

R for Gene Ontology Analysis

Genome-wide studies

- Sanger sequencing
- Next generation sequencing
- Microarray
- ChIP-chip and ChIP-seq
- RNA-seq
- Tandem mass spectrometry
-

An Example

5 normal sample and 9 myeloma (MM) samples 12558 genes (rows)

probe set	gene	Normal m4	Normal m4	Normal m4	Normal m4	Normal m4	MM m282	MM m331a	MM m332a	MM m333a	MM m334a	MM m353a	MM m408a	MM m423a
31307_at	pre-T/NK c	28.53	32.61	29.56	36.55	33.19	25.1	32.79	34.3	35.44	28.48	29.55	22.28	28.77
31308_at	pre-T/NK c	69.14	53.69	52.78	62.07	58.74	67.88	85.82	83.54	85.91	60.93	62.82	47.17	77.07
31309_r_a	Human bre	16.9	67.7	27.61	46.16	51.46	45.62	35.57	32.62	35.14	96.18	45.94	63.2	38.27
31310_at	glycine rec	67.42	49.55	55.51	59.57	68.42	91.06	91.23	83.66	76.37	71.23	74.95	74.04	100.77
31311_at	Homo sapi	78.73	62.91	60.84	72.98	72.9	79.39	85.52	82.57	69.69	63.72	64.29	62.85	67.58
31312_at	potassium	66.65	59.46	55.47	61.75	69.92	75.28	85.53	97.91	69.92	74.77	71.83	58.17	72.15
31313_at	mannosyl	115.33	95.51	84.48	94.99	109.04	105.05	118.68	106.76	142.88	103.72	106.19	98.58	104.13
31314_at	bone morp	71.89	36.24	41.86	46.99	45.94	46.67	67.56	66.14	53.95	40.97	47.96	43.63	53.54
31315_at	immunoglo	103.99	88.27	83.81	81.81	254.63	87.12	99.11	109.56	86.37	75.03	74.97	69.02	97.22
31316_at	Human vac	16.79	10.08	9.53	16.48	11.98	12.8	16.7	18.76	11.25	12.09	18.89	10.81	19.49
31317_r_a	Human un	316.75	269.61	254.92	352.61	342.4	327.12	366.39	346	308.43	279.81	312.4	318.06	334.27
31318_at	Stem cell f	32.68	19.79	27.45	29.56	28.34	26.55	38.04	41.05	31.91	22.76	23.58	28.29	22.61
31319_at	Cluster Inc	252.78	441.07	143.32	400.01	373.4	105.06	105.72	87.02	110.75	161.69	84.88	240.91	210.54
31320_at	Cluster Inc	101.42	89.07	79.51	100.69	120.06	116.74	121.41	134.74	131.36	137.4	114.15	119.89	126.74
31321_at	Cluster Inc	112.27	62.17	62.44	80.17	110.97	53.89	55.04	55.16	63.37	54.35	57.79	48.07	47.89
31322_at	Cluster Inc	44.15	52.5	44.8	46.25	55.96	50.01	53.2	52.24	62.16	49.94	47.24	40.64	50.1
31323_r_a	Glutamate	141.44	177.7	138.58	142.61	167.28	169.49	199.64	185.22	218.79	196.56	150.14	185.24	226.37
31324_at	Cluster Inc	70.87	57.8	61.61	65.93	84.05	106.41	106.73	87.01	112.12	78.47	111	89.08	100.53
31325_at	Cluster Inc	68.63	167.66	69.04	112.84	120.46	126.72	107.04	100	116.83	207.5	125.65	155.19	102.55
31326_at	Cluster Inc	157.67	127.49	123.37	146.18	150.95	159.46	184.08	206.02	182.95	139.01	154.57	143.09	175.27
31327_at	Cluster Inc	35.57	28.17	33.64	32.36	38.76	43.13	40.16	46.8	34.47	33.71	25.74	29.45	37.37
31328_at	solute carr	61.61	48.23	50.76	58	57.58	57.91	69.91	72.34	70.29	54.98	59.74	45.55	63.02
31329_at	Human pur	12.23	18.91	15.36	19.99	21.15	15.9	20.76	22.26	16.15	28.86	13.59	16.06	23.85
31330_at	ribosomal	108.87	133.3	89.84	113.02	147.61	169.87	156.81	136.47	153.07	220.54	220.96	332.11	183
31331_at	surfactant	28.21	17.99	23.56	26.37	30.35	28.84	31.54	35.06	22.53	24.45	23	21.37	30.86
31332_at	RIG-like 1	20.77	18.58	19.03	18.29	20.86	23.56	25.11	24.43	19.3	28.72	17.27	23.18	25.35
31333_at	tolloid-like	22.97	52.9	26.95	41.22	48.38	48.85	42.09	40.13	40.73	89.86	46.96	59.74	40.87
31334_at	G protein-c	98.57	100.16	78.76	119.09	118.58	97.42	110.67	104.95	143.47	111.28	102.88	115.9	133.17
31335_at	clone 1900	65.79	54.3	54.79	57.23	60.75	66.98	72.89	86.97	76.34	57.65	59.83	49.21	70.83
31336_at	Cluster Inc	40.97	26.15	32.55	26.26	33.73	36.15	36.03	34.93	24.12	26.26	22.55	23.64	28.11

