

## Exercises for the GeneMANIA Resource (Version 1, 2010)

**You can choose to do these using the questions as your only guide—or see the following pages for the step-by-step checklist to finding these answers.**

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**1)** You are interested in DNA replication and repair in humans. Analyze a list of 6 genes (MSH2; DMC1; RAD54B; RAD50; RAD51, MSH6) using GeneMANIA and then explore your search results.

*Skills: GeneMANIA Gene List Search; Navigating Search Results; Saving Results*

**2)** Imagine that you are interested in exploring the worm development genes in GeneMANIA's *C. elegans* example gene list (cpg-2; cpg-1; tba-2; ima-2; tsr-1; mei-2; ran-1; mei-1; ebp-2; gei-17). How does the network change if only datasets involving shared domains are used in the analysis?

*Skills: Searching; Navigating Search Results; Altering Analyzed Datasets*

**3)** You are working on the TGF-beta response in mouse and have a list of genes (Rab34; Smad4; Rab2b; Smad2; bmp1a; uhmk1; rasd2) that you are interested in. Not only do you want to obtain additional related genes predicted by GeneMANIA's algorithm, you also want to explore how network weighting affects those predictions.

*Skills: GeneMANIA Gene List Search; Altering Network Weighting; Comparing Search Results*

**NOTE: Network layouts are flexible and can be rearranged. What you see when you perform these exercises may not be identical to what you see in the tutorial, or what you have seen other times that you have performed the exercises. Exact layouts and predictions can also be affected by updates to the networks database that GeneMANIA uses. However it is expected that the network weights and predicted genes will be similar to those shown here.**

**GeneMANIA Exercises, Version 1.  
Correspond to the data available in August 2010.**

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## Step-by-Step checklist/instructions for the GeneMANIA introduction exercises

1) You are interested in DNA replication and repair in humans. Analyze a list of 6 genes (MSH2; DMC1; RAD54B; RAD50; RAD51, MSH6) using GeneMANIA and then explore your search results.

Step	Action	✓
1	Go to GeneMANIA's homepage at <a href="http://www.genemania.org/">http://www.genemania.org/</a>	
2	In the search window, <b>ensure that the 'Find genes in' menu is set to human.</b>	
3	<b>Enter the following gene list:</b> MSH2 DMC1 RAD54B RAD50 RAD51 MSH6	
4	<b>Click 'Go'</b> to run your search.	
5	When your search results load, <b>examine the network.</b> <i>Note, the network will be on the left of the results window and include input genes (filled circles), predicted genes (open circles), and colored links representing the interactions that connect the nodes.</i>	
6	Locate the Network summary tab (on the right) and <b>look at what data has been used</b> to create the network and predictions. <i>Note that Physical Interactions (periwinkle blue lines, score over 40%) influence the results the most, but Co-Expression (purple) data are also included.</i>	
7	<b>Click any link</b> connecting two nodes to highlight information about it. <i>Note that if you expand the Network summary tab all you can see highlights on the networks that support the link you clicked.</i>	
8	To see the details of the genes involved in this network, <b>locate the Genes tab</b> (in the right panel) and <b>click it.</b>	
9	Now <b>click on the 'Expand: all' option</b> to see a list of gene descriptions.	
10	<b>Scroll</b> through the expanded gene list and <b>read some of the descriptions.</b> <i>Note that the descriptions for the predicted genes indicate similar functions as for our gene list, including DNA replication and repair, etc.</i>	
11	Generate and save a report of your results by <b>locating the upper left 'Save' menu</b> , clicking it open, and then <b>clicking 'Save Report as PDF'.</b> <i>Note the PDF report provides a detailed description of your search and results, and can be saved to your computer.</i>	

Notes:

- 2) Imagine that you are interested in exploring the worm development genes in GeneMANIA's *C. elegans* example gene list (cpg-2; cpg-1; tba-2; ima-2; tsr-1; mei-2; ran-1; mei-1; ebp-2; gei-17). How does the network change if only datasets involving shared domains are used in the analysis?

Step	Action	✓
1	Go to <a href="http://www.genemania.org/">http://www.genemania.org/</a>	
2	In the search window, <b>set the 'Find genes in' menu to C. elegans (worm). Click 'Go'</b> to run the following gene list: cpg-2; cpg-1; tba-2; ima-2; tsr-1; mei-2; ran-1; mei-1; ebp-2; gei-17.	
3	Once your search results are completely loaded, <b>locate the Genes tab</b> in the right panel and <b>click it</b> to view a list of the genes in your network.	
4	In the Genes list, <b>locate the gene cpg-1</b> , and click on its gene name. <i>Note that the cpg-1 node is now highlighted in yellow in the left panel network. You could click the triangle to expand and view its full gene description.</i>	
5	From the 'Actions' menu, <b>click the 'Highlight neighbours'</b> option to see more clearly which genes it interacts with. <i>Note that cpg-1 links to nodes from our original gene list (cpg-2, ima-2, mei-1 and tba-2) as well as predicted nodes (clec-87 and cyb-3). Updates to the networks database may change the links described here.</i>	
6	From the 'Actions' menu, <b>click the 'Remove neighbours highlight'</b> option to return to the normal results view of all interactions.	
7	Immediately under the gene input window, <b>click on the link labeled 'Show advanced options'</b> . <i>Note that a window of advanced search options will open.</i>	
8	<b>Click</b> the network option to Enable: <b>'none'</b> , then <b>click the checkbox</b> to the left of 'Shared protein domains' to select the InterPro and Pfam datasets.	
9	<b>Click 'Go'</b> to run your new analysis. <i>Note that the new network graph looks significantly different and highlights connections between proteins in the network with similar domains. If you'd like your network layout to be different, at the top of the graph panel you can click Actions &gt; Reset layout, or use your mouse to drag any gene to a different position.</i>	

Notes:

3) You are working on the TGF-beta response in mouse and have a list of genes (Rab34; Smad4; Rab2b; Smad2; bmp1a; uhmk1; rasd2) that you are interested in. Not only do you want to obtain additional related genes predicted by GeneMANIA's algorithm, you also want to explore how weighting affects those predictions.

*Note, you may want to generate a report from each of your analyses so that it is easier to compare how different weighting affects the results.*

Step	Action	✓
1	Go to <a href="http://www.genemania.org/">http://www.genemania.org/</a>	
2	In the search window, <b>set the 'Find genes in' menu to M. musculus (mouse).</b>	
3	<b>Enter the following gene list:</b> Rab34 Smad4 Rab2b Smad2 Bmpr1a Uhmk1 Rasd2 <b>Then click 'Go' to run the example gene list.</b>	
4	When your search results load, in the right panel <b>examine the network weights</b> , and the <b>list of genes</b> in your results network. <i>Note, five different data types were used in the analysis with 'Other' having the highest score.</i>	
5	<b>Click to open the advanced options</b> window and in the network weighting area, <b>click the radio button</b> labeled 'Molecular function based'. <b>Then click 'Go'</b> to run the analysis. <i>Note that again there are six different data types used in the analysis but 'Physical interactions' has the highest score.</i>	
6	Next, <b>change the network weighting</b> to 'Equal by network', which is the top right choice in the weighting area, then <b>click Go</b> . <i>Note that 'Physical interactions' again has the highest score, but the order of other data types has changed. If you 'expand all' networks, you will see that each individual dataset is weighted the same as all other datasets.</i>	
7	As an optional step, <b>repeat this exercise</b> with this list of genes (Clock; Cry1; Lgals8; Per1; Arntl, one gene per line) to see networks that are less affected by weighting.	

**Notes:**