

GSE19383 Carrier Sample

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1 Background of GSE19383

Organism: Homo sapiens

Summary: 36 BRCA1 and BRCA2 carrier samples, 6 were derived from RNA from Breast BRCA1 mutant, 6 were derived from RNA from Breast BRCA2 mutant, 6 were derived from RNA from Breast WT, 6 were derived from RNA from Ovary WT.

2 BRCA1 versus WT

2.1 Gene ontology (GO) based enrichment analysis

Top 20 GO enrichment terms

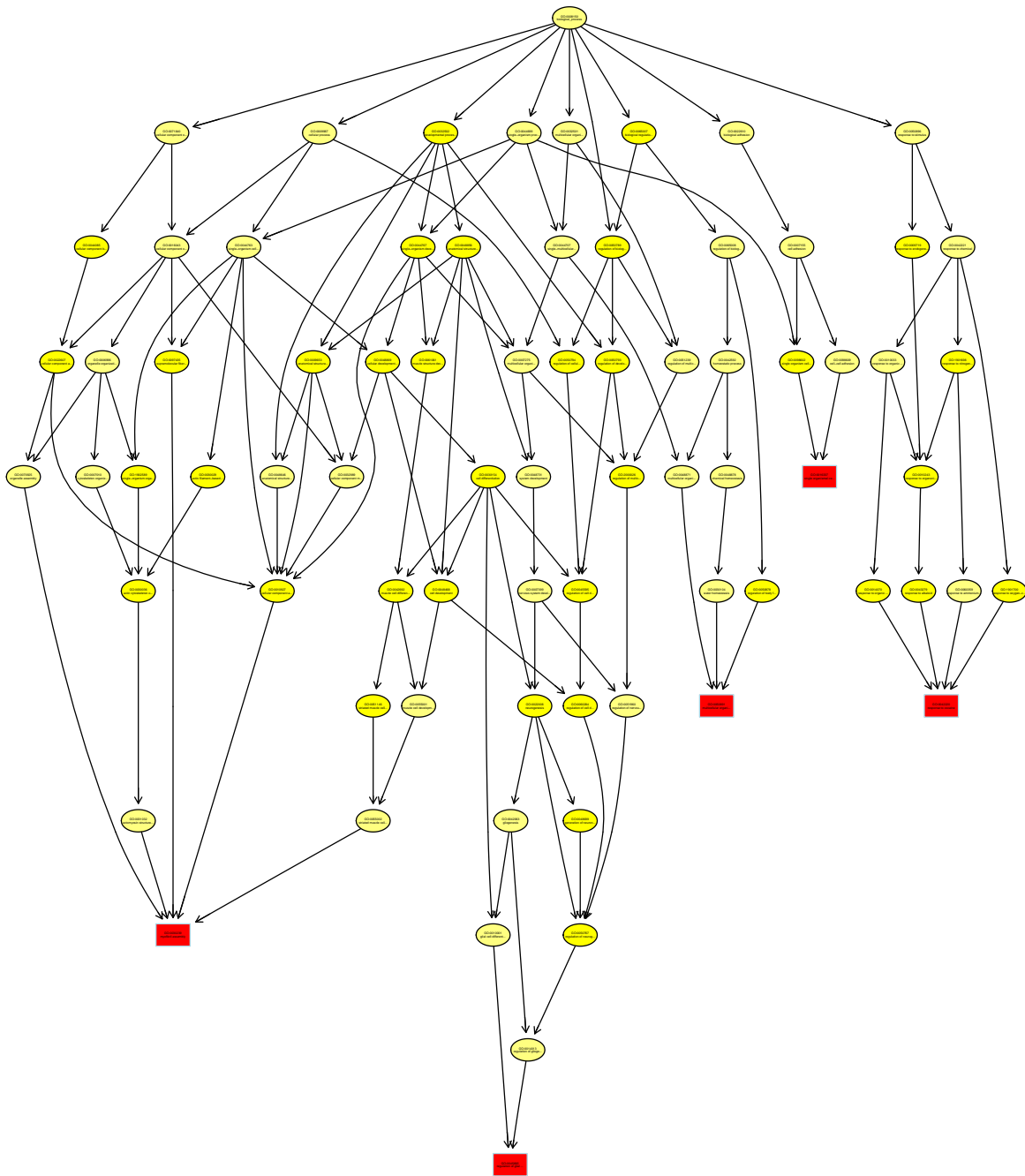
** Using P-value under 0.005 for functional enrichment analysis **

```
head(res_top_GO[,1:8], 20)
```

