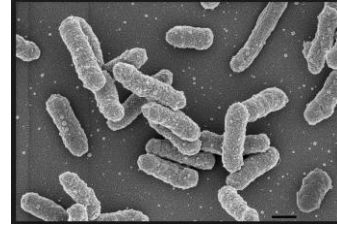


Exploring gene expression in *Yersinia pestis*



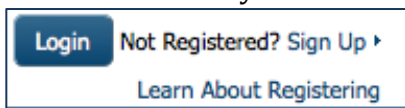
In 541-542, a plague swept in and killed 40% of the population in Europe. Almost 100 years later, a similar plague, infamously referred to as “The Black Death” resulted in the deaths of an estimated 75 to 200 million people, or 30% of the European population, with the epidemic peaking in Europe in the years 1346–53[1]. In 1894, Alexandre Yersin, a Swiss/French physician and bacteriologist from the Pasteur Institute, discovered the bacterium that caused plague, and the organism was named *Yersinia pestis* in his honor in 1967[2]. This bacterium is small, rod-shaped, and is able to infect both fleas and mammals. The bacterium must survive in both hosts to infect humans, as in most cases it is transmitted by the bite of an infected flea.

Fleas have a body temperature of 26°C, while the human body temperature is 37°C. Scientists wanted to explore what genes *Y. pestis* turned on (called up-regulated) and turned off (called down-regulated) at these two temperatures. They looked specifically at a strain of *Y. pestis* that they had made mutant at one critical gene, called Lpp, which was essential for survival in the mammal host[3].

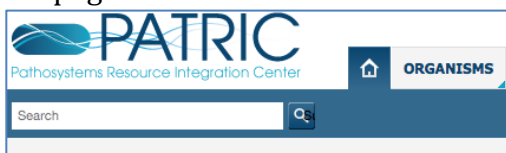
We will examine this experiment and, using PATRIC tools, we will explore the up- and down-regulation of genes at the two different temperatures.

I. Exploring an experiment

1. Login to the PATRIC website so that you can use your workspace in the downstream analysis.



2. On the PATRIC homepage (patricbrc.org), open the Organisms tab at the top of the page.



3. When the tab opens to reveal the box listing the names of pathogens, click on *Yersinia*.

ORGANISMS DATA SERVICES TOOLS

Genera Containing NIAID Category A-C / Emerging / Re-emerging Bacteria Pathogens

- Bacillus
- Bartonella
- Borrelia
- Bruceella
- Burkholderia
- Campylobacter
- Chlamydomphila
- Clostridium
- Coxiella
- Ehrlichia
- Escherichia
- Francisella
- Helicobacter
- Listeria
- Mycobacterium
- Rickettsia
- Salmonella
- Shigella
- Staphylococcus
- Streptococcus
- Vibrio
- Yersinia**

Complete Lists of Bacteria:

- All Bacteria
- All Archaea

4. This will take you to the landing page for *Yersinia*, which summarizes all the information that PATRIC has about the genus, including the number of genomes, experiments associated with it, publications on it, and tools that can analyze the available data sorted at that taxonomic level.

Bacteria > Proteobacteria > Gammaproteobacteria > Enterobacteriales > Enterobacteriaceae > Yersinia

Data Overview Tutorial > Download genome data >

Overview Taxonomy Phylogeny Genome List Feature Table Specialty Genes Protein Families Pathways Transcriptomics Interactions Diseases Literature

Search Tools

- Genome Finder
- Feature Finder
- Comparative Pathway Tool
- Protein Family Sorter

Experiment Summary

Transcriptomics from GEO	81
Transcriptomics from ArrayExpress	53
Proteomics from PRIDE	0
Structure from NCBI	290
Protein Protein Interaction from IntAct	4060

more >

Recent PubMed Articles

Taxonomy Summary

Taxonomy ID	629
Lineage	cellular organisms > Bacteria > Proteobacteria > Gammaproteobacteria > Enterobacteriales > Enterobacteriaceae > Yersinia
External Links	Immune Epitope Database and Analysis Resource
Summary Terms	Click on number to view genomes associated with term (see PATRIC FAQs)
Genome Status	WGS (130), Complete (44)
Reference Genome	Representative (12), Reference (2)
Antimicrobial Resistance	
Antimicrobial Resistance Evidence	
Isolation Country	Peru (60), USA (19), show all 128 genomes
Host Name	Human, Homo sapiens (38), Black rat, Rattus rattus (16), show all 110 genomes
Disease	Bubonic plague (83), Pneumonic plague (60), show all 217 genomes
Collection Date	2010 (45), 2009 (13), show all 100 genomes
Completion Date	2012 (73), 2013 (24), show all 174 genomes

5. Find the tab across the top that is labeled “Transcriptomics” and click on it.

Bacteria > Proteobacteria > Gammaproteobacteria > Enterobacteriales > Enterobacteriaceae > Yersinia

Overview Taxonomy Phylogeny Genome List Feature Table Specialty Genes Protein Families Pathways **Transcriptomics**

6. This will take you to the landing page for the transcriptomics experiments that are available through the PATRIC resource. The left side has a filter to help people find specific experiments, and on the right is a table that summarizes the experiments available.

The list below provides all of the available transcriptionomics experiments and associated metadata at this taxonomic level. The list of experiments can be filtered by metadata or keyword. To learn more about PATRIC's transcriptionomics data and associated metadata, see [Transcriptionomics FAQs](#).

Filter By: Clear All

6 experiments found

Title	Comparisons	Genes	PubMed	Link Out	Organism	Strain	Gene Modifc
<input type="checkbox"/> Comparative transcriptomics in <i>Yersinia pestis</i> : a global view of environmental modula...	24	3655	17963531	GSE5279	<i>Yersinia pestis</i>	201	fut,ompR...
<input type="checkbox"/> Gene expression analysis of <i>Yersinia Pestis</i> temperature shift.	12	28357	22479471	GSE30634	<i>Yersinia pestis</i> , <i>Yersinia ps...</i>	CO92, PB1...	
<input type="checkbox"/> Gene expression profiles of wild-type <i>Yersinia pestis</i> CO92 and its Braun lipoprotein m...	2	2655	20508723	GSE19840	<i>Yersinia pestis</i>	CO92	LPP
<input type="checkbox"/> Involvement of the post-transcriptional regulator Hfq in <i>Yersinia pestis</i> virulence	1	3655	2704395	GSE15579	<i>Yersinia pestis</i>	201	Hfq
<input type="checkbox"/> KIMS intracellular expression profiling	6	2834	20566923	GSE22168	<i>Yersinia pestis</i>	KIMS	
<input type="checkbox"/> Phenotypic and transcriptional analysis of the osmotic regulator OmpR in <i>Yersinia pestis</i>	1	3704	21345179	GSE26601	<i>Yersinia pestis</i>	201	ompR

7. Find the experiment with the title “Gene expression profiles of wild-type *Yersinia pestis* CO92 and its Braun lipoprotein mutant at flea and human temp” and click the check box in front of it.

