

# **netGO :**

R/shiny Package for network-integrated pathway enrichment analysis

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## ≡ **What is netGO?**

- R/shiny Package for network-integrated pathway enrichment analysis
- Open source program to use in Statistical analysis.
- Find how genes are significantly included in pathways
- Using Network information ( Protein-Protein Interaction )

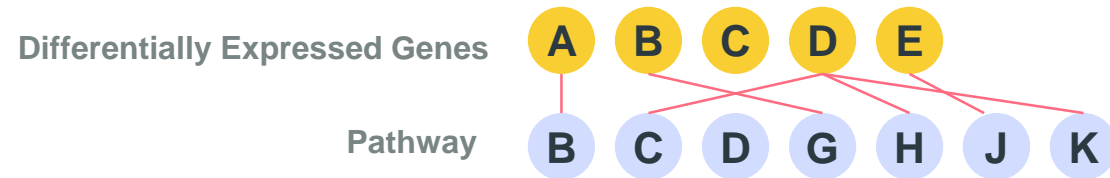
## How it works?

### Traditional Pathway analysis



$$\frac{|G \cap P|}{\min(|G|, |P|)} = \frac{3}{5}$$

### netGO



$$\frac{|G \cap P|}{\min(|G|, |P|)} + \text{net} = \frac{3}{5} + \text{net}$$

$$D(G \rightarrow P) = \omega \cdot \left( \frac{|G \cap P|}{|G|} \right) + (1 - \omega) \cdot \left( \frac{\alpha}{|T|} \sum_{x \in G-P} AI(x, P)^\beta \cdot RI(x, P)^{1-\beta} \right)$$

$$AI(x, P) = \frac{1}{|P|} \sum_{y \in P} I(x, y), RI(x, P) = \frac{1}{|N(x)|} \sum_{y \in P} I(x, y)$$

## ≡ **How can I use?**

- Install R, netGO package via Github (<https://github.com/unistbig/netGO>)
- Run netGO with own Data. (Also, example data is prepared)
- Get insight !



# How can I use?

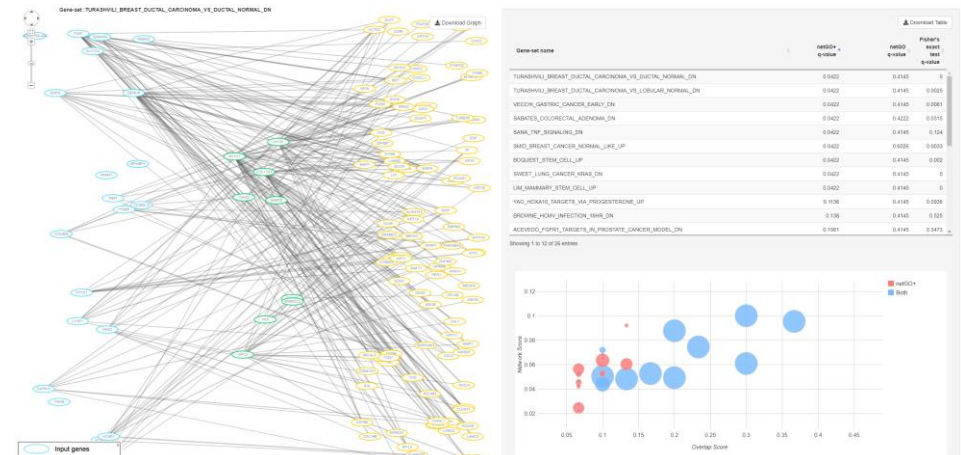
```
> obj3 = netGO(brca[1:30], genesets, network, genesetV)
```

Parallel function loads  
netGO calculation start  
Progress - each = means 5%

=====  
netGO calculation finished  
netGO+ calculation start  
Progress - each = means 5%

