

# SPIA-PCC: Signaling pathway impact analysis incorporated the change of Pearson correlation coefficient between two groups

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## spiapcc pathway signatures

This R package provides function that uses the previous SPIA method and integrate the change of genes Pearson coefficient(PCC) from two groups. We proposed a set of three pathway analysis methods based on the change of PCC. We applied these approaches to colorectal cancer, lung cancer and Alzheimer's disease datasets and so on.

## Scoring the KEGGandMetacoreDzPathwaysGEO package data for pathway analysis

This is to outline how to prepare expression data, in this case from the KEGGandMetacoreDzPathwaysGEO package for pathway analysis using spiap.

### Preparing the gene expression matrix

```
library(EnrichmentBrowser)
library(KEGGandMetacoreDzPathwaysGEO)
library(KEGGdzPathwaysGEO)
library(SPIA)

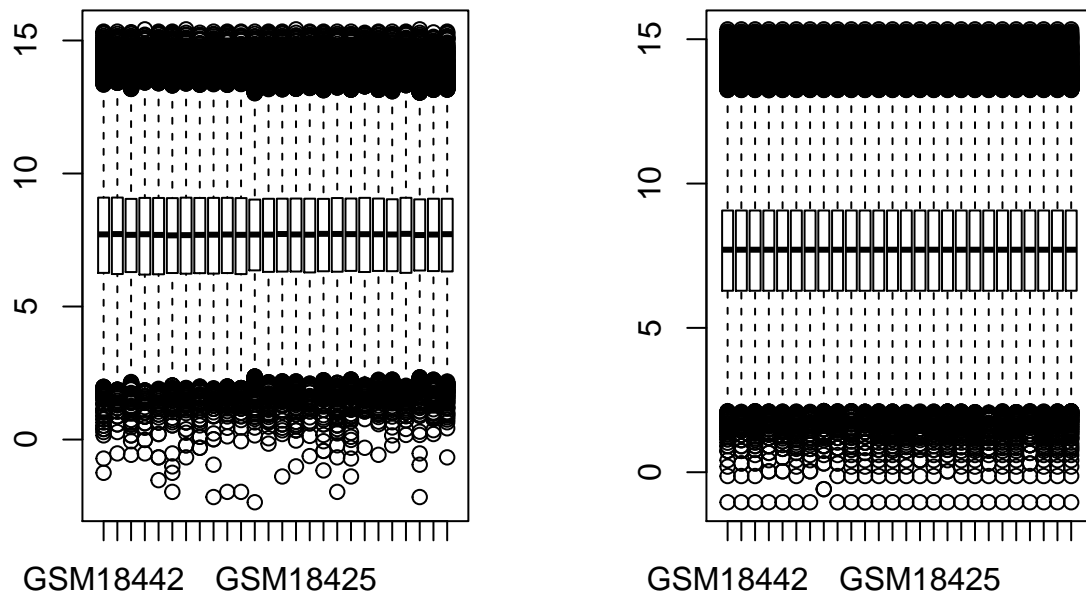
# load the dataset
data("GSE1145")
# get the gene expression matrix
exprs_all <- exprs(GSE1145)
# get the gene symbol of gene expression matrix
all.eset <- probe.2.gene.eset(GSE1145)
head(featureNames(all.eset))

## [1] "780" "5982" "3310" "7849" "2978" "7318"

# Normalization of gene expression profile
before.norm <- exprs(all.eset)
all.eset <- normalize(all.eset, norm.method="quantile")
after.norm <- exprs(all.eset)

# Change matrix to dataframe style
exprs_all1 <- data.frame(after.norm)

# plot of normalization
par(mfrow=c(1,2))
boxplot(before.norm)
boxplot(after.norm)
```



Obtaining case and control samples

```
table(pData(all.eset)$Group)
```

```
##
##  c  d
## 11 15
```

```
pData(all.eset)$GROUP <- ifelse(pData(all.eset)$Group == "d", 1, 0)
normal <- length(which(pData(all.eset)$GROUP == '0'))
tumor <- length(which(pData(all.eset)$GROUP == '1'))
```

