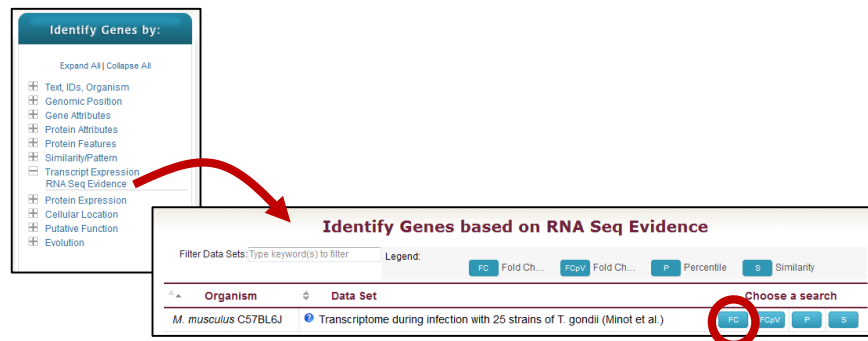


Host Response

- Find host genes that are upregulated in infected mouse cells compared to uninfected ones.

For this exercise use <http://hostdb.org>

- Navigate to the “Transcript Expression” section then select “RNA Seq Evidence”. Select the fold change query for the “Transcriptome during infection with 25 strains of *T. gondii* (Minot et al.)” experiment.



- Configure the search to compare all infected samples to the uninfected control. Make sure to select upregulated. In the example below a fold change of 10 was selected and the “average” operation was applied on the comparison samples.

Upregulated 10 fold

Not infected

Average

All samples except 'not infected'

Identify Genes based on M.mus. Transcriptome during infection with 25 strains of *T. gondii* RNASeq (fold change)

For the Experiment
Transcriptome during infection with 25 strains of *T. gondii*

return protein coding Genes

that are up-regulated

with a Fold change ≥ 10

between each gene's expression value
in the following Reference Samples

☐ TgC14183 infected
☐ VAND infected
☐ VEG infected
☐ WTD3 infected
☒ not infected

select all | clear all

and its average expression value
in the following Comparison Samples

☐ TgC14183 infected
☒ VAND infected
☒ VEG infected
☒ WTD3 infected
☐ not infected

select all | clear all

[Get Answer](#)

Example showing one gene that would meet search criteria

(Dots represent this gene's expression values for selected samples)

Up-regulated

Average Comparison

Reference

10 fold

Reference Samples

Comparison Samples

A maximum of four samples are shown when more than four are selected.

You are searching for genes that are up-regulated between one reference sample and at least two comparison samples.

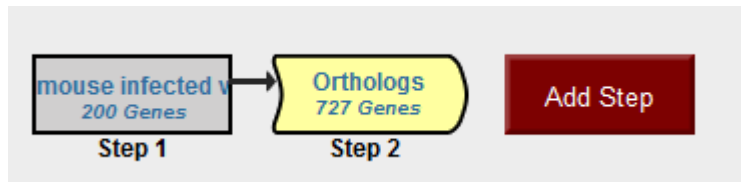
For each gene, the search calculates:

$$\text{fold change} = \frac{\text{average expression value in comparison samples}}{\text{reference expression value}}$$

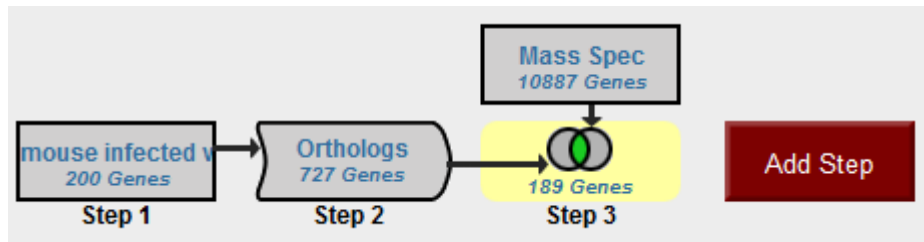
and returns genes when fold change ≥ 10 . To narrow the window, use the minimum comparison value. To broaden the window, use the maximum comparison value.

