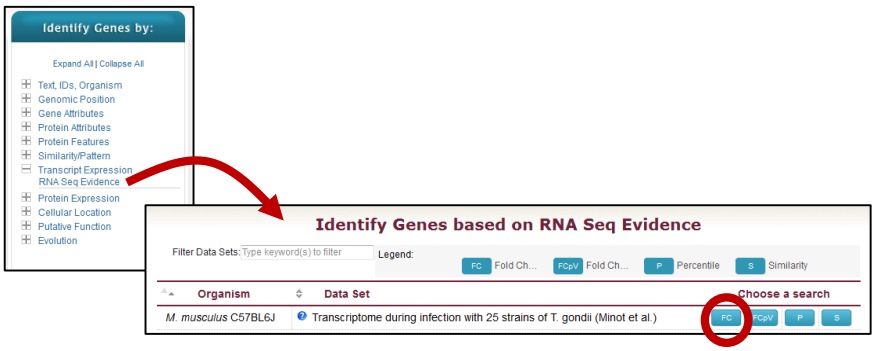
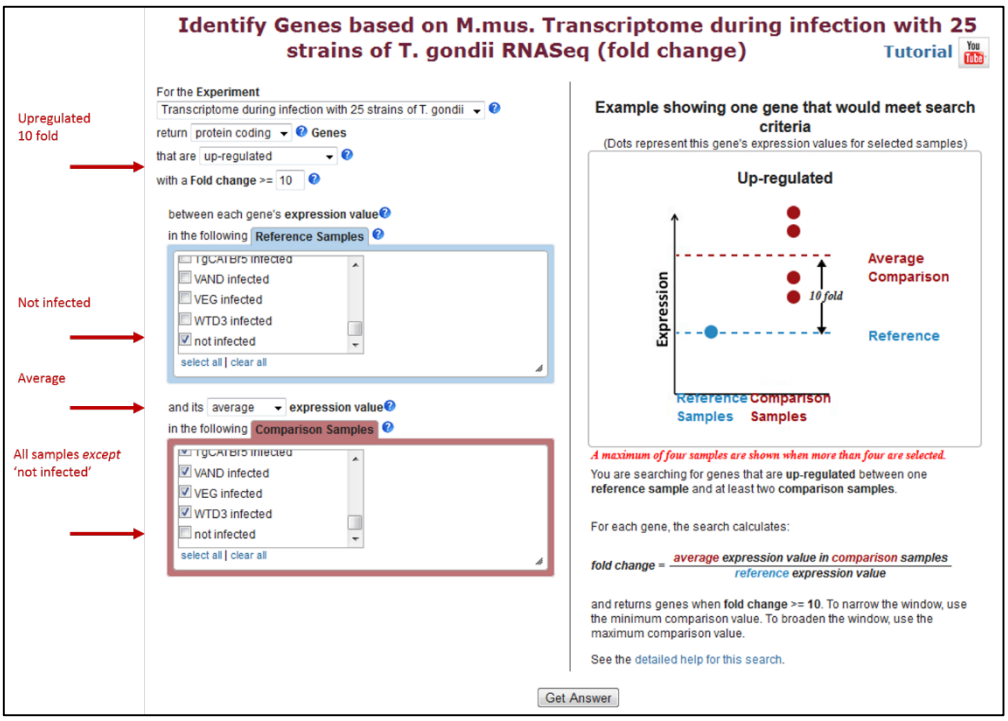
Host Response