Get differential expression genes

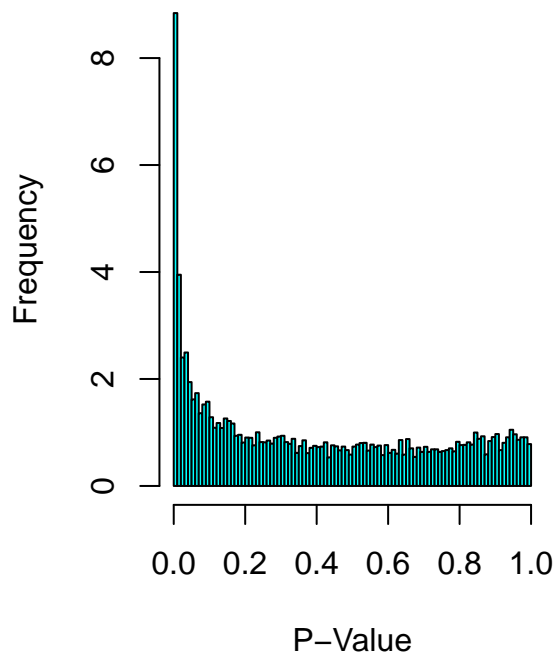
```
# get differential expression genes
all.eset <- de.ana(all.eset)
head(fData(all.eset), n=4)
```

```
##           FC    ADJ.PVAL  limma.STAT
## 780  -0.0662664 0.74712418 -0.5423112
## 5982 -0.3378525 0.01977145 -3.3337793
## 3310 -0.7570934 0.32848640 -1.4348586
## 7849  0.1140257 0.47175743  1.0961393
```

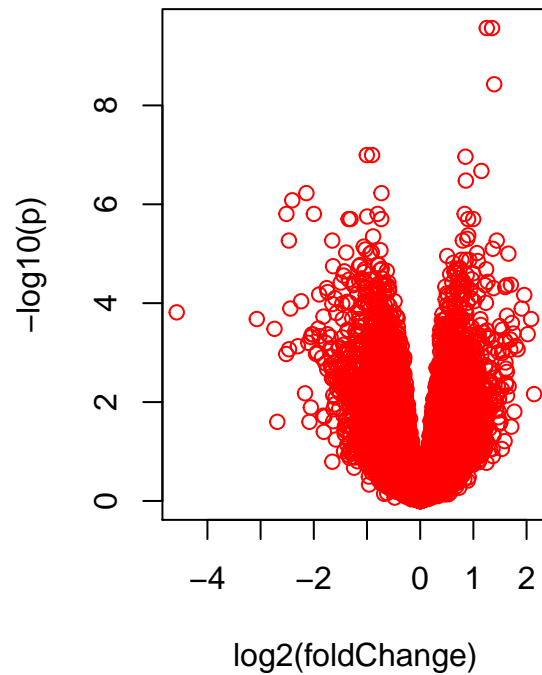
```
all_de <- fData(all.eset)

#The plot of differential expression genes
par(mfrow=c(1,2))
pdistr(fData(all.eset)$ADJ.PVAL)
volcano(fData(all.eset)$FC, fData(all.eset)$ADJ.PVAL)
```

**P-Value Distribution**



**Volcano Plot**



Get database of signaling pathways from KEGG

```
# get pathway dataset
kegg.gs <- get.kegg.genesets("hsa")
```

Get the results of SPIA method and spiap method, we use colorectal cancer dataset from GSE8671

```
library(spiapcc)

# get differential expression genes on threshold 0.1
tg <- all_de[all_de$ADJ.PVAL < 0.1,]
# get fold change pf differential expression genes
DE_colorectal = tg$FC
names(DE_colorectal)<-as.vector(rownames(tg))
# get all gene names
```

```

ALL_colorectal = rownames(all_de)
#The result of spia method
res_spia = spia(de = DE_colorectal, all=ALL_colorectal, organism="hsa",nB=2000,plots=FALSE,beta=NULL,cor

##
## Done pathway 1 : RNA transport..
## Done pathway 2 : RNA degradation..
## Done pathway 3 : PPAR signaling pathway..
## Done pathway 4 : Fanconi anemia pathway..
## Done pathway 5 : MAPK signaling pathway..
## Done pathway 6 : ErbB signaling pathway..
## Done pathway 7 : Calcium signaling pathway..
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## Done pathway 9 : Chemokine signaling pathway..
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## Done pathway 17 : SNARE interactions in vesicula..
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## Done pathway 19 : Protein processing in endoplas..
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## Done pathway 47 : B cell receptor signaling path..
## Done pathway 48 : Fc epsilon RI signaling pathwa..
## Done pathway 49 : Fc gamma R-mediated phagocytos..