##	GO.ID	Term	Annotated
## 1	G0:0045685	regulation of glial cell differentiation	15
## 2	G0:0016337	single organismal cell-cell adhesion	131
## 3	G0:0030239	myofibril assembly	12
## 4	G0:0042220	response to cocaine	12
## 5	G0:0050891	multicellular organismal water homeostas...	12
## 6	G0:0051701	interaction with host	86
## 7	G0:0043122	regulation of I-kappaB kinase/NF-kappaB ...	87
## 8	G0:0046578	regulation of Ras protein signal transdu...	57
## 9	G0:0007507	heart development	155

## 10	G0:0071312	cellular response to alkaloid	14
## 11	G0:0043278	response to morphine	14
## 12	G0:0033002	muscle cell proliferation	39
## 13	G0:0002011	morphogenesis of an epithelial sheet	15
## 14	G0:0000186	activation of MAPKK activity	23
## 15	G0:0038094	Fc-gamma receptor signaling pathway	32
## 16	G0:0038096	Fc-gamma receptor signaling pathway invo...	32
## 17	G0:0002431	Fc receptor mediated stimulatory signali...	32
## 18	G0:0002433	immune response-regulating cell surface ...	32
## 19	G0:0043901	negative regulation of multi-organism pr...	51
## 20	G0:0051817	modification of morphology or physiology...	42
##	Significant Expected Rank in Fisher.classic Fisher.elim Fisher.classic		
## 1	5	0.96	1 0.0019 0.0019
## 2	17	8.42	5 0.0039 0.0039
## 3	4	0.77	6 0.0055 0.0055
## 4	4	0.77	7 0.0055 0.0055
## 5	4	0.77	8 0.0055 0.0055
## 6	12	5.53	9 0.0082 0.0082
## 7	12	5.59	11 0.0090 0.0090
## 8	9	3.66	14 0.0096 0.0096
## 9	18	9.96	15 0.0097 0.0097
## 10	4	0.90	16 0.0100 0.0100
## 11	4	0.90	17 0.0100 0.0100
## 12	7	2.51	20 0.0109 0.0109
## 13	4	0.96	24 0.0130 0.0130
## 14	5	1.48	25 0.0136 0.0136
## 15	6	2.06	26 0.0146 0.0146
## 16	6	2.06	27 0.0146 0.0146
## 17	6	2.06	28 0.0146 0.0146
## 18	6	2.06	29 0.0146 0.0146
## 19	8	3.28	30 0.0149 0.0149
## 20	7	2.70	31 0.0162 0.0162

A graphical representation of the topGO results.



```
## $dag
## A graphNEL graph with directed edges
## Number of Nodes = 76
## Number of Edges = 135
##
## $complete.dag
```

```
## [1] "A graph with 76 nodes."
```