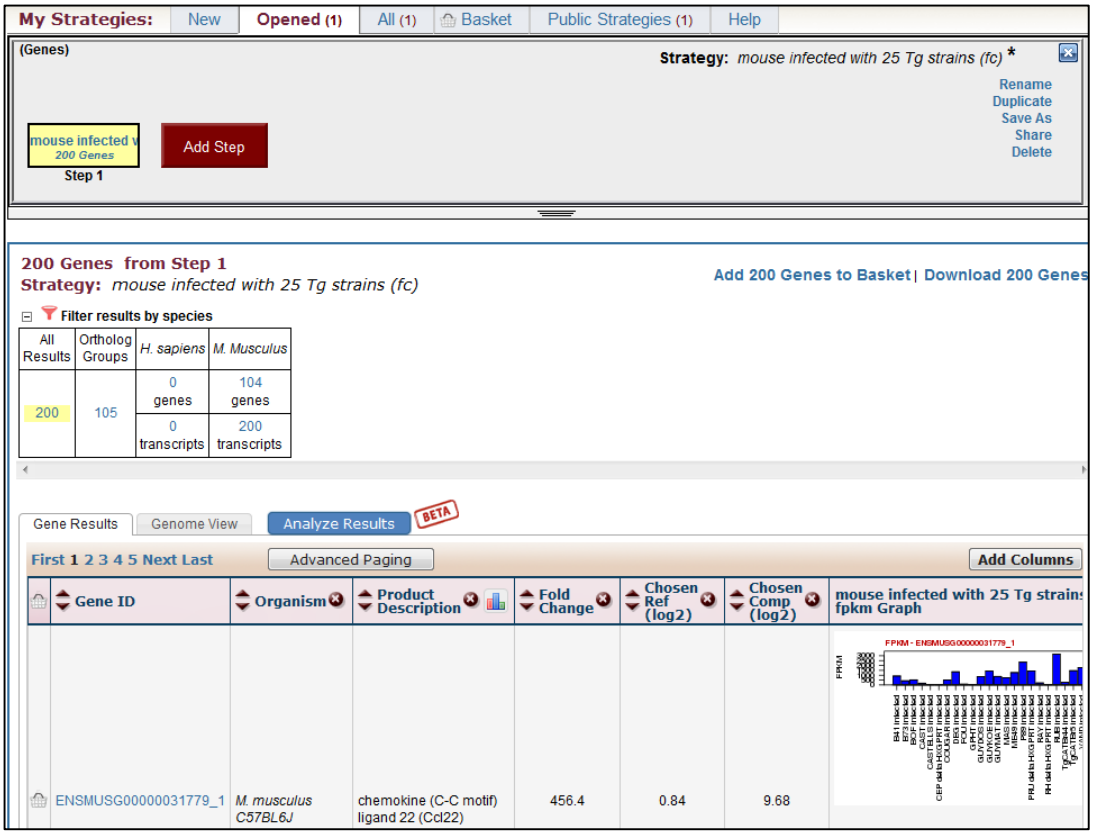
1. **Find host genes that are upregulated in infected mouse cells compared to uninfected ones.**
   For this exercise use http://hostdb.org

   a. 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.