```

```

## Done pathway 50 : Leukocyte transendothelial mig..
## Done pathway 51 : Intestinal immune network for ..
## Done pathway 52 : Circadian rhythm - mammal..
## Done pathway 53 : Long-term potentiation..
## Done pathway 54 : Neurotrophin signaling pathway..
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## Done pathway 87 : Prion diseases..
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## Done pathway 97 : Salmonella infection..
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## Done pathway 100 : Leishmaniasis..
## Done pathway 101 : Chagas disease (American trypan..
## Done pathway 102 : African trypanosomiasis..
## Done pathway 103 : Malaria..

```

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## Done pathway 104 : Toxoplasmosis..
## Done pathway 105 : Amoebiasis..
## Done pathway 106 : Staphylococcus aureus infectio..
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## Done pathway 127 : Chronic myeloid leukemia..
## Done pathway 128 : Acute myeloid leukemia..
## Done pathway 129 : Small cell lung cancer..
## Done pathway 130 : Non-small cell lung cancer..
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## Done pathway 132 : Autoimmune thyroid disease..
## Done pathway 133 : Systemic lupus erythematosus..
## Done pathway 134 : Rheumatoid arthritis..
## Done pathway 135 : Allograft rejection..
## Done pathway 136 : Graft-versus-host disease..
## Done pathway 137 : Arrhythmogenic right ventricul..
## Done pathway 138 : Dilated cardiomyopathy..
## Done pathway 139 : Viral myocarditis..
```

```
res_spia <- res_spia[,-12]
head(res_spia)
```

##		Name	ID	pSize	NDE	pNDE
## 1		Huntington's disease	05016	178	76	8.083864e-06
## 2		Alzheimer's disease	05010	164	70	1.826593e-05
## 3		Chagas disease (American trypanosomiasis)	05142	102	45	2.177596e-04
## 4		ECM-receptor interaction	04512	85	33	1.485504e-02
## 5		Malaria	05144	50	24	1.539524e-03
## 6		Amoebiasis	05146	106	43	2.341983e-03
##	tA	pPERT	pG	pGFdr	pGFWER	Status
## 1	-0.3699900	0.821	0.0000857672	0.01085692	0.01175011	Inhibited
## 2	1.4164091	0.708	0.0001584953	0.01085692	0.02171385	Activated
## 3	-0.4637171	0.942	0.0019470630	0.06751252	0.26674763	Inhibited
## 4	7.1971982	0.014	0.0019711685	0.06751252	0.27005008	Activated
## 5	-1.1799883	0.199	0.0027850850	0.07631133	0.38155665	Inhibited
## 6	-3.5320157	0.185	0.0037885538	0.08650531	0.51903187	Inhibited

```

gse_madat2 <- exprs_all1

# The results of spia_nt method
res_nt = spiapcc(de=DE_colorectal, all=ALL_colorectal, normal = normal, tumor = tumor, gse_madat2 = gse_madat2,
                 beta=NULL, combine="fisher", verbose=T, flag = 1)

##
## Done pathway 1 : RNA transport..
## Done pathway 2 : RNA degradation..
## Done pathway 3 : PPAR signaling pathway..
## Done pathway 4 : Fanconi anemia pathway..
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```



```

## Done pathway 102 : African trypanosomiasis..
## Done pathway 103 : Malaria..
## Done pathway 104 : Toxoplasmosis..
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```

```

res_nt <- res_nt[, -12]
head(res_nt)

```

##		Name	ID	pSize	NDE	pNDE
## 1		Huntington's disease	05016	178	76	8.083864e-06
## 2		Alzheimer's disease	05010	164	70	1.826593e-05
## 3		Malaria	05144	50	24	1.539524e-03
## 4		Chagas disease (American trypanosomiasis)	05142	102	45	2.177596e-04
## 5		Neurotrophin signaling pathway	04722	120	49	1.026966e-03
## 6		ECM-receptor interaction	04512	85	33	1.485504e-02
##	tA	pPERT	pG	pGFdr	pGFWER	Status
## 1	0.01743747	0.956	9.869372e-05	0.01120103	0.01371843	Activated
## 2	0.29422231	0.721	1.611659e-04	0.01120103	0.02240205	Activated
## 3	0.65849958	0.060	9.504738e-04	0.04347802	0.13211586	Activated
## 4	-0.50339814	0.720	1.530338e-03	0.04347802	0.21271700	Inhibited
## 5	1.72720784	0.203	1.975438e-03	0.04347802	0.27458583	Activated