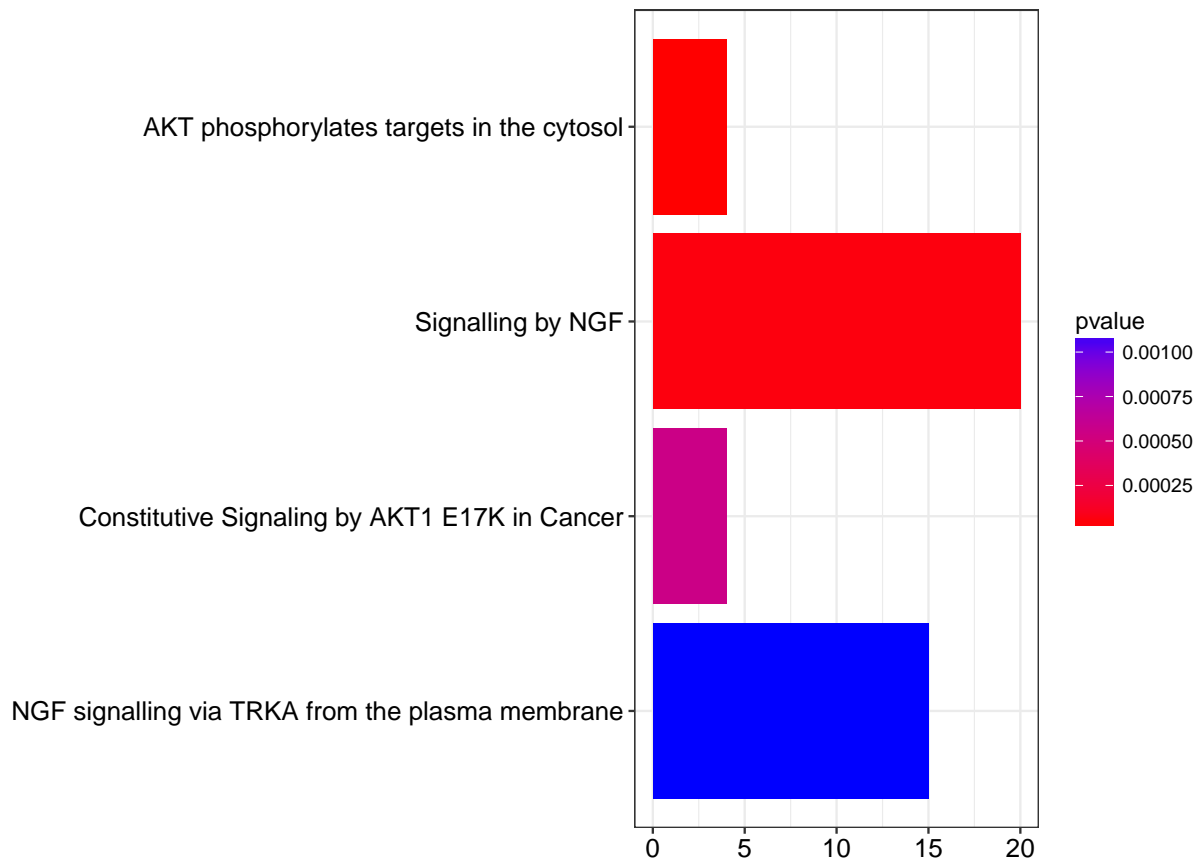
2.2 A pathway enrichment analysis using Reactome

**** Using P-value under 0.005 for pathway enrichment analysis ****

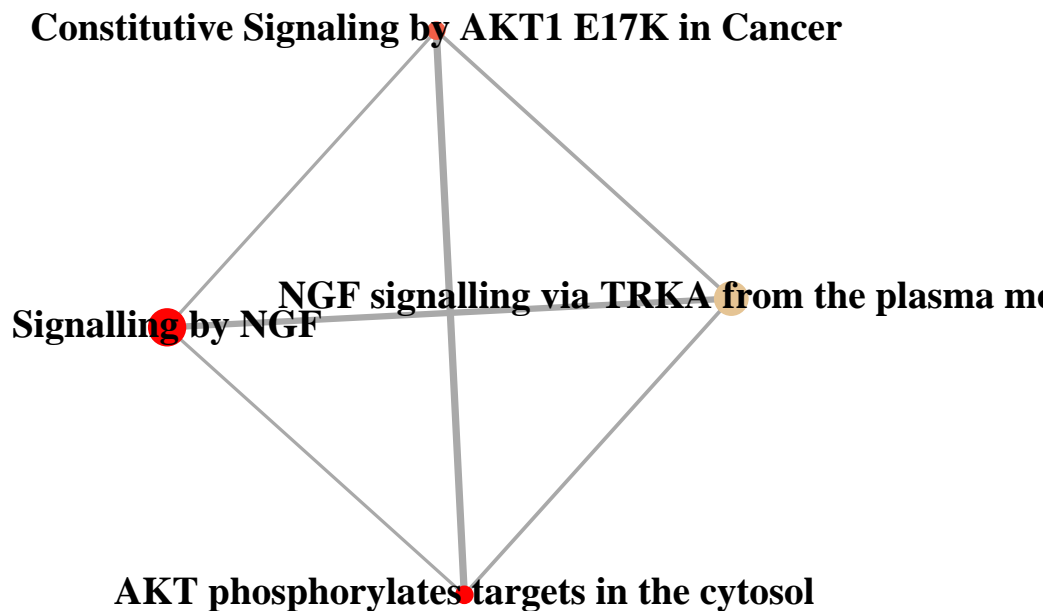
Enriched Reactome pathways and their p-values as a bar chart. - The top pathways can be displayed as a bar chart that displays all categories with a p-value below the specified cutoff.