=====  
netGO+ calculation finished

```
> obj3[1:50,]
      gene-set  netGO  netGO+  FisherQ  OverlapScore  NetworkScore
1139  TURASHVILI_BREAST_DUCTAL_CARCINOMA_VS_DUCTAL_NORMAL_DN  0.4145493  0.04216245  3.424567e-06  0.30000000  0.06101461
1141  TURASHVILI_BREAST_DUCTAL_CARCINOMA_VS_LOBULAR_NORMAL_DN  0.4145493  0.04216245  2.512230e-03  0.13333333  0.04834635
1225  VECCHI_GASTRIC_CANCER_EARLY_DN  0.4145493  0.04216245  8.085328e-03  0.20000000  0.04940671
1327  SABATES_COLORECTAL_ADENOMA_DN  0.4221829  0.04216245  3.146580e-02  0.16666667  0.05279270
2051  SANA_TNF_SIGNALING_DN  0.4145493  0.04216245  1.239918e-01  0.10000000  0.05052787
2882  SMID_BREAST_CANCER_NORMAL_LIKE_UP  0.6026084  0.04216245  3.295149e-03  0.23333333  0.07457959
2932  BOQUEST_STEM_CELL_UP  0.4145493  0.04216245  1.964674e-03  0.20000000  0.08784530
3104  SWEET_LUNG_CANCER_KRAS_DN  0.4145493  0.04216245  1.200892e-05  0.30000000  0.10019266
3723  LIM_HAEMATOGENESIS_STEM_CELL_UP  0.4145493  0.04216245  1.126134e-07  0.36666667  0.09533468
2153  YAO_HOXA10_TARGETS_VIA_PROGESTERONE_UP  0.4145493  0.11383862  9.377171e-02  0.10000000  0.04425761
2493  BROWNE_HCMV_INFECTION_18HR_DN  0.4145493  0.13798620  5.250471e-01  0.10000000  0.06359878
3721  ACEVEDO_FGFRL1_TARGETS_IN_PROSTATE_CANCER_MODEL_DN  0.4145493  0.15810919  3.473165e-01  0.13333333  0.06049468
2346  WESTON_VEGFA_TARGETS_GHR  0.4145493  0.16262659  6.115580e-01  0.06666667  0.05644747
3198  VALK_AML_CLUSTER_9  0.4145493  0.16262659  3.656684e-01  0.06666667  0.02465327
2879  SMID_BREAST_CANCER_LUMINAL_A_UP  0.4145493  0.22767723  8.584529e-01  0.06666667  0.05252725
682  REACTOME_GLYCOSAMINOGLYCAN_METABOLISM  0.4145493  0.23189348  2.083634e-01  0.10000000  0.07210894
1144  TURASHVILI_BREAST_LOBULAR_CARCINOMA_VS_DUCTAL_NORMAL_DN  0.4145493  0.23189348  9.279819e-01  0.06666667  0.04564789
3556  MIYAGAWA_TARGETS_OF_EWSR1_LETS_FUSIONS_DN  0.4145493  0.23189348  6.960037e-01  0.10000000  0.05291238
2633  WANG_SMACCEL_TARGETS_UP  0.4145493  0.23966024  9.279819e-01  0.10000000  0.06535960
1145  TURASHVILI_BREAST_LOBULAR_CARCINOMA_VS_LOBULAR_NORMAL_UP  0.4145493  0.24810980  9.445829e-01  0.06666667  0.04647504
1397  DELYS_THYROID_CANCER_DN  0.4145493  0.24810980  6.960037e-01  0.10000000  0.06798274
1946  LEE_TARGETS_OF_PTCH1_AND_SUFU_UP  0.8798944  0.24810980  5.698235e-01  0.06666667  0.02726989
2017  ROSS_AML_WITH_CBP_PWWL_FUSION  0.6128952  0.24810980  5.698235e-01  0.06666667  0.02256462
2934  BOQUEST_STEM_CELL_CULTURED_VS_FRESH_UP  0.5234852  0.24810980  6.115580e-01  0.13333333  0.09225607