```
## 6 1.44392628 0.017 2.344530e-03 0.04347802 0.32588972 Activated
```

```
#The results of spia_tn method
```

```
res_tn = spiapcc( de=DE_colorectal, all=ALL_colorectal, normal = normal, tumor = tumor, gse_madat2 = gse.  
                 beta=NULL, combine="fisher", verbose=T, flag = -1)
```

```
##
```

```
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## 5		Neurotrophin signaling pathway	04722	120	49	1.026966e-03
## 6		ECM-receptor interaction	04512	85	33	1.485504e-02
##	tA	pPERT	pG	pGFdr	pGFWER	Status
## 1	0.01743747	0.956	9.869372e-05	0.01120103	0.01371843	Activated
## 2	0.29422231	0.721	1.611659e-04	0.01120103	0.02240205	Activated
## 3	0.65849958	0.060	9.504738e-04	0.04347802	0.13211586	Activated
## 4	-0.50339814	0.720	1.530338e-03	0.04347802	0.21271700	Inhibited
## 5	1.72720784	0.203	1.975438e-03	0.04347802	0.27458583	Activated
## 6	1.44392628	0.017	2.344530e-03	0.04347802	0.32588972	Activated

*#The results of spia\_abs method*

```
res_abs = spiapcc( de=DE_colorectal, all=ALL_colorectal,normal = normal,tumor = tumor, gse_madat2 = gs  
                  beta=NULL,combine="fisher",verbose=T, flag = 0)
```