##	ID	Description	GeneRatio
##	R-HSA-198323	AKT phosphorylates targets in the cytosol	4/160
##	R-HSA-166520	Signalling by NGF	20/160
##	R-HSA-5674400	Constitutive Signaling by AKT1 E17K in Cancer	4/160
##	R-HSA-187037	NGF signalling via TRKA from the plasma membrane	15/160

##	BgRatio	pvalue	p.adjust	
##	R-HSA-198323	13/10281	3.6e-05	0.021
##	R-HSA-166520	484/10281	6.0e-05	0.021
##	R-HSA-5674400	25/10281	5.5e-04	0.128
##	R-HSA-187037	390/10281	1.1e-03	0.191



Enriched Reactome pathways enrichment results as a graph.



3 BRCA2 versus WT

3.1 Gene ontology (GO) based enrichment analysis

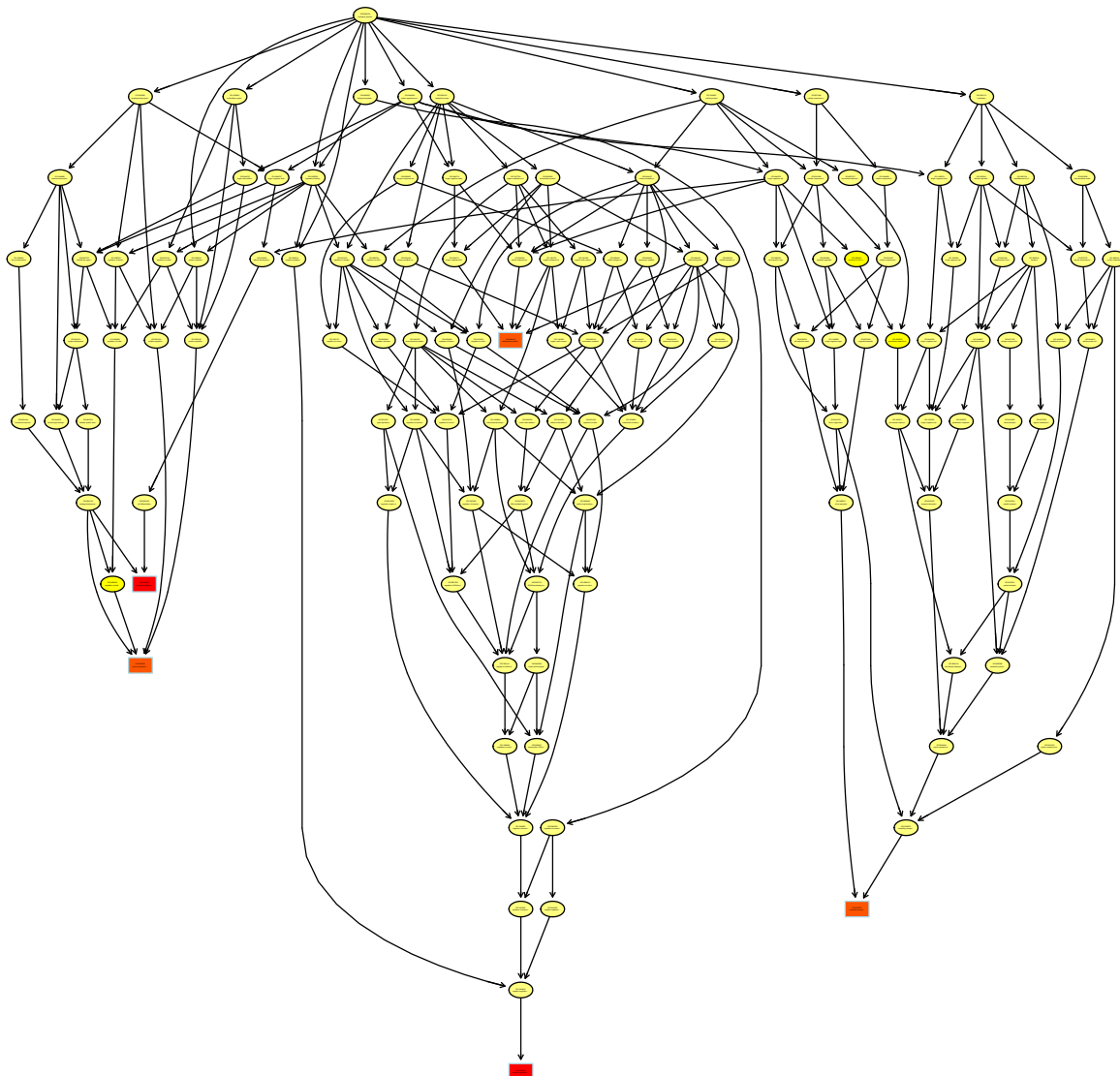
Top 20 GO enrichment terms

Using P-value under 0.01 for functional enrichment analysis

##	GO.ID	Term	Annotated
## 1	GO:0002062	chondrocyte differentiation	64
## 2	GO:0032088	negative regulation of NF-kappaB transcr...	39
## 3	GO:0061036	positive regulation of cartilage develop...	30
## 4	GO:0035735	intraciliary transport involved in ciliu...	31
## 5	GO:0046184	aldehyde biosynthetic process	10
## 6	GO:0010922	positive regulation of phosphatase activ...	15
## 7	GO:0097553	calcium ion transmembrane import into cy...	34
## 8	GO:0050690	regulation of defense response to virus ...	