



CBW Module 8 Lab Answers

Example 1

1. The overall sub-network consists of 250 nodes and 517 edges. The largest component of the subnetwork consists of 212 nodes and 448 edges, with the remainder of nodes and edges distributed amongst 11 other small subnetworks and interactions.
2. The most frequently mutated gene in the samples could be the driver mutations. node size is proportional to the number of samples where the gene is mutated. The largest node is TP53, ie. mutations in the TP53 gene are highly prevalent, occurring in at least 96% of HGS-OvCa samples. Other prominent genes include BRCA1, BRCA2, FAT3,
3. Annotated Functional Interaction based upon data from the TRED database. This targeted interaction describes an interaction between TP53 (regulator) and PEG3 (target). An immunoprecipitation experiment demonstrates the interaction, and the supporting evidence has been published in the paper with a PubMed ID: 11679586.
4. Predicted Functional Interaction based upon data (2/9 sources are true) from a human interaction database and GO (GO BP sharing). FI score: 0.64
5. After clustering, there are 27 modules with 10 modules of 10 \geq genes.
6. 17 modules, depending on the results of the enrichment analysis. Some pathways gene sets at the cutoff threshold may come or go but those highly significant gene sets are always there.
7. 0: ECM and Integrin signalling, 2: Calcium signalling, 3: Cell Cycle, 5: TP53 Signaling and Cell Cycle Checkpoints
8. Yes, ECM organization and Cell adhesion.
9. Nuclear terms (matrix, envelope, membrane, etc), spindle, nucleoplasm.
10. Modules 0, 15, and 16 will be highlighted. Navigate through hierarchy. Neoplasm > Neoplasm_by_Site > Breast Neoplasm > Malignant_Breast_Neoplasm > Breast Carcinoma > Stage_IV_Breast_Cancer. Go back to the Network Module Browser. Genes in the modules that have 'Stage IV Breast Cancer' annotations will be yellow-highlighted: BRCA1, NRG1, TP53, INSR, EGFR.
11. 3 modules: 0, 2, 8

Results Panel

Survival Analysis

Analysis: Coxph (all modules)

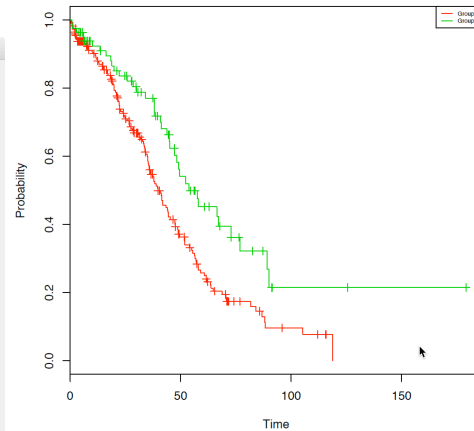
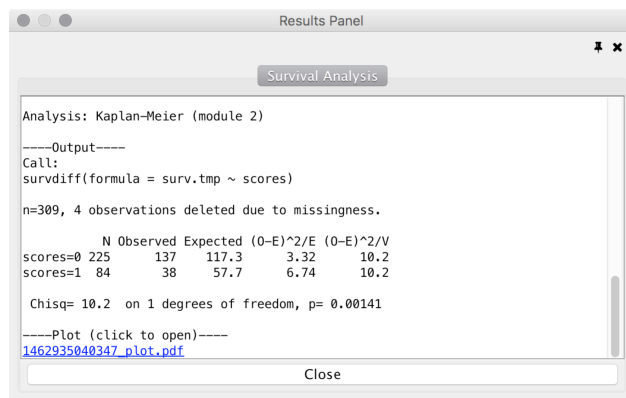
-----Output-----

Note: Click underlined modules in blue for single module-based analysis. You may not see any underlined module if all p-values > 0.05.

Module	Coefficient	P-value
<u>0</u>	-0.4152029	0.007307736
1	-0.00750872	0.5261241
<u>2</u>	-0.53092491	0.00163052
3	0.03746824	0.825179
4	-0.2262933	0.2135214
5	-0.310467	0.3918302
6	0.003930039	0.9834405
7	-0.2440726	0.203739
<u>8</u>	-0.3747218	0.04612862
9	-0.04482006	0.8114485
10	-0.300604	0.1456164
11	-0.4143405	0.115162
12	-0.05341417	0.8587009
13	-0.124334	0.6901617
14	0.3042236	0.2767055
15	-0.1042551	0.7185266
16	-0.1243374	0.7041014
17	-0.2705508	0.5514837
18	-0.7495018	0.1394324
19	-0.4211600	0.5544945
20	-0.5240063	0.3004151
21	0.3076683	0.426012
22	-0.2223146	0.5671013
23	0.1764907	0.7277737
24	0.202935	0.5995571

Close

12. In Modules 2 (KM: $p = 0.00141$), patient with genes mutated (green line) have a better prognosis than patients with no gene mutations (red line). Module 2 is the most statistically significant module from the CoxPH analysis. The ReactomeFIViz app splits samples into two groups: samples having genes mutated in a module (red line), and samples having no genes mutated in the module (green line). The plugin uses the log-rank test to compare the two survival curves, and estimates p-values.



13. In Module 2, the Calcium signaling, Chemical Synapse/Neurotransmission and Muscle Contraction annotations reflect a shared set of genes. These genes represent voltage-gated ion channels, which are a group of transmembrane ion channels that activated by changes in electrical potential difference. Even though ion channels are especially critical in neurons and muscle tissue, they are common in many types of cells, controlling the influx and outflux of ions. There are a number of genetic disorders, which disrupt normal functioning of ion channels. Calcium homeostasis is essential for cell migration, and tumor metastasis in particular. It may be that mutations in Module 2 genes disrupt calcium homeostasis, thereby impairing the tumour's ability to metastasize, and extending patient's overall survival.