.186	-0.054	1.196	2.787	8.131	12.668	41.058	76.32	3 32.737	16.954	-0.376	-3.265	0.575	0.160	0.121	0.091
0	4.031 2.401	3.598	6.297	7.255	10.582	5.686	-29.344	43.29	3 -6.746	27.116	-0.452	0.066	0.433	0.205	-0.453	-0.688
9	1.515 2.374	3.740	4.440	8.103	12.772	12.448	14.424	4 <b>5.2</b> 8	4 16.353	58.690	5.942	2.550	-0.851	0.088	-2.133	-1.190
0	0.693 2.635	1.586	1.492	7.467	3.035	15.279	-23.029	65.83	5 -40.806	42.841	10.222	3.888	3.987	0.170	-2.146	-2.589
	0.778 2.096	1.154	2.103	6.557	3.309	9.712	-16.883	51 <b>.6</b> 6	0-25.789	46.193	3.134	2.661	6.421	0.591	-1.317	-4.095
0	0.866 -1.625	1.156	0.517	6.418	2.126	6.597	-33.233	38.38	0 28.862	29.817	0.475	-0.008	1.491	-0.498	-2.102	-0.315
5	3.104 1.721	2.600	0.827	3.370	-7.618	11.408	-33.038	4 <b>9.3</b> 8	7 -1.760	56.628	7.129	-2.601	2.540	0.537	-3.642	-3.424
4	1.023 -4.176	-2.734	-0.457	10.280	-10.089	-7.889	-37.395	4 <b>4.6</b> 4	9 2.696	65.498	15.834	1.335	7.550	0.307	-3.733	-0.545
3	-3.857 -0.795	-1.407	1.506	7.086	-1.291	-8.114	-50.828	65.31	1 -18.844	39.592	-3.819	2.623	-2.522	-0.387	-4.126	-0.715
2	-5.860 -1.289	-4.252	0.215	1.370	2.451	-0.682	-36.576	32.33	<mark>8</mark> -20.239	10.954	-1.307	0.409	1.522	-4.939	-0.090	-1.412
1	-5.761 5.488	-4.735	12.372	7.468	15.919	-35.058	-32.376	47.34	4 -8.836	26.688	-12.632	-33.351	23.934	5.317	-3.435	-3.390
0	1.458 -2.533	-2.940	-1.930	6.293	9.087	-10.644	14.931	60.57	2 10.519	41.828	-0.500	0.248	-0.014	2.446	-0.614	0.794
embeddings	-2.905 0.707	4.800	5.773	5.332	-1.487	0.904	-0.386	7.242	6.091	11.238	16.226	-1.650	1.032	-2.435	0.429	0.244