See the detailed help for this search.

- d. Expand the result set to include orthologs/paralogs of these genes. *Hint:* add a “Transform by Orthology” step choosing Homo sapiens.



- e. Do any of these human genes also have peptide evidence for their expression during infection? *Hint:* add a step and explore the “Mass Spec Evidence” data in the protein expression section. Run the search using the default parameters.



2. Find *Plasmodium falciparum* antigens that are immunogenic.

For this exercise use <http://plasmodb.org>

- a. Identify antigens (genes) that exhibited an increased immunogenicity in children (ages 0-18) with no disease (normal) compared to children with disease (infected). *Hint:* the “Protein Array” search is available in the “Host Response” menu item in the “Identify Genes By” section of the home page. Choose the experiment Protein targets of serum antibodies in response to infection (Crompton et al.).

Identify Genes by:

Expand All | Collapse All

- Text, IDs, Organism
- Genomic Position
- Gene Attributes
- Protein Attributes
- Protein Features
- Similarity/Pattern
- Transcript Expression
- Protein Expression
- Cellular Location
- Putative Function
- Evolution
- Population Biology
- Host Response
- Protein Array

Identify Genes based on Protein Array

id(s) to filter Legend: TSTU T-Test (u...

Organism	Data Set	Choose a
<i>P. falciparum</i> 3D7	Protein targets of serum antibodies in response to infection (Crompton et al.)	TSTU
<i>P. falciparum</i> 3D7	International Centers of Excellence for Malaria Research (International Centers of Excellence for Malaria Research (ICEMR))	TSTU
<i>P. falciparum</i> 3D7	Treatment-time to reinfection cohort from Kisumu area, Kenya collected in 2003 (Dent et al.)	TSTU

Identify Genes based on P.fal. Protein targets of serum antibodies in response to infection Antibody Array (p-value)

T-Test (unequal variance)

