

Direct inhibition of the NOTCH TF. Differential expression analysis

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1 Array expression profiling

Summary

NOTCH proteins regulate signaling pathways involved in cellular differentiation, proliferation and death. Overactive Notch signaling has been observed in numerous cancers and has been extensively studied in the context of T-cell acute lymphoblastic leukemia (T-ALL) where more than 50% of patients harbour mutant NOTCH1. Small molecule modulators of these proteins would be important for understanding the role of NOTCH proteins in malignant and normal biological processes.

We were interested to measure the global changes in gene expression upon treatment of the human T-ALL cell lines HPB-ALL and KOPT-K1 with either vehicle alone (DMSO) or SAHM1, an alpha-helical hydrocarbon stapled peptide derived from the MAML1 co-activator protein.

Overall design Triplicate cultures of KOPT-K1 or HPB-ALL cells were treated with either DMSO alone or SAHM1 (20 uM) for 24 hours. Total RNA was extracted and hybridized to Affymetrix human U133 plus 2.0 microarrays (three arrays per treatment per cell line for a total of 12 arrays).

1.1 Pipeline

1.2 Python imports

Script 1.2.1 (python)

```
1 import rpy2.rinterface
2 %reload_ext rpy2.ipython
```

1.3 R imports

Script 1.3.1 (R)

```
1 %%R
2 ##1. Load libraries
3 library("affy")
4 library("limma")
5 library("genefilter")
6 library(hgu133plus2.db)
7 wd <- "/Users/nandoide/misc_work/Desktop/uni/TRREP"
8 setwd(wd)
```

1.4 Functions

Script 1.4.1 (R)

```
1 %%R
2
3 import_CEL <- function(pattern) {
4   # Import CEL files into affiBatch object
5   files <- list.files(pattern = pattern)
6   names <- gsub(".CEL.gz", "", files)
```

```

7   abatch <- ReadAffy(fileNames = files, compress = TRUE, sampleNames = names)
8   return(abatch)
9 }
10
11 create_eset <- function(affyBatch) {
12   # Generates object eset (class ExprSet),
13   # espresso function provides intensities in log scale
14   return(espresso(affyBatch,
15     bg.correct = TRUE,
16     bgcorrect.method="rma",
17     normalize = TRUE,
18     normalize.method="quantiles",
19     pmcorrect.method="pmonly",
20     summary.method="medianpolish",
21     verbose = TRUE))
22 }
23
24 boxplots <- function(affyBatch, eset, title) {
25   # Generate BOXPLOTS before and after normalization
26   boxplot(affyBatch,
27     main=paste0("Boxplot Before Normalization ", title),
28     col = "lightgrey")
29   df_eset <- as.data.frame(exprs(eset))
30
31   boxplot(data.frame(df_eset),
32     main=paste0("Boxplot After Normalization (log scale) ", title), col = "white")
33 }
34
35 create_TopTable <- function(eset, control_samples=c(1,1,1,0,0,0)) {
36   # Generate TopTable with limma
37
38   # Data filtering using IQR.
39   esetIQR <- varFilter(eset, var.func=IQR, var.cutoff=0.5, filterByQuantile=TRUE)
40
41   # Differential expression analysis.#####
42   r_control_samples <- 1 - control_samples
43   design <- cbind(DMSO=control_samples, SAHM1=r_control_samples)
44
45   rownames(design) <- colnames(eset)
46
47   #7. Contrasts matrix.
48   cont.matrix <- makeContrasts(DMSO_SAHM1 = SAHM1 - DMSO, levels = design)
49
50   #8. Obtaining differentially expressed genes (DEGs)
51   #Linear model and eBayes
52   fit <- lmFit(esetIQR, design) ##getting DEGs from IQR
53   fit2 <- contrasts.fit(fit, cont.matrix)
54   fit2 <- eBayes(fit2)
55
56   #Table with DEGs results
57   toptableIQR <- topTable(fit2, number=dim(exprs(esetIQR))[1], adjust.method="BH",
   ↪ sort.by="p")

```

```

58   return(toptableIQR)
59 }
60
61 anotate_TopTable <- function(toptable) {
62   # Obtain gene names from probe names and chip symbol dataset
63   probenames_toptable <- as.character(rownames(toptable))
64   genesymbols_toptable <- as.character(mget(probenames_toptable, hgu133plus2SYMBOL))
65   # Annotated gene table
66   toptable_annot <- cbind(Symbol = genesymbols_toptable, toptable)
67   return(toptable_annot)
68 }
69
70 generank_table <- function(toptable, rnk.file) {
71   # Generate rank of table top 50 upregulated and top 50 downregulated from 250 better
72   # adjusts p-values
73   more_significant = toptable[order(toptable$adj.P.Val, decreasing = FALSE),][1:250,]
74   up_50 = more_significant[which(toptable$logFC > 0), ] [1:50,] # up reg top 50
75   down_50 = more_significant[which(toptable$logFC < 0), ] [1:50,] # down reg top 50
76
77   print("Down-regulated genes")
78   print(down_50[order(down_50$logFC), c(1,2,6)])
79
80   print("Up-regulated genes")
81   print(up_50[order(up_50$logFC), c(1,2,6)])
82
83   d <- rbind(down_50[order(down_50$logFC), c(1,2,6)], up_50[order(up_50$logFC), c(1,2,6)])
84
85   #df <- data.frame(paste0(d$Symbol,'|',row.names(d)),d$logFC)
86   df <- data.frame(row.names(d), d$logFC)
87   write.table(df,row.names=FALSE,col.names=FALSE,
88               quote=FALSE,sep="\t",file=paste0(rnk.file, ".rnk"))
89 }

```

1.5 Load raw data

Script 1.5.1 (R)

```

1  %%R
2  setwd("GSE18198_data")
3  affyBatch_HPBB = import_CEL("HPB*")
4  affyBatch_KOPT = import_CEL("KOPT*")
5  setwd(wd)

```

1.6 Create expression sets

Script 1.6.1 (R)

```
1 %%R
2 eset_HPB <- create_eset(affyBatch_HPB)
3 eset_KOPT <- create_eset(affyBatch_KOPT)
```

```
background correction: rma
normalization: quantiles
PM/MM correction : pmonly
expression values: medianpolish
background correcting...done.
normalizing...done.
54675 ids to be processed
|                               |
|#####|
background correction: rma
normalization: quantiles
PM/MM correction : pmonly
expression values: medianpolish
background correcting...done.
normalizing...done.
54675 ids to be processed
|                               |
|#####|
```

Script 1.6.2 (R)

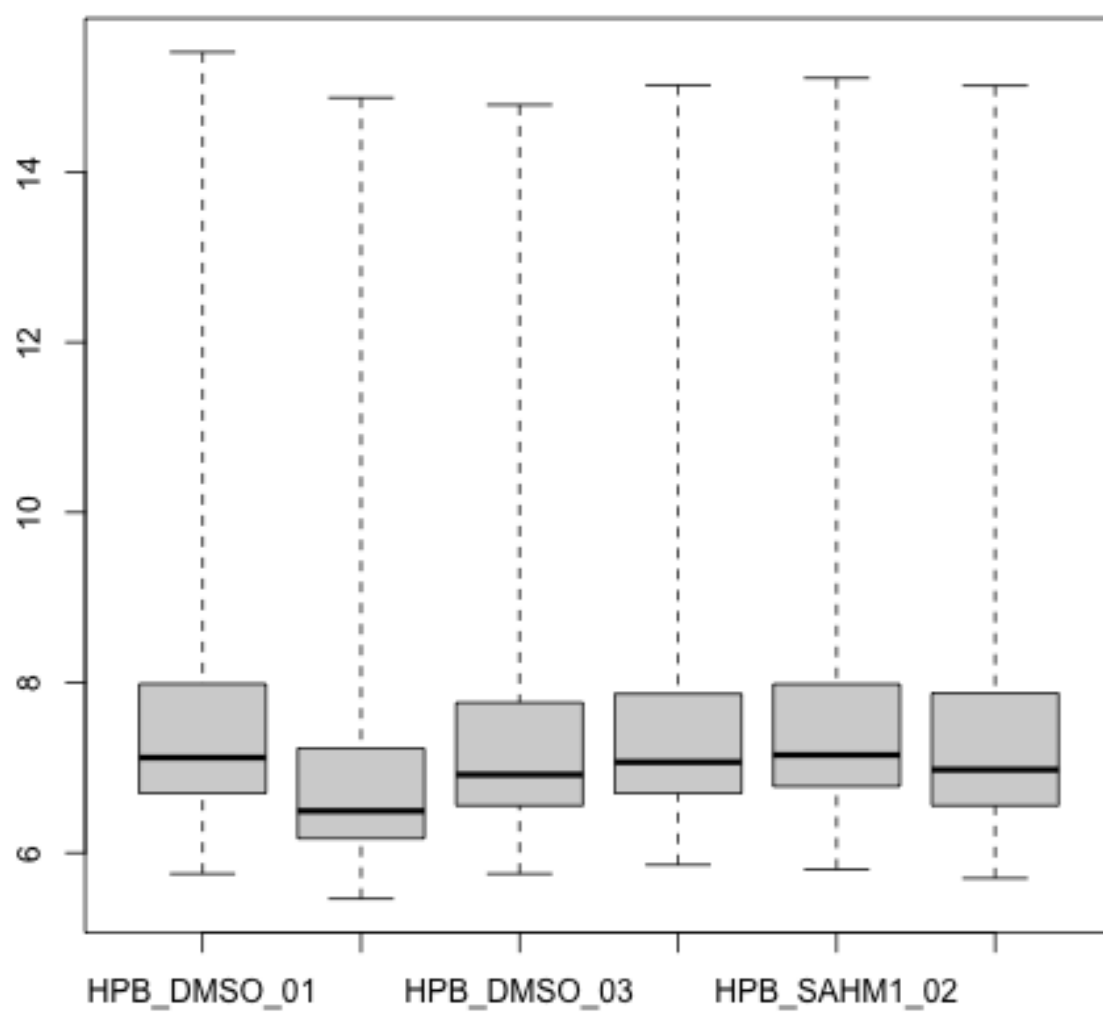
```
1 %%R
2 save(eset_HPB, file="eset_HPB.RData")
3 save(eset_KOPT, file="eset_KOPT.RData")
```