23	<b>ĠThe Ġformation</b>	Ġof Ġa	Ġstable	Ġtetrameric	Ġ	[unused]	ı <b>) -</b> (	unused	1] Ġcomplex	,	Ġwhich	Ġrequired	Ġthe	Ġdimerization	Ġdomain
22	0.000 0.000	0.000 0.000	0.000	0.000	0.000	0.000	0.000 0	.00 <mark>0</mark> 0.(	0.000	0.000	0.000	0.000	0.000	0.000	0.000
21	1.531 3.358	4.568 6.362	2.490	5.186	9.769	9.920	9.712	0.513	7.224	3.558	0.717	0.392	0.453	0.432	0.357
20	0.166 2.214	3.321 8.529	1.309	6.305	31.516	34.723	30.925	9.330	12.245	0.316	0.337	0.307	0.248	0.253	0.290
19	-0.600 1.099	1.568 5.060	0.626	1.849	25.754	39.092	50.523	9. <mark>007</mark>	7.805	3.590	0.050	0.077	-0.109	-0.139	0.020
18	-1.008 0.586	0.588 1.735	0.354	1.537	19.917	36.754	46.165	7.417	7.517	-7.077	0.158	0.214	0.109	0.164	0.437
17	-0.524 -0.441	-1.075 -1.297	-0.280	-0.317	9.072	58.563	27.092	5.014	-0.713	3.248	-0.170	0.086	0.310	0.155	0.159
16	-0.422 -0.426	-0.451 -0.341	-0.667	-1.011	2.003	74.995	8.566	5.0 <b>26</b>	-0.847	-2.921	-0.146	0.017	0.161	-0.123	-0.090
15	-0.732 2.142	1.444 0.787	0.078	-2.099	4.496	73.162	29.060	9. <b>009</b>	2.967	1.683	0.104	-0.451	-0.003	0.040	-0.058
14	-1.702 1.460	2.146 2.287	2.549	2.247	3.443	59.614	60.360	5. <b>958</b>	21.414	1.110	-0.469	-0.144	-0.173	0.095	-0.116
13	-2.352 1.425	1.776 2.583	4.649	7.468	7.370	55.175	45.217	8.128	32.410	1.677	-1.243	-1.132	-0.490	0.127	-0.339
12	-3.934 -0.383	0.963 3.722	4.673	7.945	10.543	35.450	83.759	5.693	26.498	-2.475	-1.211	0.328	-0.527	0.006	-0.497
11	-4.516 0.183	1.168 4.041	7.488	11.607	17.723	24.354	63.085	1.438	52.631	-3.128	-1.698	-2.574	-1.188	0.504	-0.522
10	-1.618 0.186	-0.054 1.196	2.787	8.131	12.668	41.058	76.323	2.737	16.954	0.376	-3.265	0.575	0.160	0.121	0.091
9	4.031 2.401	3.598 6.297	7.255	10.582	5.686	-29.344	43.293 -	6.746	27.116	-0.452	0.066	0.433	0.205	-0.453	-0.688
8	1.515 2.374	3.740 4.440	8.103	12.772	12.448	14.424	45.284	6.353	58.690	5.942	2.550	-0.851	0.088	-2.133	-1.190
7	0.693 2.635	1.586 1.492	7.467	3.035	15.279	-23.029	65.835 -	40.806	42.841	10.222	3.888	3.987	0.170	-2.146	-2.589
6	0.778 2.096	1.154 2.103	6.557	3.309	9.712	-16.883	51.660 -	25.789	46.193	3.134	2.661	6.421	0.591	-1.317	-4.095
5	0.866 -1.625	1.156 0.517	6.418	2.126	6.597	-33.233	38.380 2	8.862	29.817	0.475	-0.008	1.491	-0.498	-2.102	-0.315
3	3.104 1.721	2.600 0.827	3.370	-7.618	11.408	-33.038	49.387	1.760	56.628	7.129	-2.601	2.540	0.537	-3.642	-3.424
3	1.023 -4.176	-2.734 -0.457	10.280	-10.089	-7.889	-37.395	44.649		65.498	15.834	1.335	7.550	0.307	-3.733	-0.545
3	-3.857 -0.795	-1.407 1.506	7.086	-1.291	-8.114	-50.828	65.311	18.844	39.592	-3.819	2.623	-2.522	-0.387	-4.126	-0.715
2	-5.860 -1.289	-4.252 0.215	1.370	2.451	-0.682	-36.576	32.338	20.239	10.954	-1.307	0.409	1.522	-4.939	-0.090	-1.412
1	-5.761 5.488	-4.735 12.372	2 7.468	15.919	-35.058	-32.376	47.344	8.836	26.688	-12.632	-33.351	23.934	5.317	-3.435	-3.390
0	1.458 -2.533	-2.940 -1.930	6.293	9.087	-10.644	14.931	60.572	0.519	41.828	-0.500	0.248	-0.014	2.446	-0.614	0.794
mbeddings	-2.905 0.707	4.800 5.773	5.332	-1.487	0.904	-0.386	7.242 (	0.091	11.238	16.226	-1.650	1.032	-2.435	0.429	0.244



### **RegulaTome corpus:**

- 10499 regulatory relationships
  - 2294 Regulation
  - 2131 Positive Regulation
  - **1920** Negative Regulation
  - 521 Regulation of Gene Expression
  - ... 40 different types



### Model run:

- - 3 mln abstracts • 3 mln full-text
- 1200 mln pairs

### Documents with at least 1 pair

 18.4 mln with at least one positive label < 100k high confidence labels</li>

# REGULATION

# Available Later This Year





# STRING **Textmining viewer**



tro 4 [h1260]

• (IPA [D1200]				
Tryptophan synthase, alpha subunit; T responsible for the aldol cleavage of i to indole and glyceraldehyde 3-phosp family.	The alpha subunit is indoleglycerol phosphate hate; Belongs to the TrpA	$\leftrightarrow$	Tryptophan synthase, beta subunit; The beta is responsible for the synthesis of L- tryptoph from indole and L-serine; Belongs to the TrpE	subunit nan 8 family.
	Evidence suggesting	g a functi	onal link:	
Neighborhood in the Genome:	yes, intergenic distance 0 b neighbors in other genome	p (score s (score (	0.773). In addition, homologous genes are 0.154).	show
Gene Fusions:	yes (score 0.900).			show
Cooccurrence Across Genomes:	yes (score 0.775).			show
Co-Expression:	yes (score 0.999).			show
Experimental/Biochemical Data:	yes (score 0.802). In addition organisms (score 0.738).	on, putati	ve homologs were found interacting in other	show
Association in Curated Databases:	yes (score 0.900).			show
Co-Mentioned in Pubmed Abstracts:	yes (score 0.990). In addition other organisms (score 0.2	on, putati :00).	ve homologs are mentioned together in	show
Combined Score:	0.999		Full interac	tion pag