34 taste genes

- NM_199153
- NM_207011
- NM_020501
- NM_207016
- NM_199154
- NM_020502
- NM_207017
- NM_199155
- NM_207018
- NM_207019
- NM_207020
- NM_053212
- NM_207021
- NM_207022
- NM_020503
- NM_207023
- NM_207024
- NM_001039128
- NM_207025
- NM_207026
- NM_207027
- NM_207028
- NM_207029
- NM_199156
- NM_207030
- NM_199158
- NM_199159
- NM_181276
- NM_001025385
- NM_001001451
- NM_181275
- NM_021562
- NM_001001452
- NM_001001453



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Gene Ontology Home

The Gene Ontology project provides a controlled vocabulary to describe gene and gene product attributes in any organism. [Read more...](#)

Popular Links

Search the Gene Ontology Database

☒ gene or protein name ☐ GO term or ID

This search uses the browser [AmiGO](#). [Browse](#) the Gene Ontology using AmiGO.

<http://www.geneontology.org/>

cellular component, biological process and molecular function.

A gene product might be associated with or located in one or more cellular components; it is active in one or more biological processes, during which it performs one or more molecular functions.

For example, the gene product cytochrome c can be described by the molecular function term oxidoreductase activity, the biological process terms oxidative phosphorylation and induction of cell death, and the cellular component terms mitochondrial matrix and mitochondrial inner membrane.

Cellular component

A cellular component is just that, a component of a cell, but with the proviso that it is part of some larger object; this may be an anatomical structure (e.g. rough endoplasmic reticulum or nucleus) or a gene product group (e.g. ribosome, proteasome or a protein dimer). See the [documentation on the cellular component ontology](#) for more details.

Biological process

A biological process is series of events accomplished by one or more ordered assemblies of molecular functions. Examples of broad biological process terms are cellular physiological process or signal transduction. Examples of more specific terms are pyrimidine metabolism or alpha-glucoside transport. It can be difficult to distinguish between a biological process and a molecular function, but the general rule is that a process must have more than one distinct steps.

A biological process is not equivalent to a pathway; at present, GO does not try to represent the dynamics or dependencies that would be required to fully describe a pathway.

Further information can be found in the [process ontology documentation](#).

