

## Final Project

In this project I worked with DataSet Record GDS3116, “Letrozole effect on breast cancer tumors,” from the GEO database [1]. This expression set contains microarray data from a group of 58 patients measured at two points in time, baseline and 10-14 days post-treatment with letrozole, an aromatase inhibitor. Based on percentage of tumor shrinkage, patients were labeled as “responders” or “nonresponders.” Using after-the-fact knowledge of who is a responder and who is not, I looked at tumor gene expression at baseline and used some of our modeling methods to attempt to predict which patients would respond to letrozole treatment. I also used a correlation network and annotation enrichment to see which pathways might be overrepresented between responders and nonresponders at baseline.

[1] Miller, W.R., Larionov, A. (2010). Changes in expression of oestrogen regulated and proliferation genes with neoadjuvant treatment highlight heterogeneity of clinical resistance to the aromatase inhibitor, letrozole. *Breast Cancer Res.* **12(4)**: R52.

```
library(GEOquery)
library(Biobase)
library(gplots)
library(class)
library(e1071)
library(graph)
library(hgu133a.db)
library(reactome.db)

# Retrieve expression set from GEO database and store exprs() data
gds3116 <- getGEO('GDS3116', destdir=".")
eset3116 <- GDS2eSet(gds3116, do.log2=TRUE)
ex3116 <- exprs(eset3116)

# 116 columns are 58 patients measured at two points in time
> dim(ex3116)
[1] 22283    116

# Six patients were not assessable for various reasons and the corresponding
# columns are removed from the expression matrix
not.assessable = grep("not assessable", pData(eset3116)[,4])
genematrix = ex3116[, -not.assessable]

# Save the baseline measurements to a separate matrix from the post-treatment
# measurements
genematrix.base = genematrix[, 1:(0.5*dim(genematrix)[2])]
> dim(genematrix.base)
[1] 22283    52

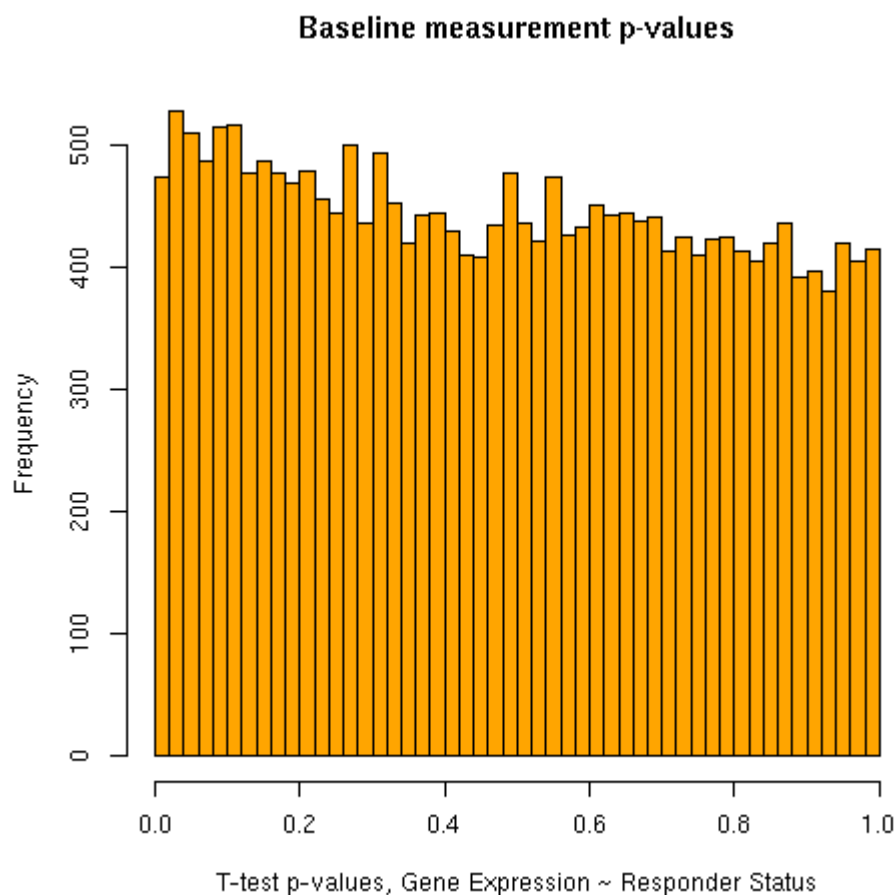
# Remove non-assessable rows from pData as well so that pData row numbers continue
# to match up to expression matrix column numbers
pData.assess = pData(eset3116)[-not.assessable,]

# Get row numbers for responders and non-responders
nonresponders = grep("nonresponder", pData.assess[,4])
responders = grep(" responder", pData.assess[,4])
```

```
# Use responder/nonresponder information to create a vector of 0s (responders)
# and 1s (nonresponders) which can be used to create models and predictions
description = vector()
for(g in 1:dim(pData.assess)[1]){
  if(g %in% responders){
    description = c(description, 0)
  }else if(g %in% nonresponders){
    description = c(description, 1)
  }
}
description = as.factor(description)
> description
 [1] 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 1 0 1 0 1 1 1 0 0 0 1 1 0 0 0 0 0 0 1
[38] 1 0 0 0 1 0 0 0 0 1 1 0 0 1 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 1 0 1 0
[75] 1 1 1 0 0 0 1 1 0 0 0 0 0 0 1 1 0 0 0 1 0 0 0 0 1 1 0 0 1 0
Levels: 0 1

# Save the first half separately for working with baseline information only
description.base = description[1:(0.5*length(description))]
```

```
# Find genes most strongly associated with outcome
test.pvals=apply(genematrix.base,1,function(x) t.test(x~description.base)$p.value)
hist(test.pvals,col="orange",breaks=50, main="Baseline measurement p-values",
xlab="T-test p-values, Gene Expression ~ Responder Status")
```



It looks like there is a slight overrepresentation of small, significant p-values. This makes sense to me; all patients are at baseline anyway and I would not expect the differences between them to be too strong. We are possibly only looking for a small number of genes to begin with. Next, a few models, starting with logistical regression run on the single most significant gene:

```
# The assess.prediction() is as from notes
M = glm(description.base ~ genematrix.base[which.min(test.pvals),],family="binomial")
assess.prediction(description.base,as.numeric(predict(M,type="response")>0.5))
Total cases that are not NA: 52
Correct predictions (accuracy): 38(73.1%)
TPR (sensitivity)=TP/P: 26.7%
TNR (specificity)=TN/N: 91.9%
PPV (precision)=TP/(TP+FP): 57.1%
FDR (false discovery)=1-PPV: 42.9%
FPR =FP/N=1-TNR: 8.11%

df.final=as.data.frame(t(genematrix.base[order(test.pvals),]))
```

The accuracy in predicting responders seems respectable. The sensitivity/specificity split is not very even, though, with a very low result for the former and a high result for the latter. This is using the single most significant gene; I attempted logistic regression with the top 20 most significant genes and received these warning messages:

```
1: glm.fit: algorithm did not converge
2: glm.fit: fitted probabilities numerically 0 or 1 occurred
```

This can occur if the fit is somehow *too* good, and indeed running the `assess.prediction()` function showed that accuracy, sensitivity, and specificity were all 100%. I tried dialing it back to the top five most significant genes and got usable results:

```
M = glm(description.base ~ . , data=df.final[1:5], family="binomial",
na.action="na.exclude")
assess.prediction(description.base,as.numeric(predict(M,type="response")>0.5))
Total cases that are not NA: 52
Correct predictions (accuracy): 46(88.5%)
TPR (sensitivity)=TP/P: 80%
TNR (specificity)=TN/N: 91.9%
PPV (precision)=TP/(TP+FP): 80%
FDR (false discovery)=1-PPV: 20%
FPR =FP/N=1-TNR: 8.11%
```

Going back to the 20 most significant genes, I did get reasonable numbers when cross-validating using the function from the notes (N=1000, n.out=5):

```
predictor.LR$train(description.base ~ ., df.final[1:20])
set.seed(456)
cv.LR.20=cross.validate(predictor.LR, description.base ~ ., df.final[1:20])
assess.prediction(cv.LR.20$truth,cv.LR.20$prediction)
Total cases that are not NA: 5000
Correct predictions (accuracy): 3921(78.4%)
TPR (sensitivity)=TP/P: 74.6%
TNR (specificity)=TN/N: 80%
PPV (precision)=TP/(TP+FP): 60.2%
FDR (false discovery)=1-PPV: 39.8%
FPR =FP/N=1-TNR: 20%
```