3276  MIKKELSEN_IPS_ICP_WITH_H3K4ME3_AND_H327ME3  0.4145493  0.24810980  1.000000e+00  0.06666667  0.04208265
3519  PANGAS_TUMOR_SUPPRESSION_BY_SMAD1_AND_SMAD5_UP  0.4145493  0.24810980  1.000000e+00  0.06666667  0.04310035
3318  KORKOLA_EMBRYONIC_CARCINOMA_VS_SEMINOMA_UP  0.4145493  0.27104432  1.000000e+00  0.03333333  0.03483580
3738  WARTERS_LR_RESPONSE_SGY  0.9938063  0.27104432  5.250471e-01  0.06666667  0.02339494
2439  NIELSEN_LIPOCARCINOMA_UP  0.4145493  0.30831292  1.000000e+00  0.03333333  0.01860542
2452  WESTON_VEGFA_TARGETS  0.4145493  0.30831292  1.000000e+00  0.06666667  0.06738126
2841  RIGOT_EWING_SARCOMA_PROGENITOR_DN  0.4145493  0.30831292  1.000000e+00  0.06666667  0.05853074
3212  POOLA_INVASIVE_BREAST_CANCER_DN  0.4145493  0.30831292  1.000000e+00  0.06666667  0.05517289
1853  SCHAEFFER_PROSTATE_DEVELOPMENT_GHR_UP  0.8310391  0.31046895  5.250471e-01  0.10000000  0.03657326
2712  LEIN_CHOROIOD_PLEXUS_MARKERS  0.4145493  0.33729960  1.000000e+00  0.06666667  0.03102362
3265  MIKKELSEN_MCV6_HCP_WITH_H3K27ME3  0.4145493  0.33729960  6.355794e-01  0.13333333  0.07089955
0389  YAO_TEMPORAL_RESPONSE_TO_PROGESTERONE_CLUSTER_1  0.6579220  0.33729960  6.960037e-01  0.06666667  0.03453843
3752  NABA_COLLAGENS  0.4145493  0.35895059  5.250471e-01  0.06666667  0.08224751
989  REACTOME_METABOLISM_OF_CARBOHYDRATES  0.4145493  0.36139243  7.709060e-01  0.10000000  0.09484623
1539  WONG_ENDOMETRIUM_CANCER_DN  0.4145493  0.36139243  1.000000e+00  0.03333333  0.04578543
2390  BROWNE_HCMV_INFECTION_24HR_DN  0.4145493  0.36139243  1.000000e+00  0.06666667  0.0667856
3655  PLASARI_TGFR1_TARGETS_10HR_DN  0.6351316  0.36139243  7.709060e-01  0.10000000  0.05209529
3758  NABA_CORE_MATRISOME  0.4145493  0.36139243  9.279819e-01  0.10000000  0.08268774
3792  HOLLERN_SOLID_NODULAR_BREAST_TUMOR_DN  0.4145493  0.37946205  1.000000e+00  0.03333333  0.03191635
1807  INGRAM_SHH_TARGETS_DN  0.4145493  0.40420958  1.000000e+00  0.03333333  0.04165000
2173  WANG_IMMORTALIZED_PV_HOXA9_AND_MET1_DN  0.4145493  0.40420958  1.000000e+00  0.03333333  0.02428975
3087  SCHRAETS_MLL_TARGETS_UP  0.4145493  0.40420958  1.000000e+00  0.03333333  0.04255129
107  KEGG_ECM_RECEPTOR_INTERACTION  0.4145493  0.40922378  8.584529e-01  0.06666667  0.10727309
1076  NAKAMURA_CANCER_MICROENVIRONMENT_UP  0.4145493  0.40922378  1.000000e+00  0.03333333  0.03799837
1150  WILCOX_RESPONSE_TO_PROGESTERONE_DN  0.4145493  0.40922378  1.000000e+00  0.03333333  0.05394571
2960  LU_TUMOR_ENDOTHELIAL_MARKERS_UP  0.4145493  0.40922378  1.000000e+00  0.03333333  0.02734533
```