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		Search	Download	Help	My Data
TEXTMI	INING				
				SUMMARIZ	TE (AI) BETA
Relevant publications mentioning your query species (Escher PMD:27597847 Candidate Essential Genes in Burkholderia renormania J2015 Iduardia	ichia coli K12): d by Genome Wide Tra	05.			public a
Wong YL, Alad El Ghany M, Necem R, Lee Kit, Tan YC, Pain A, Nathan S Front Microbiol. 7:1288 2016. Abstract:					Public
turnencemes cencocepacie antection often leads to fatal cepacia syndrome in o eradication of the pathogen due to its intimice resistance or many clinically ava genes as the proteins encoded by these genes may serve as potential targe (Transpopen Directed Insertion alla Enumerical as a measure ide	systic fibrosis patien ilable antibiotics. Re ts for development il to facilitate the idea	cent attention ha of novel antimic ntification of R	work therapy rais s turned to the ic obials. In this s mocepania	tudy, we up to provide to the top	i in complete n of essential tilized TraDIS for its growth
and viability. A transposon mutant pool consisting of approximately 500,000 mut insertion sites identified by computational analysis of TraDIS datasets. The satural essential in B. cencocpacia. We extended the application of TraDIS to identify con reporting of 470 agrees to be occurring for B.	tants was successful ated library allowed f iditionally essential g	By constructed, w or the identification enes required for the library of the	th more than 400 in of 383 genes t in vitro growth an	0,000 uniqui hat were prid revealed	e transposon redicted to be J an additional becuently be
subjected to various biologically related conditions to facilitate the discovery of ge Excepts from full text: conditionally essential are genes involved in the conversion of chorismate	to phenylalanine an	adaptation as we d tyrosine (pheA	II as pathogenicit BCAL2953, and	y and virule BCAL300-	nce. 4) as well as
tryptophen ( <b>IBpA</b> (0), <b>IBp</b> A (0), <b>IBpA</b> (0), <b>IbpA</b> (0)). We suspect that trp mutants r environment. It had been demonst PMD-18221558. The tryptophen pathway ones of the Samasso Sea metacenome new	may be tryptophan a	the prevalence of p	unable to grow	in a tryptop	shan-depleted
Kapan J, Sharon I, Beja G, Kuhn JC Genome Biol. 9(1) R20 2008. Abstract: BACK00(2) R07. The economics. Activities of microbiol.	Same for	abarrow of a	a a pair a	where a	
participating in different biosynthetic pathways and to attempt to understand the sargasso Sea metagenome is made with respect to the seven genes of the type acid biosynthesis are tryptophan (typ) genes. Many contigs and scatflods con	re relationship and e ophan pathway. RES ntain whole or split	volution of those ULTS: At least 5% operons that are	genes. In this at of all the genes to similar to previo	rticle, an ar hat are reli ously analy	nalysis of the ated to amino yzed trp gene
organizations. Only two scattoros discovered in this analysis possess a different Many mainic organisms lack an operon-type cognization of these genes in have i search reveal that the dichotomous division between trp8,1 and trp1,2 also occu sequences that were closely related to each other but distinct from most known to	operon organization mini-operons contain ars in organisms from pB sequences. CONC	of tryptophan pati ing only two trp g in the Sargasso S LUSION: The data	tway genes than enes. In addition, ra. One cluster w show that trp ge	those prev the trpB ge as found to nes are wid	nes from this p contain trpB dely dispersed
within this metagenome. The novel organization of these genes and an unusual g bacteria indicate that there is much to be discovered about both the reason fo bacteria. Excerpts from full text:	roup of trp8_1 sequ r certain gene order	ences that were for s and the regulat	und among som ion of tryptophar	e of these biosynthe	Sargasso Sea Isis in marine
n be concluded that this gene must be functional in tryptophan biosynthesis and and tige (□)+ept (b) + (b)	d not a pseudogene. I es of the second split	P. ubique contains operon is: (gene	two split operon not mentioned ab	s: trpE-trpG ove) himD-	·trpD-trp© ( <sup>©</sup> ) рутF-trpF ( <sup>©</sup> )-
PMID:27190007 Reinventing the Wheel and Making It Round Again: Evolutionary Convery Related Lachman Aphdio Tuberotachnus salignus and Cinara cedri. Manuson-Marin A, Simon JLC (atome A Garwane Billiot Idan). 817:1440.82016.	gence in Buchnera-Gen	atia Symbiotic Con	sortia between the	Distantly	Pub
Abstract: Virtually aphids (Aphididae) harbor Buchnera aphidicola as an obligate endos Mary species within the Lachrinae subfamily seem to be consistently associat	nymbiont to compen- ted also with Serrati	ate nutritional de a symbiotica We	ficiencies arising have previously	from their shown that	r phloem diet. It both Cinara
(Unitan) Oracin and Unitary (Updepactually significant (Updepactually significant and Updepact) symbolics. However, while Bouchness genomes of both Cinara species are similar gain insight into the essentiality and degree of integration of S. symbolics within endosymbionts from the distantly related aphild Tuberolechnuss salignuss (Lachn).	; genome degradatio the Lachninae, we s inae: Tuberolachnini	n differs greatly b equenced the gen tribe). We found	etween the two to come of both Buc a striking level o	5. symbioti hnera and f similarity	ca strains. To S. symbiotica y between the