Next I tried naïve Bayes with the top 20 genes:

```
MB20=naiveBayes(description.base ~ ., data=df.final[,1:20])
assess.prediction(description.base, predict(MB20,df.final[,1:20]))
Total cases that are not NA: 52
Correct predictions (accuracy): 48 (92.3%)
TPR (sensitivity)=TP/P: 100%
TNR (specificity)=TN/N: 89.2%
PPV (precision)=TP/(TP+FP): 78.9%
FDR (false discovery)=1-PPV: 21.1%
FPR =FP/N=1-TNR: 10.8%
```

And K nearest neighbors:

```
set.seed(234)
n=0
n.out=5
Nrep=1000
for(i in 1:Nrep){
  leave.out=sample(nrow(df.final),size=n.out)
  pred = knn(df.final[-
leave.out,1,drop=F],df.final[leave.out,1,drop=F],description.base[-leave.out],k=1)
  n=n+sum(pred==description.base[leave.out])
}
n/(n.out*Nrep)
[1] 0.6942
```

Using SVM I got perfect results identical to `glm()` with top 20 most significant genes, though this changed upon cross-validation:

```
predictor.SVM$train(description.base~.,df.final[1:20], kernel="radial")
assess.prediction(description.base, predictor.SVM$predict(df.final[1:20]))
Total cases that are not NA: 52
Correct predictions (accuracy): 52 (100%)
TPR (sensitivity)=TP/P: 100%
TNR (specificity)=TN/N: 100%
PPV (precision)=TP/(TP+FP): 100%
FDR (false discovery)=1-PPV: 0%
FPR =FP/N=1-TNR: 0%
```

```
set.seed(789)
cv.SVM.20 = cross.validate(predictor.SVM, description.base ~ ., df.final[1:20])
assess.prediction(cv.SVM.20$truth, cv.SVM.20$prediction)
Total cases that are not NA: 5000
Correct predictions (accuracy): 4345 (86.9%)
TPR (sensitivity)=TP/P: 75.9%
TNR (specificity)=TN/N: 91.4%
PPV (precision)=TP/(TP+FP): 78.2%
FDR (false discovery)=1-PPV: 21.8%
FPR =FP/N=1-TNR: 8.61%
```

It looks like a variety of modeling methods can produce some respectably accurate predictions as to whether or not a patient will end up being a letrozole responder or nonresponder based upon gene expression at baseline. To see which pathways might be involved in the difference between responders and nonresponders, I used a correlation network and annotation enrichment.

```
# Prepare the graph as in the notes
DE.data = as.data.frame(
  t(
    apply(genematrix.base,1,function(x){
      tt = t.test(x~description.base)
      return(c(diff(tt$estimate),tt$p.value))
    })
  )
)

colnames(DE.data) = c("LogFC","p.value")
DE.data$transcript = rownames(DE.data)

vars = apply(genematrix.base,1,var)
gene.sel.cr = order(vars,decreasing=T)[1:300]
gb.300 = genematrix.base[gene.sel.cr,]
# "gb" is a shortening of genematrix.base

c.null = numeric()
for (trial in 1:100) {
  gb.test = t(apply(gb.300,1,sample))
  corr.t = cor(t(gb.test),use="pairwise")
  diag(corr.t) = 0
  c.null = c(c.null,as.numeric(corr.t))
}

gb.cor = cor(t(gb.300),use="pairwise")
diag(gb.cor) = 0
adj.mat = ifelse(gb.cor>0.6,1,0)
connected = apply(adj.mat,1,sum) > 0
adj.mat = adj.mat[connected,connected]
G.corr = graphAM(adj.mat)

G.corr = as(G.corr,"graphNEL")
G.corr.cc = connComp(G.corr)
> length(G.corr.cc)
[1] 12
# It looks like there are 12 components to this graph

> G.corr.cc
[[1]]
[1] "205979_at" "206799_at" "206378_at"
```

These appear to be Affymetrix IDs and indeed the paper states that Affymetrix U133A chips were used. I found an annotation database that works for converting these and adapted the code from our notes to convert the Affy IDs to Entrez IDs.

```
affy2entrez = function(ids) {
  require(hgu133a.db)
  entrez.a =
mapIds(hgu133a.db,keys=ids,keytype="PROBEID",column="ENTREZID",multiVals="first")
  entrez = ifelse(
    !is.na(entrez.a),entrez.a,NA)
  return(entrez)
}
```

```

}
G.corr.entrez = lapply(G.corr.cc, affy2entrez)
G.corr.entrez = lapply(G.corr.entrez, unname)

# Retrieve pathway annotations and count table, stored separately for each component
path.cnt.tables = vector("list", length=length(G.corr.entrez))
for (q in 1:length(G.corr.entrez)) {
  if (all(G.corr.entrez[[q]] %in% keys(reactome.db) == FALSE)) {
    next
  } else {
    path.annot = select(reactome.db, keys=G.corr.entrez[[q]],
keytype="ENTREZID", columns="PATHNAME")
    path.cnt.tables[[q]] = table(path.annot$PATHNAME)
  }
}

# Convert array to Entrez IDs, eliminate duplicate entries
gb.entrez = affy2entrez(row.names(genematrix.base))
gb.entrez = unique(unname(gb.entrez))

> length(gb.entrez)
[1] 22283
> gb.entrez = unique(unname(gb.entrez))
> length(gb.entrez)
[1] 12994

# List of tables containing total counts of genes in various pathways
path.cnt.total = vector("list", length=length(path.cnt.tables))
for (w in 1:length(path.cnt.tables)) {
  if (is.null(path.cnt.tables[[w]])) {
    next
  } else {
    path.annot = select(reactome.db, keys=names(path.cnt.tables[[w]]),
keytype="PATHNAME", columns="ENTREZID")
    ind = vector()
    for (i in path.annot$ENTREZID) {
      ind = c(ind, i %in% gb.entrez)
    }
    path.annot = path.annot[ind,]
    path.cnt.total[[w]] = table(path.annot$PATHNAME)
  }
}

# Enrichment function provided in homework 8
test.enrichment = function(N, total.cnt, n.selected, n.overlap) {
  fisher.test(matrix(c(n.overlap, total.cnt-n.overlap, n.selected-n.overlap,
N-n.selected-total.cnt+n.overlap), ncol=2), alternative="greater")$p.value
}

results = vector("list", length=length(path.cnt.total))
for (g in 1:length(results)) {
  if (is.null(path.cnt.total[[g]])) {
    next
  } else {
    results[[g]] = data.frame("PATHWAY" = names(path.cnt.total[[g]]))
    for (y in 1:length(path.cnt.total[[g]])) {
      if (path.cnt.tables[[g]][[y]] > path.cnt.total[[g]][[y]]) {
        next
      } else {
        results[[g]]$N.COMP[y] = path.cnt.tables[[g]][[y]]
        results[[g]]$N.ARRAY[y] = path.cnt.total[[g]][[y]]
      }
    }
  }
}

```

```

        results[[g]]$P.VALUE[y] = test.enrichment(length(gb.entrez),
path.cnt.total[[g]][[y]], length(G.corr.entrez[[g]]), path.cnt.tables[[g]][[y]])
    }
}
}

```

I had an unexpected error that I didn't run into during the week 8 homework. In a few spots the value in `path.cnt.tables` was greater than the value in `path.cnt.total`, which meant that when the enrichment function was called, `total.cnt - n.overlap` gave a negative value. In other words, more genes in the graph component were involved in a particular pathway than total genes in the entire array participating in that pathway. At that point the enrichment function would quit and throw up the error. I have not been able to make sense of that and am currently bypassing those few spots with `if (path.cnt.tables[[g]][[y]] > path.cnt.total[[g]][[y]]){ next }`.