Title

Comparative transcriptomics in *Yersinia pestis*: a global view of environmental modula...

Gene expression analysis of *Yersinia Pestis* temperature shift.

Gene expression profiles of wild-type *Yersinia pestis* CO92 and its Braun lipoprotein m...

Involvement of the post-transcriptional regulator Hfq in *Yersinia pestis* virulence

KIMS intracellular expression profiling

Phenotypic and transcriptional analysis of the osmotic regulator OmpR in *Yersinia pestis*

8. Next, in the header across the top of the table in the category called “View” click on the “Gene List” tool.

6 experiments found

Workspace View

Add Experiment(s) Gene List

9. This will take you to the Transcriptionomics Gene list for the experiment that you chose. There is a filter on the right side, and a table that will show the results of the filter on the left. When the page opens up and before any actions are taken, all genes available in the experiment are listed in the table.

Transcriptionomics Gene List

The gene list below provides details about gene regulation across a given set of experiments and comparisons. The gene list can be filtered based on regulation within each comparison as well as by locus tag and keyword. To learn more, see our [Transcriptionomics Gene List FAQs](#).

Filter By: Table Heatmap

2 comparison(s) in 1 experiment(s)

7655 genes found

Workspace View Download Tools Columns Help

Add Feature(s) FASTA DNA FASTA Pathway Summary Multiple Seq Alignment Show/Hide Default PATRIC

Genome Name	PATRIC ID	RefSeq Locus T	Alt Locus Tag	Gene Symbol	Product Description	Comparisons	Up	Down
<input type="checkbox"/> <i>Yersinia pestis</i> CO92	fig 214092...	YPO0001	VBIYerPes7...		Flavoprotein MicC	2	0	2
<input type="checkbox"/> <i>Yersinia pestis</i> CO92	fig 214092...	YPO0002	VBIYerPes7...	asnC	Regulatory protein AsnC	2	1	1
<input type="checkbox"/> <i>Yersinia pestis</i> CO92	fig 214092...	YPO0003	VBIYerPes7...	asnA	Aspartate-ammonia ligase (...)	2	1	0
<input type="checkbox"/> <i>Yersinia pestis</i> CO92	fig 214092...	YPO0004	VBIYerPes7...	yleM	FIG01221722: hypothetical p...	2	1	1
<input type="checkbox"/> <i>Yersinia pestis</i> CO92	fig 214092...	YPO0005	VBIYerPes7...		Putative regulator protein	2	2	0
<input type="checkbox"/> <i>Yersinia pestis</i> CO92	fig 214092...	YPO0006	VBIYerPes7...	trkD	Kup system potassium uptak...	2	2	0
<input type="checkbox"/> <i>Yersinia pestis</i> CO92	fig 214092...	YPO0007	VBIYerPes7...		Ribose ABC transport system...	2	0	2
<input type="checkbox"/> <i>Yersinia pestis</i> CO92	fig 214092...	YPO0008	VBIYerPes7...	rbkK	Ribokinase (EC 2.7.1.15)	2	0	2
<input type="checkbox"/> <i>Yersinia pestis</i> CO92	fig 214092...	YPO0009	VBIYerPes7...		Permeases of the major facil...	2	1	1
<input type="checkbox"/> <i>Yersinia pestis</i> CO92	fig 214092...	YPO0010	VBIYerPes7...		Transcriptional regulator, Gnt...	2	2	0
<input type="checkbox"/> <i>Yersinia pestis</i> CO92	fig 214092...	YPO0011	VBIYerPes7...		Mobile element protein	2	2	0
<input type="checkbox"/> <i>Yersinia pestis</i> CO92	fig 214092...	YPO0012	VBIYerPes7...	mobB	Molybdopterin-guanine dinuc...	2	1	1
<input type="checkbox"/> <i>Yersinia pestis</i> CO92	fig 214092...	YPO0013	VBIYerPes7...	mobA	Molybdopterin-guanine dinuc...	2	1	1
<input type="checkbox"/> <i>Yersinia pestis</i> CO92	fig 214092...	YPO0013a	VBIYerPes7...		Protein yihD	2	1	1
<input type="checkbox"/> <i>Yersinia pestis</i> CO92	fig 214092...	YPO0014	VBIYerPes7...		YiE protein, a ser/thr kinase...	2	2	0
<input type="checkbox"/> <i>Yersinia pestis</i> CO92	fig 214092...	YPO0015	VBIYerPes7...	dsbA	Periplasmic thiol-disulfide int...	2	2	0
<input type="checkbox"/> <i>Yersinia pestis</i> CO92	fig 214092...	YPO0017	VBIYerPes7...	polA	DNA polymerase I (EC 2.7.7.7)	2	2	0

Filter by Genome:

Filter by one or more keywords or locus tags

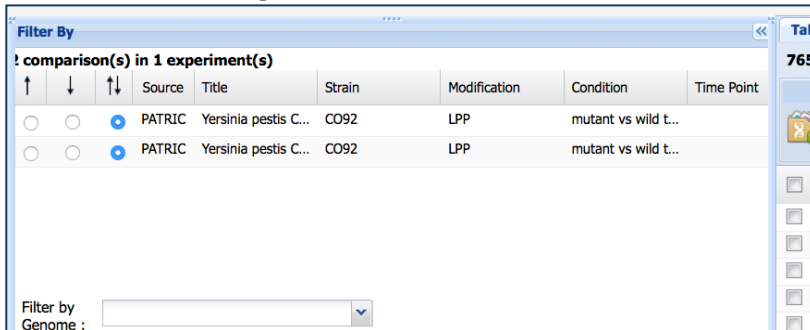
e.g. VBIYerPes7_0001, Transcription factor

Filter by |Log Ratio|:

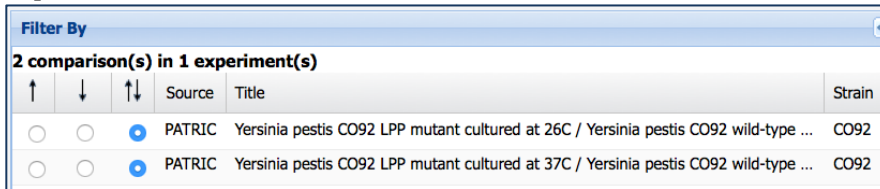
Filter by |Z-score|:

Filter

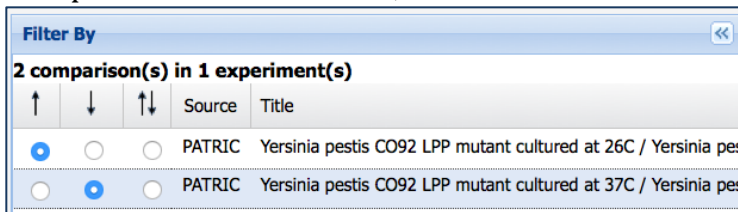
10. To find the experimental conditions and see the two different temperatures, you will first need to expand the filter box by grabbing the right edge with your cursor and then increasing the width of the box.