Reference Samples 421 of 421 selected
Select Reference Samples

Comparison Samples 421 of 421 selected
Select Comparison Samples

Metadata category to color graph by DiseaseState

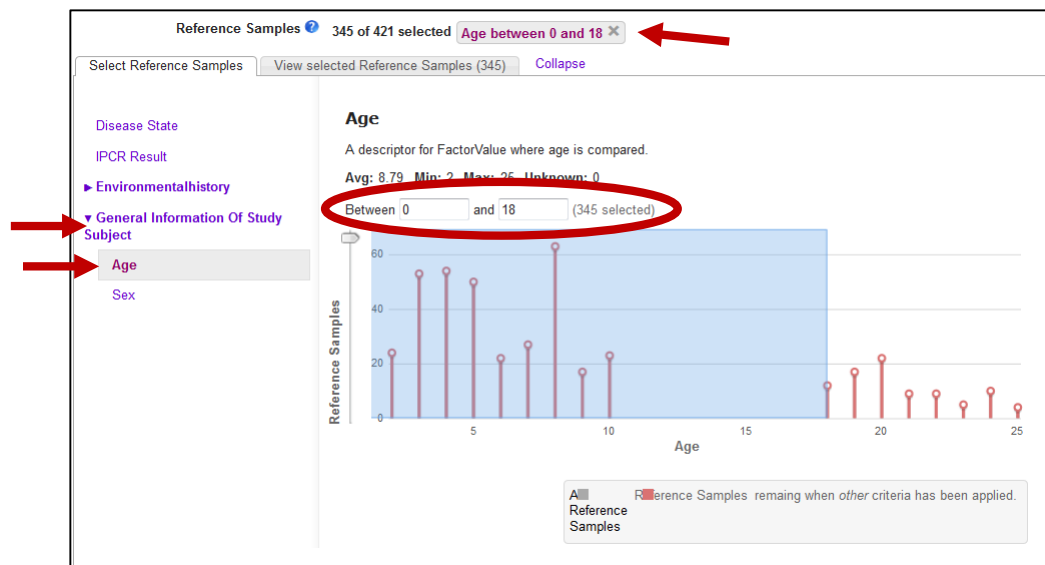
Direction increased immunogenicity

P value less than or equal to 0.05

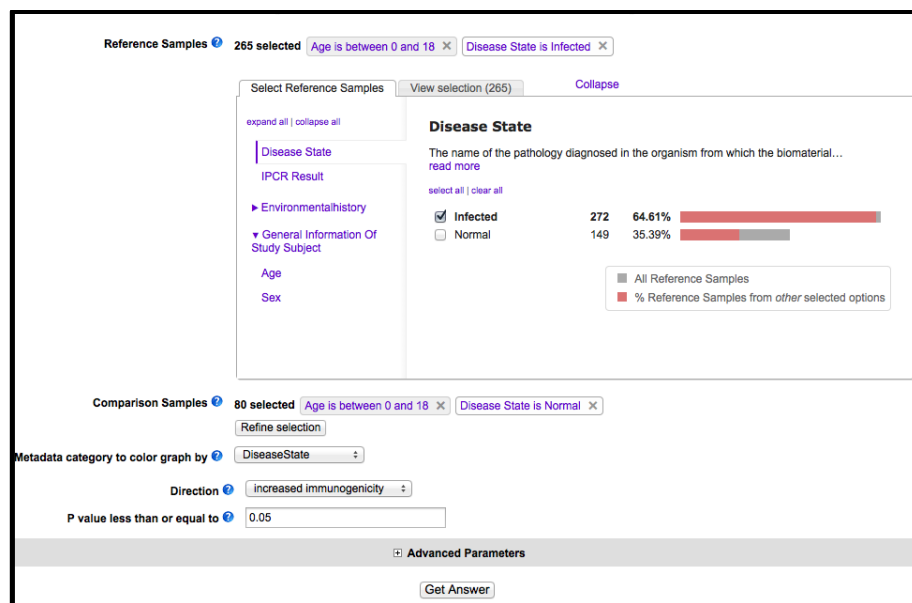
Get Answer

This is a view of the search page with the reference and comparison sample parameters collapsed.

In this example, your **comparison samples will be normal children** and your **reference samples will be infected children**. So each set of samples (reference and comparison) has two parameters that need to be set, age and disease state. The age parameter should be set to 0-18 years for both the reference and the comparison samples. To set the age parameter for the reference samples, choose the ‘General Information of Study Subject’ and then ‘Age’ from the left menu to reveal choices for the parameter on the right. Set the range to 0-18 (see image below).



Now set the disease state for the reference samples to infected. Move on the comparison samples and set the age to 0-18 and the disease state to normal. The default settings for other parameters are good – increased immunogenicity and p-value = 0.05.



You are ready to click Get Answer! What do your results look like? Could these represent potential protective antigens? (result image below)

My Strategies: New Opened (1) All (1) Basket Public Strategies (33) Help

(Genes) Strategy: Serum Ab Response (p-val) * Rename Duplicate Save As Share Delete

Serum Ab Respo 31 Genes Add Step

Step 1

31 Genes from Step 1 Strategy: Serum Ab Response (p-val) Add 31 Genes to Basket | Download 31 Genes

Click on a number in this table to limit/filter your results

Gene Results Genome View **Analyze Results** BETA

First 1 2 Next Last Advanced Paging Add Columns

Gene ID	Organism	Product Description	P Value	Avg Ref (arcsinh(1+50x))	Avg Comp (arcsinh(1+50x))	Expression - graph
PF3D7_0304600	P. falciparum 3D7	circumsporozoite (CS) protein (CSP)	1.72E-04	4.696921	5.00801	

3. Find *falciparum* antigens that may be protective from reoccurrence of malaria (and potentially reinfection)

For this exercise use <http://plasmodb.org>

A recently published study from Kenya ([view paper](#)) where participants were followed for 12 weeks following an initial screening for malaria and treatment with anti-malarials is available in PlasmoDB. Each week patients were assessed for presence of parasites and clinical symptoms of malaria. Select the “Treatment-time to reinfection cohort from Kisumu area, Kenya collected in 2003 (Dent et al.)” experiment from the protein array searches and configure the parameters to see if you can reproduce the results of the paper. They concluded that increased antigenicity was present in children who did not show clinical symptoms of malaria, and suggest that these antigens are protective in children who did not get a recurrence of symptomatic malaria (compared to those children who did exhibit malaria symptoms). They also concluded that there did not appear to be a correlation between antigenicity and time to re-infection (could be asymptomatic). Test both these conclusions.