##

```
## Done pathway 1 : RNA transport..  
## Done pathway 2 : RNA degradation..  
## Done pathway 3 : PPAR signaling pathway..  
## Done pathway 4 : Fanconi anemia pathway..  
## Done pathway 5 : MAPK signaling pathway..  
## Done pathway 6 : ErbB signaling pathway..  
## Done pathway 7 : Calcium signaling pathway..  
## Done pathway 8 : Cytokine-cytokine receptor int..  
## Done pathway 9 : Chemokine signaling pathway..  
## Done pathway 10 : NF-kappa B signaling pathway..  
## Done pathway 11 : Phosphatidylinositol signaling..  
## Done pathway 12 : Neuroactive ligand-receptor in..  
## Done pathway 13 : Cell cycle..  
## Done pathway 14 : Oocyte meiosis..  
## Done pathway 15 : p53 signaling pathway..  
## Done pathway 16 : Sulfur relay system..  
## Done pathway 17 : SNARE interactions in vesicula..  
## Done pathway 18 : Regulation of autophagy..  
## Done pathway 19 : Protein processing in endoplas..  
## Done pathway 20 : Lysosome..  
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## Done pathway 22 : Apoptosis..  
## Done pathway 23 : Vascular smooth muscle contrac..  
## Done pathway 24 : Wnt signaling pathway..  
## Done pathway 25 : Dorso-ventral axis formation..  
## Done pathway 26 : Notch signaling pathway..  
## Done pathway 27 : Hedgehog signaling pathway..  
## Done pathway 28 : TGF-beta signaling pathway..  
## Done pathway 29 : Axon guidance..  
## Done pathway 30 : VEGF signaling pathway..  
## Done pathway 31 : Osteoclast differentiation..  
## Done pathway 32 : Focal adhesion..  
## Done pathway 33 : ECM-receptor interaction..  
## Done pathway 34 : Cell adhesion molecules (CAMs)..  
## Done pathway 35 : Adherens junction..  
## Done pathway 36 : Tight junction..  
## Done pathway 37 : Gap junction..  
## Done pathway 38 : Complement and coagulation cas..  
## Done pathway 39 : Antigen processing and present..  
## Done pathway 40 : Toll-like receptor signaling p..  
## Done pathway 41 : NOD-like receptor signaling pa..  
## Done pathway 42 : RIG-I-like receptor signaling ..  
## Done pathway 43 : Cytosolic DNA-sensing pathway..  
## Done pathway 44 : Jak-STAT signaling pathway..  
## Done pathway 45 : Natural killer cell mediated c..  
## Done pathway 46 : T cell receptor signaling path..  
## Done pathway 47 : B cell receptor signaling path..  
## Done pathway 48 : Fc epsilon RI signaling pathwa..  
## Done pathway 49 : Fc gamma R-mediated phagocytos..
```

```

## Done pathway 50 : Leukocyte transendothelial mig..
## Done pathway 51 : Intestinal immune network for ..
## Done pathway 52 : Circadian rhythm - mammal..
## Done pathway 53 : Long-term potentiation..
## Done pathway 54 : Neurotrophin signaling pathway..
## Done pathway 55 : Retrograde endocannabinoid sig..
## Done pathway 56 : Glutamatergic synapse..
## Done pathway 57 : Cholinergic synapse..
## Done pathway 58 : Serotonergic synapse..
## Done pathway 59 : GABAergic synapse..
## Done pathway 60 : Dopaminergic synapse..
## Done pathway 61 : Long-term depression..
## Done pathway 62 : Olfactory transduction..
## Done pathway 63 : Taste transduction..
## Done pathway 64 : Phototransduction..
## Done pathway 65 : Regulation of actin cytoskelet..
## Done pathway 66 : Insulin signaling pathway..
## Done pathway 67 : GnRH signaling pathway..
## Done pathway 68 : Progesterone-mediated oocyte m..
## Done pathway 69 : Melanogenesis..
## Done pathway 70 : Adipocytokine signaling pathwa..
## Done pathway 71 : Type II diabetes mellitus..
## Done pathway 72 : Type I diabetes mellitus..
## Done pathway 73 : Maturity onset diabetes of the..
## Done pathway 74 : Aldosterone-regulated sodium r..
## Done pathway 75 : Endocrine and other factor-reg..
## Done pathway 76 : Vasopressin-regulated water re..
## Done pathway 77 : Salivary secretion..
## Done pathway 78 : Gastric acid secretion..
## Done pathway 79 : Pancreatic secretion..
## Done pathway 80 : Carbohydrate digestion and abs..
## Done pathway 81 : Bile secretion..
## Done pathway 82 : Mineral absorption..
## Done pathway 83 : Alzheimer's disease..
## Done pathway 84 : Parkinson's disease..
## Done pathway 85 : Amyotrophic lateral sclerosis ..
## Done pathway 86 : Huntington's disease..
## Done pathway 87 : Prion diseases..
## Done pathway 88 : Cocaine addiction..
## Done pathway 89 : Amphetamine addiction..
## Done pathway 90 : Morphine addiction..
## Done pathway 91 : Alcoholism..
## Done pathway 92 : Bacterial invasion of epitheli..
## Done pathway 93 : Vibrio cholerae infection..
## Done pathway 94 : Epithelial cell signaling in H..
## Done pathway 95 : Pathogenic Escherichia coli in..
## Done pathway 96 : Shigellosis..
## Done pathway 97 : Salmonella infection..
## Done pathway 98 : Pertussis..
## Done pathway 99 : Legionellosis..
## Done pathway 100 : Leishmaniasis..
## Done pathway 101 : Chagas disease (American trypan..
## Done pathway 102 : African trypanosomiasis..
## Done pathway 103 : Malaria..