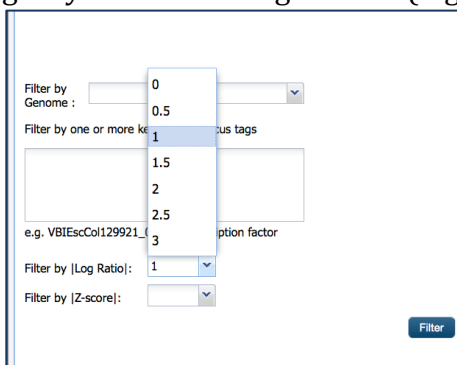
11. Then you will have to grab the right edge of the column header called “Title” and use your cursor to increase the width of that box. Then you will be able to see which experimental condition was done at 26°C, and which at 37°C.



12. To see which genes are up-regulated at 26°C and down-regulated at 37°C, click the up arrow on the 26C row, and the down arrow on the row for 37C.



13. You will want to see which genes are significantly expressed. To do this, look at the bottom of the filter, and where it says “Filter by |Log Ratio|:” there is an arrow. Click the arrow and you will see a box with numbers in it. Choose 1, and this will give you a fold-change of two (log2). Then click “Filter”.



14. This will filter the table to show that there are 38 genes that meet those criteria. These genes are up-regulated at 26C (the temperature of the flea host) and down regulated at 37C (the temperature of the human host).

Genome Name	PATRIC ID	RefSeq Locus Tag	Alt Locus Tag	Gene Symbol	Product Description
Yersinia pestis CO92	fig1214092.21...	YPO0163	VBIYerPes784...		TsgA protein homolog
Yersinia pestis CO92	fig1214092.21...	YPO0222	VBIYerPes784...	rplE	LSU ribosomal protein L5p (L11e)
Yersinia pestis CO92	fig1214092.21...	YPO0224	VBIYerPes784...	rplF	LSU ribosomal protein L6p (L9e)
Yersinia pestis CO92	fig1214092.21...	YPO0444	VBIYerPes784...	nadR	NadR transcriptional regulator / ...
Yersinia pestis CO92	fig1214092.21...	YPO1142	VBIYerPes784...	modF	Putative molybdenum transport A...
Yersinia pestis CO92	fig1214092.21...	YPO1168	VBIYerPes784...	betT	High-affinity choline uptake prote...
Yersinia pestis CO92	fig1214092.21...	YPO1326	VBIYerPes784...		TrxA_Potassium channel-family p...

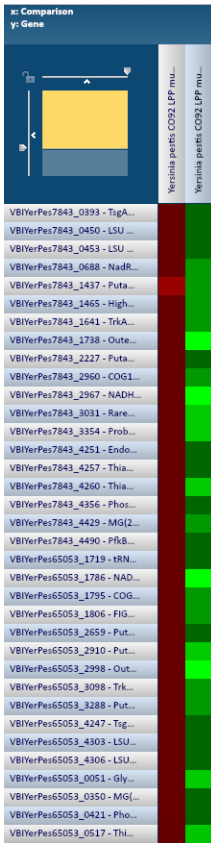
15. To see all the genes, you will need to scroll down to the bottom of the table and resize it to 38 and hit return.

Page 1 of 2 Show 38 per page

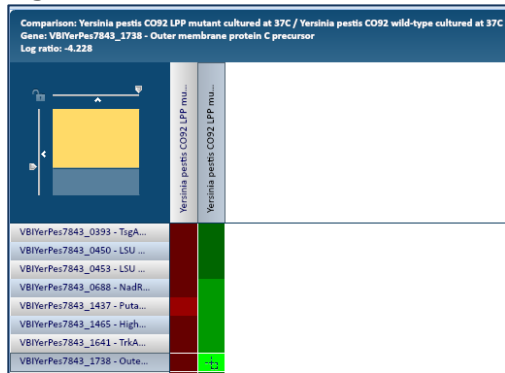
16. To visualize these genes, PATRIC provides a heatmap view. To see the genes, click on the “Heatmap” tab.

Table Heatmap
38 genes found
Flip Axis Heatmap Color

17. You will notice that there are two columns. One is varying degrees of red, and the other is varying degrees of green. The red color signifies up-regulation, so this is the 26C column. Green is down-regulation (37C).

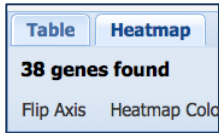


18. To get more details on specific genes, you can mouse a single cell of interest. I moused over a light green box in the 37C. When you do that, you can see details on that gene in the blue band at the top of the heatmap. In this example, that gene is the “Outer membrane protein C precursor” that is strongly down-regulated with a log ratio of -4.228.

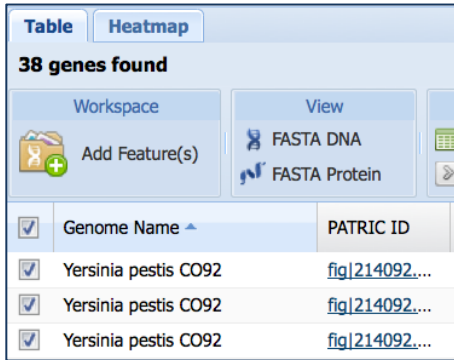


II. Discovering if genes of interest have any functional significance.

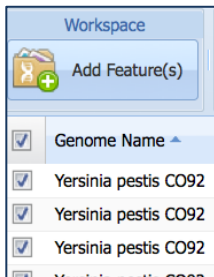
1. From the previous example, return to the table by clicking on the Table tab.