1.7 Quality plots

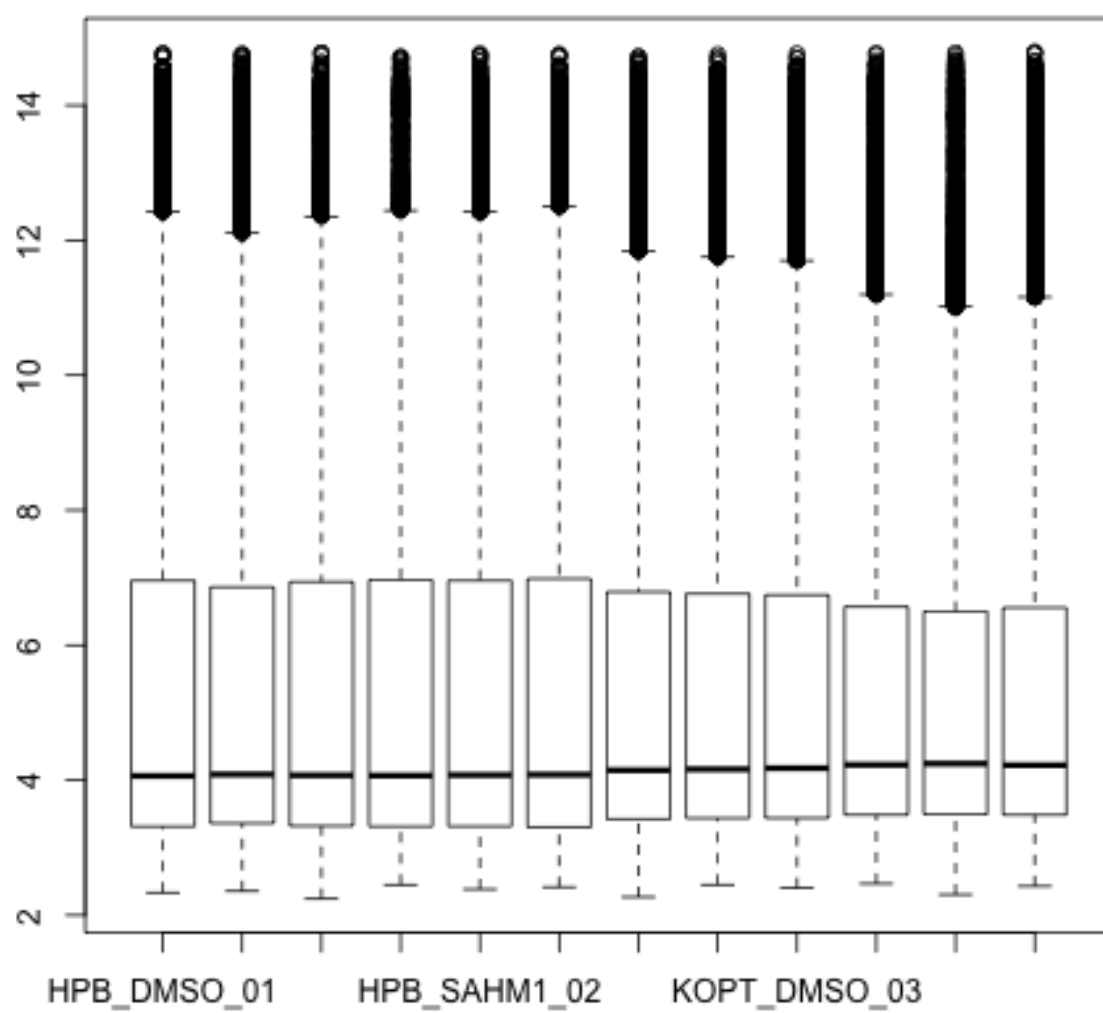
Script 1.7.1 (R)

```
1 %%R
2 boxplots(affyBatch_HPB, eset, "HPB Cell Line")
3 boxplots(affyBatch_KOPT, eset, "KOPT Cell Line")
```

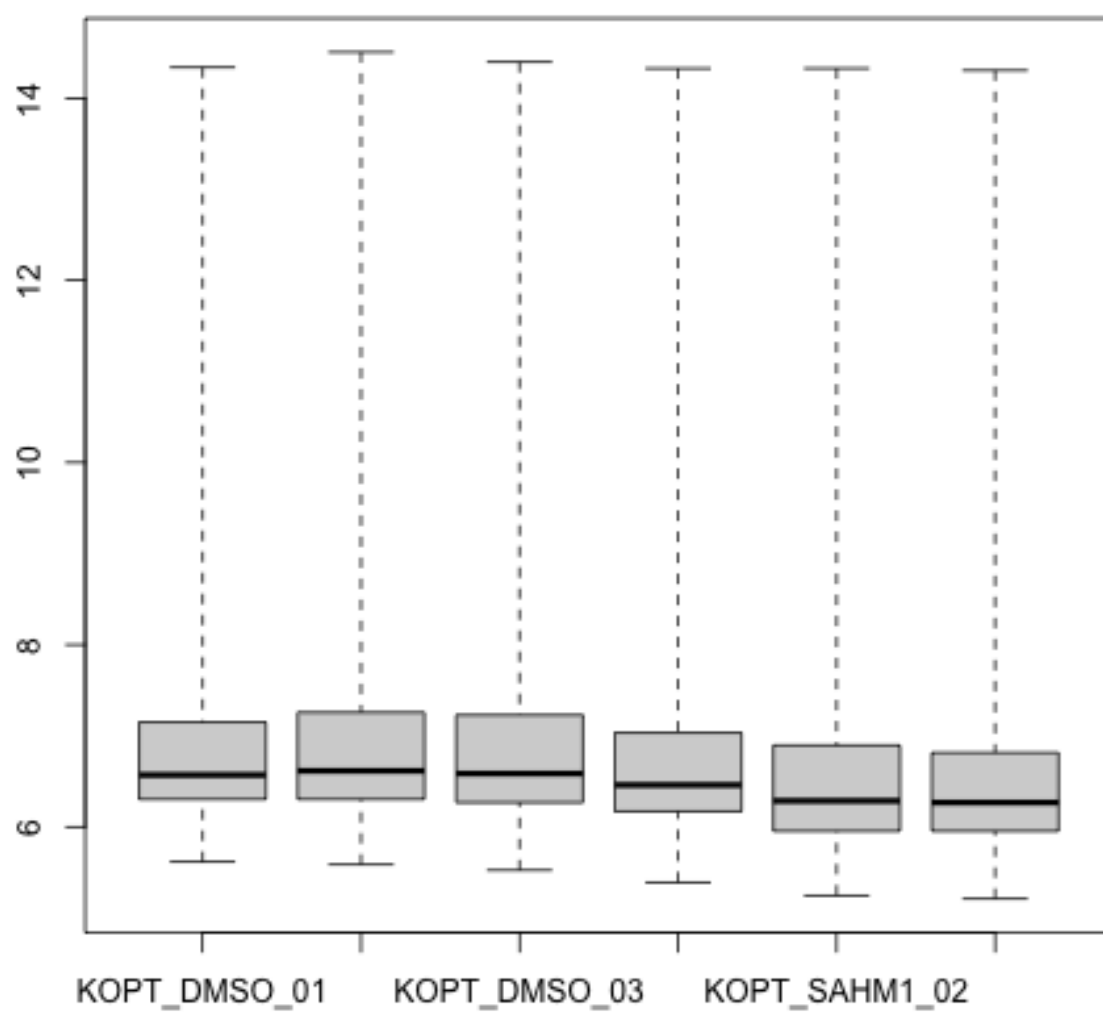
Boxplot Before Normalization HPB Cell Line