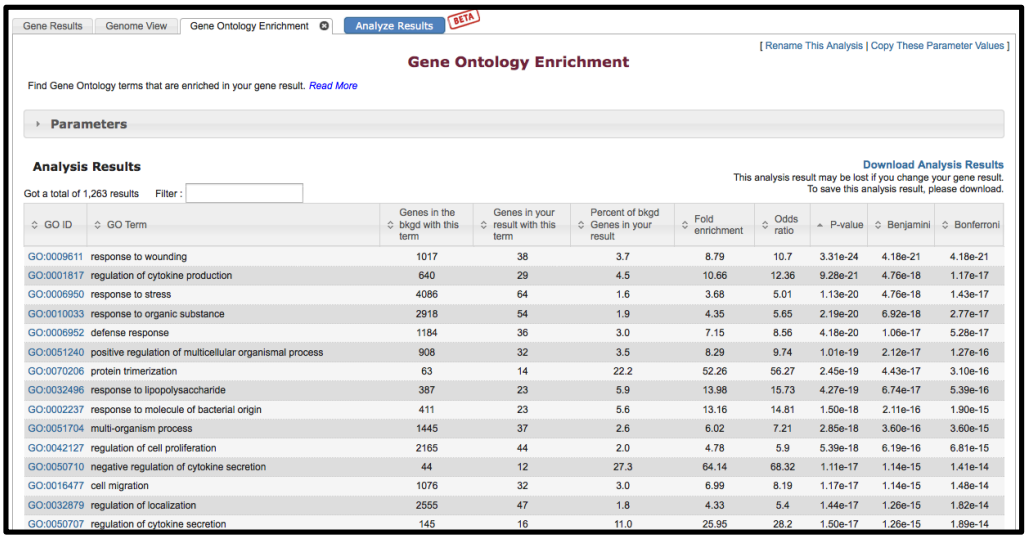


   b. Configure the search to compare all infected samples to the uninfected control. Make sure to select upregulated. In the example below a fold change of 10 was selected and the "average" operation was applied on the comparison samples.





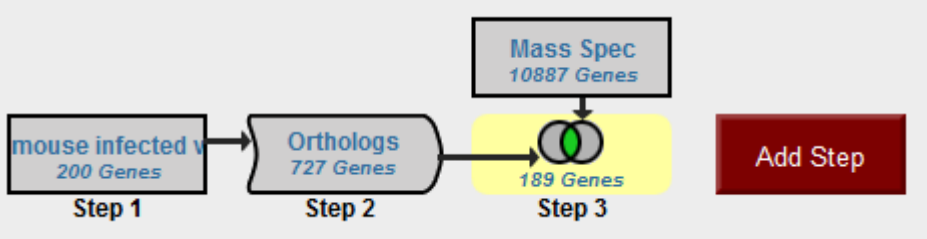
c. What are the functional characteristics of the genes in this result? What kinds of GO terms are enriched? *Hint*: click on the "Analyze Results" tab and select the GO enrichment analysis.



GO ID	GO Term	Genes in the bkgd with this term	Genes in your result with this term	Percent of bkgd Genes in your result	Fold enrichment	Odds ratio	P-value	Benjamini	Bonferroni
GO:0009611	response to wounding	1017	38	3.7	8.79	10.7	3.31e-24	4.18e-21	4.18e-21
GO:0001817	regulation of cytokine production	640	29	4.5	10.66	12.36	9.28e-21	4.76e-18	1.17e-17
GO:0006950	response to stress	4086	64	1.6	3.68	5.01	1.13e-20	4.76e-18	1.43e-17
GO:0010033	response to organic substance	2918	54	1.9	4.35	5.65	2.19e-20	6.92e-18	2.77e-17
GO:0006952	defense response	1184	36	3.0	7.15	8.56	4.18e-20	1.06e-17	5.28e-17
GO:0051240	positive regulation of multicellular organismal process	908	32	3.5	8.29	9.74	1.01e-19	2.12e-17	1.27e-16
GO:0070206	protein trimerization	63	14	22.2	52.26	56.27	2.45e-19	4.43e-17	3.10e-16
GO:0032496	response to lipopolysaccharide	387	23	5.9	13.98	15.73	4.27e-19	6.74e-17	5.39e-16
GO:0002237	response to molecule of bacterial origin	411	23	5.6	13.16	14.81	1.50e-18	2.11e-16	1.90e-15
GO:0051704	multi-organism process	1445	37	2.6	6.02	7.21	2.85e-18	3.60e-16	3.60e-15
GO:0042127	regulation of cell proliferation	2165	44	2.0	4.78	5.9	5.39e-18	6.19e-16	6.81e-15
GO:0050710	negative regulation of cytokine secretion	44	12	27.3	64.14	68.32	1.11e-17	1.14e-15	1.41e-14
GO:0016477	cell migration	1076	32	3.0	6.99	8.19	1.17e-17	1.14e-15	1.48e-14
GO:0032879	regulation of localization	2555	47	1.8	4.33	5.4	1.44e-17	1.26e-15	1.82e-14
GO:0050707	regulation of cytokine secretion	145	16	11.0	25.95	28.2	1.50e-17	1.26e-15	1.89e-14