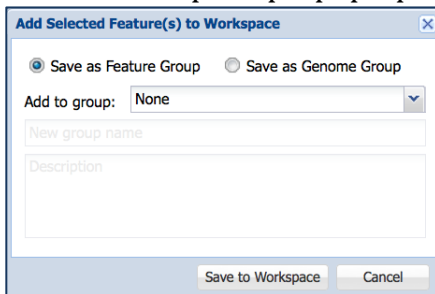
2. In the column titled "Genome Name", click on the box to the left of it select all the genes



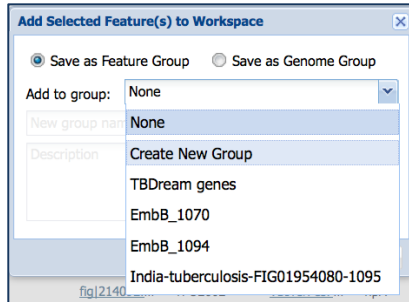
3. We need to save these features to a workspace. Click on the "Add Feature" and folder.



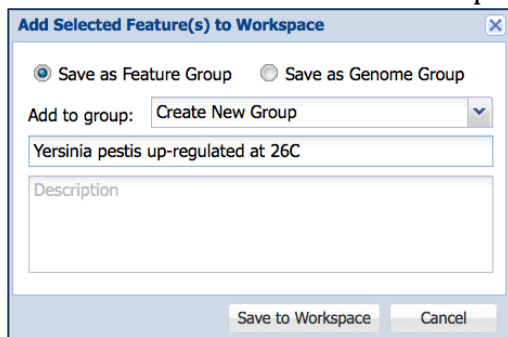
4. This will open up a pop-up window that allows you to save the group.



5. Select the "Create New Group" option.



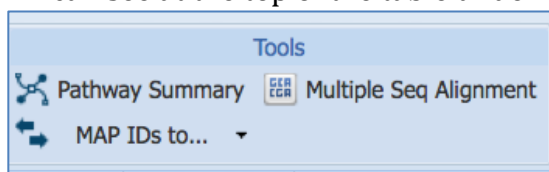
6. Name the group and click “Save to Workspace”. Now that data is saved and you can use a number of tools to explore it.



7. This data is now safely in the Workspace, but we can also examine it here from this table. To look at the data with the Pathway tool, you first need to select all the features in this table again.

Table		Heatmap	
38 genes found			
Workspace		View	
Add Feature(s)		FASTA DNA	
		FASTA Protein	
<input checked="" type="checkbox"/>	Genome Name		PATRIC ID
<input checked="" type="checkbox"/>	Yersinia pestis CO92		fig 214092...
<input checked="" type="checkbox"/>	Yersinia pestis CO92		fig 214092...
<input checked="" type="checkbox"/>	Yersinia pestis CO92		fig 214092...

8. Once the genes are selected, you can use the Pathway Summary tool that you can see at the top of the table under the Tools heading. Click on that.



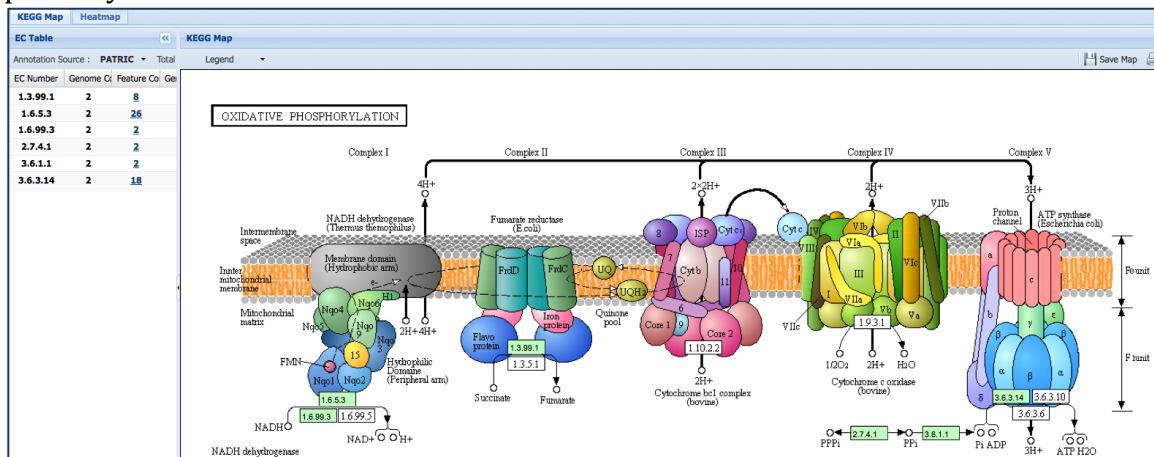
9. This will return a table that shows you the list of pathways that the genes you selected are involved in.

Pathway Summary

Out of 38 genes selected, 5 genes found in 5 pathways

Pathway Name	# of Genes Selected	# of Genes Annotated
Thiamine metabolism	1	20
Oxidative phosphorylation	2	58
Glycerolipid metabolism	1	36
Nitrogen metabolism	2	75
Nicotinate and nicotinamide metabolism	1	41

10. Clicking on any of the pathway names in the table will take you to a KEGG map that shows how many the genes you selected acted as enzymes are involved in that pathway.



III. Exploring specific genes that are significantly expressed in an experiment

1. In the heatmap view above we saw that a gene called “Outer membrane protein C precursor” was strongly down-regulated at 37°C. Return to the workspace by clicking on Workspace at the top of the page.

Welcome Workshop
 Not Workshop? Logout »
 My Account »

WORKSPACE: HOME »

2. We’re going to return to the group created earlier, so double-click on the name Feature Groups as you did before.

- ↑ Parent Folder
- Experiment Groups
- Experiments
- Feature Groups**
- Genome Groups

3. Once again, double-click on the name you selected for your group. I called mine “Yersinia pestis up-regulated at 26C”.