endosymbiotic system of this aprild and that of C. cedri lis both aprild hosts, intracellularly inside bacterico/sets. Interestingly, T. salignut endosymbiotits pres- which is not present in C. tujafilina's. Moreover, we corroborate the ribofiliaribot provide further evidence for the previously proposed establishment of a seconda	<ol> <li>symbiotica poss ent the same tryptop osynthetic-role take- ry co-obligate endos</li> </ol>	esses a highly re han biosynthetic over/rescue by S. ymbiont in the co	duced genome a metabolic compli symbiotica in T. mmon ancestor (	ementation salignus, a of the Lach	id exclusively i as C. cedrils, and therefore, ininae aphids.
Finally, we propose that the putative convergent split of the tryptophan biosynthetic S. symbotics as an obligate invacefular symbiont and the triggering of further ger Excerpts from full text: etaped neit the obscriptic trustrophan biosynthetic onese trut. and trut (config	c role between Buchr nome degradation.	era and S. symbio	rtica could be beh	ind the est	ablishment of
(trgA (iii), trgB, trgB (iii) and trpD). These retentions and losses of genes in Buchni of tryptophan now bo- material and tryptophan or bo- tryptophan on bo- material and tryptophanet and tryptophanet and tryptophanet provide the tryptophanet and tryptophanet and tryptophanet provide tryptophanet and tryptophanet and tryptophanet provide tryptophanet and tryptophanet and tryptophanet provide tryptophanet and tryptophanet provide tryptophanet and tryptophanet provide tryptophanet prov	era complement thos	e in the S. symbic	tica genome, res	ulting in the	biosynthesis
Instruction sub-set environment or (pressegnar(id) carrier enzymes: establishing pholp Evran S, Telefoncu: A, Sterner R Protein Eng Des Set 25(6):285-93 2012. Abstract:		consistent activ	, on the scanoid (		Public
Abstract: Phosphoribosylambranilate (PRA) isomerase (TBPE (©)) and tryptophan synthase the biosynthesis of tryptophan. They contain a conserved phosphate binding site, this hypothesis, we have established TBPE (©) activity on the scaffold of TBPI	alpha-subunit (TrpA which indicates a c (III) from Salmone	(*)) are (betaalp ommon evolution fla typhimurium	ha)(8)-barrel enzy ary origin. In orde using protein en	mes that a r to expering.	ire involved in mentally back Based on the
superposition of crystal structures with bound ligands, two residues in the active directed mutagenesis. This <b>TryA</b> (•) variant as well as wild stype <b>TryA</b> (•) were a <b>tryA</b> (•) gene libraries were used to transform an auxotrophic Escherichia coli <b>try</b> isolated by in vivo complementation. The amina acid substitutions of the same	site of TrpA (*) wer ach subjected to ran F (*) deletion strain, cted TrpA (*) varian	e replaced with co dom mutagenesis and TrpA (*) vari its were recombin	using error-prom ants with PRA iso ned by DNA shot	rom TrpF ( e PCR. The omerisation filing, age	<ul> <li>using site- two resulting activity were in followed by</li> </ul>
complementation in vivo. Several TrpA ( $^{\circ}$ ) variants were produced in E. coli and p state enzyme kinetics. Our results support that TrpA ( $^{\circ}$ ) and TrpF ( $^{\circ}$ ) have eppedecessor, and provide insights into the minimum requirements for the catalysis	urified, and their cat volved by gene dupl of PRA isomerisatio	alytic TrpF (0) act lication and diver	ivities were deter sification from e	mined in vi ach other o	tro by steady- or a common
PMID 22056666 Unexpected electron transfer in crystochrome identified by time resolve ♥ Biokup Z. Hitsmi K. Getzoff ED, Xiapf S. Koslawski T. Schleicher E. Weber S Angew Chem int Ed Engl. 50(52):12647-51 2011.	d EPR spectroscopy.				Pub
Abstract: Subtle differences in the local sequence and conformation of amino acids can structural conservation of the redox partners. For individual ET steps, distance is the ET partners, and thus the stabilization of the charge-secarated states <i>maniful</i>	result in diversity a not necessarily the te substantially.	nd specificity in o decisive parameter	ectron transfer er; orientation and	(ET) in pro d solvent a	teins, despite ocessibility of
Excerpts from full text: rence of the Gibbs free energy. We computed free energy changes for movin k.i/mol, to Tript (III) (Tript (III) -> Tript (III)) as 42 k.i/mol, and to Tript (III) (Tript population on Tript (III) in excess of 99% at most term	g a positive charge t t (⊜)' → TrpA (⊜)) an	from TrpA (=) to s -81 kJ/mol. This	TrpB (TrpB → Tr translates into a	pA ( <sup>e</sup> )) as n equilibriu	i DeltaG = -49 im Boltzmann
[truncated after 5 items <u>view more]</u>					
PMID:35011212. Transient Receptor Potential (TRP) and Thermoregulation in Animals: S 	tructural Biology and N . Gomez J, de Mira Gen	ieurophysiological i aldo A, Lendez P, Hi	lspects. mandez-Availos (, i	Falcon (	Pub
<sup>C</sup> Otroo-Homandez A, Warg D Animats (Base): 12(1) 2022. Abstract: This review presents and analyzes recent scientific findings on the structure, physi	iology, and neurotran	smission mechan	isms of transient	receptor p	otential (TRP)