```

```
## Done pathway 104 : Toxoplasmosis..
## Done pathway 105 : Amoebiasis..
## Done pathway 106 : Staphylococcus aureus infectio..
## Done pathway 107 : Tuberculosis..
## Done pathway 108 : Hepatitis C..
## Done pathway 109 : Measles..
## Done pathway 110 : Influenza A..
## Done pathway 111 : HTLV-I infection..
## Done pathway 112 : Herpes simplex infection..
## Done pathway 113 : Epstein-Barr virus infection..
## Done pathway 114 : Pathways in cancer..
## Done pathway 115 : Transcriptional misregulation ..
## Done pathway 116 : Viral carcinogenesis..
## Done pathway 117 : Colorectal cancer..
## Done pathway 118 : Renal cell carcinoma..
## Done pathway 119 : Pancreatic cancer..
## Done pathway 120 : Endometrial cancer..
## Done pathway 121 : Glioma..
## Done pathway 122 : Prostate cancer..
## Done pathway 123 : Thyroid cancer..
## Done pathway 124 : Basal cell carcinoma..
## Done pathway 125 : Melanoma..
## Done pathway 126 : Bladder cancer..
## Done pathway 127 : Chronic myeloid leukemia..
## Done pathway 128 : Acute myeloid leukemia..
## Done pathway 129 : Small cell lung cancer..
## Done pathway 130 : Non-small cell lung cancer..
## Done pathway 131 : Asthma..
## Done pathway 132 : Autoimmune thyroid disease..
## Done pathway 133 : Systemic lupus erythematosus..
## Done pathway 134 : Rheumatoid arthritis..
## Done pathway 135 : Allograft rejection..
## Done pathway 136 : Graft-versus-host disease..
## Done pathway 137 : Arrhythmogenic right ventricul..
## Done pathway 138 : Dilated cardiomyopathy..
## Done pathway 139 : Viral myocarditis..
```

```
res_abs <- res_abs[,-12]
head(res_abs)
```

##		Name	ID	pSize	NDE	pNDE
## 1		Huntington's disease	05016	178	76	8.083864e-06
## 2		Alzheimer's disease	05010	164	70	1.826593e-05
## 3		Chagas disease (American trypanosomiasis)	05142	102	45	2.177596e-04
## 4		Neurotrophin signaling pathway	04722	120	49	1.026966e-03
## 5		Bacterial invasion of epithelial cells	05100	70	25	8.068118e-02
## 6		ECM-receptor interaction	04512	85	33	1.485504e-02
##	tA	pPERT	pG	pGFdr	pGFWER	Status
## 1	0.03239039	0.971	0.0001001201	0.008879475	0.01391669	Activated
## 2	0.54172743	0.560	0.0001277622	0.008879475	0.01775895	Activated
## 3	-0.80660388	0.700	0.0014921229	0.057945449	0.20740508	Inhibited
## 4	-3.19554279	0.168	0.0016674949	0.057945449	0.23178180	Inhibited
## 5	-4.46271459	0.004	0.0029170156	0.071802353	0.40546517	Inhibited
## 6	2.53667607	0.024	0.0031869824	0.071802353	0.44299055	Activated

```

#
data("GSE3467")
result <- process(GSE3467)
exprs_nrom <- result$exprs
normal <- result$normal
tumor <- result$tumor
DE <- result$DE
ALL <- result$ALL

res = spiapcc( de=DE, all=ALL,normal = normal,tumor = tumor, gse_madat2 = exprs_nrom, organism="hsa",n
              beta=NULL,combine="fisher",verbose=T, flag = 0)

```

```

##
## Done pathway 1 : RNA transport..
## Done pathway 2 : RNA degradation..
## Done pathway 3 : PPAR signaling pathway..
## Done pathway 4 : Fanconi anemia pathway..
## Done pathway 5 : MAPK signaling pathway..
## Done pathway 6 : ErbB signaling pathway..
## Done pathway 7 : Calcium signaling pathway..
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## Done pathway 19 : Protein processing in endoplas..
## Done pathway 20 : Lysosome..
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## Done pathway 22 : Apoptosis..
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## Done pathway 26 : Notch signaling pathway..
## Done pathway 27 : Hedgehog signaling pathway..
## Done pathway 28 : TGF-beta signaling pathway..
## Done pathway 29 : Axon guidance..
## Done pathway 30 : VEGF signaling pathway..
## Done pathway 31 : Osteoclast differentiation..
## Done pathway 32 : Focal adhesion..
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## Done pathway 34 : Cell adhesion molecules (CAMs)..
## Done pathway 35 : Adherens junction..
## Done pathway 36 : Tight junction..
## Done pathway 37 : Gap junction..
## Done pathway 38 : Complement and coagulation cas..
## Done pathway 39 : Antigen processing and present..
## Done pathway 40 : Toll-like receptor signaling p..
## Done pathway 41 : NOD-like receptor signaling pa..