22
## 9	GO:0016055	Wnt signaling pathway	254
## 10	GO:0048704	embryonic skeletal system morphogenesis	65
## 11	GO:0030168	platelet activation	83
## 12	GO:0033688	regulation of osteoblast proliferation	12
## 13	GO:2000352	negative regulation of endothelial cell ...	12

## 14	G0:0002224	toll-like receptor signaling pathway	67
## 15	G0:0044003	modification by symbiont of host morphol...	24
## 16	G0:0030501	positive regulation of bone mineralizati...	18
## 17	G0:0010975	regulation of neuron projection developm...	213
## 18	G0:0051293	establishment of spindle localization	13
## 19	G0:1902895	positive regulation of pri-miRNA transcr...	19
## 20	G0:0030010	establishment of cell polarity	62
##	Significant	Expected Rank in Fisher.classic	Fisher.elim Fisher.classic
## 1	15	4.93	5 7.5e-05 7.5e-05
## 2	11	3.00	8 0.00012 0.00012
## 3	9	2.31	20 0.00029 0.00029
## 4	9	2.39	26 0.00038 0.00038
## 5	5	0.77	28 0.00048 0.00048
## 6	6	1.15	31 0.00055 0.00055
## 7	9	2.62	38 0.00081 0.00081
## 8	7	1.69	40 0.00094 0.00094
## 9	34	19.56	42 0.00096 0.00096
## 10	13	5.00	51 0.00114 0.00114
## 11	18	6.39	2 0.00132 4.5e-05
## 12	5	0.92	54 0.00133 0.00133
## 13	5	0.92	55 0.00133 0.00133
## 14	13	5.16	57 0.00153 0.00153
## 15	7	1.85	59 0.00168 0.00168
## 16	6	1.39	60 0.00168 0.00168
## 17	29	16.40	62 0.00171 0.00171
## 18	5	1.00	64 0.00203 0.00203
## 19	6	1.46	69 0.00230 0.00230
## 20	12	4.77	71 0.00234 0.00234

A graphical representation of the topGO results.