## Example Run

- Breast tumor data set ( GSE3744 )
- 40 Tumor vs 7 Normal
- DEG calculated with default GEO2R and 30 genes selected.

## ≡ Result

- Based on Q value
- netGO found **26** gene-sets as significant ( Qvalue <0.25 )  
And **6** gene-sets of them are intersect with Breast tumor related gene-sets
- Where, Fisher Exact Test ( traditional method ) found **11** gene-sets ( Qvalue <0.25 )  
And **3** gene-sets of them are intersect with Breast tumor related gene-sets
- Based on Rank
- In netGO's top **50** gene-sets,  
**8** gene-sets of them are intersect with Breast tumor related gene-sets
- and, Fisher Exact Test's top **50** gene-sets,  
And **6** gene-sets of them are intersect with Breast tumor related gene-sets





## Result

ACEVEDO_FGFR1_TARGETS_IN_PROSTATE_CANCER_MODEL_DN	SANA_TNF_SIGNALING_DN
BOQUEST_STEM_CELL_CULTURED_VS_FRESH_UP	SMID_BREAST_CANCER_LUMINAL_A_UP
BOQUEST_STEM_CELL_UP	SMID_BREAST_CANCER_NORMAL_LIKE_UP
BROWNE_HCMV_INFECTION_18HR_DN	SWEET_LUNG_CANCER_KRAS_DN
DELYS_THYROID_CANCER_DN	TURASHVILI_BREAST_DUCTAL_CARCINOMA_VS_DUCTAL_NORMAL_DN
LEE_TARGETS_OF_PTCH1_AND_SUFU_UP	TURASHVILI_BREAST_DUCTAL_CARCINOMA_VS_LOBULAR_NORMAL_DN
LIM_MAMMARY_STEM_CELL_UP	TURASHVILI_BREAST_LOBULAR_CARCINOMA_VS_DUCTAL_NORMAL_DN
MIKKELSEN_IPS_ICP_WITH_H3K4ME3_AND_H327ME3	TURASHVILI_BREAST_LOBULAR_CARCINOMA_VS_LOBULAR_NORMAL_UP
MIYAGAWA_TARGETS_OF_EWSR1_ETS_FUSIONS_DN	VALK_AML_CLUSTER_9
PANGAS_TUMOR_SUPPRESSION_BY_SMAD1_AND_SMAD5_UP	VECCHI_GASTRIC_CANCER_EARLY_DN
REACTOME_GLYCOSAMINOGLYCAN_METABOLISM	WANG_SMARCE1_TARGETS_UP
ROSS_AML_WITH_CBFB_MYH11_FUSION	WESTON_VEGFA_TARGETS_6HR
SABATES_COLORECTAL_ADENOMA_DN	YAO_HOXA10_TARGETS_VIA_PROGESTERONE_UP

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BOQUEST_STEM_CELL_UP
LIM_MAMMARY_STEM_CELL_UP
REACTOME_GLYCOSAMINOGLYCAN_METABOLISM
SABATES_COLORECTAL_ADENOMA_DN
SANA_TNF_SIGNALING_DN
SMID_BREAST_CANCER_NORMAL_LIKE_UP
SWEET_LUNG_CANCER_KRAS_DN
TURASHVILI_BREAST_DUCTAL_CARCINOMA_VS_DUCTAL_NORMAL_DN
TURASHVILI_BREAST_DUCTAL_CARCINOMA_VS_LOBULAR_NORMAL_DN
VECCHI_GASTRIC_CANCER_EARLY_DN
YAO_HOXA10_TARGETS_VIA_PROGESTERONE_UP

— Evidence with overlap is not good,  
but Strong in network score



## Q&A

Thanks for listening