Molecular function

Molecular function describes activities, such as catalytic or binding activities, that occur at the molecular level. GO molecular function terms represent activities rather than the entities (molecules or complexes) that perform the actions, and do not specify where or when, or in what context, the action takes place. Molecular functions generally correspond to activities that can be performed by individual gene products, but some activities are performed by assembled complexes of gene products. Examples of broad functional terms are catalytic activity, transporter activity, or binding; examples of narrower functional terms are adenylate cyclase activity or Toll receptor binding.

Search GO

- ☐ Exact Match
☒ Terms
☐ Gene Symbol/Name

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Gene Product Filters

Species

- All
- A. japonica
- A. niger
- A. platyrhynchos

Datasource

- All
- FlyBase
- SGD
- MGI

Evidence Code

- All Curator Approved
- IC
- IMP
- IGI

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Last updated: 2006-01-05

all : all (166170)

GO:0008150 : biological_process (118045)

GO:0000004 : biological process unknown (33123)

GO:0009987 : cellular process (70992)

GO:0007275 : development (12234)

GO:0040007 : growth (3010)

GO:0051704 : interaction between organisms (1392)

GO:0051705 : behavioral interaction between organisms (196)

GO:0042710 : biofilm formation (17)

GO:0000746 : conjugation (204)

GO:0000128 : flocculation (10)

GO:0009292 : genetic transfer (70)

GO:0044419 : interspecies interaction between organisms (820)

GO:0044402 : competition with another organism (0)

GO:0044403 : symbiosis, encompassing mutualism through parasitism (818)

GO:0051703 : intraspecies interaction between organisms (8)

GO:0051706 : physiological interaction between organisms (135)

GO:0007582 : physiological process (72983)

GO:0043473 : pigmentation (86)

GO:0050789 : regulation of biological process (13235)

GO:0000003 : reproduction (3883)

GO:0050896 : response to stimulus (13945)

GO:0016032 : viral life cycle (289)

GO:0005575 : cellular_component (103652)

GO:0003674 : molecular_function (114778)

obsolete_biological_process : obsolete_biological_process (0)

obsolete_cellular_component : obsolete_cellular_component (0)

obsolete_molecular_function : obsolete_molecular_function (0)

[Graphical View](#)

http://www.geneontology.org/GO.current.annotations.shtml

5 - GEO DataSets Free Hotmail Windows Marketplace Windows Media Windows

Species, Database	Gene Products Annotated	Annotations	Submission date MM/DD/YYYY	Download filtered files
<i>Anaplasma phagocytophilum</i> HZ TIGR	1292	3559 (3559 non-IEA)	1/13/2007	 annotations [38.7 kb]  README
<i>Arabidopsis thaliana</i> TAIR/TIGR	35026	105826 (83959 non-IEA)	4/28/2007	 annotations [2.3 mb]  README
<i>Bacillus anthracis</i> Ames TIGR	5289	13393 (13393 non-IEA)	3/19/2007	 annotations [148.6 kb]  README
<i>Bos taurus</i> GO Annotations @ EBI	22780	84862 (3010 non-IEA)	4/28/2007	 annotations [1.1 mb]  README
<i>Carboxydothermus hydrogenoformans</i> Z-2901 TIGR	2616	6610 (6610 non-IEA)	4/18/2007	 annotations [79.7 kb]  README
<i>Caenorhabditis elegans</i> WormBase	14011	93427 (33378 non-IEA)	4/28/2007	 annotations [745.9 kb]  README
<i>Campylobacter jejuni</i> RM1221 TIGR	1834	4791 (4791 non-IEA)	1/13/2007	 annotations [60.0 kb]  README
<i>Candida albicans</i> CGD	1280	5425 (5214 non-IEA)	4/11/2007	 annotations [68.2 kb]  README
<i>Coxiella burnetii</i> RSA 493 TIGR	2038	5294 (5294 non-IEA)	1/13/2007	 annotations [58.0 kb]  README
<i>Danio rerio</i> ZFIN	12961	70855 (20485 non-IEA)	4/28/2007	 annotations [1.1 mb]  README
<i>Dehalococcoides ethenogenes</i> 195 TIGR	1584	4068 (4068 non-IEA)	3/19/2007	 annotations [47.4 kb]  README
<i>Dictyostelium discoideum</i> DictyBase	6581	27438 (15179 non-IEA)	4/22/2007	 annotations [330.7 kb]  README
<i>Drosophila melanogaster</i> FlyBase	11605	70438 (47970 non-IEA)	4/7/2007	 annotations [862.4 kb]  README