Name	Size	Owner	Created
Parent Folder			
EmbB_1070	160 features	Workshop	4/14/15, 3:56 PM
EmbB_1094	90 features	Workshop	4/14/15, 3:57 PM
India-tuberculosis-FIG01954080-1095	125 features	Workshop	4/14/15, 7:33 PM
TBDream genes	1348 features	Workshop	4/14/15, 3:08 PM
Yersinia pestis genes up-regulated at 37C	43 features	Workshop	4/17/15, 6:22 PM
Yersinia pestis up-regulated at 26C	58 features	Workshop	4/17/15, 3:49 PM
Yersinia pestis up-regulated at 26C Arlington	38 features	Workshop	5/2/15, 6:46 PM

Yersinia pestis up-regulated at 26C

Type: feature_group
 Owner: Workshop@patricbrc.org
 Created: 4/17/15, 3:49 PM
 Path: /Workshop@patricbrc.org/home/Feature Groups/Yersinia pestis up-regulated at 26C

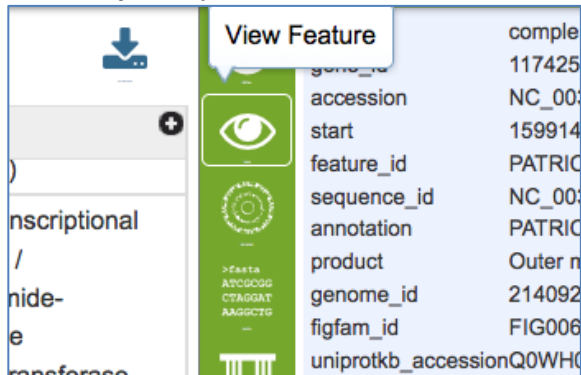
4. Scroll down until you see the gene called “Outer membrane protein C precursor” and click on it once to select it.

Genome Name	PATRIC ID	RefSeq Locus Tag	Alt Locus Tag	Gene Symbol	Product
Yersinia pestis CO92	fig 214092.21.peg.688	YPO0444	VBIYerPes7843_0688	nadR	NadR transcriptional regulator / Nicotinamide-nucleotide adenyltransferase, NadR family (EC 2.7.7.1) / Ribosylnicotinamide kinase (EC 2.7.1.22)
Yersinia pestis CO92	fig 214092.21.peg.1437	YPO1142	VBIYerPes7843_1437	modF	Putative molybdenum transport ATP-binding protein modF
Yersinia pestis CO92	fig 214092.21.peg.1465	YPO1168	VBIYerPes7843_1465	betT	High-affinity choline uptake protein BetT
Yersinia pestis CO92	fig 214092.21.peg.1641	YPO1326	VBIYerPes7843_1641		TrkA, Potassium channel-family protein
Yersinia pestis CO92	fig 214092.21.peg.1738	YPO1411	VBIYerPes7843_1738	ompF	Outer membrane protein C precursor

5. When you click on it, the description panel to the right shows information related to the gene. The informative band that separates the table from the description panel also shows tools that you can use with your selection.

<p>Product L6p (L9e)</p> <p>NadR transcriptional regulator / Nicotinamide-nucleotide adenyltransferase, NadR family (EC 2.7.7.1) / Ribosylnicotinamide kinase (EC 2.7.1.22)</p> <p>Putative molybdenum transport ATP-binding protein modF</p> <p>High-affinity choline uptake protein BetT</p> <p>TrkA, Potassium channel-family protein</p> <p>Outer membrane protein C precursor</p>	<p>location complement(1599145..1600227)</p> <p>gene_id 1174252</p> <p>accession NC_003143</p> <p>start 1599145</p> <p>feature_id PATRIC.214092.21.NC_003143.CDS.159</p> <p>sequence_id NC_003143</p> <p>annotation PATRIC</p> <p>product Outer membrane protein C precursor</p> <p>genome_id 214092.21</p> <p>figfam_id FIG00633937</p> <p>uniprotkb_accession Q0WH04</p> <p>gi 218928559</p> <p>gene ompF</p> <p>p2_feature_id 108115791</p> <p>pos_group NC_003143:1599145:-</p> <p>alt_locus_tag VBIYerPes7843_1738</p> <p>na_length 1083</p> <p>strand -</p> <p>refseq_locus_tag YPO1411</p> <p>segments 1599145..1600227</p> <p>feature_type CDS</p> <p>taxon_id 214092</p> <p>protein_id YP_002346434.1</p> <p>aa_length 360</p> <p>seed_id fig 214092.21.peg.1738</p> <p>end 1600227</p> <p>genome_name Yersinia pestis CO92</p> <p>public true</p> <p>owner PATRIC</p>
--	---

6. Mouse over the icons in the band until you see one that says “View Feature” (it’s the eyeball). Click on that.



7. This will take you to the landing page for that gene where all the information available for it in PATRIC is summarized, including its different gene identifiers, tools and resources that can be used to examine this gene, and any publications that might have been written about it.

Bacteria • Proteobacteria • Gammaproteobacteria • Enterobacteriales • Enterobacteriaceae • Yersinia • Yersinia pestis CO92 • fig | 214092.21.peg.1738 | YPO1411 | VBIYerPes7843_1738 | ompF | Outer membrane protein C precursor ⓘ

Overview Genome Browser Compare Region Viewer Pathways Transcriptomics Interactions Correlated Genes Literature

Add PATRIC Feature to Workspace

View NT Sequence
View AA Sequence

External Tools
The SEED Viewer
NCBI CDD Search
STRING: Protein-Protein Interactions
STITCH: Chemical-Protein Interactions

Recent PubMed Articles
• 2013 Nov
Outer membrane proteins all and OmpF of Yersinia pestis are involved in the adhesion of T3-related

Gene ID: **PATRIC ID:** fig|214092.21.peg.1738 **RefSeq:** YPO1411 **Alt Locus Tag:** VBIYerPes7843_1738
Protein ID: **RefSeq:** YP_002346434.1 **UnitProt:** Q0WH04 22 IDs are mapped

ompF

CDS

Annotation	Locus Tag	Start	End	NT Length	AA Length	Product
PATRIC	VBIYerPes7843_1738	1599145	1600227	1083	360	Outer membrane protein C precursor
RefSeq	YPO1411	1599145	1600227	1083	360	Outer membrane porin protein F