In the paper, the authors tracked five estrogen-regulated genes and five genes related to proliferation. It looks like there is additional overrepresentation in other pathways as well, although not every pathway here produced a low p-value. I'm seeing a number of significant immunity pathways, several neurotransmitter-related pathways (including a strongly significant result for the GABA cycle), membrane transporters, cell signaling, and modifications to chromatin and histones.

```

> results[1]
[[1]]
NULL

```

```

> results[2]
[[1]]

```

	PATHWAY	N.COMP	N.ARRAY
1	Homo sapiens: Antimicrobial peptides	1	44
2	Homo sapiens: Cell-Cell communication	1	113
3	Homo sapiens: Cell junction organization	1	78
4	Homo sapiens: Developmental Biology	4	865
5	Homo sapiens: Formation of the cornified envelope	4	79
6	Homo sapiens: Immune System	2	1765
7	Homo sapiens: Innate Immune System	2	892
8	Homo sapiens: Keratinization	4	85
9	Homo sapiens: Metal sequestration by antimicrobial proteins	1	5
10	Homo sapiens: Neutrophil degranulation	2	422
11	Homo sapiens: Type I hemidesmosome assembly	1	11

```

P.VALUE
1 3.336181e-02
2 8.366563e-02
3 5.845160e-02
4 2.960519e-03
5 2.584726e-07
6 4.026903e-01
7 1.469275e-01
8 3.475458e-07
9 3.842602e-03
10 3.984616e-02
11 8.436180e-03

```

```

> results[3]
[[1]]

```

	PATHWAY
1	Homo sapiens: Acetylcholine Neurotransmitter Release Cycle
2	Homo sapiens: Amine-derived hormones
3	Homo sapiens: Cell surface interactions at the vascular wall
4	Homo sapiens: Cytokine Signaling in Immune system
5	Homo sapiens: Disease
6	Homo sapiens: Dopamine Neurotransmitter Release Cycle
7	Homo sapiens: GABA synthesis
8	Homo sapiens: GABA synthesis, release, reuptake and degradation
9	Homo sapiens: Glutamate Neurotransmitter Release Cycle

```

10                                     Homo sapiens: Hemostasis
11                                     Homo sapiens: Immune System
12 Homo sapiens: Incretin synthesis, secretion, and inactivation
13                                     Homo sapiens: Infectious disease
14                                     Homo sapiens: Innate Immune System
15                                     Homo sapiens: Insulin processing
16 Homo sapiens: Integration of energy metabolism
17                                     Homo sapiens: Metabolism
18 Homo sapiens: Metabolism of amino acids and derivatives
19                                     Homo sapiens: Metabolism of proteins
20                                     Homo sapiens: Neuronal System
21 Homo sapiens: Neurotoxicity of clostridium toxins
22 Homo sapiens: Neurotransmitter release cycle
23 Homo sapiens: Neutrophil degranulation
24 Homo sapiens: Norepinephrine Neurotransmitter Release Cycle
25 Homo sapiens: Other interleukin signaling
26 Homo sapiens: Peptide hormone biosynthesis
27 Homo sapiens: Peptide hormone metabolism
28 Homo sapiens: Platelet activation, signaling and aggregation
29 Homo sapiens: Platelet degranulation
30 Homo sapiens: Post-translational protein modification
31 Homo sapiens: Post-translational protein phosphorylation
32 Homo sapiens: Regulation of Insulin-like Growth Factor (IGF) transport and uptake by Insulin-like Growth Factor Binding Proteins (IGFBPs)
33 Homo sapiens: Regulation of insulin secretion
34 Homo sapiens: Response to elevated platelet cytosolic Ca2+
35 Homo sapiens: Serotonin and melatonin biosynthesis
36 Homo sapiens: Serotonin Neurotransmitter Release Cycle
37 Homo sapiens: Signaling by Interleukins
38 Homo sapiens: Synthesis, secretion, and deacylation of Ghrelin
39 Homo sapiens: Synthesis, secretion, and inactivation of Glucagon-like Peptide-1 (GLP-1)
40 Homo sapiens: Synthesis, secretion, and inactivation of Glucose-dependent Insulinotropic Polypeptide (GIP)
41 Homo sapiens: Tie2 Signaling
42 Homo sapiens: Toxicity of botulinum toxin type A (BoNT/A)
43 Homo sapiens: Toxicity of botulinum toxin type C (BoNT/C)
44 Homo sapiens: Toxicity of botulinum toxin type E (BoNT/E)
45 Homo sapiens: Transmission across Chemical Synapses
46 Homo sapiens: Uptake and actions of bacterial toxins

```

	N.COMP	N.ARRAY	P.VALUE
1	1	16	1.832150e-02
2	1	16	1.832150e-02
3	1	131	1.410748e-01
4	1	759	5.947726e-01
5	1	923	6.690691e-01
6	1	22	2.511092e-02
7	1	16	1.832150e-02
8	4	16	2.075449e-09
9	1	23	2.623822e-02
10	2	588	1.457058e-01
11	2	1765	6.242940e-01
12	1	19	2.172170e-02
13	1	356	3.409272e-01
14	2	892	2.754042e-01
15	1	22	2.511092e-02
16	1	101	1.105136e-01
17	2	1736	6.146674e-01
18	1	317	3.097338e-01
19	3	1639	2.916221e-01
20	4	312	3.609585e-04
21	1	9	1.034474e-02
22	4	48	2.171259e-07
23	2	422	8.363128e-02
24	1	17	1.945612e-02
25	1	20	2.285266e-02
26	1	12	1.377073e-02
27	1	76	8.427387e-02
28	1	261	2.625269e-01
29	1	121	1.309984e-01
30	2	1075	3.557843e-01
31	2	95	5.219989e-03
32	2	112	7.185317e-03
33	1	72	8.000907e-02
34	1	126	1.360503e-01
35	1	4	4.610058e-03
36	1	17	1.945612e-02
37	1	554	4.799964e-01
38	1	16	1.832150e-02
39	1	16	1.832150e-02
40	1	10	1.148797e-02
41	1	18	2.058952e-02
42	1	4	4.610058e-03
43	1	2	2.307514e-03
44	1	3	3.459407e-03
45	4	204	7.030158e-05
46	1	29	3.297651e-02

```

> results[4]
[[1]]
NULL

```



```
> results[5]
[[1]]
```

PATHWAY

1 Homo sapiens: Adaptive Immune System

2 Homo sapiens: Binding and Uptake of Ligands by Scavenger Receptors

3 Homo sapiens: Cargo recognition for clathrin-mediated endocytosis

4 Homo sapiens: Cell surface interactions at the vascular wall

5 Homo sapiens: Chemokine receptors bind chemokines

6 Homo sapiens: Class A/1 (Rhodopsin-like receptors)

7 Homo sapiens: Clathrin-mediated endocytosis

8 Homo sapiens: Constitutive Signaling by Aberrant PI3K in Cancer

9 Homo sapiens: Cytokine Signaling in Immune system

10 Homo sapiens: Developmental Biology

11 Homo sapiens: Disease

12 Homo sapiens: Diseases associated with visual transduction

13 Homo sapiens: Diseases of signal transduction

14 Homo sapiens: Downstream TCR signaling

15 Homo sapiens: G alpha (i) signalling events

16 Homo sapiens: GPCR downstream signalling

17 Homo sapiens: GPCR ligand binding

18 Homo sapiens: Hemostasis

19 Homo sapiens: Immune System

20 Homo sapiens: Incretin synthesis, secretion, and inactivation

21 Homo sapiens: Interleukin-10 signaling

22 Homo sapiens: Interleukin-12 family signaling

23 Homo sapiens: Interleukin-4 and 13 signaling

24 Homo sapiens: Intracellular signaling by second messengers

25 Homo sapiens: Iron uptake and transport

26 Homo sapiens: Membrane Trafficking

27 Homo sapiens: Metabolism

28 Homo sapiens: Metabolism of fat-soluble vitamins

29 Homo sapiens: Metabolism of lipids

30 Homo sapiens: Metabolism of proteins

31 Homo sapiens: Metabolism of vitamins and cofactors

32 Homo sapiens: Neddylaton

33 Homo sapiens: Negative regulation of the PI3K/AKT network

34 Homo sapiens: Peptide hormone metabolism

35 Homo sapiens: Peptide ligand-binding receptors

36 Homo sapiens: PI3K/AKT Signaling in Cancer

37 Homo sapiens: PI5P, PP2A and IER3 Regulate PI3K/AKT Signaling

38 Homo sapiens: PIP3 activates AKT signaling

39 Homo sapiens: Platelet activation, signaling and aggregation

40 Homo sapiens: Platelet degranulation

41 Homo sapiens: Post-translational modification: synthesis of GPI-anchored proteins

42 Homo sapiens: Post-translational protein modification

43 Homo sapiens: Post-translational protein phosphorylation

44 Homo sapiens: Regulation of Insulin-like Growth Factor (IGF) transport and uptake by Insulin-like Growth Factor Binding Proteins (IGFBPs)