3 Microsoft... 4 Firefox 3 Internet ... Feedreader ... randomGene... 149.166.16... RGui UltraEdit-32 ... 2:46 PM

http://www.geneontology.org/GO.teaching.resources.shtml

GO Teaching Resources - Mozilla Firefox

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http://www.geneontology.org/GO.teaching.resources.shtml

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 *the Gene Ontology*

Search
 gene or protein name

GO Teaching Resources

The following posters, tutorials and presentations have been prepared and used by members of the GO Consortium to educate and disseminate information about the GO project. Please note that these items were written for specific events, and have not subsequently been updated. Some of the material in the older files may not be representative of the current state of the project. Please check the dates carefully and choose the newest relevant file.

Presentations
Tutorials
Posters
Sample Annotation Sets

Presentations

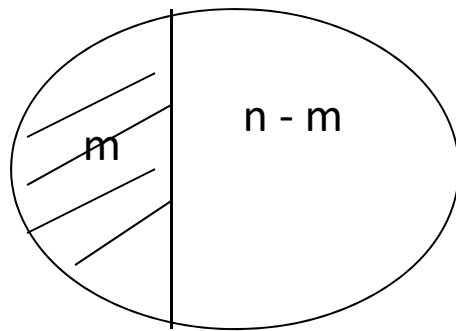
Title and author	Date	Download
Real-life Ontology Development Jane Lomax (EBI) Second Meeting of the Ontogenesis Network University of Manchester, UK.	March 2007	 ppt
Making Gene Ontology Annotations for Fungal Genomes Karen Christie, Rama Balakrishnan, and Maria Costanzo (SGD) 24th Fungal Genetics Conference, workshop Asilomar, Pacific Grove, CA	January 2007	 ppt
What's New in GO? Jennifer Clark (EBI)	January 2007	 ppt

Done

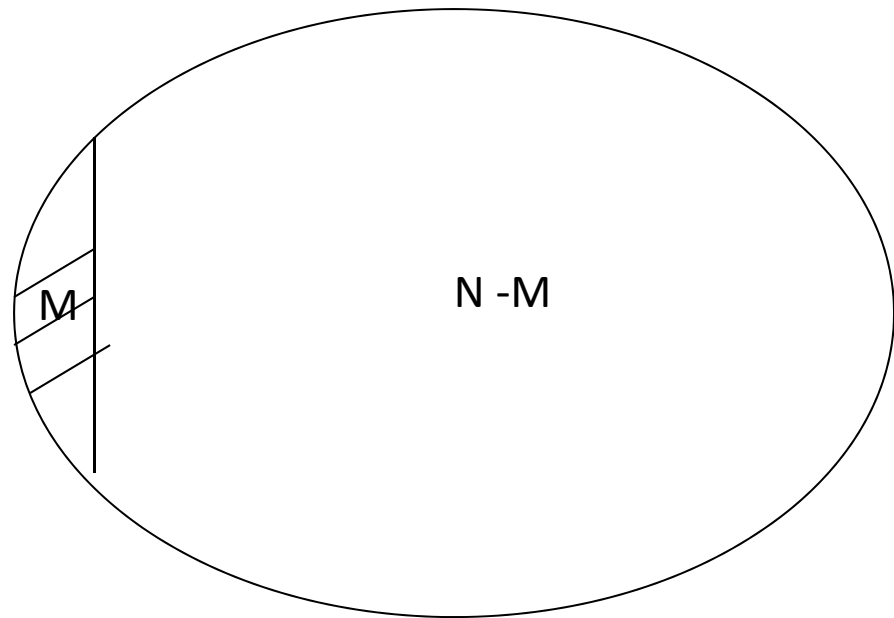
Start 3 Microsoft... 4 Firefox 3 Internet... Feedreader... randomGen... 149.166.16... RGui UltraEdit-32... 2:31 PM

Common function

What do we mean by common function? 90% genes have the function?