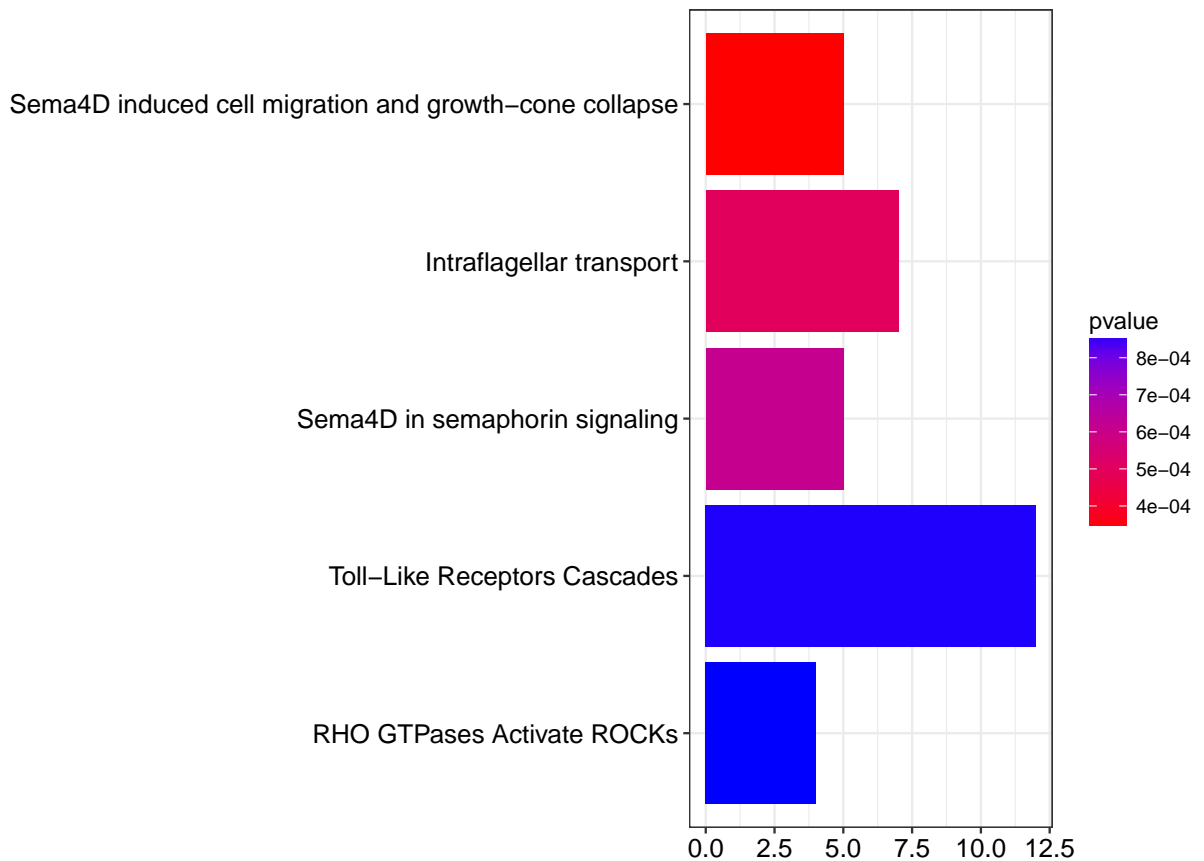
```
## $dag
## A graphNEL graph with directed edges
## Number of Nodes = 126
## Number of Edges = 250
##
## $complete.dag
## [1] "A graph with 126 nodes."
```