and their function in the thermoregulation of mammals. The aim is to better un temperature of animals, or those susceptible to thermal stress. The majority of per that function as transductors through changes in the merhane potential. THP are include continuenail associate barcarde and on our fully known the mechanism that.	idenstand the function ipheral receptors are classified into sever coverate the covering	mailty of these re TRP cation change families and two and closing of the	ceptors and their less formed from groups. The data TRP cates. Data	r role in m transmemb gathered f	aintaining the brane proteins for this review weaver succest
the intervention of machanisms related to 6 protein-coupled receptors, dishopp example, the future uses of these data for controlling themoregulatory disorders our understanding of these mechanisms and achieve substantial advances in cont	horylation, and ligan and the invitation to rolling fever, hyperth	ds. Several quest researchers to co emia, and hypoth	ons emerge from induct more exter ermia.	the review nsive studi	w as well. For es to broaden
Excerpts tream hall text: A total of 9 families are recognized and divided into two groups depending on 1 TRPE (ii), TSPV, TRPU, TRPM, TRPS, and TRPS, (iii) includes the TRP with great TRPM(), (Figure 7), 2.1.7, Classification of TRP	their degree of simila ater similarity to the	rity with the gene gene, while group	trp found in Dros 2 contains those	ophilas. Gr Iess simil	roup 1 (TRPN, lar (TRPP and
PMID:3536955 The phyliosphere microbiome shifts toward combating melanose patho V LPQ, Dru.2R, Dhang Y, Xu, J Wang H, Wang Z, Li H Microbiome. 10(1):55 42022.	igen.				Pub
Abstract: RACK/CV/RIP: Please and some it has faint mission to achieve their shifts to do					
the rhizosphere microbiome in suppressing plant pathogens, the collective come pathogen invasion remains lamak elisities. BESUITS: Here, we interested 145	efend against pathog munity-level change metabarcoding, sh	ens. However, in and effect of the otrust	contrast to the int phyllosphere mic	tensively st probiome in dependent	udied roles of n response to 1 methods to
buckdoncorbs realiss can recruit periencial minicolores of ensurine view adary too the histoghne microbiome in suppressing plant pathogeni, the collective com pathogen imasion remains largely elusive. RESUITS: Here, we integrated 156 systematically investigate the charges in phylosphere microbiome batteres infer metanose disease worldwide. Multitle microbiome features suppetted a shift reduction of community evenines, the emispirace of lange numbers of new mi	efend against pathop munity-level change metabarcoding, sh cted and uninfected in phyllosphere micr crobes, and the inte	ens. However, in and effect of the otgun metagenor citrus leaves by 0 obiome upon D. tse microbial net	contrast to the int phyllosphere mic nics and culture Naporthe citri, a f citri infection, hig work. We also id	ensively st crobiome is dependen/ lungal path shlighted b entified the	tudied roles of n response to t methods to logen causing y the marked a microbiome
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The shoughes microlations in appreseng plant pathogens, the collectine course pathogenization means in pages values, RESOLTS Here, we integrated 160 systematically investigate the charges in phylosphere microbios belawani for reduction of constructive prevents. The sengence of days mathematically investigates and constructive prevents. The sengence of days mathematically methods and the sended approximation of the sense features from functional perspectives in infected leaves, such as enriched more microbast barefullar groups characteristics. Calabolase experiments for Methylobartetion and the sense integration of the sense Methylobartetion and the infected leaves, such as enriched more contributor for file nactional enricement growth, Sphiogenomeas spo- combibility for file nactional enrichment of two complex outer membrane inco- combibility for file nactional enrichment of two complex outer membranes in the statement of the sense of the sense of the sense contributor for file nactional enrichment and the method of the sense entroporties cacher. CONCLUSION: Summark, our shart prevealed how phylinght	efend against pathog munity-level change i metabarcoding, sh cted and uninfected in phylicophere micro crobes, and the inter- bial functions for ire monstrated that sev disease index rangi ves, exhibited antage presented beneficial protor protein in the is incn-sufficient condi- tere microbiomes d	ens. However, in and effect of the otgun metagenou offusa leaves by 0 obiome upon D. is microbial net in competition an eral bacteria asse insistic activities to personic charact flected leaves. M ions, suggesting fixed between i	contrast to the int phyllosphere mix- nics and culture hisporthe citi, a 1 citi infection, his work. We also id g potential artiflue sociated with the L8.4%. Among th D. citri both in w D. citri both in w creative. Sphingo a role of ison c fected and unit	tensively st crobiome in dependen/ ungal path phighted bi- ngal traits, microbiom em, Panto- tro and in v e found to monas asy competition fected citt	tudied roles of n response to t methods to togen causing y the marked e microbiome and enriched te althit could ea anyt0 and vibe the main 20 showed a t during their us leaves by
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TITING is a Core Data Resource as designated by Shibal Bodelta Coalition and SLIDE.