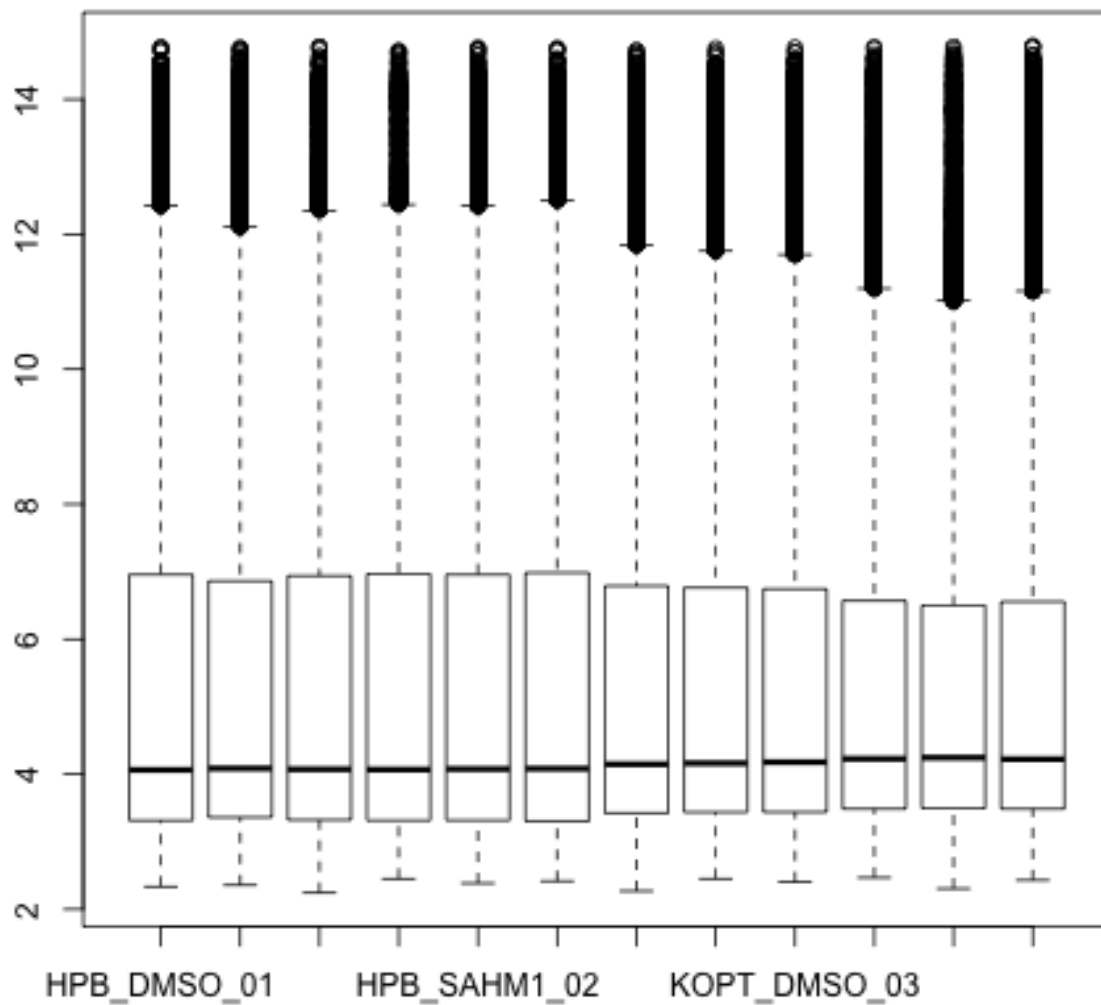
Boxplot After Normalization (log scale) HPB Cell Line



Boxplot Before Normalization KOPT Cell Line



Boxplot After Normalization (log scale) KOPT Cell Line



1.8 Differential expressed genes

Script 1.8.1 (R)

```
1 %%R
2 toptable_HPBB <- create_TopTable(eset_HPBB)
3 toptable_anot_HPBB <- anotate_TopTable(toptable_HPBB)
4 generank_table(toptable_anot_HPBB, "generank_HPBB")
```

[1] "Down-regulated genes"

	Symbol	logFC	adj.P.Val
225342_at	AK4	-2.1078858	1.128982e-05
230710_at	MIR210HG	-1.9761492	7.688286e-06
227336_at	DTX1	-1.3841443	8.636324e-05
201842_s_at	EFEMP1	-1.3678548	6.004820e-05
204348_s_at	AK4	-1.3491612	3.350727e-04
227347_x_at	HES4	-1.2640712	1.228528e-04
200953_s_at	CCND2	-1.2357909	7.997079e-05
202464_s_at	PFKFB3	-1.1937490	1.228528e-04
202022_at	ALDOC	-1.1753644	1.248092e-04
240546_at	LINC01120	-1.1131135	1.552628e-04
227337_at	ANKRD37	-1.1079168	2.110727e-04
200894_s_at	FKBP4	-1.0737202	5.300330e-04
217078_s_at	CD300A	-1.0719092	8.239876e-04
201170_s_at	BHLHE40	-1.0402130	2.549012e-04
202934_at	HK2	-1.0377714	2.104071e-04
201848_s_at	BNIP3	-1.0052154	6.744018e-04
218051_s_at	NT5DC2	-1.0049990	2.851346e-03
203394_s_at	HES1	-0.9993973	7.294799e-04
219371_s_at	KLF2	-0.9800918	3.918155e-04
201251_at	PKM	-0.9787897	4.328581e-03
201849_at	BNIP3	-0.9724936	6.167814e-04
213746_s_at	FLNA	-0.9705676	1.430899e-03
201516_at	SRM	-0.9428084	1.627743e-03
203523_at	LSP1	-0.9360851	2.263449e-03
225944_at	NLN	-0.9317256	1.421369e-03
214183_s_at	TKTL1	-0.9290362	2.452591e-03
236180_at	NA	-0.9287828	3.049302e-03
201194_at	SELENOW	-0.9285463	6.167814e-04
231922_at	ZNF276	-0.9269927	4.098501e-03
209933_s_at	CD300A	-0.9049911	8.239876e-04
214752_x_at	FLNA	-0.9018607	1.636952e-03
226348_at	FUT11	-0.8976507	1.075839e-03
201212_at	LGMN	-0.8972886	1.381530e-03
218305_at	IP04	-0.8783786	1.923264e-03
205544_s_at	CR2	-0.8502424	1.206402e-03
202145_at	LY6E	-0.8406636	2.534145e-03
200859_x_at	FLNA	-0.8368746	2.851346e-03
202887_s_at	DDIT4	-0.8271607	1.813467e-03
200965_s_at	ABLIM1	-0.8229490	1.522219e-03
203504_s_at	ABCA1	-0.8211483	1.430899e-03
208116_s_at	MAN1A1	-0.7931451	4.037398e-03
202472_at	MPI	-0.7831169	2.929531e-03
207543_s_at	P4HA1	-0.7783781	2.263449e-03
201563_at	SORD	-0.7663457	4.281959e-03
222150_s_at	GSAP	-0.7532244	4.098501e-03
207539_s_at	IL4	-0.7404704	4.098501e-03

205895_s_at	NOLC1	-0.7357033	4.328581e-03
219389_at	SUSD4	-0.7347418	3.852969e-03
201562_s_at	SORD	-0.7343969	4.098501e-03
218984_at	PUS7	-0.7076878	4.281959e-03
[1] "Up-regulated genes"			
	Symbol	logFC	adj.P.Val
204962_s_at	NA	0.8016614	1.927646e-03
222670_s_at	MAFB	0.8314472	1.414249e-03
244075_at	NA	0.8555977	1.927646e-03
205047_s_at	ASNS	0.8566562	1.373571e-03
236153_at	NA	0.8615325	1.373571e-03
228999_at	CHD2	0.8640573	1.731300e-03
202847_at	PCK2	0.8839066	1.373571e-03
242388_x_at	TAGAP	0.8933876	1.116736e-03
243368_at	NA	0.9077303	1.731300e-03
1558212_at	NA	0.9381646	1.381530e-03
212907_at	SLC30A1	0.9572462	5.305252e-04
241505_at	NA	0.9630797	1.430899e-03
230659_at	NA	0.9742286	8.892420e-04
203279_at	EDEM1	0.9785129	3.944123e-04
218923_at	CTBS	0.9839137	1.116736e-03
1558920_at	SLC8A1-AS1	0.9839933	1.272470e-03
215071_s_at	HIST1H2AC	0.9867407	1.634677e-03
217678_at	SLC7A11	1.0002602	6.787587e-04
235795_at	PAX6	1.0066337	6.744018e-04
1556294_at	FXD2	1.0219109	1.381530e-03
229538_s_at	IQGAP3	1.0315469	5.922793e-04
206864_s_at	HRK	1.0324569	1.969355e-03
243495_s_at	ZNF652	1.0513033	1.522219e-03
218145_at	TRIB3	1.0673820	2.149263e-04
219892_at	TM6SF1	1.0684116	7.475097e-04
244377_at	SLC1A4	1.0880295	2.042060e-04
201010_s_at	TXNIP	1.1062690	1.552628e-04
209921_at	SLC7A11	1.1333321	1.248092e-04
209822_s_at	VLDLR	1.1350680	2.104071e-04
230795_at	NA	1.1699268	2.104071e-04
213931_at	NA	1.1702639	3.804126e-04
201009_s_at	TXNIP	1.2328092	1.663743e-04
244042_x_at	NA	1.2501748	1.080676e-03
218559_s_at	MAFB	1.2553755	5.305252e-04
225957_at	CREBRF	1.2981952	4.382754e-04
222853_at	FLRT3	1.3254635	1.138577e-04
219270_at	CHAC1	1.3362724	3.651273e-05
202672_s_at	ATF3	1.3481402	3.651273e-05
218280_x_at	NA	1.3495011	1.272470e-03
207076_s_at	ASS1	1.4918960	3.651273e-05
201008_s_at	TXNIP	1.4920023	1.663743e-04
243871_at	LOC100130476	1.5055489	4.060560e-04