```



```

## Done pathway 42 : RIG-I-like receptor signaling ..
## Done pathway 43 : Cytosolic DNA-sensing pathway..
## Done pathway 44 : Jak-STAT signaling pathway..
## Done pathway 45 : Natural killer cell mediated c..
## Done pathway 46 : T cell receptor signaling path..
## Done pathway 47 : B cell receptor signaling path..
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## Done pathway 50 : Leukocyte transendothelial mig..
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## Done pathway 52 : Circadian rhythm - mammal..
## Done pathway 53 : Long-term potentiation..
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## Done pathway 77 : Salivary secretion..
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## Done pathway 88 : Cocaine addiction..
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## Done pathway 91 : Alcoholism..
## Done pathway 92 : Bacterial invasion of epitheli..
## Done pathway 93 : Vibrio cholerae infection..
## Done pathway 94 : Epithelial cell signaling in H..
## Done pathway 95 : Pathogenic Escherichia coli in..

```

```

## Done pathway 96 : Shigellosis..
## Done pathway 97 : Salmonella infection..
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## Done pathway 102 : African trypanosomiasis..
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## Done pathway 106 : Staphylococcus aureus infectio..
## Done pathway 107 : Tuberculosis..
## Done pathway 108 : Hepatitis C..
## Done pathway 109 : Measles..
## Done pathway 110 : Influenza A..
## Done pathway 111 : HTLV-I infection..
## Done pathway 112 : Herpes simplex infection..
## Done pathway 113 : Epstein-Barr virus infection..
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## Done pathway 115 : Transcriptional misregulation ..
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## Done pathway 120 : Endometrial cancer..
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## Done pathway 125 : Melanoma..
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## Done pathway 132 : Autoimmune thyroid disease..
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## Done pathway 134 : Rheumatoid arthritis..
## Done pathway 135 : Allograft rejection..
## Done pathway 136 : Graft-versus-host disease..
## Done pathway 137 : Arrhythmogenic right ventricul..
## Done pathway 138 : Dilated cardiomyopathy..
## Done pathway 139 : Viral myocarditis..

```

```

res <- res[,-12]
head(res)

```

##		Name	ID	pSize	NDE	pNDE	tA
## 1	Cell adhesion molecules (CAMs)	04514	130	63	1.475773e-07	6.036699	
## 2	Staphylococcus aureus infection	05150	51	32	9.937630e-08	4.498668	
## 3	ECM-receptor interaction	04512	85	33	1.188292e-02	6.390686	
## 4	Viral myocarditis	05416	68	34	4.626103e-05	3.292822	
## 5	Tuberculosis	05152	176	73	2.298166e-05	6.895598	
## 6	Salmonella infection	05132	81	38	1.005036e-04	3.155768	

```
##      pPERT      pG      pGFdr      pGFWER      Status
## 1 5.0e-06 2.135074e-11 2.967753e-09 2.967753e-09 Activated
## 2 6.3e-02 1.245190e-07 8.654072e-06 1.730814e-05 Activated
## 3 5.0e-06 1.047998e-06 4.855725e-05 1.456718e-04 Activated
## 4 2.0e-03 1.590993e-06 5.528699e-05 2.211480e-04 Activated
## 5 8.0e-03 3.035257e-06 8.438015e-05 4.219008e-04 Activated
## 6 5.6e-02 7.366033e-05 1.706464e-03 1.023879e-02 Activated
```

## R version information

```
## R version 3.4.1 (2017-06-30)
## Platform: i386-w64-mingw32/i386 (32-bit)
## Running under: Windows 7 (build 7601) Service Pack 1
##
## Matrix products: default
##
## locale:
## [1] LC_COLLATE=Chinese (Simplified)_People's Republic of China.936
## [2] LC_CTYPE=Chinese (Simplified)_People's Republic of China.936
## [3] LC_MONETARY=Chinese (Simplified)_People's Republic of China.936
## [4] LC_NUMERIC=C
## [5] LC_TIME=Chinese (Simplified)_People's Republic of China.936
##
## attached base packages:
## [1] stats4      parallel  stats      graphics  grDevices  utils      datasets
## [8] methods    base
##
## other attached packages:
## [1] spiapcc_0.1.0
## [2] hgu133plus2.db_3.2.3
## [3] SPIA_2.28.0
## [4] KEGGgraph_1.38.0
## [5] KEGGdzPathwaysGEO_1.14.0
## [6] KEGGandMetacoreDzPathwaysGEO_0.110.0
## [7] EnrichmentBrowser_2.6.0
## [8] pathview_1.16.1
## [9] org.Hs.eg.db_3.4.1
## [10] GSEABase_1.38.0
## [11] graph_1.54.0
## [12] annotate_1.54.0
## [13] XML_3.98-1.9
## [14] AnnotationDbi_1.38.1
## [15] IRanges_2.10.2
## [16] S4Vectors_0.14.3
## [17] Biobase_2.36.2
## [18] BiocGenerics_0.22.0
## [19] knitr_1.20
##
## loaded via a namespace (and not attached):
## [1] httr_1.2.1      munsell_0.5.0
## [3] latticeExtra_0.6-28 KEGGREST_1.16.0
## [5] pillar_1.2.1    pkgconfig_2.0.1
## [7] R.utils_2.5.0   BSgenome_1.44.2
```