3.2 A pathway enrichment analysis using Reactome

Using P-value under 0.01 for pathway enrichment analysis

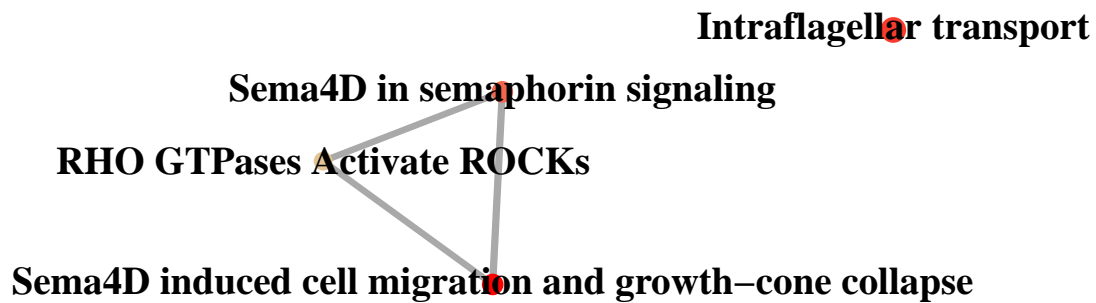
Enriched Reactome pathways and their p-values as a bar chart. - The top pathways can be displayed as a bar chart that displays all categories with a p-value below the specified cutoff.

##	ID				
##	R-HSA-416572	R-HSA-416572			
##	R-HSA-5620924	R-HSA-5620924			
##	R-HSA-400685	R-HSA-400685			
##	R-HSA-168898	R-HSA-168898			
##	R-HSA-5627117	R-HSA-5627117			
##		Description			
##	R-HSA-416572	Sema4D induced cell migration and growth-cone collapse			
##	R-HSA-5620924	Intraflagellar transport			
##	R-HSA-400685	Sema4D in semaphorin signaling			
##	R-HSA-168898	Toll-Like Receptors Cascades			
##	R-HSA-5627117	RHO GTPases Activate ROCKs			
##	GeneRatio	BgRatio	pvalue	p.adjust	
##	R-HSA-416572	5/271	24/10281	0.00035	0.14
##	R-HSA-5620924	7/271	54/10281	0.00050	0.14
##	R-HSA-400685	5/271	27/10281	0.00062	0.14
##	R-HSA-168898	12/271	156/10281	0.00085	0.14
##	R-HSA-5627117	4/271	17/10281	0.00086	0.14



Enriched Reactome pathways enrichment results as a graph.

Toll-Like Receptors Cascades



4 Conclusion

4.1 BRCA1 vs WT Function Analysis

Top GO terms are:

1. regulation of glial cell differentiation
2. single organismal cell-cell adhesion
3. myofibril assembly
4. response to cocaine
5. multicellular organismal water homeostasis
6. interaction with host
7. regulation of I-kappaB kinase/NF-kappaB signaling
8. regulation of Ras protein signal transduction
9. heart development
10. cellular response to alkaloid

4.2 BRCA1 vs WT Pathway enrichment analysis using Reactome

Top Affected Pathways:

1. AKT phosphorylates targets in the cytosol
2. Signalling by NGF

3. Constitutive Signaling by AKT1 E17K in Cancer
4. NGF signalling via TRKA from the plasma membrane

4.3 BRCA2 vs WT Function Analysis

Top GO terms are:

1. chondrocyte differentiation
2. negative regulation of NF-kappaB transcription factor activity
3. positive regulation of cartilage development
4. intraciliary transport involved in cilium assembly
5. aldehyde biosynthetic process
6. positive regulation of phosphatase activity
7. calcium ion transmembrane import into cytosol
8. regulation of defense response to virus by virus
9. Wnt signaling pathway
10. embryonic skeletal system morphogenesis

4.4 BRCA2 vs WT Pathway enrichment analysis using Reactome

Top Affected Pathways:

1. Sema4D induced cell migration and growth-cone collapse
2. Intraflagellar transport
3. Sema4D in semaphorin signaling
4. Toll-Like Receptors Cascades
5. RHO GTPases Activate ROCKs