45 Homo sapiens: Response to elevated platelet cytosolic Ca2+

46 Homo sapiens: Retinoid cycle disease events

47 Homo sapiens: Retinoid metabolism and transport

48 Homo sapiens: Retinoid metabolism disease events

49 Homo sapiens: Scavenging of heme from plasma

50 Homo sapiens: Signaling by GPCR

51 Homo sapiens: Signaling by Interleukins

52 Homo sapiens: Signaling by Leptin

53 Homo sapiens: Signal Transduction

54 Homo sapiens: Synthesis, secretion, and deacylation of Ghrelin

55 Homo sapiens: Synthesis, secretion, and inactivation of Glucagon-like Peptide-1 (GLP-1)

56 Homo sapiens: TCR signaling

57 Homo sapiens: The canonical retinoid cycle in rods (twilight vision)

58 Homo sapiens: TNFR2 non-canonical NF-kB pathway

59 Homo sapiens: TNFs bind their physiological receptors

60 Homo sapiens: Transcriptional regulation of white adipocyte differentiation

61 Homo sapiens: Transferrin endocytosis and recycling

62 Homo sapiens: Transport of small molecules

63 Homo sapiens: Triglyceride catabolism

64 Homo sapiens: Triglyceride metabolism

65 Homo sapiens: Vesicle-mediated transport

66 Homo sapiens: Visual phototransduction

	N.COMP	N.ARRAY	P.VALUE
1	1	628	0.9029444200
2	1	37	0.1256373289
3	1	90	0.2790958499
4	1	131	0.3794121082
5	3	46	0.0006037034
6	4	269	0.0159533957
7	1	127	0.3702601976
8	1	59	0.1928716056
9	4	759	0.2940025864
10	2	865	0.8296955054
11	2	923	0.8565434393
12	1	10	0.0355995748
13	2	335	0.3427115148
14	1	93	0.2869450073
15	3	195	0.0333025133
16	3	530	0.3003069533
17	4	370	0.0441853071

18	2	588	0.6343543235
19	5	1765	0.7837427680
20	1	19	0.0665766546
21	2	46	0.0119781838
22	1	55	0.1810355987
23	1	104	0.3150160821
24	1	263	0.6181650884
25	1	51	0.1690297703
26	1	532	0.8603106091
27	2	1736	0.9903381140
28	1	40	0.1351185300
29	1	589	0.8874322698
30	5	1639	0.7235335327
31	1	149	0.4190102638
32	1	175	0.4718759071
33	1	94	0.2895427582
34	1	76	0.2413341008
35	4	160	0.0026162266
36	1	83	0.2604508275
37	1	88	0.2738161644
38	1	232	0.5718382480
39	1	261	0.6153304368
40	1	121	0.3562841533
41	2	60	0.0198397511
42	4	1075	0.5524429696
43	1	95	0.2921312459
44	1	112	0.3347491424
45	1	126	0.3679516592
46	1	10	0.0355995748
47	1	37	0.1256373289
48	1	1	0.0036170540
49	1	12	0.0425691560
50	5	702	0.1081189174
51	3	554	0.3243255737
52	1	11	0.0390905499
53	7	1951	0.5718362374
54	1	16	0.0563607476
55	1	16	0.0563607476
56	1	113	0.3371763113
57	1	18	0.0631834380
58	1	95	0.2921312459
59	1	26	0.0899946602
60	2	74	0.0293256605
61	1	27	0.0932927980
62	1	578	0.8826347626
63	1	21	0.0733270398
64	1	27	0.0932927980
65	2	566	0.6132858237
66	1	85	0.2658256066

```
> results[6]
[[1]]
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PATHWAY	
1	Homo sapiens: Activation of Ca-permeable Kainate Receptor
2	Homo sapiens: Activation of kainate receptors upon glutamate binding
3	Homo sapiens: Activation of Na-permeable kainate receptors
4	Homo sapiens: Biological oxidations
5	Homo sapiens: Defective CP causes aceruloplasminemia (ACERULOP)
6	Homo sapiens: Defective FMO3 causes Trimethylaminuria (TMAU)
7	Homo sapiens: Deubiquitination
8	Homo sapiens: Disease
9	Homo sapiens: Diseases of metabolism
10	Homo sapiens: Disorders of transmembrane transporters
11	Homo sapiens: FMO oxidises nucleophiles
12	Homo sapiens: Gene expression (Transcription)

```

13 Homo sapiens: Generic Transcription Pathway
14 Homo sapiens: Glucuronidation
15 Homo sapiens: Ionotropic activity of kainate receptors
16 Homo sapiens: Iron uptake and transport
17 Homo sapiens: Josephin domain DUBs
18 Homo sapiens: Metabolic disorders of biological oxidation enzymes
19 Homo sapiens: Metabolism
20 Homo sapiens: Metabolism of proteins
21 Homo sapiens: Metal ion SLC transporters
22 Homo sapiens: Mitochondrial protein import
23 Homo sapiens: Neurexins and neuroligins
24 Homo sapiens: Neuronal System
25 Homo sapiens: Neurotransmitter receptors and postsynaptic signal transmission
26 Homo sapiens: Phase I - Functionalization of compounds
27 Homo sapiens: Phase II - Conjugation of compounds
28 Homo sapiens: Post-translational protein modification
29 Homo sapiens: Post-translational protein phosphorylation
30 Homo sapiens: Protein-protein interactions at synapses
31 Homo sapiens: Regulation of Insulin-like Growth Factor (IGF) transport and uptake by Insulin-like Growth Factor Binding Proteins (IGFBPs)
32 Homo sapiens: RNA Polymerase II Transcription
33 Homo sapiens: SLC-mediated transmembrane transport
34 Homo sapiens: SLC transporter disorders
35 Homo sapiens: Sodium-coupled sulphate, di- and tri-carboxylate transporters
36 Homo sapiens: Transmission across Chemical Synapses
37 Homo sapiens: Transport of bile salts and organic acids, metal ions and amine compounds
38 Homo sapiens: Transport of small molecules

```

	N.COMP	N.ARRAY	P.VALUE
1	1	12	0.020137387
2	1	27	0.044765122
3	1	2	0.003383442
4	2	180	0.036764513
5	1	1	0.001693089
6	1	1	0.001693089
7	1	240	0.336665388
8	2	923	0.469866469
9	1	95	0.149189106
10	1	130	0.198595811
11	1	3	0.005071062
12	1	1075	0.850639446
13	1	863	0.779792345
14	1	15	0.025110916
15	1	12	0.020137387
16	1	51	0.082944760
17	1	11	0.018474168
18	1	30	0.049619247
19	2	1736	0.812955951
20	3	1639	0.537279995
21	1	17	0.028413206
22	1	52	0.084503534
23	1	48	0.078253222
24	2	312	0.096932151
25	1	137	0.208142868
26	1	94	0.147735631
27	1	81	0.128623455
28	2	1075	0.553751136
29	1	95	0.149189106
30	1	72	0.115153031
31	1	112	0.173539099
32	1	964	0.816818572
33	2	185	0.038645021
34	1	57	0.092259544
35	1	4	0.006755955
36	1	204	0.294193386
37	2	62	0.004866110
38	2	578	0.256104099

```

> results[7]
[[1]]

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	PATHWAY	N.COMP
1	Homo sapiens: Adaptive Immune System	3
2	Homo sapiens: Costimulation by the CD28 family	3

3	Homo sapiens: Cytokine Signaling in Immune system	3
4	Homo sapiens: Downstream TCR signaling	3
5	Homo sapiens: Generation of second messenger molecules	3
6	Homo sapiens: Immune System	3
7	Homo sapiens: Interferon gamma signaling	3
8	Homo sapiens: Interferon Signaling	3
9	Homo sapiens: MHC class II antigen presentation	3
10	Homo sapiens: PD-1 signaling	3
11	Homo sapiens: Phosphorylation of CD3 and TCR zeta chains	3
12	Homo sapiens: TCR signaling	3
13	Homo sapiens: Translocation of ZAP-70 to Immunological synapse	3