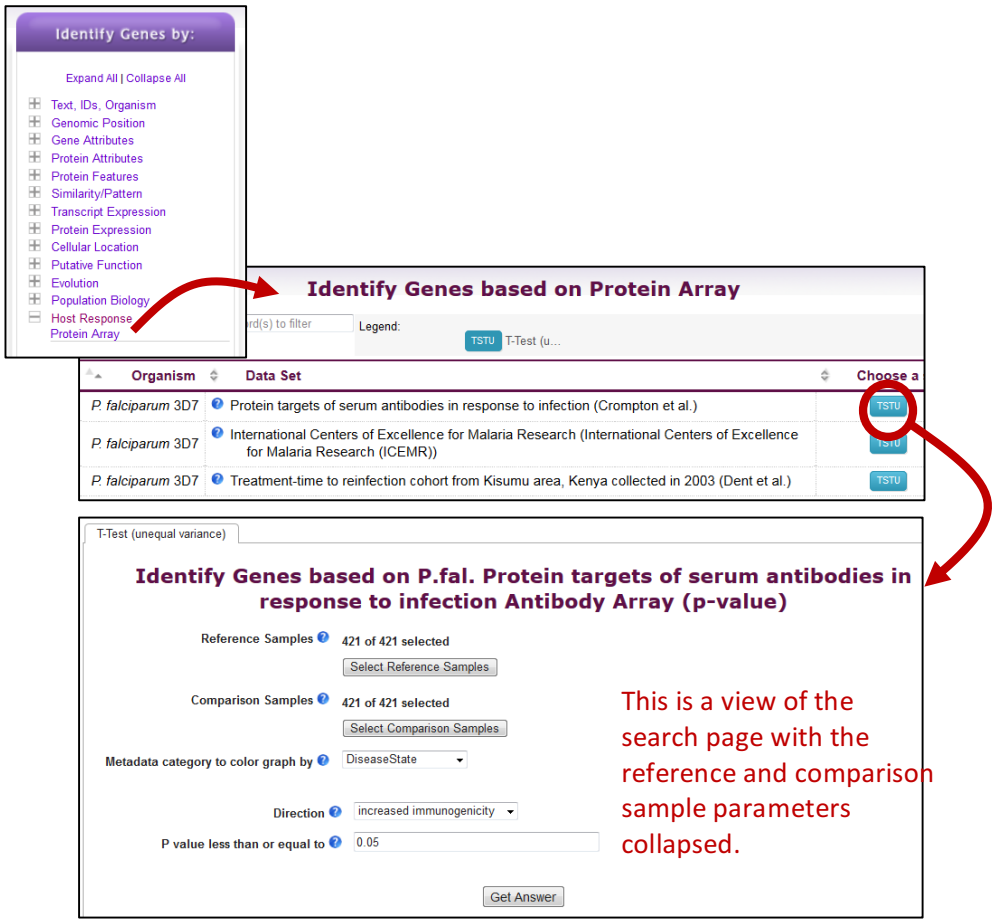
d. Expand the result set to include orthologs/paralogs of these genes. *Hint:* add a "Transform by Orthology" step choosing Homo sapiens.

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.



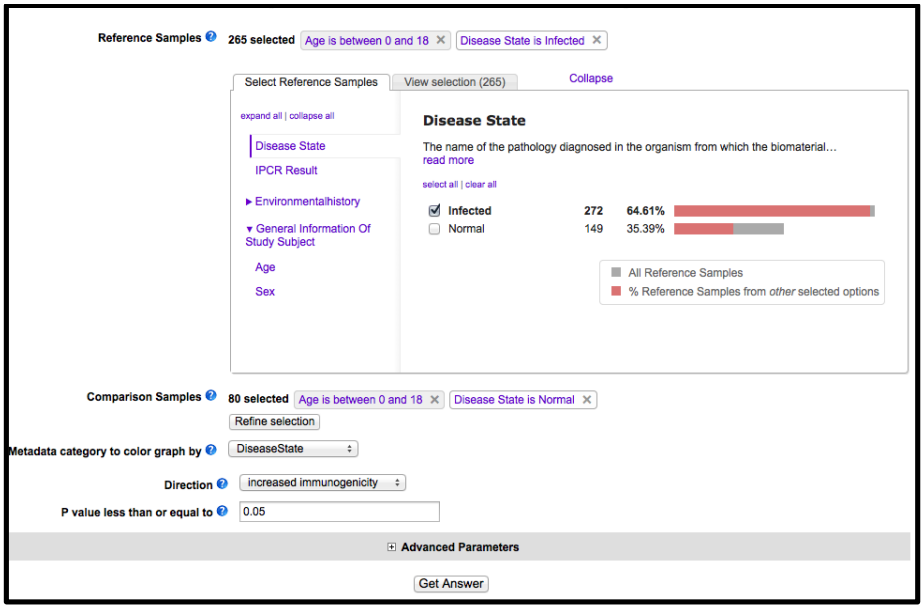
2. Find *Plasmodium falciparum* antigens that are immunogenic.
For this exercise use http://plasmodb.org