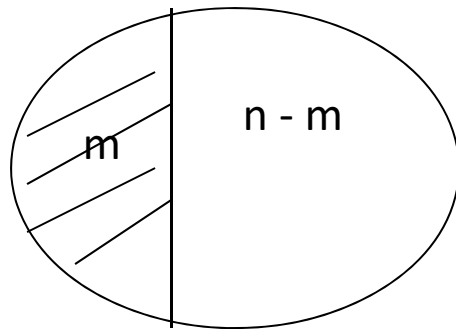
Genes under consideration



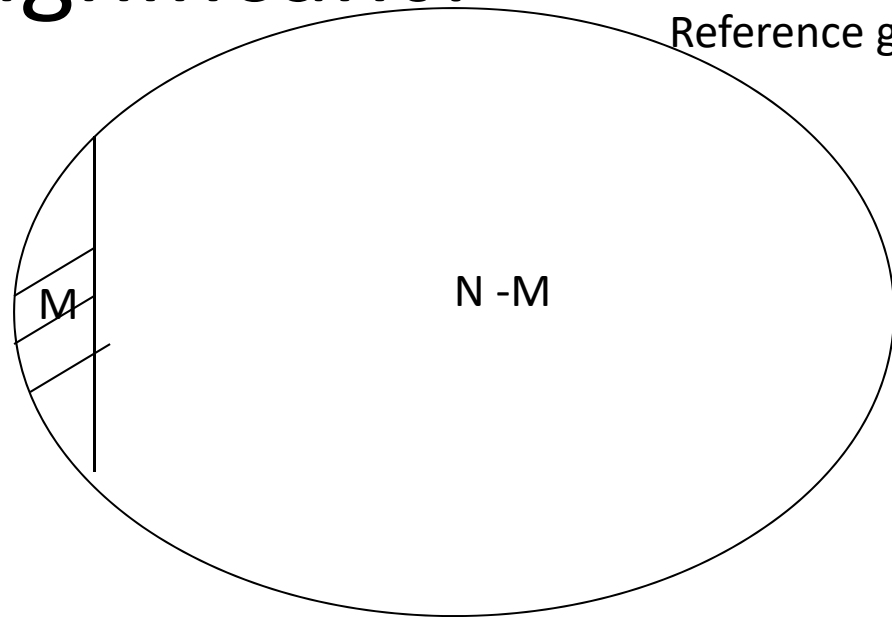
Reference genes

How significant?