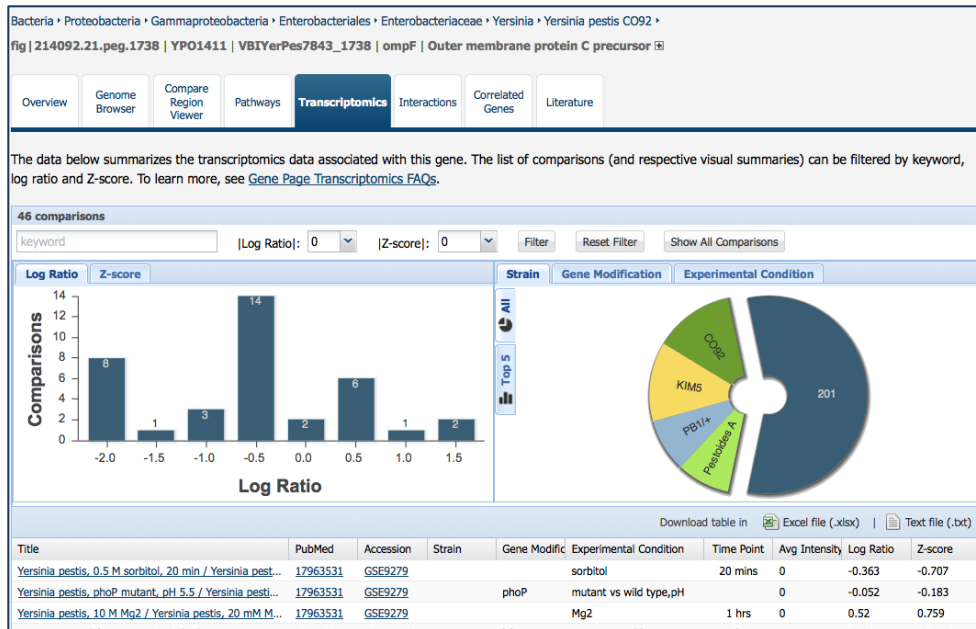
Functional Properties

GO Assignments	-
EC Assignments	-
FIGfam Assignments	FIG00633937

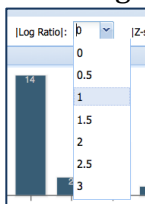
8. Along the top panel, click on the tab called “Transcriptomics.”



9. This takes you to all the experimental evidence for these gene that is available in the PATRIC website. The page is broken down to show the expression pattern for the gene across all the available experiments, a list of those experiments, and a circular diagram that can display different experimental conditions. Above the diagrams you will see some tools that allow you to filter the experiments.



10. As in the example above, we are going to filter the experiments displayed by the level of expression. Next to |Log Ratio|: there is an arrow. Click the arrow and you will see a box with numbers in it. Choose 1, and this will give you a fold-change of two (log2).

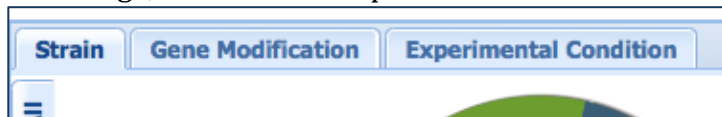


11. This will set the log ratio to 1, but to see the results you have to click the “Filter” button

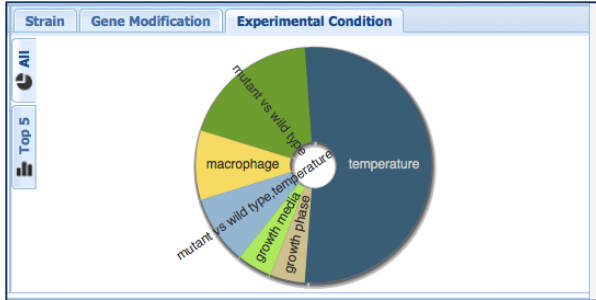
46 comparisons

keyword |Log Ratio|: 1 |Z-score|: 0 Filter

12. This will filter the table and the graphs to show those results. To see a visual representation of the experimental conditions where this gene had this fold-change, click on the “Experimental Condition” button above the bar graph.



13. This will show you that the majority of the experimental conditions where this gene was significantly up- or down-regulated dealt with temperature.



14. You can also see that in the table that has been filtered to match the log ratio selection. You can also see the log ratio values. Note that many of them are negative, as we saw in the initial experiment we were looking at.

Title	PubMed	Accession	Strain	Gene Modific	Experimental Condition	Time Point	Avg Intensity	Log Ratio	Z-score
Yersinia pestis, ompR mutant (high osmolarity), 30 ...	17963531	GSE9279		ompR	mutant vs wild type	30 mins	0	-4.037	-8.279
Yersinia pestis, Exponential growth phase, TMH / Ye...	17963531	GSE9279			growth media		0	-1.979	-2.294
Yersinia pestis, grown at 37 C / Yersinia pestis	17963531	GSE9279			temperature	3 hrs	0	-2.619	-2.323
Yersinia pestis, ompR mutant, high salinity, 30 min / ...	17963531	GSE9279		ompR	mutant vs wild type	30 mins	0	-1.68	-3.659
ompR null mutant (ompR) / WT	21345178	GSE26601		ompR	mutant vs wild type		0	-4.533	-6.363
Yersinia pestis, 10 degree, 1 hr / Yersinia pestis, bef...	17963531	GSE9279			temperature	1 hrs	0	1.573	1.398
Yersinia pestis CO92 LPP mutant cultured at 26C / Y...	20508723	GSE19840		LPP	mutant vs wild type,te...		0	1.006	1.106
Yersinia pestis, Exponential phase, TMH / Yersinia p...	17963531	GSE9279			growth phase		0	-1.073	-2.105
Yersinia pestis, phoP mutant, 10 M Mg2 / Yersinia p...	17963531	GSE9279		phoP	mutant vs wild type		0	-2.116	-1.8
Yersinia pestis, 45 degree, 10min / Yersinia pestis, 37...	17963531	GSE9279			temperature	10 mins	0	-1.575	-1.733
COW5 Total RNA extracted after 1 hour at 37 degr...	22479471	GSE30634			temperature	1 hrs	0	-1.9	-2.138
PBIB15 Total RNA extracted after 1 hour at 37 degr...	22479471	GSE30634			temperature	1 hrs	0	-1.639	-2.846
PBIB15 Total RNA extracted after 2 hours at 37 degr...	22479471	GSE30634			temperature	2 hrs	0	-1.998	-2.33
PBIB15 Total RNA extracted after 4 hours at 37 degr...	22479471	GSE30634			temperature	4 hrs	0	-1.698	-3.053
PBIB15 Total RNA extracted after 8 hours at 37 degr...	22479471	GSE30634			temperature	8 hrs	0	-1.925	-3.807
PesF Total RNA extracted after 2 hours at 37 degr...	22479471	GSE30634			temperature	2 hrs	0	-2.171	-4.669

15. To see what other genes have a similar expression pattern, scroll to the top of the page and select the Correlated Genes tab.

Bacteria · Proteobacteria · Gammaproteobacteria · Enterobacteriales · Enterobacteriaceae · Yersinia · Yersinia pestis CO92 · fig | 214092.21.peg.1738 | YPO1411 | VBIYerPes7843_1738 | ompF | Outer membrane protein C precursor

Overview Genome Browser Compare Region Viewer Pathways Transcriptomics Interactions **Correlated Genes** Literature

16. The page that returns will show you what genes have a similar expression pattern to the gene we chose, Outer membrane protein C precursor.