	N.ARRAY	P.VALUE
1	628	1.123759e-04
2	65	1.194828e-07
3	759	1.985540e-04
4	93	3.549636e-07
5	31	1.229568e-08
6	1765	2.502461e-03
7	82	2.422482e-07
8	183	2.748354e-06
9	108	5.584510e-07
10	20	3.118371e-09
11	19	2.650615e-09
12	113	6.404587e-07
13	17	1.860081e-09

```
> results[8]
[[1]]
```

```
PATHWAY
1 Homo sapiens: ABC-family proteins mediated transport
2 Homo sapiens: ABC transporter disorders
3 Homo sapiens: Activation of APC/C and APC/C:Cdc20 mediated degradation of mitotic proteins
4 Homo sapiens: Activation of gene expression by SREBF (SREBP)
5 Homo sapiens: Activation of Matrix Metalloproteinases
6 Homo sapiens: Activation of NF-kappaB in B cells
7 Homo sapiens: Adaptive Immune System
8 Homo sapiens: Antigen processing-Cross presentation
9 Homo sapiens: Antigen processing: Ubiquitination & Proteasome degradation
10 Homo sapiens: Antimicrobial peptides
11 Homo sapiens: APC/C:Cdc20 mediated degradation of mitotic proteins
12 Homo sapiens: APC/C:Cdc20 mediated degradation of Securin
13 Homo sapiens: APC/C:Cdh1 mediated degradation of Cdc20 and other APC/C:Cdh1 targeted proteins in late mitosis/early G1
14 Homo sapiens: APC:Cdc20 mediated degradation of cell cycle proteins prior to satisfaction of the cell cycle checkpoint
15 Homo sapiens: APC/C-mediated degradation of cell cycle proteins
16 Homo sapiens: Apoptosis
17 Homo sapiens: Asparagine N-linked glycosylation
18 Homo sapiens: Assembly of collagen fibrils and other multimeric structures
19 Homo sapiens: Assembly of the pre-replicative complex
20 Homo sapiens: Asymmetric localization of PCP proteins
21 Homo sapiens: Attenuation phase
22 Homo sapiens: AUF1 (hnRNP D0) binds and destabilizes mRNA
23 Homo sapiens: Autodegradation of Cdh1 by Cdh1:APC/C
24 Homo sapiens: Autodegradation of the E3 ubiquitin ligase COP1
25 Homo sapiens: Axon guidance
26 Homo sapiens: Basigin interactions
27 Homo sapiens: Beta-catenin independent WNT signaling
28 Homo sapiens: BMAL1:CLOCK,NPAS2 activates circadian gene expression
29 Homo sapiens: Cdc20:Phospho-APC/C mediated degradation of Cyclin A
30 Homo sapiens: CDK-mediated phosphorylation and removal of Cdc6
31 Homo sapiens: CDT1 association with the CDC6:ORC:origin complex
32 Homo sapiens: Cell-Cell communication
33 Homo sapiens: Cell-cell junction organization
34 Homo sapiens: Cell Cycle
35 Homo sapiens: Cell Cycle Checkpoints
36 Homo sapiens: Cell Cycle, Mitotic
37 Homo sapiens: Cell-extracellular matrix interactions
38 Homo sapiens: Cell junction organization
39 Homo sapiens: Cell surface interactions at the vascular wall
40 Homo sapiens: Cellular responses to external stimuli
41 Homo sapiens: Cellular responses to stress
42 Homo sapiens: Cellular response to heat stress
43 Homo sapiens: Cellular response to hypoxia
44 Homo sapiens: Cellular Senescence
45 Homo sapiens: Chromatin modifying enzymes
46 Homo sapiens: Chromatin organization
47 Homo sapiens: Circadian Clock
48 Homo sapiens: Class I MHC mediated antigen processing & presentation
49 Homo sapiens: Cleavage of Growing Transcript in the Termination Region
```

50 Homo sapiens: CLEC7A (Dectin-1) signaling  
 51 Homo sapiens: Collagen biosynthesis and modifying enzymes  
 52 Homo sapiens: Collagen chain trimerization  
 53 Homo sapiens: Collagen degradation  
 54 Homo sapiens: Collagen formation  
 55 Homo sapiens: Complement cascade  
 56 Homo sapiens: Complex I biogenesis  
 57 Homo sapiens: COPI-dependent Golgi-to-ER retrograde traffic  
 58 Homo sapiens: COPII (Coat Protein 2) Mediated Vesicle Transport  
 59 Homo sapiens: COPI-mediated anterograde transport  
 60 Homo sapiens: CRMPs in Sema3A signaling  
 61 Homo sapiens: Cross-presentation of soluble exogenous antigens (endosomes)  
 62 Homo sapiens: C-type lectin receptors (CLRs)  
 63 Homo sapiens: Cyclin A:Cdk2-associated events at S phase entry  
 64 Homo sapiens: Cyclin E associated events during G1/S transition  
 65 Homo sapiens: Cytokine Signaling in Immune system  
 66 Homo sapiens: Dectin-1 mediated noncanonical NF-kB signaling  
 67 Homo sapiens: Defective CFTR causes cystic fibrosis  
 68 Homo sapiens: Degradation of AXIN  
 69 Homo sapiens: Degradation of beta-catenin by the destruction complex  
 70 Homo sapiens: Degradation of DVL  
 71 Homo sapiens: Degradation of GLI1 by the proteasome  
 72 Homo sapiens: Degradation of GLI2 by the proteasome  
 73 Homo sapiens: Degradation of the extracellular matrix  
 74 Homo sapiens: Deubiquitination  
 75 Homo sapiens: Developmental Biology  
 76 Homo sapiens: Disease  
 77 Homo sapiens: Diseases of signal transduction  
 78 Homo sapiens: Disorders of transmembrane transporters  
 79 Homo sapiens: DNA Replication  
 80 Homo sapiens: DNA Replication Pre-Initiation  
 81 Homo sapiens: Downstream signaling events of B Cell Receptor (BCR)  
 82 Homo sapiens: Downstream TCR signaling  
 83 Homo sapiens: ECM proteoglycans  
 84 Homo sapiens: Elastic fibre formation  
 85 Homo sapiens: EPHA-mediated growth cone collapse  
 86 Homo sapiens: EPH-Ephrin signaling  
 87 Homo sapiens: Epigenetic regulation of gene expression  
 88 Homo sapiens: ERCC6 (CSB) and EHMT2 (G9a) positively regulate rRNA expression  
 89 Homo sapiens: ER-Phagosome pathway  
 90 Homo sapiens: ER to Golgi Anterograde Transport  
 91 Homo sapiens: Extracellular matrix organization  
 92 Homo sapiens: Factors involved in megakaryocyte development and platelet production  
 93 Homo sapiens: FBXL7 down-regulates AURKA during mitotic entry and in early mitosis  
 94 Homo sapiens: Fc epsilon receptor (FCERI) signaling  
 95 Homo sapiens: FCERI mediated NF-kB activation  
 96 Homo sapiens: Formation of the beta-catenin:TCF transactivating complex  
 97 Homo sapiens: G1/S DNA Damage Checkpoints  
 98 Homo sapiens: G1/S Transition  
 99 Homo sapiens: G2/M Checkpoints  
 100 Homo sapiens: G2/M Transition  
 101 Homo sapiens: Gene expression (Transcription)  
 102 Homo sapiens: Generic Transcription Pathway  
 103 Homo sapiens: GLI3 is processed to GLI3R by the proteasome  
 104 Homo sapiens: Golgi-to-ER retrograde transport  
 105 Homo sapiens: Hedgehog ligand biogenesis  
 106 Homo sapiens: Hedgehog 'off' state  
 107 Homo sapiens: Hedgehog 'on' state  
 108 Homo sapiens: Hemostasis  
 109 Homo sapiens: Hh mutants abrogate ligand secretion  
 110 Homo sapiens: Hh mutants that don't undergo autocatalytic processing are degraded by ERAD  
 111 Homo sapiens: HIV Infection  
 112 Homo sapiens: Host Interactions of HIV factors  
 113 Homo sapiens: HSF1 activation  
 114 Homo sapiens: HSF1-dependent transactivation  
 115 Homo sapiens: Immune System  
 116 Homo sapiens: Infectious disease  
 117 Homo sapiens: Innate Immune System  
 118 Homo sapiens: Integrin cell surface interactions  
 119 Homo sapiens: Interferon alpha/beta signaling  
 120 Homo sapiens: Interferon Signaling  
 121 Homo sapiens: Interleukin-1 family signaling  
 122 Homo sapiens: Interleukin-20 family signaling  
 123 Homo sapiens: Interleukin-7 signaling  
 124 Homo sapiens: Intracellular signaling by second messengers  
 125 Homo sapiens: Intra-Golgi and retrograde Golgi-to-ER traffic  
 126 Homo sapiens: Intra-Golgi traffic  
 127 Homo sapiens: Localization of the PINCH-ILK-PARVIN complex to focal adhesions  
 128 Homo sapiens: MAPK1/MAPK3 signaling  
 129 Homo sapiens: MAPK6/MAPK4 signaling  
 130 Homo sapiens: MAPK family signaling cascades  
 131 Homo sapiens: Membrane Trafficking  
 132 Homo sapiens: Metabolism  
 133 Homo sapiens: Metabolism of amino acids and derivatives  
 134 Homo sapiens: Metabolism of lipids  
 135 Homo sapiens: Metabolism of polyamines  
 136 Homo sapiens: Metabolism of proteins  
 137 Homo sapiens: Metabolism of RNA  
 138 Homo sapiens: Metabolism of steroids  
 139 Homo sapiens: MET activates PTK2 signaling  
 140 Homo sapiens: MET promotes cell motility  
 141 Homo sapiens: M/G1 Transition  
 142 Homo sapiens: Mitochondrial biogenesis  
 143 Homo sapiens: Mitochondrial translation  
 144 Homo sapiens: Mitochondrial translation elongation