# STRING Textmining viewer

PMID:35022438 Sonic Hedgehog (●) acts as a macrophage chemoattractant during regeneration of the gastric epithelium.
Chakrabarti J, Dua-Awereh M, Schumacher M, Engevik A, Hawkins J, Helmrath MA, Zavros Y
NPJ Regen Med. 7(1):3 2022.

### Abstract:

Sonic Hedgehog () (Shh ()), secreted from gastric parietal cells, contributes to the regeneration of the epithelium. The recruitment of macrophages plays a central role in the regenerative process. The mechanism that regulates macrophage recruitment in response to gastric injury is largely unknown. Here we tested the hypothesis that Shh () stimulates macrophage chemotaxis to the injured epithelium and contributes to gastric regeneration. A mouse model expressing a myeloid cell-specific deletion of Smoothened () (LysMcre/+;Smof/f) was generated using transgenic mice bearing loxP sites flanking the Smo () gene (Smo () loxP) and mice expressing a Cre recombinase transgene from the Lysozyme M locus (LysMCre). Acetic acid injury was induced in the stomachs of both control and LysMcre/+;Smof/f (SmoKO) mice and gastric epithelial regeneration and macrophage recruitment analyzed over a period of 7 days post-injury. Bone marrow-derived macrophage (BM-Moe) were collected from control and SmoKO mice. Human-derived gastric organoid/macrophage co-cultures were established, and macrophage chemotaxis measured. Compared to control and SmoKO animals exhibited inhibition of ulcer repair and normal epithelial regeneration, which correlated with decreased macrophage infiltration at the site of injury. Bone marrow chimera experiments using SmoKO donor cells showed that control chimera mice transplanted with SmoKO bone marrow donor cells exhibited a loss of ulcer repair, and transplantation of control bone marrow donor cells to SmoKO mice rescued epithelial cell regeneration. Histamine-stimulated Shh () secretion in human organoid/macrophage co-cultures resulted in macrophage migration toward the gastric epithelial cell regeneration. Histamine-stimulated Shh () inhibitor Vismodegib. Shh ()-induced macrophage migration was mediated by AKT signaling. In conclusion, Shh () signaling acts as a macrophage chemoattractant via a Smo ()-dependent mechanism during gastric epithelial regeneration in response to injury.

### Excerpts from full text:

... ite chamber (Fig. 9A). Collection of conditioned media from the chamber with organoid/ILC2 co-cultures revealed that histamine-induced significant secretion of Shh (
) that was blocked by Smo (
) inhibitor vismodegib (Fig. 9B). Similarly, IL-33 (Fig. 9C) and IL-13 Fig. 9D) secretion was induced by histamine, a response that was also blocked by vismod ...





![](_page_41_Figure_0.jpeg)

# STRING **Textmining viewer**

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Pub Med

![](_page_42_Picture_8.jpeg)

... re tested at 2x and 8x MIC of each compound. The enzymes involved in de novo tryptophan biosynthesis are encoded on the trp operon PMID:33078454 (5'-3'): trpE, Rv1610, trpC, trpB, trpA. To confirm that compounds 1, 2 and 3, target biological components of the tryptophan biosynthesis, and more specifically tryptophan synthase, the MIC of M ...

PMID:31311884

..., representing 4% of the genome, five categories were equally represented with 3 genes each: energy metabolism (glgA, lpdA, and glmS), amino acid biosynthesis (trpA, trpB, and aroL), DNA replication and repair (nrdA, recA, and dnaQ), type III secretion (mcsC, CTL0085, and CTL0043), and translation (pheT, cysS, and thrS). Of ...