201464_x_at	JUN	1.5541848	7.688286e-06
236962_at	NA	1.5966520	1.522219e-03
235412_at	ARHGEF7	1.5978442	2.999663e-04
229541_at	NA	1.6143542	2.042060e-04
229147_at	RASSF6	1.6458323	7.688286e-06
235638_at	RASSF6	1.7804932	7.997079e-05
201466_s_at	JUN	2.1333931	2.108830e-06
201465_s_at	JUN	2.2743608	1.053822e-05

Script 1.8.2 (R)

```

1 %%R
2 toptable_KOPT <- create_TopTable(eset_KOPT)
3 toptable_annot_KOPT <- anotate_TopTable(toptable_KOPT)
4 generank_table(toptable_annot_KOPT, "generank_KOPT")

```

[1] "Down-regulated genes"

	Symbol	logFC	adj.P.Val
209921_at	SLC7A11	-2.916468	2.066610e-11
205047_s_at	ASNS	-2.757747	2.764706e-11
209369_at	ANXA3	-2.661459	2.066610e-11
219270_at	CHAC1	-2.264373	7.569090e-10
226517_at	BCAT1	-2.216157	2.899776e-10
214452_at	BCAT1	-2.166267	3.402665e-09
225285_at	BCAT1	-2.072317	2.630231e-10
217678_at	SLC7A11	-2.058710	7.569090e-10
230748_at	SLC16A6	-2.004791	6.729951e-09
219892_at	TM6SF1	-1.957664	1.012031e-09
220892_s_at	PSAT1	-1.938100	4.136414e-10
204351_at	S100P	-1.902944	5.924315e-09
223195_s_at	SESN2	-1.889417	7.569090e-10
214079_at	DHRS2	-1.873374	5.924315e-09
209822_s_at	VLDLR	-1.863734	4.214321e-09
212290_at	SLC7A1	-1.860735	2.786337e-08
202847_at	PCK2	-1.828534	1.164949e-09
225520_at	NA	-1.790127	1.147212e-09
223062_s_at	PSAT1	-1.786577	1.164949e-09
223196_s_at	SESN2	-1.730910	3.463629e-08
200924_s_at	SLC3A2	-1.698282	2.186020e-08
1553972_a_at	CBS	-1.682036	3.595785e-09
207076_s_at	ASS1	-1.675254	2.113541e-08
229787_s_at	OGT	-1.662192	1.743772e-07
222632_s_at	LZTFL1	-1.643945	9.106004e-08
212816_s_at	CBS	-1.599989	1.068633e-07
224839_s_at	GPT2	-1.553796	1.734549e-08

240983_s_at	CARS	-1.552793	5.615021e-08
215411_s_at	TRAF3IP2	-1.540251	2.113541e-08
221539_at	EIF4EBP1	-1.533442	1.149078e-08
201195_s_at	SLC7A5	-1.511384	1.336464e-08
214390_s_at	BCAT1	-1.459915	2.424870e-07
204999_s_at	ATF5	-1.451634	2.113541e-08
210512_s_at	VEGFA	-1.448871	5.654616e-08
200878_at	EPAS1	-1.435966	3.072051e-07
212501_at	CEBPB	-1.428290	2.844253e-08
224580_at	SLC38A1	-1.428164	1.068633e-07
204744_s_at	IARS	-1.419418	2.844253e-08
208693_s_at	GARS	-1.406661	4.090508e-08
223059_s_at	FAM107B	-1.392809	5.070038e-08
218437_s_at	LZTFL1	-1.332751	1.769993e-07
1558212_at	NA	-1.308392	1.982077e-07
205653_at	CTSG	-1.279331	2.502696e-07
217078_s_at	CD300A	-1.278830	2.424870e-07
203627_at	IGF1R	-1.275358	3.751987e-07
221933_at	NLGN4X	-1.272235	4.113388e-07
231894_at	SARS	-1.263321	2.424870e-07
214095_at	SHMT2	-1.235111	1.982077e-07
201263_at	TARS	-1.197960	3.751987e-07
226181_at	TUBE1	-1.189891	3.344154e-07

[1] "Up-regulated genes"

	Symbol	logFC	adj.P.Val
224429_x_at	NA	0.9259213	6.376426e-06
220725_x_at	DNAH3	0.9423323	6.447180e-06
210686_x_at	SLC25A16	0.9631964	4.491576e-06
213605_s_at	NA	0.9632616	6.833714e-06
1556206_at	LINC00408	0.9653901	4.353339e-06
244114_x_at	NA	0.9679377	6.750428e-06
241632_x_at	NA	0.9686426	4.885508e-06
239017_at	NA	0.9834736	7.316357e-06
1558496_at	LINC02053	0.9853247	5.091816e-06
211585_at	NPAT	0.9926606	6.429684e-06
236389_x_at	NA	1.0027588	4.491576e-06
208120_x_at	FKSG49	1.0184438	2.815681e-06
206323_x_at	OPHN1	1.0212889	5.601191e-06
224284_x_at	FKSG49	1.0251308	3.950099e-06
201464_x_at	JUN	1.0348832	3.490668e-06
220828_s_at	LINC01949	1.0397500	4.491576e-06
81737_at	LOC100505915	1.0462560	5.662707e-06
210800_at	TIMM8A	1.0479516	4.730744e-06
215182_x_at	NA	1.0559763	4.491576e-06
243489_at	NA	1.0626878	4.070717e-06
240988_x_at	NA	1.0629756	4.779299e-06
224288_x_at	FKSG49	1.0813463	1.113017e-06
AFFX-r2-Ec-bioB-5_at	NA	1.1020958	5.322529e-06

242862_x_at	NA	1.1113007	1.113017e-06
1563674_at	FCRL2	1.1127799	6.945728e-06
AFFX-BioC-5_at	NA	1.1199525	6.430788e-06
210718_s_at	NA	1.1396478	6.670158e-06
1562755_at	NA	1.1425399	2.235176e-06
232964_at	NA	1.1460961	1.656041e-06
220232_at	SCD5	1.1545960	1.183928e-06
1569940_at	SLC6A16	1.1781696	8.464513e-07
211454_x_at	FKSG49	1.1800267	5.834686e-07
AFFX-BioB-M_at	NA	1.1849198	6.376426e-06
209700_x_at	PDE4DIP	1.1871538	8.406263e-07
1566145_s_at	NA	1.1918754	3.003518e-07
234949_at	FRG1BP	1.1922760	1.231065e-06
1560144_at	NA	1.2077566	1.790306e-06
1553185_at	RASEF	1.2129105	6.160739e-07
231597_x_at	NA	1.2169048	1.477715e-06
242619_x_at	NA	1.2257718	4.302148e-07
1553186_x_at	RASEF	1.2330332	6.881976e-07
227952_at	ZNF595	1.2408024	5.034675e-07
1561754_at	NA	1.2457988	9.800827e-07
224159_x_at	TRIM4	1.2471076	7.904835e-07
243689_s_at	FRG1BP	1.3748167	6.160739e-07
231598_x_at	NA	1.4418759	1.469974e-07
228919_at	NA	1.4589605	1.682330e-06
1562527_at	LOC441666	1.4936054	7.062932e-08
1558048_x_at	NA	1.5005510	2.186020e-08
211565_at	SH3GL3	1.5671795	2.844253e-08

1.9 Generate GSEA gct, cls files

Script 1.9.1 (R)

```
1 %%R
2 exprs2_HPB <- cbind(c(" "), exprs(eset_HPB))
3 write.table(exprs2_HPB, row.names=TRUE, col.names=FALSE, quote=FALSE, file="eset_HPB.tsv", sep =
  → "\t")
4 exprs2_KOPT <- cbind(c(" "), exprs(eset_KOPT))
5 write.table(exprs2_KOPT, row.names=TRUE, col.names=FALSE, quote=FALSE, file="eset_KOPT.tsv", sep
  → = "\t")
```

