Functional analysis of cancer-specific gene list and mutation by Cytoscape

Analyze gene lists and somatic mutation data to identify biology that contributes to GBM and ovarian cancer.

Example 1: Pathway-based analysis of GBM genelist

- Open up Cytoscape.
- Go to Apps >Reactome FI>Reactome Pathways.
- Unfurl the Signal Transduction events, by clicking the triangle to the left of the event name, in the Reactome tab on the left.
- Click on Signaling by EGFR or your favourite pathway.
- Right-click on highlighted pathway name to display drop-down menu, select Show Diagram to display Signaling by EGFR pathway.
- Right-click on highlighted pathway name to display drop-down menu, select Analyze Pathway Enrichment
- Upload/Browse GBM_genelist.txt into Reactome Pathway Enrichment Analysis, and click OK.

Questions:

1. What are the most significant biological pathways when the FDR Filter is set to 0.05?
   (Hint: Right-click on selected pathway in Table Panel, and click “View in Diagram”. Purple-coloured nodes reflect hits in the dataset. Right-click on highlighted nodes to invoke additional features.)

Example 2: Network-based analysis of GBM gene-sample data

- Open up Cytoscape.
- Go to Apps>Reactome FI and Select Gene Set/Mutational Analysis.
- Choose “2016” (Latest) Version.
- Upload/Browse GBM_genesample.txt file.
- Select Gene/sample number pair and Choose sample cutoff value of 4.
- Select Fetch FI annotations.
- Click OK.

Questions:

2. Describe the size and composition of the GBM sub-network.
3. Describe the TP53-PEG3 interaction, and the source information to support this interaction?
4. Describe the data sources for the TAF1-TAF7L FI?
5. After clustering, how many modules are there?
6. How many pathway gene sets are there in TP53 module when the FDR Filter is set to 1.0E-4 and Module Size Filter to 10?
   (Hint: Analyze Module Functions>Pathway Enrichment. Select appropriate filters at each step)

7. What are the most significant pathway gene sets (Top 3) in Module 0, 1, and 3?

Example 3: Network-based analysis of OvCa somatic mutation

- Open up Cytoscape.
- Go to Apps>Reactome FI and Select Gene Set/Mutational Analysis.
- Choose 2016 (Latest) Version.
- Upload/Browse OVCA_TCGA_MAF.txt file.
- Select NCI MAF (Mutation Annotation File) and choose sample cutoff value of 4.
- Do not select Fetch FI annotations.

Questions:

8. Describe the size and composition of the OvCa network?
9. What are the most frequently mutated genes?
10. After clustering, how many modules are there?
11. How many pathway gene sets are there in CREBBP module when the FDR Filter is set to 0.005 and Module Size Filter to 10?
12. What are the most significant pathway gene sets in Module 1, 2, 3 and 4?
13. Do the GO Biological Process annotations correlate with the significant pathway annotations for IGTA2B module? (Hint: Analyze Module Functions>GO Biological Process.)
14. Are any of the modules annotated with the NCI Disease term: “Stage_IV_Breast_Cancer” [malignant cancer]? (Hint: Load Cancer Gene Index>Neoplasm>Neoplasm_by_Site>Breast Neoplasm>…….)
15. What are the targets of drug Imatinib Mesylate?