145 Homo sapiens: Mitochondrial translation initiation  
146 Homo sapiens: Mitochondrial translation termination  
147 Homo sapiens: Mitotic Anaphase  
148 Homo sapiens: Mitotic G1-G1/S phases  
149 Homo sapiens: Mitotic G2-G2/M phases  
150 Homo sapiens: Mitotic Metaphase and Anaphase  
151 Homo sapiens: Molecules associated with elastic fibres  
152 Homo sapiens: M Phase  
153 Homo sapiens: mRNA 3'-end processing  
154 Homo sapiens: mRNA Splicing  
155 Homo sapiens: mRNA Splicing - Major Pathway  
156 Homo sapiens: Muscle contraction  
157 Homo sapiens: NCAM1 interactions  
158 Homo sapiens: NCAM signaling for neurite out-growth  
159 Homo sapiens: Neddylation  
160 Homo sapiens: Neutrophil degranulation  
161 Homo sapiens: NIK-->noncanonical NF-kB signaling  
162 Homo sapiens: Non-integrin membrane-ECM interactions  
163 Homo sapiens: Nuclear Receptor transcription pathway  
164 Homo sapiens: Orcl removal from chromatin  
165 Homo sapiens: Organelle biogenesis and maintenance  
166 Homo sapiens: Other semaphorin interactions  
167 Homo sapiens: Oxygen-dependent proline hydroxylation of Hypoxia-inducible Factor Alpha  
168 Homo sapiens: p53-Dependent G1 DNA Damage Response  
169 Homo sapiens: p53-Dependent G1/S DNA damage checkpoint  
170 Homo sapiens: p53-Independent DNA Damage Response  
171 Homo sapiens: p53-Independent G1/S DNA damage checkpoint  
172 Homo sapiens: PCP/CE pathway  
173 Homo sapiens: PIP3 activates AKT signaling  
174 Homo sapiens: PKMTs methylate histone lysines  
175 Homo sapiens: Platelet activation, signaling and aggregation  
176 Homo sapiens: Platelet degranulation  
177 Homo sapiens: Positive epigenetic regulation of rRNA expression  
178 Homo sapiens: Post-translational modification: synthesis of GPI-anchored proteins  
179 Homo sapiens: Post-translational protein modification  
180 Homo sapiens: PPARA activates gene expression  
181 Homo sapiens: Processing of Capped Intron-Containing Pre-mRNA  
182 Homo sapiens: Programmed Cell Death  
183 Homo sapiens: PTEN Regulation  
184 Homo sapiens: RAF/MAP kinase cascade  
185 Homo sapiens: Regulation of activated PAK-2p34 by proteasome mediated degradation  
186 Homo sapiens: Regulation of APC/C activators between G1/S and early anaphase  
187 Homo sapiens: Regulation of Apoptosis  
188 Homo sapiens: Regulation of cholesterol biosynthesis by SREBP (SREBF)  
189 Homo sapiens: Regulation of Complement cascade  
190 Homo sapiens: Regulation of cytoskeletal remodeling and cell spreading by IPP complex components  
191 Homo sapiens: Regulation of DNA replication  
192 Homo sapiens: Regulation of expression of SLITs and ROBOs  
193 Homo sapiens: Regulation of HSF1-mediated heat shock response  
194 Homo sapiens: Regulation of Hypoxia-inducible Factor (HIF) by oxygen  
195 Homo sapiens: Regulation of lipid metabolism by Peroxisome proliferator-activated receptor alpha (PPARalpha)  
196 Homo sapiens: Regulation of mitotic cell cycle  
197 Homo sapiens: Regulation of mRNA stability by proteins that bind AU-rich elements  
198 Homo sapiens: Regulation of ornithine decarboxylase (ODC)  
199 Homo sapiens: Regulation of PTEN stability and activity  
200 Homo sapiens: Regulation of RAS by GAPs  
201 Homo sapiens: Regulation of RUNX2 expression and activity  
202 Homo sapiens: Regulation of RUNX3 expression and activity  
203 Homo sapiens: Regulation of TP53 Activity  
204 Homo sapiens: Regulation of TP53 Activity through Methylation  
205 Homo sapiens: Removal of licensing factors from origins  
206 Homo sapiens: Respiratory electron transport  
207 Homo sapiens: Respiratory electron transport, ATP synthesis by chemiosmotic coupling, and heat production by uncoupling proteins.  
208 Homo sapiens: Response to elevated platelet cytosolic Ca2+  
209 Homo sapiens: RHO GTPase Effectors  
210 Homo sapiens: RHO GTPases activate CIT  
211 Homo sapiens: RHO GTPases activate PAKs  
212 Homo sapiens: RHO GTPases activate PKNs  
213 Homo sapiens: RHO GTPases Activate ROCKs  
214 Homo sapiens: RMTs methylate histone arginines  
215 Homo sapiens: RNA Polymerase II Transcription  
216 Homo sapiens: RNA Polymerase II Transcription Termination  
217 Homo sapiens: RNA Polymerase I Promoter Clearance  
218 Homo sapiens: RNA Polymerase I Transcription  
219 Homo sapiens: RNA Polymerase I Transcription Initiation  
220 Homo sapiens: RORA activates gene expression  
221 Homo sapiens: RUNX1 interacts with co-factors whose precise effect on RUNX1 targets is not known  
222 Homo sapiens: RUNX1 regulates genes involved in megakaryocyte differentiation and platelet function  
223 Homo sapiens: RUNX1 regulates transcription of genes involved in differentiation of HSCs  
224 Homo sapiens: RUNX3 regulates YAP1-mediated transcription  
225 Homo sapiens: SCF-beta-TrCP mediated degradation of Emi1  
226 Homo sapiens: SCF(Skp2)-mediated degradation of p27/p21  
227 Homo sapiens: Sema3A PAK dependent Axon repulsion  
228 Homo sapiens: SEMA3A-Plexin repulsion signaling by inhibiting Integrin adhesion  
229 Homo sapiens: Sema4D induced cell migration and growth-cone collapse  
230 Homo sapiens: Sema4D in semaphorin signaling  
231 Homo sapiens: Semaphorin interactions  
232 Homo sapiens: Senescence-Associated Secretory Phenotype (SASP)  
233 Homo sapiens: Separation of Sister Chromatids  
234 Homo sapiens: Signaling by Hedgehog  
235 Homo sapiens: Signaling by Interleukins  
236 Homo sapiens: Signaling by MET  
237 Homo sapiens: Signaling by PDGF  
238 Homo sapiens: Signaling by Receptor Tyrosine Kinases  
239 Homo sapiens: Signaling by Rho GTPases