Script 1.9.2 (bash)

```
1 %%bash
2 echo "#1.2" > gct.head.HPB
3 echo "$(cat eset_HPB.tsv | wc -l) 6" >> gct.head.HPB
```

```

4 echo "GID      NAME      HPB_DMSO_01      HPB_DMSO_02      HPB_DMSO_03      HPB_SA
   ↪ HM1_01      HPB_SAHM1_02      HPB_SAHM1_03" >>
   ↪ gct.head.HPB
5
6 echo "#1.2" > gct.head.KOPT
7 echo "$(cat eset_KOPT.tsv | wc -l) 6" >> gct.head.KOPT
8 echo "GID      NAME      KOPT_DMSO_01      KOPT_DMSO_02      KOPT_DMSO_03      KOP
   ↪ T_SAHM1_01      KOPT_SAHM1_02      KOPT_SAHM1_03" >>
   ↪ gct.head.KOPT
9
10 cat gct.head.HPB eset_HPB.tsv > eset_HPB.gct
11 cat gct.head.KOPT eset_KOPT.tsv > eset_KOPT.gct
12 head eset_KOPT.gct
13
14 echo "6      2      1" > phenotypes.cls
15 echo "#DMSO SAHM1" >> phenotypes.cls
16 echo "0      0      0      1      1      1" >> phenotypes.cls
17 cat phenotypes.cls

```

Output

```

#1.2
54675 6
GID      NAME      KOPT_DMSO_01      KOPT_DMSO_02      KOPT_DMSO_03      KOPT_SAHM1
   ↪ _01      KOPT_SAHM1_02      KOPT_SAHM1_03
1007_s_at      6.39550778914434      6.63361329719407      6.6375785381641
   ↪      7.00665069446903      6.68384761746578      6.81043796741411
1053_at      8.27291684544428      8.04195281624978      8.13203974449545
   ↪      8.07153608599753      7.85863717382127      8.02719895633383
117_at      3.14729311345973      2.94262593114145      3.15131758375372
   ↪      3.05034281709199      3.23612638945269      3.14794105723779
121_at      6.87870865041484      6.88129495627018      6.82820532797191
   ↪      6.86631576689715      6.95693356773948      6.83081218004268
1255_g_at      2.81967249987976      2.88648735903777      2.88201717529506
   ↪      2.97379457130539      2.98461193851988      3.01905325883313
1294_at      6.87006027265826      6.80399928959987      6.65695733746297
   ↪      6.57214844234865      6.65606153751673      6.80098950326962
1316_at      3.77034812760452      3.82602264159359      4.09195191846965
   ↪      3.72596001077624      4.2350082264062      4.00773283062547
6      2      1
#DMSO SAHM1
0      0      0      1      1      1

```

1.10 Processing all samples

Script 1.10.1 (R)

```
1 %%R
2 setwd("GSE18198_data")
3 affyBatch = import_CEL("*")
4 setwd(wd)
5 eset <- create_eset(affyBatch)
6 toptable <- create_TopTable(eset, control_samples=c(1,1,1,0,0,0,1,1,1,0,0,0))
7 toptable_anot <- anotate_TopTable(toptable)
8 generank_table(toptable_anot, "generank")
9 save(eset, file="eset.RData")
```

background correction: rma

normalization: quantiles

PM/MM correction : pmonly

expression values: medianpolish

background correcting...done.

normalizing...done.

54675 ids to be processed

|

|#####|

[1] "Down-regulated genes"

	Symbol	logFC	P.Value
227347_x_at	HES4	-1.2391846	4.541483e-05
227336_at	DTX1	-1.0787341	1.772044e-03
230263_s_at	DOCK5	-1.0589452	2.174812e-04
218051_s_at	NT5DC2	-0.9507155	1.126824e-03
205544_s_at	CR2	-0.9438572	5.961088e-05
202464_s_at	PFKFB3	-0.9408542	1.077045e-04
226452_at	PDK1	-0.8325181	2.019305e-05
223364_s_at	DHX37	-0.8207408	1.605856e-03
206686_at	PDK1	-0.8172945	9.936732e-04
203627_at	IGF1R	-0.8050123	1.277490e-03
203867_s_at	NLE1	-0.7963720	7.746991e-04
204513_s_at	ELM01	-0.7885410	1.839908e-04
207543_s_at	P4HA1	-0.7663495	3.287902e-05
212063_at	CD44	-0.7621344	1.769410e-03
227337_at	ANKRD37	-0.7620441	3.022164e-04
239410_at	HK2	-0.7615742	2.557385e-03
1554918_a_at	ABCC4	-0.7263246	1.912084e-03
231094_s_at	NA	-0.7232606	9.131629e-04
200965_s_at	ABLIM1	-0.7085777	6.009393e-04
210625_s_at	AKAP1	-0.6987526	1.183409e-04
231310_at	TRIM71	-0.6679915	6.024183e-04
219253_at	TMEM185B	-0.6494920	1.313180e-03
215195_at	PRKCA	-0.6258312	2.255091e-04

228205_at	TKT	-0.6126859	8.915350e-04
218806_s_at	VAV3	-0.5936019	2.050231e-03
206923_at	PRKCA	-0.5924819	2.694018e-04
201367_s_at	ZFP36L2	-0.5879670	1.331411e-03
236180_at	NA	-0.5535885	1.051495e-03
221989_at	NA	-0.5531493	1.744579e-04
223058_at	FAM107B	-0.5499447	2.198129e-03
208858_s_at	ESYT1	-0.5411513	2.844208e-04
1555434_a_at	SLC39A14	-0.5382917	2.440482e-03
1553138_a_at	ANKLE1	-0.5306391	5.104033e-04
227099_s_at	C11orf96	-0.5289498	2.627354e-03
203612_at	BYSL	-0.5257364	1.818973e-04
226938_at	DCAF4	-0.5161954	1.874088e-03
214484_s_at	SIGMAR1	-0.5153579	1.465927e-03
206653_at	POLR3G	-0.5067532	2.177288e-03
226498_at	FLT1	-0.5041981	2.319967e-03
208758_at	ATIC	-0.4943349	1.053895e-03
208997_s_at	UCP2	-0.4905291	2.479831e-03
209461_x_at	WDR18	-0.4862286	8.241993e-04
201161_s_at	YBX3	-0.4839871	9.730003e-04
225883_at	ATG16L2	-0.4745402	2.113101e-03
201692_at	SIGMAR1	-0.4727785	1.380736e-03
217139_at	VDAC1	-0.4553310	2.588750e-03
229236_s_at	SFXN4	-0.4251656	1.858039e-03
224824_at	COX20	-0.4173264	2.375617e-03
204027_s_at	METTL1	-0.4116541	2.046282e-03
201250_s_at	SLC2A1	-0.3947427	2.225655e-03

[1] "Up-regulated genes"

	Symbol	logFC	P.Value
232059_at	DSCAML1	0.3346000	0.0068497056
209392_at	ENPP2	0.3540105	0.0052561029
205381_at	LRRC17	0.3645748	0.0064690771
214710_s_at	CCNB1	0.3671989	0.0073863284
1569680_at	NA	0.3814353	0.0033810217
1559023_a_at	EFCAB14	0.3845018	0.0052968042
236353_at	NA	0.3952903	0.0082999985
206448_at	ZNF365	0.4055256	0.0032538740
226936_at	CENPW	0.4121128	0.0055882829
243469_at	NA	0.4133233	0.0048561664
201896_s_at	PSRC1	0.4219794	0.0084642203
1568596_a_at	TROAP	0.4261581	0.0017179111
238875_at	NA	0.4288226	0.0078367183
242966_x_at	RFX2	0.4321379	0.0027616154
236253_at	ZNF546	0.4657924	0.0075436998
1557290_at	NA	0.4742477	0.0041564711
243992_at	NA	0.4761079	0.0040639088
204641_at	NEK2	0.4770373	0.0034259514
220167_s_at	NA	0.4845848	0.0045882849

241685_x_at	PURA	0.4879466	0.0058069390
239735_at	NA	0.4897705	0.0030891034
202644_s_at	TNFAIP3	0.4934166	0.0004891236
242476_at	NA	0.5030038	0.0056605223
238595_at	NA	0.5058669	0.0059647137
213605_s_at	NA	0.5068902	0.0050211914
244427_at	KIF23	0.5209074	0.0015710943
242637_at	NA	0.5222779	0.0047282688
232953_at	LINC00266-1	0.5259613	0.0041673250
1559156_at	NA	0.5325258	0.0057922093
228390_at	RAB30	0.5332846	0.0071758418
238407_at	NA	0.5390014	0.0066182068
216756_at	NA	0.5406353	0.0019487381
239248_at	SDCBP2-AS1	0.5441412	0.0010999281
213544_at	ING2	0.5513826	0.0046805162
239531_at	NA	0.5536821	0.0026133238
243709_at	SLC38A9	0.5569113	0.0009694726
241745_at	LOC100507557	0.5600510	0.0027569686
1557813_at	NA	0.5691647	0.0029037060
215599_at	NA	0.5931984	0.0012579337
244114_x_at	NA	0.6411913	0.0034400322
213281_at	JUN	0.6419108	0.0061333797
228834_at	TOB1	0.6427144	0.0006729806
244532_x_at	NA	0.6470301	0.0046383310
230795_at	NA	0.6509000	0.0039752814
216094_at	NA	0.6647132	0.0040965858
234759_at	LOC100287497	0.6758224	0.0008985553
244075_at	NA	0.6914067	0.0071383024
215071_s_at	HIST1H2AC	0.7357238	0.0038095135
210718_s_at	NA	0.7879121	0.0013751119
201465_s_at	JUN	1.5137055	0.0061879051