Genes under consideration



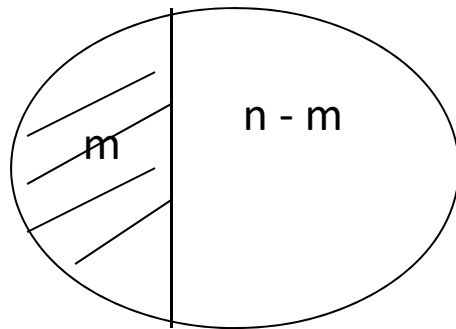
Reference genes



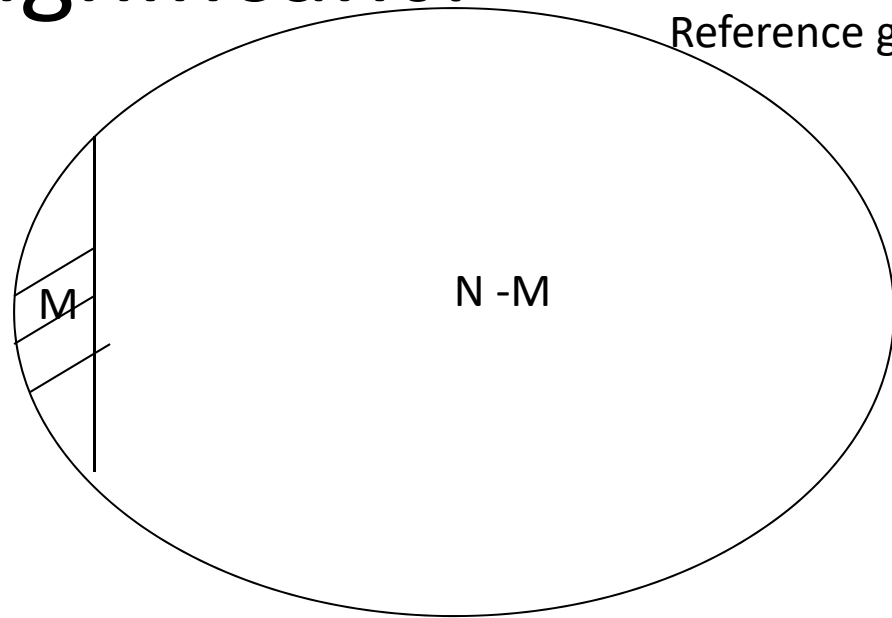
n	m	N	M
34	10	25000	2000
34	10	25000	200
34	2	25000	400

How significant?

Genes under consideration



Reference genes



n	m	N	M	significance
34	10	25000	2000	0.0002304588
34	10	25000	200	9.503509e-14
34	2	25000	400	0.1025492

P-value

In statistical hypothesis testing, the **p-value** is the probability of obtaining a result at least as extreme as the one that was actually observed, assuming that the null hypothesis is true. The fact that p-values are based on this assumption is crucial to their correct interpretation.

Hypergeometric testing

	Annotated with term A	Annotated w/o term A
Reference gene set	m	n - m
Target gene set	M	N-M

$$p - value = \sum_{i=m}^{\min(n, M)} \frac{C_M^i C_{N-M}^{n-i}}{C_N^n}, \quad C_i^j = \frac{j(j-1)\cdots 1}{i(i-1)\cdots 1}.$$

GO enrichment analysis

<http://genemerge.cbcb.umd.edu/>

<http://david.abcc.ncifcrf.gov/home.jsp>

http://www.informatics.jax.org/gotools/MGI_Term_Finder.html

<http://go.princeton.edu/cgi-bin/GOTermFinder>

<http://gostat.wehi.edu.au/cgi-bin/goStat.pl>

Multiple comparisons and false discovery rate

multiple comparisons problem occurs when one considers a set, or family, of statistical inferences simultaneously.

Dealing with Multiple Comparison

- **Bonferroni inequality:** To control the **family-wise error rate** for testing m hypotheses at level α , we need to control the FPR for each individual test at α/m
- Then $P(\text{false rejection at least one hypothesis}) < \alpha$
or $P(\text{no false rejection}) > 1 - \alpha$
- This is appropriate for some applications (e.g. testing a new drug versus several existing ones), but is too conservative for our task of gene selection.

GOstats

- `if (!require("BiocManager", quietly = TRUE))
install.packages("BiocManager")`
- `#install Bioconductor if not installed`
- `BiocManager::install("GOstats")`
- `#any Bioconductor packages should be install by such a
command`
- Google “how to use Gostats”, you will have “*How To Use GOstats and Category to do Hypergeometric testing with unsupported model organisms*” by M. Carlson. October 26, 2021 in the pdf format.