## [9] dichromat_2.0-0	compiler_3.4.1
## [11] DBI_0.7	lazyeval_0.2.0
## [13] tibble_1.4.2	PFAM.db_3.4.1
## [15] httpuv_1.3.5	R6_2.2.2
## [17] ensemblDb_2.0.3	yaml_2.1.14
## [19] BiocInstaller_1.26.1	data.table_1.10.4
## [21] reshape_0.8.6	xtable_1.8-2
## [23] tools_3.4.1	stringr_1.3.0
## [25] rtracklayer_1.36.4	mime_0.5
## [27] shiny_1.0.3	png_0.1-7
## [29] R.oo_1.21.0	G0stats_2.42.0
## [31] digest_0.6.12	G0.db_3.4.1
## [33] GenomeInfoDb_1.12.2	GGally_1.3.1
## [35] base64enc_0.1-3	GenomicAlignments_1.12.1
## [37] genefilter_1.58.1	scales_1.0.0
## [39] memoise_1.1.0	stringi_1.1.7
## [41] locfit_1.5-9.1	R.methodsS3_1.7.1
## [43] limma_3.32.3	GenomeInfoDbData_0.99.0
## [45] lattice_0.20-35	AnnotationForge_1.18.1
## [47] bit64_0.9-7	interactiveDisplayBase_1.14.0
## [49] biovizBase_1.24.0	Rcpp_0.12.19
## [51] OrganismDbi_1.18.0	Hmisc_4.0-3
## [53] Formula_1.2-2	ggplot2_3.0.0
## [55] htmlTable_1.9	Category_2.42.1
## [57] ProtGenerics_1.8.0	grid_3.4.1
## [59] ReportingTools_2.16.0	blob_1.1.0
## [61] GenomicRanges_1.28.4	plyr_1.8.4
## [63] RBGL_1.52.0	survival_2.41-3
## [65] edgeR_3.18.1	AnnotationFilter_1.0.0
## [67] DelayedArray_0.2.7	rprojroot_1.3-2
## [69] acepack_1.4.1	matrixStats_0.52.2
## [71] rpart_4.1-11	Rgraphviz_2.20.0
## [73] magrittr_1.5	SummarizedExperiment_1.6.3
## [75] VariantAnnotation_1.22.3	Biostrings_2.44.1
## [77] gridExtra_2.2.1	htmlwidgets_0.9
## [79] curl_2.7	checkmate_1.8.3
## [81] biomaRt_2.32.1	htmltools_0.3.6
## [83] RSQLite_2.0	ggbio_1.24.1
## [85] nnet_7.3-12	gtable_0.2.0
## [87] zlibbioc_1.22.0	colorspace_1.3-2
## [89] geneplotter_1.54.0	MASS_7.3-47
## [91] cluster_2.0.6	XVector_0.16.0
## [93] RCurl_1.95-4.8	DESeq2_1.16.1
## [95] bitops_1.0-6	RColorBrewer_1.1-2
## [97] Matrix_1.2-10	foreign_0.8-69
## [99] hwriter_1.3.2	bit_1.1-12
## [101] GenomicFeatures_1.28.4	reshape2_1.4.2
## [103] rmarkdown_1.9	AnnotationHub_2.8.2
## [105] splines_3.4.1	evaluate_0.10.1
## [107] rlang_0.2.0	BiocParallel_1.10.1
## [109] backports_1.1.0	Rsamtools_1.28.0