Script 1.10.2 (R)

```

1 %%R
2 # Create files for GSEA
3 # Add description column for gct
4 exprs2 <- cbind(c(" "), exprs(eset))
5 write.table(exprs2,row.names=TRUE,col.names=FALSE,quote=FALSE,file="eset.tsv", sep = "\t")

```

Script 1.10.3 (bash)

```

1 %%bash
2 echo "#1.2" > gct.head
3 echo "$(cat eset.tsv | wc -l) 12" >> gct.head

```

```

4 echo "GID      NAME      HPB_DMSO_01      HPB_DMSO_02      HPB_DMSO_03      HPB_SA
  ↳ HM1_01      HPB_SAHM1_02      HPB_SAHM1_03      KOPT_DMSO_01      KOPT_DMSO_02
  ↳      KOPT_DMSO_03      KOPT_SAHM1_01      KOPT_SAHM1_02      KOPT_SAHM1_03" >>
  ↳ gct.head
5 #head gct.head
6 cat gct.head eset.tsv > eset.gct
7 head eset.gct
8
9 echo "12      2      1" > phenotypes_all.cls
10 echo "#DMSO SAHM1" >> phenotypes_all.cls
11 echo "0      0      0      1      1      1      0      0      0      1
  ↳      1      1" >>
  ↳ phenotypes_all.cls
12 cat phenotypes_all.cls

```

Output

```

#1.2
54675 12
GID      NAME      HPB_DMSO_01      HPB_DMSO_02      HPB_DMSO_03      HPB_SAHM1_01
  ↳      HPB_SAHM1_02      HPB_SAHM1_03      KOPT_DMSO_01      KOPT_DMSO_02      K
  ↳ OPT_DMSO_03      KOPT_SAHM1_01      KOPT_SAHM1_02      KOPT_SAHM1_03
1007_s_at      7.93312670379653      8.0542010037019      7.95037177526279
  ↳      8.14888412184819      8.07040224126479      8.13284175160718      7.8540586
  ↳ 2605073      7.93163674386994      7.98141396242764      8.23905406061932      7.
  ↳ 67867201107947      7.99642963218746
1053_at      9.27929486368929      9.09842264841232      9.13663090431202
  ↳      9.17708364564691      9.25193771745009      9.25935418937713      9.1979174
  ↳ 8340989      9.01830505039165      9.10266422012541      9.00617077213224      8.
  ↳ 847158491907      8.96969656837736
117_at      3.57098005665705      3.72380927817243      3.74780750590507
  ↳      3.43028679172995      3.58735116951185      3.67221660949905      3.7380732
  ↳ 0168918      3.56701089801695      3.83082492669122      3.64438471116145      3.
  ↳ 73805379638288      3.76775757547126
121_at      6.63358355634922      7.03665979693398      6.56807516112594
  ↳      6.67607356294671      6.64106588645408      6.66741769078119      7.8046532
  ↳ 8459714      7.84417420209367      7.78011537263602      7.82982021440325      7.
  ↳ 98585760475067      7.8937469606581
1255_g_at      3.27294190916313      3.18180831594297      3.26783472739394
  ↳      3.22214757689712      3.19485091845378      3.13889560789193      3.4986396
  ↳ 3223639      3.44357829099314      3.41671075173184      3.6416140029546      3.6
  ↳ 5297571299999      3.51910174405494
1294_at      6.06025742402608      6.28475689755523      6.29919659174142
  ↳      5.7718487881919      5.82726956747749      6.00959670335518      7.55405588
  ↳ 978221      7.33787628232827      7.14016037992714      7.11627582476523      7.2
  ↳ 7368560476569      7.50759676384855
1316_at      5.01972637826717      4.54787382581301      4.39018774324754
  ↳      5.05461423958757      5.06386915983787      4.8042459612599      4.79285162
  ↳ 533848      5.3855916031891      5.31415139553623      4.55392090437712      5.17
  ↳ 463822538147      4.90567702437559

```

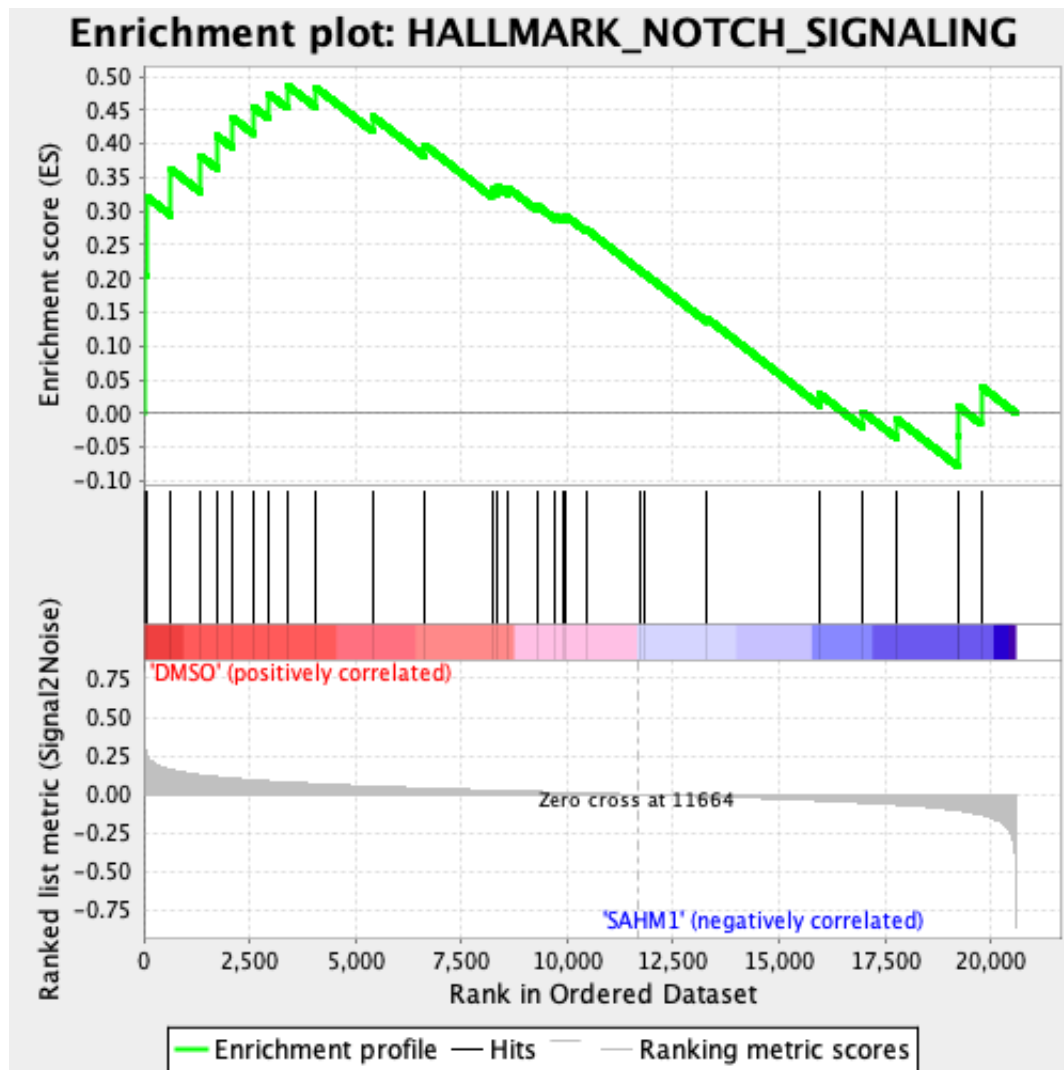


Figure 1: Enrichment plot Notch Signalling Pathway

```

12      2      1
#DMSO SAHM1
0      0      0      1      1      1      0      0      0      1      1
↪      1