240 Homo sapiens: Signaling by ROBO receptors  
 241 Homo sapiens: Signaling by the B Cell Receptor (BCR)  
 242 Homo sapiens: Signaling by WNT  
 243 Homo sapiens: Signal Transduction  
 244 Homo sapiens: Smooth Muscle Contraction  
 245 Homo sapiens: S Phase  
 246 Homo sapiens: Sphingolipid de novo biosynthesis  
 247 Homo sapiens: Sphingolipid metabolism  
 248 Homo sapiens: Stabilization of p53  
 249 Homo sapiens: Switching of origins to a post-replicative state  
 250 Homo sapiens: Synthesis of DNA  
 251 Homo sapiens: TCF dependent signaling in response to WNT  
 252 Homo sapiens: TCR signaling  
 253 Homo sapiens: Terminal pathway of complement  
 254 Homo sapiens: The citric acid (TCA) cycle and respiratory electron transport  
 255 Homo sapiens: The role of GTSE1 in G2/M progression after G2 checkpoint  
 256 Homo sapiens: Tight junction interactions  
 257 Homo sapiens: TNFR2 non-canonical NF-kB pathway  
 258 Homo sapiens: Transcriptional activation of mitochondrial biogenesis  
 259 Homo sapiens: Transcriptional Regulation by E2F6  
 260 Homo sapiens: Transcriptional regulation by RUNX1  
 261 Homo sapiens: Transcriptional regulation by RUNX2  
 262 Homo sapiens: Transcriptional regulation by RUNX3  
 263 Homo sapiens: Transcriptional Regulation by TP53  
 264 Homo sapiens: Transcriptional regulation of white adipocyte differentiation  
 265 Homo sapiens: Translation  
 266 Homo sapiens: Transport of Mature mRNA derived from an Intron-Containing Transcript  
 267 Homo sapiens: Transport of Mature Transcript to Cytoplasm  
 268 Homo sapiens: Transport of small molecules  
 269 Homo sapiens: Transport to the Golgi and subsequent modification  
 270 Homo sapiens: Ubiquitin-dependent degradation of Cyclin D  
 271 Homo sapiens: Ubiquitin-dependent degradation of Cyclin D1  
 272 Homo sapiens: Ubiquitin Mediated Degradation of Phosphorylated Cdc25A  
 273 Homo sapiens: Ub-specific processing proteases  
 274 Homo sapiens: UCH proteinases  
 275 Homo sapiens: Vesicle-mediated transport  
 276 Homo sapiens: Vif-mediated degradation of APOBEC3G  
 277 Homo sapiens: Vpu mediated degradation of CD4  
 278 Homo sapiens: YAP1- and WWTR1 (TAZ)-stimulated gene expression

	N.COMP	N.ARRAY	P.VALUE
1	1	92	0.2944730504
2	1	73	0.2416192159
3	1	69	0.2300076283
4	1	39	0.1371911935
5	1	33	0.1173542456
6	1	64	0.2152480132
7	1	628	0.9121318640
8	1	96	0.3051313515
9	1	229	0.5822533433
10	1	44	0.1533878179
11	1	68	0.2270776271
12	1	60	0.2032410968
13	1	65	0.2182219380
14	1	66	0.2211848218
15	1	79	0.2587156556
16	1	158	0.4515078359
17	2	264	0.2625513038
18	3	54	0.0010919537
19	1	65	0.2182219380
20	1	60	0.2032410968
21	1	14	0.0515440353
22	1	54	0.1848925796
23	1	58	0.1971703388
24	1	49	0.1692864902
25	4	521	0.1323840236
26	1	25	0.0902086430
27	1	132	0.3942239396
28	1	43	0.1501725027
29	1	65	0.2182219380
30	1	49	0.1692864902
31	1	56	0.1910542767
32	2	113	0.0676811568
33	1	52	0.1786849142
34	1	566	0.8876776679
35	1	256	0.6234966845

36	1	475	0.8392996012
37	1	17	0.0622457320
38	2	78	0.0348810390
39	1	131	0.3919074868
40	3	455	0.2454032911
41	3	391	0.1824655670
42	1	82	0.2671217155
43	1	71	0.2358350267
44	1	175	0.4860568945
45	2	230	0.2150355419
46	2	230	0.2150355419
47	1	63	0.2122630072
48	1	290	0.6697947223
49	1	56	0.1910542767
50	1	96	0.3051313515
51	3	54	0.0010919537
52	3	33	0.0002539182
53	3	57	0.0012779498
54	3	75	0.0028123750
55	1	54	0.1848925796
56	1	40	0.1404546155
57	1	82	0.2671217155
58	1	60	0.2032410968
59	2	91	0.0461252748
60	1	14	0.0515440353
61	1	48	0.1661303328
62	1	127	0.3825545913
63	1	78	0.2558927028
64	1	79	0.2587156556
65	2	759	0.7889494125
66	1	58	0.1971703388
67	1	56	0.1910542767
68	1	52	0.1786849142
69	1	79	0.2587156556
70	1	55	0.1879791533
71	1	57	0.1941179914
72	1	57	0.1941179914
73	4	121	0.0010968473
74	1	240	0.5995645948
75	5	865	0.2254564290
76	1	923	0.9731461990
77	1	335	0.7225865211
78	1	130	0.3895823574
79	1	104	0.3259769127
80	1	81	0.2643301238
81	1	79	0.2587156556
82	1	93	0.2971525435
83	1	72	0.2387325028
84	1	41	0.1437059451
85	1	26	0.0936460534
86	1	87	0.2809247627
87	1	125	0.3778254448
88	1	63	0.2122630072
89	1	80	0.2615281165
90	2	137	0.0942016981
91	5	269	0.0033208526
92	1	145	0.4235625350
93	1	52	0.1786849142
94	1	128	0.3849059416
95	1	77	0.2530592200
96	1	76	0.2502151685



97	1	64	0.2152480132
98	1	124	0.3754475840
99	1	153	0.4409203308
100	1	178	0.4919284187
101	6	1075	0.2163065573
102	5	863	0.2240649359
103	1	57	0.1941179914
104	1	113	0.3486963683
105	1	58	0.1971703388
106	1	103	0.3234051068
107	1	74	0.2444952053
108	3	588	0.3833376510
109	1	54	0.1848925796
110	1	52	0.1786849142
111	1	213	0.5557576409
112	1	122	0.3706651248
113	1	12	0.0443432024
114	1	21	0.0763308400
115	4	1765	0.9149070698
116	1	356	0.7443010445
117	3	892	0.6631970687
118	1	81	0.2643301238
119	1	69	0.2300076283
120	1	183	0.5015685922
121	1	114	0.3511739615
122	1	235	0.5917847581
123	1	42	0.1469452263
124	1	263	0.6335209871
125	2	168	0.1320047942
126	1	35	0.1240156992
127	1	4	0.0150004998
128	1	228	0.5806437195
129	1	82	0.2671217155
130	1	262	0.6321051177
131	2	532	0.6018350452
132	4	1736	0.9080469800
133	1	317	0.7025442120
134	2	589	0.6579069398
135	1	78	0.2558927028
136	5	1639	0.7573290571
137	4	584	0.1770817139
138	1	133	0.3965317477
139	2	28	0.0049464705
140	2	38	0.0089815565
141	1	81	0.2643301238
142	1	83	0.2699029296
143	1	62	0.2092668796
144	1	60	0.2032410968
145	1	58	0.1971703388
146	1	58	0.1971703388
147	1	174	0.4840849885
148	1	142	0.4169181785
149	1	180	0.4958062095
150	1	175	0.4860568945
151	1	36	0.1273279325
152	1	342	0.7300181523
153	1	49	0.1692864902
154	2	166	0.1294680808
155	2	162	0.1244309856
156	1	184	0.5034750116
157	1	40	0.1404546155

158	1	63	0.2122630072
159	1	175	0.4860568945
160	1	422	0.8022614715
161	1	57	0.1941179914
162	2	58	0.0201341891
163	1	49	0.1692864902
164	1	68	0.2270776271
165	1	244	0.6056837198
166	1	18	0.0657866089
167	1	62	0.2092668796
168	1	62	0.2092668796
169	1	62	0.2092668796
170	1	51	0.1755637385
171	1	51	0.1755637385
172	1	87	0.2809247627
173	1	232	0.5870459880
174	1	58	0.1971703388
175	1	261	0.6306838902
176	1	121	0.3682604609
177	1	91	0.2917835513
178	1	60	0.2032410968
179	4	1075	0.5861385804
180	1	104	0.3259769127
181	3	212	0.0455939345
182	1	159	0.4536016436
183	1	126	0.3801944364
184	1	222	0.5708576128
185	1	48	0.1661303328
186	1	73	0.2416192159
187	1	50	0.1724309446
188	1	52	0.1786849142
189	1	43	0.1501725027
190	1	8	0.0297805091
191	1	73	0.2416192159
192	1	163	0.4618988571
193	1	65	0.2182219380
194	1	71	0.2358350267
195	1	106	0.3310918286
196	1	79	0.2587156556
197	1	83	0.2699029296
198	1	49	0.1692864902
199	1	67	0.2241367049
200	1	60	0.2032410968
201	1	70	0.2329267483
202	1	55	0.1879791533
203	1	140	0.4124469884
204	1	16	0.0586917094
205	1	70	0.2329267483
206	1	76	0.2502151685
207	1	96	0.3051313515
208	1	126	0.3801944364
209	1	272	0.6460259391
210	1	19	0.0693143876
211	1	24	0.0867584629
212	1	80	0.2615281165
213	1	18	0.0657866089
214	1	62	0.2092668796
215	6	964	0.1528614723
216	1	56	0.1910542767
217	1	94	0.2998220672
218	1	96	0.3051313515