Bacteria · Proteobacteria · Gammaproteobacteria · Enterobacteriales · Enterobacteriaceae · Yersinia · Yersinia pestis CO92 · fig | 214092.21.peg.1738 | YPO1411 | VBIYerPes7843_1738 | ompF | Outer membrane protein C precursor

Overview Genome Browser Compare Region Viewer Pathways Transcriptomics Interactions **Correlated Genes** Literature

Correlation Cutoff: 0.4 Correlation: positive Filter

294 features found

Gene Name	PATRIC ID	Alt Locus Tag	RefSeq Locus Tag	Gene Symbol	Product Description	Correlation	Comparisons
Yersinia pestis CO92	fig 214092.21.peg.1738	VBIYerPes7843_1738	YPO1411	ompF	Outer membrane protein C precursor	1.000	46
Yersinia pestis CO92	fig 214092.21.peg.4151	VBIYerPes7843_4151	YPO0949		4-carboxymuconolactone decarboxylase (EC 4.1.1.44)	0.666	46
Yersinia pestis CO92	fig 214092.21.peg.3024	VBIYerPes7843_3024	YPO2278		Cell division inhibitor Shi22 (YerA-EC), curtsin ep...	0.678	46
Yersinia pestis CO92	fig 214092.21.peg.878	VBIYerPes7843_8878	YPO0623		Aspartate aminotransferase (EC 2.6.1.1)	0.655	46
Yersinia pestis CO92	fig 214092.21.peg.268	VBIYerPes7843_2768	YPO0516		FIG1220427: hypothetical protein	0.644	46
Yersinia pestis CO92	fig 214092.21.peg.1052	VBIYerPes7843_1052	YPO0800		Metallo-beta-lactamase superfamily protein PA0057	0.639	46
Yersinia pestis CO92	fig 214092.21.peg.1550	VBIYerPes7843_1550	YPO1255		FIG1220999: hypothetical protein	0.638	46
Yersinia pestis CO92	fig 214092.21.peg.879	VBIYerPes7843_8879	YPO0624		Putative membrane protein	0.629	46
Yersinia pestis CO92	fig 214092.21.peg.2630	VBIYerPes7843_2630	YPO2234	csfA	Carbon starvation protein A paralog	0.624	46
Yersinia pestis CO92	fig 214092.21.peg.4610	VBIYerPes7843_4610	YPO3516	mdh	Malate dehydrogenase (EC 1.1.1.37)	0.623	46
Yersinia pestis CO92	fig 214092.21.peg.2928	VBIYerPes7843_2928	YPO2311		Uncharacterized conserved protein	0.621	46
Yersinia pestis CO92	fig 214092.21.peg.3722	VBIYerPes7843_3722	YPO2362		FIG1220554: hypothetical protein	0.619	46
Yersinia pestis CO92	fig 214092.21.peg.3726	VBIYerPes7843_3726	YPO2361		Asp-tRNA ^{Asp} -Glu-tRNA ^{Gln} aminotransferase A subunit ...	0.619	46
Yersinia pestis CO92	fig 214092.21.peg.4152	VBIYerPes7843_4152	YPO0650		Putative metabolite transport protein	0.614	46
Yersinia pestis CO92	fig 214092.21.peg.4024	VBIYerPes7843_4024	YPO3529	cytQ	3'(2',5'-bisphosphate nucleotidase (EC 3.1.3.7)	0.611	46
Yersinia pestis CO92	fig 214092.21.peg.4150	VBIYerPes7843_4150	YPO0648		2-hydroxy-3-oxopropionate reductase (EC 1.1.1.60)	0.611	46
Yersinia pestis CO92	fig 214092.21.peg.248	VBIYerPes7843_248	YPO0027		probable haloperoxidase-like hydrolase STY3852	0.603	46

17. Notice that the default parameters are set to a correlation cutoff of 0.4, with positive correlation.

Correlation Cutoff: 0.4 Correlation: positive Filter

18. Click on the arrow next to positive and select “negative,” then hit filter.

Correlation: positive Filter
 positive
 negative

19. This will show you all the genes that are also negatively correlated with this gene.

Genome Name	PATRIC ID	Alt Locus Tag	RefSeq Locus Tag	Gene Symbol	Product Description	Correlation
Yersinia pestis CO92	fsj214592.21.pep.1197	YerPes7843_1197	YPO0921	pgk	Phosphoglycerate kinase (EC 2.7.2.3)	-0.400
Yersinia pestis CO92	fsj214592.21.pep.4514	YerPes7843_4514	YPO0983		FG01220178: hypothetical protein	-0.400
Yersinia pestis CO92	fsj214592.21.pep.2222	YerPes7843_2222	YPO0632	hlypK	ATP-dependent helicase HlypK	-0.401
Yersinia pestis CO92	fsj214592.21.pep.4114	YerPes7843_4114	YPO0616		FG01221499: hypothetical protein	-0.403
Yersinia pestis CO92	fsj214592.21.pep.1828	YerPes7843_1828	YPO1498		Putative exported protein precursor	-0.403
Yersinia pestis CO92	fsj214592.21.pep.912	YerPes7843_0912	YPO0653	gHf	Glutamate-ammonia-ligase adenyltransferase (EC 2.7...	-0.404
Yersinia pestis CO92	fsj214592.21.pep.1312	YerPes7843_1312	YPO0925	mBA	Membrane-bound lytic murein transglycosylase A precu...	-0.404
Yersinia pestis CO92	fsj214592.21.pep.3945	YerPes7843_3945	YPO0452		Dipeptide transport ATP-binding protein DppD (TC 3.A.1...	-0.405
Yersinia pestis CO92	fsj214592.21.pep.1609	YerPes7843_1609	YPO1499	lucK	1-phosphotransferase (EC 4.2.1.96)	-0.406

20. At the bottom of the page, resize the table to show all 146 of the negatively correlated genes.

YerPes7843 4649
 Show 146 per page
 PATRIC Fun

21. At the top of the table, click on the column header called “RefSeq Locus Tag”.

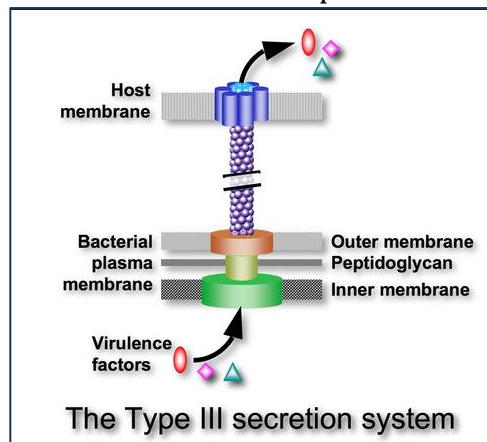
RefSeq Locus Tag	Gene Symbol
YPCD1.26c	yopM

22. This will sort the results showing the genes in the order they appear in the genome. Look at the results...talk about **AWESOME!** All the members of a Type III Secretion System are correlated, and have similar correlation values. Certain pathogenic bacteria use these structures to inject proteins into the cell that helps the bacteria infect the host.