```

1.11 GSEA results

1.12 Conclusions

NAME	SIZE	ES	NES	NOM p-val	FDR q-val	FWER p-val	RANK AT MAX	LEADING EDGE
HALLMARK_WNT_BETA_CATENIN_SIGNALING	40	0.49850842	1.3996072	0.0	0.9853856	277	2947	tags=23%, list=14%, signal=26%
HALLMARK_NOTCH_SIGNALING	29	0.48723552	1.3520839	0.09484536	0.7166934	374	3383	tags=31%, list=16%, signal=37%
HALLMARK_GLYCOLYSIS	186	0.42253992	1.3206861	0.0	0.64004976	473	4630	tags=35%, list=22%, signal=45%
HALLMARK_INTERFERON_ALPHA_RESPONSE	88	0.34315822	1.279187	0.096114516	0.6929842	527	4447	tags=27%, list=22%, signal=35%
HALLMARK_REACTIVE_OXIGEN_SPECIES_PATHWAY	46	0.3981605	1.2701172	0.09168444	0.5729008	527	7669	tags=57%, list=37%, signal=90%
HALLMARK_INTERFERON_GAMMA_RESPONSE	187	0.3087745	1.2654618	0.08958333	0.49679276	527	5351	tags=32%, list=26%, signal=43%
HALLMARK_ADIPOGENESIS	184	0.2826048	1.2613991	0.0911017	0.43812412	527	7541	tags=42%, list=37%, signal=65%
HALLMARK_OXIDATIVE_PHOSPHORYLATION	188	0.35985056	1.2546434	0.10103093	0.4135756	577	9489	tags=56%, list=46%, signal=104%
HALLMARK_MTORC1_SIGNALING	183	0.26467624	1.2359246	0.19502075	0.4407044	0.69	5436	tags=35%, list=26%, signal=47%
HALLMARK_IL2_STAT5_SIGNALING	182	0.31952778	1.2251521	0.0	0.44391555	0.69	2989	tags=23%, list=15%, signal=27%
HALLMARK_FATTY_ACID_METABOLISM	150	0.27257207	1.2249079	0.09663866	0.40792337	0.69	4963	tags=24%, list=24%, signal=31%
HALLMARK_PEROXISOME	98	0.30541733	1.2229942	0.091649696	0.38731882	0.69	4429	tags=26%, list=21%, signal=32%
HALLMARK_HYPOXIA	188	0.38151017	1.2137458	0.0	0.3664674	0.69	4409	tags=35%, list=21%, signal=44%
HALLMARK_UV_RESPONSE_UP	150	0.26630923	1.2116135	0.18930042	0.3437194	0.69	5540	tags=34%, list=27%, signal=46%
HALLMARK_ALLOGRAFT_REJECTION	191	0.3419296	1.1964117	0.09033614	0.3680125	739	4439	tags=28%, list=22%, signal=36%
HALLMARK_MYC_TARGETS_V2	47	0.65528375	1.1840152	0.0	0.3599941	739	4315	tags=66%, list=21%, signal=83%
HALLMARK_INFLAMMATORY_RESPONSE	189	0.34822693	1.1837027	0.097363085	0.34164155	739	4313	tags=33%, list=21%, signal=41%
HALLMARK_MYC_TARGETS_V1	173	0.4086298	1.1757741	0.19381443	0.3362698	788	7640	tags=44%, list=37%, signal=69%
HALLMARK_APICAL_JUNCTION	193	0.31684956	1.1519539	0.28781512	0.3974107	835	4296	tags=26%, list=21%, signal=33%
HALLMARK_ESTROGEN_RESPONSE_EARLY	183	0.29886743	1.119735	0.2801636	0.43835357	888	4844	tags=32%, list=24%, signal=42%
HALLMARK_ANGIOGENESIS	34	0.43509555	1.1002749	0.29411766	0.47263375	888	3335	tags=26%, list=16%, signal=32%
HALLMARK_ESTROGEN_RESPONSE_LATE	194	0.29403758	1.0978482	0.28305784	0.45791104	888	4138	tags=30%, list=20%, signal=38%
HALLMARK_MYOGENESIS	196	0.37049508	1.0864803	0.18958333	0.4909446	888	4781	tags=37%, list=23%, signal=47%
HALLMARK_CHOLESTEROL_HOMEOSTASIS	71	0.2772793	1.0851066	0.28661087	0.47539067	888	5068	tags=35%, list=25%, signal=47%
HALLMARK_COMPLEMENT	192	0.26265764	1.0589281	0.31237322	0.4991516	888	3189	tags=18%, list=15%, signal=21%
HALLMARK_PROTEIN_SECRETION	88	0.20329766	1.0475459	0.38381743	0.49959674	888	6061	tags=24%, list=29%, signal=34%
HALLMARK_ANDROGEN_RESPONSE	94	0.2609074	1.039261	0.2897959	0.52019876	0.95	5980	tags=31%, list=29%, signal=43%
HALLMARK_DNA_REPAIR	145	0.17039137	1.031202	0.2790224	0.526112	0.95	7845	tags=36%, list=38%, signal=58%
HALLMARK_KRAS_SIGNALING_DN	188	0.33348864	1.0201786	0.38655463	0.5383922	0.95	5627	tags=38%, list=27%, signal=52%
HALLMARK_UV_RESPONSE_DN	135	0.19810459	0.95020545	0.77867204	0.70491356	1.0	2015	tags=11%, list=10%, signal=12%
HALLMARK_KRAS_SIGNALING_UP	192	0.26940593	0.9457102	0.70416665	0.6904847	1.0	4576	tags=28%, list=22%, signal=35%
HALLMARK_HEDGEHOG_SIGNALING	35	0.30286688	0.94172853	0.58906883	0.6778487	1.0	3103	tags=26%, list=15%, signal=30%
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION	192	0.2777393	0.9384078	0.4926004	0.6730365	1.0	4711	tags=30%, list=23%, signal=38%
HALLMARK_IL6_JAK_STAT3_SIGNALING	85	0.2657967	0.93745136	0.5821501	0.6546528	1.0	4439	tags=28%, list=22%, signal=36%
HALLMARK_XENOBIOTIC_METABOLISM	194	0.2366412	0.93364125	0.68541664	0.6441654	1.0	5724	tags=29%, list=28%, signal=40%
HALLMARK_PI3K_AKT_MTOR_SIGNALING	98	0.17684619	0.9051278	0.4888438	0.69095284	1.0	2157	tags=12%, list=10%, signal=14%
HALLMARK_SPERMATOGENESIS	124	0.25800297	0.8618422	0.7	0.7451759	1.0	2215	tags=15%, list=11%, signal=17%
HALLMARK_APICAL_SURFACE	42	0.21887365	0.7824094	0.8102767	0.90781873	1.0	7749	tags=45%, list=38%, signal=72%
HALLMARK_COAGULATION	133	0.23493658	0.76809555	0.9	0.89633375	1.0	7086	tags=38%, list=34%, signal=58%

Figure 2: Gene sets enriched in phenotype DMSO(Cell Line HPB-ALL)

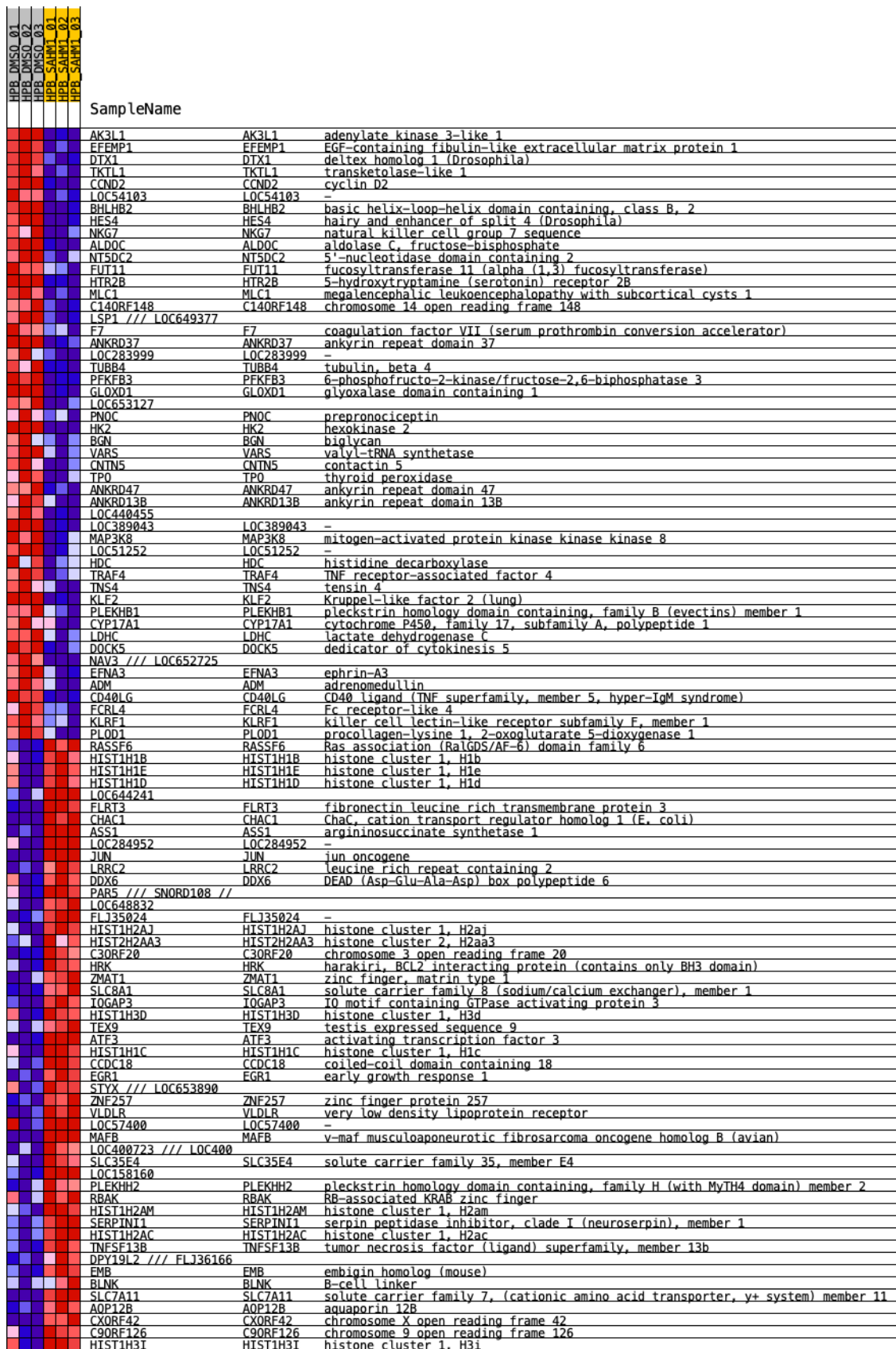


Figure 3: Heatmap(Cell Line HPB-ALL)