Hint: compare children (age 0-12.5) who got clinical malaria during the study (time to first malaria Dx weeks 4-9) compared to those who didn't (week 11+). Try running with increased immunogenicity then revise and change to decreased immunogenicity. See image below for help configuring the search.

Do these results make sense?

Ask the same question (age 0-12.5) except compare time to re-infection weeks 3 and 4 with time to reinfection weeks 9,10,11,11+. Do you get significant results? Does this agree with the conclusions of the paper? Revise the search and remove the age limits, just keeping the times to re-infection.

T-Test (unequal variance)

Identify Genes based on P.fal. Treatment-time to reinfection cohort from Kisumu area, Kenya collected in 2003 Antibody Array (p-value)

Reference Samples 19 of 172 selected Age between 0.61 and 12.64 Time to first malaria dx is We...

Select Reference Samples View selected Reference Samples (19) Collapse

▼ General Information

Age

▼ Specimen Collection Information

▶ Sample Collection Location

Date Sample Collected

End Of Observation Period

Sample Id

▼ Laboratory Methods And Results

▶ Parasite Detection

Blood Smear Result Summary

Time To First Malaria Dx

Time To Reinfection

Time To First Malaria Dx

[select all](#) | [clear all](#)

Time to first malaria dx	Total Reference Samples	Matching Reference Samples	Distribution
<input type="checkbox"/> Week 11+	151	64	<div><div></div></div>
<input type="checkbox"/> Week 111+	2	2	<div><div></div></div>
<input checked="" type="checkbox"/> Week 4	3	3	<div><div></div></div>
<input checked="" type="checkbox"/> Week 5	2	2	<div><div></div></div>
<input checked="" type="checkbox"/> Week 6	2	2	<div><div></div></div>
<input checked="" type="checkbox"/> Week 7	5	5	<div><div></div></div>
<input checked="" type="checkbox"/> Week 8	5	5	<div><div></div></div>
<input checked="" type="checkbox"/> Week 9	2	2	<div><div></div></div>

☐ All Reference Samples

Reference Samples remaining when other criteria has been applied.

Comparison Samples 66 of 172 selected Age between 0.61 and 12.55 Time to first malaria dx is We...

Select Comparison Samples View selected Comparison Samples (66) Collapse

▼ General Information

Age

▶ Specimen Collection Information

▼ Laboratory Methods And Results

▶ Parasite Detection

Blood Smear Result Summary

Time To First Malaria Dx

Time To Reinfection

Time To First Malaria Dx

[select all](#) | [clear all](#)

Time to first malaria dx	Total Comparison Samples	Matching Comparison Samples	Distribution
<input checked="" type="checkbox"/> Week 11+	151	64	<div><div></div></div>
<input checked="" type="checkbox"/> Week 111+	2	2	<div><div></div></div>
<input type="checkbox"/> Week 4	3	3	<div><div></div></div>
<input type="checkbox"/> Week 5	2	2	<div><div></div></div>
<input type="checkbox"/> Week 6	2	2	<div><div></div></div>
<input type="checkbox"/> Week 7	5	5	<div><div></div></div>
<input type="checkbox"/> Week 8	5	5	<div><div></div></div>
<input type="checkbox"/> Week 9	2	2	<div><div></div></div>

☐ All Comparison Samples

Comparison Samples remaining when other criteria has been applied.

Metadata category to color graph by age

Direction increased immunogenicity

P value less than or equal to 0.05

Get Answer

Treatment-time to
39 Genes
Step 1

Add Step