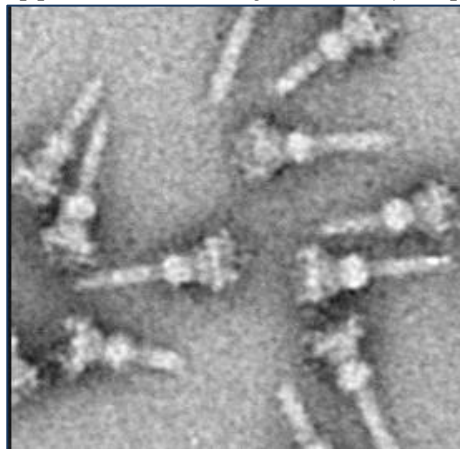
146 features found

Genome Name	PATRIC ID	Alt Locus Tag	RefSeq Locus Tag	Gene Symbol	Product Description	Correlation
Yersinia_pestis_C092	fig 214092.21.peq.33	VBIYerPes7843_0033	YPCD1_26c	yopM	Type III secretion possible injected virulence protein (Y...	-0.434
Yersinia_pestis_C092	fig 214092.21.peq.41	VBIYerPes7843_0041	YPCD1_30c	syncD	Type III secretion chaperone protein for YopD (SyncD)	-0.462
Yersinia_pestis_C092	fig 214092.21.peq.42	VBIYerPes7843_0042	YPCD1_31c	lcrV	Type III secretion cytoplasmic LcrG inhibitor (LcrV,secre...	-0.422
Yersinia_pestis_C092	fig 214092.21.peq.46	VBIYerPes7843_0046	YPCD1_35c	yscY	Chaperone protein YscY (Yop proteins translocation prot...	-0.454
Yersinia_pestis_C092	fig 214092.21.peq.56	VBIYerPes7843_0056	YPCD1_45	yscS	Type III secretion inner membrane protein (YscS,homol...	-0.592
Yersinia_pestis_C092	fig 214092.21.peq.57	VBIYerPes7843_0057	YPCD1_46	yscT	Type III secretion inner membrane protein (YscT,HrcT,S...	-0.429
Yersinia_pestis_C092	fig 214092.21.peq.59	VBIYerPes7843_0059	YPCD1_49	virF	Type III secretion thermoregulatory protein (LcrF,VirF,Tr...	-0.580
Yersinia_pestis_C092	fig 214092.21.peq.60	VBIYerPes7843_0060	YPCD1_51	yscB	Type III secretion chaperone protein for YopN (SyncN,Ys...	-0.435
Yersinia_pestis_C092	fig 214092.21.peq.63	VBIYerPes7843_0063	YPCD1_53	yscD	Type III secretion inner membrane protein (YscD,homol...	-0.495
Yersinia_pestis_C092	fig 214092.21.peq.64	VBIYerPes7843_0064	YPCD1_54	yscE	Type III secretion protein (YscE)	-0.567
Yersinia_pestis_C092	fig 214092.21.peq.65	VBIYerPes7843_0065	YPCD1_55	yscF	Type III secretion cytoplasmic protein (YscF)	-0.417
Yersinia_pestis_C092	fig 214092.21.peq.68	VBIYerPes7843_0068	YPCD1_58	lcrO	Type III secretion cytoplasmic protein (YscI)	-0.423
Yersinia_pestis_C092	fig 214092.21.peq.69	VBIYerPes7843_0069	YPCD1_59	ypb	Type III secretion bridge between inner and outermem...	-0.472
Yersinia_pestis_C092	fig 214092.21.peq.70	VBIYerPes7843_0070	YPCD1_60	yscK	Type III secretion cytoplasmic protein (YscK)	-0.486
Yersinia_pestis_C092	fig 214092.21.peq.71	VBIYerPes7843_0071	YPCD1_61	yscL	Type III secretion cytoplasmic protein (YscL)	-0.562
Yersinia_pestis_C092	fig 214092.21.peq.72	VBIYerPes7843_0072	YPCD1_62	lcrQ	Type III secretion negative regulator of effector product...	-0.486

Just for fun...here's a picture of what they think the Type III secretion system looks like and how the proteins line up.



And here's a transmission electron microscope image of one a Type III secretion system from *Salmonella*. You can clearly see the needle-like apparatus that they use to inject proteins into the host cell.



Assignment: Answer the following questions using the PATRIC website.

1. Choose one of the Type III Secretion System genes and get to the landing page for it. Open the Correlation Tab.
 - a. Look at the genes that are positively correlated with the gene you chose. Adjust the correlation cut-off (located above the table) to narrow the number of genes you see.
 - b. Which genes are the most strongly correlated?
2. Go to your workspace and select other genes from the group you created Part II, Number 6. Examine the positively and negatively correlated genes for several of them. Are there any pathways that these correlated genes share?
3. Follow the same protocol above, but in this case select the 37°C condition as the one that is up-regulated, and the 26°C condition as the one that is down-regulated. Set the log ratio to 1 and filter. Then follow all the steps listed above, and chose one specific gene to drill down on.
 - a. How many genes are significantly up-regulated at that specific log-ratio when you choose those conditions.
 - b. How many pathways do the genes appear in?
 - c. What gene(s) did you choose to examine?
 - i. What log ratio did you filter on to examine this gene, and what experimental conditions surfaced when you changed that?
 - ii. When you did the positive and negative correlation, did you see any genes of interest (Hint: The flagellar genes looked interesting to me)?
 - d. Bonus question: We haven't discussed this, but look at the tabs across the gene landing page. How would you look at the gene you chose and its gene neighborhood (the genes around it)? Which tab did you choose and what did you see?

References

1. Raoult, D., et al., *Plague: history and contemporary analysis*. J Infect, 2013. **66**(1): p. 18-26.
2. Butler, T., *Plague history: Yersin's discovery of the causative bacterium in 1894 enabled, in the subsequent century, scientific progress in understanding the disease and the development of treatments and vaccines*. Clin Microbiol Infect, 2014. **20**(3): p. 202-9.
3. Galindo, C.L., et al., *Comparative Global Gene Expression Profiles of Wild-Type Yersinia pestis CO92 and Its Braun Lipoprotein Mutant at Flea and Human Body Temperatures*. Comp Funct Genomics, 2010: p. 342168.