PMID:22086606

... T to generate the RP state FAD\*...TrpB \*via FAD\*...TrpA could basically still occur. However, without the terminal TrpC, the photo-generated radicals on FAD and TrpA/TrpB are not sufficiently spatially separated for stable charge separation on a longer time scale. Thus, efficient backward ET and radical recombination would I ...

![](_page_43_Figure_5.jpeg)

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### normalized names

![](_page_43_Picture_8.jpeg)

... re tested at 2x and 8x MIC of each compound. The enzymes involved in de novo tryptophan biosynthesis are encoded on the trp operon PMID:33078454 (5'-3'): trpE, Rv1610, trpC, trpB, trpA. To confirm that compounds 1, 2 and 3, target biological components of the tryptophan biosynthesis, and more specifically tryptophan synthase, the MIC of M ...

..., representing 4% of the genome, five categories were equally represented with 3 genes each: energy metabolism (glgA, lpdA, and glmS), PMID:31311884 amino acid biosynthesis (trpA, trpB, and aroL), DNA replication and repair (nrdA, recA, and dnaQ), type III secretion (mcsC, CTL0085, and CTL0043), and translation (pheT, cysS, and thrS). Of ...

... T to generate the RP state FAD\*...TrpB \*via FAD\*...TrpA could basically still occur. However, without the terminal TrpC, the photo-generated PMID:22086606 radicals on FAD and TrpA/TrpB are not sufficiently spatially separated for stable charge separation on a longer time scale. Thus, efficient backward ET and radical recombination would I ...

trpA and trpB are subunits of the tryptophan synthase enzyme. Studies have reported inhibitors that compete with IGP for the active site of trpA, bind at the trpA:trpB interface, and interact with the hydrophobic intermolecular indole channel in trpB. Mutations in trpA have been identified in various Chlamydia trachomatis strains, suggesting its involvement in organotropism. The trpA:trpB communication domain and nonsynonymous mutations have been analyzed in clinical strains. Additionally, trpA and trpB are components of the tryptophan biosynthesis pathway and are part of the trp operon. Furthermore, there is an ET step between trpB and trpA in the tryptophan synthase enzyme.

### openAl chat (gpt-3.5-turbo-1106)

![](_page_44_Figure_7.jpeg)

### GPT:

- Negligible cost for non programmatic access with user trigger
- We do not want GPT to inject knowledge
- Small models perform well at this task
- Don't overwhelm the model with text
- Frustrating to read, as there is no source

trpA and trpB are subunits of the tryptophan synthase enzyme. Studies have reported inhibitors that compete with IGP for the active site of trpA, bind at the trpA:trpB interface, and interact with the hydrophobic intermolecular indole channel in trpB. Mutations in trpA have been identified in various Chlamydia trachomatis strains, suggesting its involvement in organotropism. The trpA:trpB communication domain and nonsynonymous mutations have been analyzed in clinical strains. Additionally, trpA and trpB are components of the tryptophan biosynthesis pathway and are part of the trp operon. Furthermore, there is an ET step between trpB and trpA in the tryptophan synthase enzyme.

![](_page_46_Picture_2.jpeg)

trpA and trpB are subunits of the tryptophan synthase enzyme. Studies have reported inhibitors that compete with IGP for the active site of trpA, bind at the trpA:trpB interface, and interact with the hydrophobic intermolecular indole channel in trpB. Mutations in trpA have been identified in various Chlamydia trachomatis strains, suggesting its involvement in organotropism. The trpA:trpB communication domain and nonsynonymous mutations have been analyzed in clinical strains. Additionally, trpA and trpB are components of the tryptophan biosynthesis pathway and are part of the trp operon. Furthermore, there is an ET step between trpB and trpA in the tryptophan synthase enzyme.

trpA and trpB are subunits of the tryptophan synthase enzyme.

Additionally, trpA and trpB are components of the tryptophan biosynthesis pathway and are part of the trp operon

Studies have reported inhibitors that compete with IGP for the active site of trpA

bind at the trpA:trpB interface, and interact with the hydrophobic intermolecular indole channel in trpB

Mutations in trpA have been identified in various Chlamydia trachomatis strains

suggesting its involvement in organotropism

The trpA:trpB communication domain and nonsynonymous mutations have been analyzed in clinical strains Furthermore, there is an ET step between trpB and trpA in the tryptophan synthase enzyme.