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.).

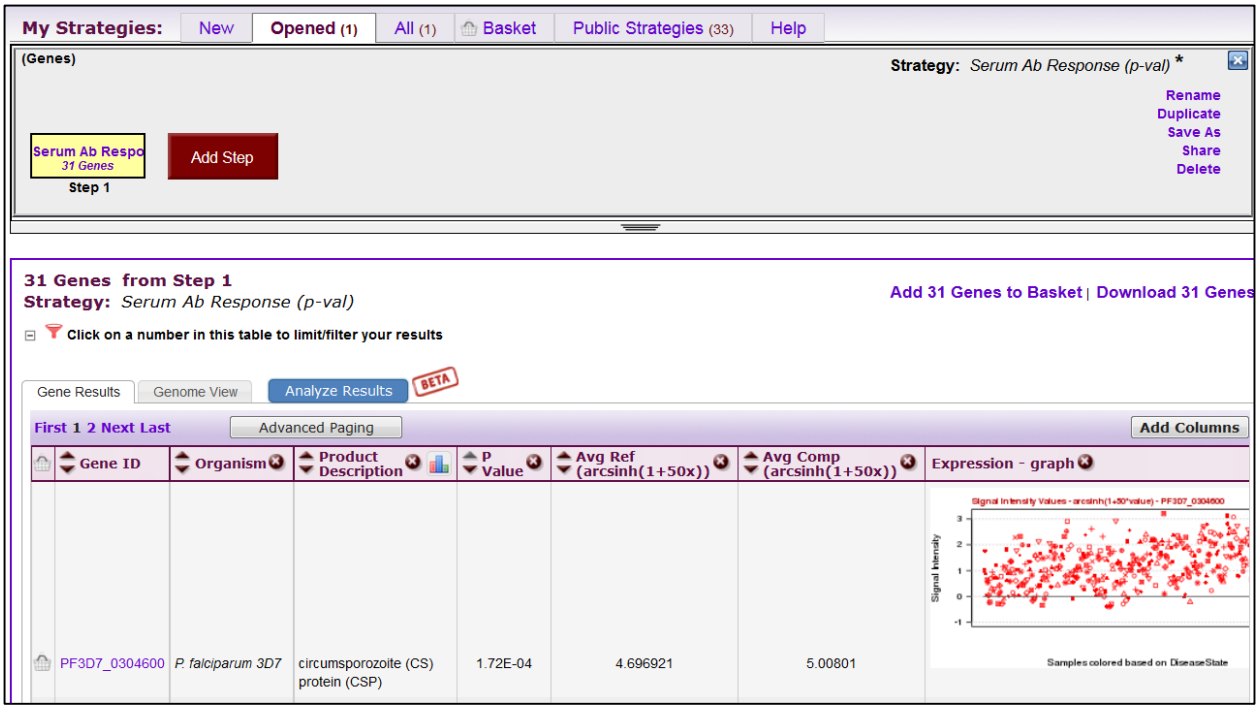


In this example, your **comparison samples will be normal children** and your **reference samples with be infected children**. So each set of samples (reference and comparison) has two parameters that need to be set, age and disease state. The age parameter should be set to 0-18 years for both the reference 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)



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.