219	1	43	0.1501725027
220	1	25	0.0902086430
221	1	34	0.1206911519
222	1	76	0.2502151685
223	1	117	0.3585514761
224	1	19	0.0693143876
225	1	53	0.1817945139
226	1	60	0.2032410968
227	1	15	0.0551244931
228	1	13	0.0479502878
229	1	24	0.0867584629
230	1	27	0.0970707406
231	2	65	0.0249168276
232	1	94	0.2998220672
233	1	164	0.4639537987
234	1	128	0.3849059416
235	2	554	0.6242345883
236	2	74	0.0316719932
237	1	55	0.1879791533
238	3	478	0.2688984462
239	1	368	0.7559523046
240	1	207	0.5454031199
241	1	111	0.3437133467
242	2	283	0.2892296582
243	6	1951	0.7649704485
244	1	36	0.1273279325
245	1	129	0.3872485197
246	1	30	0.1072689227
247	1	64	0.2152480132
248	1	54	0.1848925796
249	1	68	0.2270776271
250	1	96	0.3051313515
251	2	200	0.1739804486
252	1	113	0.3486963683
253	1	8	0.0297805091
254	1	136	0.4034036182
255	1	73	0.2416192159
256	1	21	0.0763308400
257	1	95	0.3024816578
258	1	50	0.1724309446
259	1	31	0.1106431763
260	3	206	0.0424680057
261	1	113	0.3486963683
262	2	105	0.0595051009
263	1	310	0.6943727152
264	1	74	0.2444952053
265	1	249	0.6132039324
266	1	65	0.2182219380
267	1	72	0.2387325028
268	1	578	0.8928804358
269	2	167	0.1307349566
270	1	49	0.1692864902
271	1	49	0.1692864902
272	1	51	0.1755637385
273	1	177	0.4899785826
274	1	88	0.2836546524
275	2	566	0.6360502401
276	1	52	0.1786849142
277	1	50	0.1724309446
278	1	26	0.0936460534

```
> results[9]
[[1]]
NULL

> results[10]
[[1]]
```

PATHWAY

```
1 Homo sapiens: Activation of the mRNA upon binding of the cap-binding complex and eIFs, and subsequent binding to 43S
2                                     Homo sapiens: Adaptive Immune System
3             Homo sapiens: Antigen Presentation: Folding, assembly and peptide loading of class I MHC
4                 Homo sapiens: Antigen processing-Cross presentation
5                     Homo sapiens: Asparagine N-linked glycosylation
6                         Homo sapiens: Assembly of Viral Components at the Budding Site
7                             Homo sapiens: ATF6 (ATF6-alpha) activates chaperone genes
8                                 Homo sapiens: ATF6 (ATF6-alpha) activates chaperones
9                                     Homo sapiens: Axon guidance
10                                     Homo sapiens: Binding and Uptake of Ligands by Scavenger Receptors
11                                         Homo sapiens: Calnexin/calreticulin cycle
12                                             Homo sapiens: Cap-dependent Translation Initiation
13 Homo sapiens: Class I MHC mediated antigen processing & presentation
14                                     Homo sapiens: Developmental Biology
15                                         Homo sapiens: Disease
16                                             Homo sapiens: ER-Phagosome pathway
17                                                 Homo sapiens: Eukaryotic Translation Elongation
18                                                 Homo sapiens: Eukaryotic Translation Initiation
19                                                 Homo sapiens: Eukaryotic Translation Termination
20                                 Homo sapiens: Formation of a pool of free 40S subunits
21 Homo sapiens: Formation of the ternary complex, and subsequently, the 43S complex
22                                     Homo sapiens: GTP hydrolysis and joining of the 60S ribosomal subunit
23                                         Homo sapiens: Immune System
24                                             Homo sapiens: Infectious disease
25                                                 Homo sapiens: Influenza Infection
26                                                     Homo sapiens: Influenza Life Cycle
27 Homo sapiens: Influenza Viral RNA Transcription and Replication
28 Homo sapiens: L13a-mediated translational silencing of Ceruloplasmin expression
29 Homo sapiens: Major pathway of rRNA processing in the nucleolus and cytosol
30                                     Homo sapiens: Metabolism
31                                         Homo sapiens: Metabolism of amino acids and derivatives
32                                             Homo sapiens: Metabolism of proteins
33                                                 Homo sapiens: Metabolism of RNA
34 Homo sapiens: N-glycan trimming in the ER and Calnexin/Calreticulin cycle
35                                     Homo sapiens: Nonsense-Mediated Decay (NMD)
36 Homo sapiens: Nonsense Mediated Decay (NMD) enhanced by the Exon Junction Complex (EJC)
37 Homo sapiens: Nonsense Mediated Decay (NMD) independent of the Exon Junction Complex (EJC)
38                                     Homo sapiens: Peptide chain elongation
39                                         Homo sapiens: Post-translational protein modification
40 Homo sapiens: Regulation of expression of SLITs and ROBOs
41 Homo sapiens: Ribosomal scanning and start codon recognition
42                                     Homo sapiens: rRNA processing
43 Homo sapiens: rRNA processing in the nucleus and cytosol
44                                     Homo sapiens: Scavenging by Class A Receptors
45                                     Homo sapiens: Scavenging by Class F Receptors
46                                     Homo sapiens: Selenoamino acid metabolism
47                                     Homo sapiens: Selenocysteine synthesis
48                                     Homo sapiens: Signaling by ROBO receptors
49 Homo sapiens: SRP-dependent cotranslational protein targeting to membrane
50                                     Homo sapiens: Translation
51 Homo sapiens: Translation initiation complex formation
52                                     Homo sapiens: Unfolded Protein Response (UPR)
53                                     Homo sapiens: Vesicle-mediated transport
54                                     Homo sapiens: Viral mRNA Translation
55                                     Homo sapiens: Virus Assembly and Release
```

	N.COMP	N.ARRAY	P.VALUE
1	1	58	0.0089076155
2	1	628	0.0943277481
3	1	25	0.0038443760
4	1	96	0.0147220320
5	1	264	0.0402228874
6	1	2	0.0003078225
7	1	10	0.0015386388
8	1	12	0.0018462245
9	1	521	0.0785861761
10	1	37	0.0056870466
11	1	24	0.0036907431
12	1	116	0.0177753804
13	1	290	0.0441395724
14	1	865	0.1287116975

15	2	923	0.0050405778
16	1	80	0.0122759415
17	1	90	0.0138051034
18	1	116	0.0177753804
19	1	90	0.0138051034
20	1	98	0.0150275801
21	1	50	0.0076813481
22	1	109	0.0167072475
23	1	1765	0.2532225679
24	2	356	0.0007485590
25	2	149	0.0001306158
26	2	139	0.0001136165
27	1	129	0.0197575159
28	1	108	0.0165546097
29	1	165	0.0252360582
30	1	1736	0.2493601621
31	1	317	0.0481984231
32	2	1639	0.0159015899
33	1	584	0.0878709971
34	1	33	0.0050730126
35	1	112	0.0171650898
36	1	112	0.0171650898
37	1	92	0.0141107937
38	1	86	0.0131935808
39	1	1075	0.1586224884
40	1	163	0.0249320975
41	1	57	0.0087543735
42	1	183	0.0279695721
43	1	175	0.0267551509
44	1	17	0.0026149812
45	1	6	0.0009233255
46	1	110	0.0168598734
47	1	87	0.0133464793
48	1	207	0.0316082868
49	1	107	0.0164019600
50	1	249	0.0379596188
51	1	57	0.0087543735
52	1	88	0.0134993658
53	1	566	0.0852229888
54	1	86	0.0131935808
55	1	2	0.0003078225

```
> results[11]
[[1]]
NULL
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```
> results[12]
[[1]]
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	PATHWAY	N.COMP	N.ARRAY	P.VALUE
1	Homo sapiens: Chromatin modifying enzymes	1	230	0.03508899
2	Homo sapiens: Chromatin organization	1	230	0.03508899
3	Homo sapiens: HDMs demethylate histones	1	44	0.00676115