### Split into clauses

![](_page_47_Figure_9.jpeg)

The enzymes involved in de novo tryptophan biosynthesis are encoded on the trp operon (5'-3'): trpE, Rv1610, trpC, trpB, trpA PMID:33078454

five categories were equally represented with 3 genes each: energy metabolism (glgA, lpdA, and glmS), amino acid biosynthesis (trpA, trpB, and aroL) PMID:31311884

the photo-generated radicals on FAD and TrpA/TrpB are not sufficiently spatially separated for stable charge separation on a longer time scale. PMID:22086606

> [-0.2, 3.8, 2.0, -2.1] [6.6, -4.1, -6.0, 0.1] [-0.2, 2.0, 0.1, 0.3]

![](_page_48_Figure_4.jpeg)

### embedding

The enzymes involved in de novo tryptophan biosynthesis are encoded on the trp operon (5'-3'): trpE, Rv1610, trpC, trpB, trpA PMID:33078454

five categories were equally represented with 3 genes each: energy metabolism (glgA, lpdA, and glmS), amino acid biosynthesis (trpA, trpB, and aroL) PMID:31311884

PMID:22086606 the photo-generated radicals on FAD and TrpA/TrpB are not sufficiently spatially separated for stable charge separation on a longer time scale.

> [-0.2, 3.8, 2.0, -2.1] [6.6, -4.1, -6.0, 0.1][-0.2, 2.0, 0.1, 0.3]

![](_page_49_Figure_4.jpeg)

### embedding

trpA and trpB are subunits of the tryptophan synthase enzyme (1,2). Studies have reported inhibitors that compete with IGP for the active site of trpA (2), bind at the trpA:trpB interface, and interact with the hydrophobic intermolecular indole channel in trpB (2). Mutations in trpA have been identified in various Chlamydia trachomatis strains (1), suggesting its involvement in organotropism. The trpA:trpB communication domain and nonsynonymous mutations have been analyzed in clinical strains (1,3). Additionally, trpA and trpB are components of the tryptophan biosynthesis pathway and are part of the trp operon (1). Furthermore, there is an ET step between trpB and trpA in the tryptophan synthase enzyme (1).

![](_page_49_Figure_10.jpeg)

![](_page_50_Picture_0.jpeg)

![](_page_50_Picture_1.jpeg)

### Relevant publications mentioning your query species (Homo sapiens):

PMID:31756206 Expression profile of sonic hedgehog () signaling-related molecules in basal cell carcinoma. V Kim HS, Kim YS, Lee C, Shin MS, Kim JW, Jang BG PLoS One. 14(11):e0225511 2019.

### Abstract:

Basal cell carcinoma (BCC) is the most common human cancer, characterized by aberrant activation of the hedgehog (HH) signaling pathway resulting from mutations in the patched 1 (PTCH1) or smoothened (SMO) genes. In the present study, to uncover the expression profile of HH signaling-related molecules, we thoroughly examined the mRNA and protein expression levels of six molecules including GLI1, GLI2, PTCH1, PTCH2 (), SHH (), and SMO in BCC and various other cutaneous tumors. Real-time PCR analysis demonstrated that BCC showed remarkably enhanced mRNA expression of all HH molecules, except SMO compared to other skin tumors. However, immunohistochemical analysis revealed that only GLI1 protein was specifically upregulated in BCC, while the other HHrelated proteins did not show any significant differences between the tumors. Notably, other skin malignancies such as squamous cell carcinoma, sebaceous carcinoma, and malignant melanoma showed no GLI1 expression and there was no difference in GLI1 expression between the BCC subtypes. In addition, GLI1 and

![](_page_51_Picture_0.jpeg)

![](_page_51_Figure_1.jpeg)

ltaE

dh

![](_page_52_Picture_0.jpeg)

![](_page_52_Figure_1.jpeg)

ltaE

dh

![](_page_53_Picture_2.jpeg)

- Inferential Overreach

![](_page_54_Picture_3.jpeg)

- Inferential Overreach
- Paper mills

![](_page_55_Picture_4.jpeg)

![](_page_55_Picture_7.jpeg)

- Inferential Overreach
- Paper mills
- Cuts in primary curation

![](_page_56_Picture_5.jpeg)

![](_page_56_Picture_8.jpeg)

- Inferential Overreach
- Paper mills
- Cuts in primary curation
- Web crawlers

![](_page_57_Picture_6.jpeg)

# ACKNOWLEDGMENTS

![](_page_58_Picture_1.jpeg)

![](_page_58_Picture_2.jpeg)

Universität Zürich<sup>∪zH</sup>

![](_page_58_Figure_4.jpeg)

![](_page_58_Picture_5.jpeg)

**Tao Fang** 

**Radja Hachilif** 

### **KU / NNF CPR**

### Qingyao Huang **Dawei Hu**

**Christian von Mering** 

![](_page_58_Picture_11.jpeg)

UNIVERSITY OF

COPENHAGEN

![](_page_58_Picture_12.jpeg)

Uni. Turku

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