GOstats

```
if (!require("BiocManager", quietly = TRUE))  
  install.packages("BiocManager")
```

```
BiocManager::install("GOstats")
```

```
## Fake up some data  
BiocManager::install("hgu95av2.db")  
library("hgu95av2.db")  
library("annotate")  
prbs <- ls(hgu95av2GO)[1:300]  
## Only those with GO ids  
hasGO <- lengths(lapply(mget(prbs, hgu95av2GO), names)) != 0  
prbs <- prbs[hasGO]  
prbs <- getEG(prbs, "hgu95av2")  
## remove duplicates, but keep named vector  
prbs <- prbs[!duplicated(prbs)]  
## do the same for universe  
univ <- ls(hgu95av2GO)[1:5000]  
hasUnivGO <- lengths(lapply(mget(univ, hgu95av2GO), names)) != 0  
univ <- univ[hasUnivGO]  
univ <- unique(getEG(univ, "hgu95av2"))  
p <- new("GOHyperGParams", genelds=prbs, universeGenelds=univ,  
ontology="BP", annotation="hgu95av2", conditional=TRUE)  
## this part takes time...  
if(interactive()){  
  hyp <- hyperGTest(p)  
  ps <- probeSetSummary(hyp, 0.05, 10)  
}
```

GOstats

#The following is for non-model organism.

```
library("AnnotationForge")  
available.dbschemas()
```

```
library("org.Hs.eg.db")  
#if the above line does not work, install this package in Bioconduction with the  
#command BiocManager::install("org.Hs.eg.db")
```

```
#the following 3 lines is to make your own GO database  
frame = toTable(org.Hs.egGO)  
goframeData = data.frame(frame$go_id, frame$Evidence, frame$gene_id)  
head(goframeData)
```

```
#The following is to convert your own GO database into GSEA accepting database  
goFrame=GOFrame(goframeData,organism="Homo sapiens")  
goAllFrame=GOAllFrame(goFrame)  
library("GSEABase")  
gsc <- GeneSetCollection(goAllFrame, setType = GOCollection())
```

GOstats

```
#the following section is for the GSEA GO analysis. It outputs the significant
#GO ID and terms and p-value and gene count. But not the gene IDs as in other
#tools. You need to parse the above goAllFrame and these files to obtain the
#similar output with gene names.
library("GOstats")
universe = Lkeys(org.Hs.egGO)
genes = universe[1:500]
params <- GSEAGOHyperGParams(name="My Custom GSEA based annot Params",
  geneSetCollection=gsc,
  genelds = genes,
  universeGenelds = universe,
  ontology = "MF",
  pvalueCutoff = 0.05,
  conditional = FALSE,
  testDirection = "over")

Over <- hyperGTest(params)
head(summary(Over))
```

GOstats

#the following section is for the KEGG GO analysis, similar to the aboe.

```
frame = toTable(org.Hs.egPATH)
```

```
keggframeData = data.frame(frame$path_id, frame$gene_id)
```

```
head(keggframeData)
```

```
keggFrame=KEGGFrame(keggframeData,organism="Homo sapiens")
```

```
gsc <- GeneSetCollection(keggFrame, setType = KEGGCollection())
```

```
universe = Lkeys(org.Hs.egGO)
```

```
genes = universe[1:500]
```

```
kparams <- GSEAKEGGHyperGParams(name="My Custom GSEA based annot Params",
```

```
  geneSetCollection=gsc,
```

```
  genelds = genes,
```

```
  universeGenelds = universe,
```

```
  pvalueCutoff = 0.05,
```

```
  testDirection = "over")
```

```
kOver <- hyperGTest(params)
```

```
head(summary(kOver))
```

#output the tools and versions used.

```
toLatex(sessionInfo())
```

references

- <https://bioconductor.org/packages/devel/bioc/manuals/GOstats/man/GOstats.pdf>
- *How To Use GOstats* and Category to do Hypergeometric testing with unsupported model organisms” by M. Carlson. October 26, 2021 in the pdf format.