NAME	SIZE	ES	NES	NOM p-val	FDR q-val	FWER p-val	RANK AT MAX	LEADING EDGE
HALLMARK_ANDROGEN_RESPONSE	94	0.293221	1.4200062	0.0	0.4326947	263	3888	tags=30%, list=19%, signal=37%
HALLMARK_MITOTIC_SPINDLE	185	0.386933	1.3821146	0.0	0.23884742	308	4208	tags=38%, list=20%, signal=47%
HALLMARK_MTORC1_SIGNALING	183	0.5215603	1.3441344	0.0	0.26536438	403	2776	tags=27%, list=13%, signal=31%
HALLMARK_G2M_CHECKPOINT	178	0.3373856	1.3382939	0.0	0.21027331	403	6753	tags=45%, list=33%, signal=66%
HALLMARK_PROTEIN_SECRETION	88	0.3678097	1.3335762	0.10330579	0.19757529	403	6221	tags=52%, list=30%, signal=75%
HALLMARK_MYC_TARGETS_V1	173	0.40847418	1.3236173	0.0	0.20407657	454	6363	tags=35%, list=31%, signal=51%
HALLMARK_E2F_TARGETS	173	0.33912787	1.3138137	0.0	0.20767564	454	7519	tags=48%, list=36%, signal=75%
HALLMARK_DNA_REPAIR	145	0.2616415	1.3059548	0.20245399	0.18734114	454	5134	tags=26%, list=25%, signal=34%
HALLMARK_INTERFERON_ALPHA_RESPONSE	88	0.29699197	1.3052112	0.1002004	0.17152534	454	3260	tags=26%, list=16%, signal=31%
HALLMARK_MYC_TARGETS_V2	47	0.66136664	1.2859757	0.0	0.18164015	0.5	5065	tags=62%, list=25%, signal=82%
HALLMARK_CHOLESTEROL_HOMEOSTASIS	71	0.33102265	1.2468052	0.21237114	0.22184616	604	1292	tags=15%, list=6%, signal=16%
HALLMARK_IL2_STAT5_SIGNALING	182	0.3490652	1.2443198	0.0	0.20710902	604	3186	tags=30%, list=15%, signal=35%
HALLMARK_UNFOLDED_PROTEIN_RESPONSE	104	0.6079186	1.227846	0.0	0.23289144	604	4903	tags=48%, list=24%, signal=63%
HALLMARK_ALLOGRAFT_REJECTION	191	0.26240367	1.2218562	0.0	0.23272453	604	3260	tags=23%, list=16%, signal=26%
HALLMARK_P53_PATHWAY	182	0.2778233	1.2039973	0.0	0.24092272	604	3999	tags=23%, list=19%, signal=28%
HALLMARK_HEME_METABOLISM	184	0.25559813	1.1812468	0.0	0.26794052	646	2746	tags=14%, list=13%, signal=16%
HALLMARK_PI3K_AKT_MTOR_SIGNALING	98	0.29646376	1.1782368	0.11434511	0.26249218	646	5469	tags=32%, list=27%, signal=43%
HALLMARK_GLYCOLYSIS	186	0.29053313	1.1596437	0.0	0.2764851	646	5803	tags=38%, list=28%, signal=52%
HALLMARK_HYPOXIA	188	0.26141116	1.1396848	0.2238193	0.32033673	898	3547	tags=27%, list=17%, signal=32%
HALLMARK_TGF_BETA_SIGNALING	50	0.36157095	1.1116209	0.20977597	0.39753282	945	2675	tags=24%, list=13%, signal=28%
HALLMARK_ADIPOGENESIS	184	0.2005336	1.0934803	0.22154471	0.4228268	945	5096	tags=27%, list=25%, signal=35%
HALLMARK_COMPLEMENT	192	0.25042418	1.0874768	0.18383838	0.43187666	1.0	2949	tags=19%, list=14%, signal=22%
HALLMARK_INTERFERON_GAMMA_RESPONSE	187	0.22316597	1.0854584	0.106177606	0.4260444	1.0	3581	tags=24%, list=17%, signal=29%
HALLMARK_NOTCH_SIGNALING	29	0.38857377	1.0616399	0.28716904	0.45897862	1.0	2954	tags=34%, list=14%, signal=40%
HALLMARK_FATTY_ACID_METABOLISM	150	0.21143477	1.0521207	0.28947368	0.4667693	1.0	5347	tags=33%, list=26%, signal=44%
HALLMARK_UV_RESPONSE_UP	150	0.23067562	1.0252469	0.2275574	0.5528972	1.0	2525	tags=13%, list=12%, signal=15%
HALLMARK_HEDGEHOG_SIGNALING	35	0.3210423	1.0227196	0.49588478	0.5402487	1.0	3048	tags=26%, list=15%, signal=30%
HALLMARK_TNFA_SIGNALING_VIA_NFKB	185	0.2405712	1.005899	0.40368852	0.5560466	1.0	2882	tags=20%, list=14%, signal=23%
HALLMARK_UV_RESPONSE_DN	135	0.32195312	0.99710524	0.51934826	0.5491897	1.0	3304	tags=26%, list=16%, signal=31%
HALLMARK_APOPTOSIS	159	0.20274885	0.9836564	0.39130434	0.5896945	1.0	2882	tags=18%, list=14%, signal=20%
HALLMARK_ESTROGEN_RESPONSE_EARLY	183	0.2312291	0.9552753	0.58943087	0.67311716	1.0	2938	tags=18%, list=14%, signal=21%
HALLMARK_OXIDATIVE_PHOSPHORYLATION	188	0.16545603	0.92549586	0.5323887	0.7178825	1.0	16491	tags=99%, list=80%, signal=491%
HALLMARK_PEROXISOME	98	0.16470067	0.85989714	0.7217742	0.8381856	1.0	5944	tags=28%, list=29%, signal=39%
HALLMARK_APICAL_SURFACE	42	0.24479878	0.7153503	0.81287724	0.98692274	1.0	2692	tags=21%, list=13%, signal=25%
HALLMARK_REACTIVE_OXYGEN_SPECIES_PATHWAY	46	0.101305366	0.43637094	0.9117647	1.0	1.0	4676	tags=17%, list=23%, signal=22%

Figure 4: Gene sets enriched in phenotype DMSO(Cell Line KOPT-K1)

NAME	SIZE	ES	NES	NOM p-val	FDR q-val	FWER p-val	RANK AT MAX	LEADING EDGE
HALLMARK_GLYCOLYSIS	186	0.43311334	1.6781958	0.004192872	0.036362655	25	5630	tags=47%, list=27%, signal=64%
HALLMARK_PI3K_AKT_MTOR_SIGNALING	98	0.34280387	1.6242404	0.010121457	0.030869437	45	5884	tags=36%, list=29%, signal=50%
HALLMARK_MTORC1_SIGNALING	183	0.4759005	1.6139847	0.004158004	0.023340473	51	4779	tags=42%, list=23%, signal=54%
HALLMARK_UNFOLDED_PROTEIN_RESPONSE	104	0.548177	1.5873568	0.03992016	0.024172837	64	4153	tags=38%, list=20%, signal=48%
HALLMARK_NOTCH_SIGNALING	29	0.5714514	1.5091325	0.016597511	0.04010106	116	4882	tags=55%, list=24%, signal=72%
HALLMARK_UV_RESPONSE_UP	150	0.2950838	1.4034421	0.0041237115	0.124392934	301	2906	tags=22%, list=14%, signal=25%
HALLMARK_REACTIVE_OXIGEN_SPECIES_PATHWAY	46	0.40161857	1.3443292	0.07068607	0.21853316	471	7374	tags=57%, list=36%, signal=88%
HALLMARK_MYC_TARGETS_V2	47	0.71475863	1.3281219	0.06759443	0.23772013	531	3914	tags=74%, list=19%, signal=92%
HALLMARK_UV_RESPONSE_DN	135	0.3603946	1.306755	0.05679513	0.2657795	587	2828	tags=26%, list=14%, signal=30%
HALLMARK_HYPOXIA	188	0.35863873	1.2884322	0.043392505	0.295965	651	5635	tags=44%, list=27%, signal=60%
HALLMARK_FATTY_ACID_METABOLISM	150	0.2589689	1.2816921	0.037113402	0.2849363	661	5652	tags=33%, list=27%, signal=46%
HALLMARK_INTERFERON_ALPHA_RESPONSE	88	0.3972688	1.2601771	0.18774703	0.31406602	717	4741	tags=38%, list=23%, signal=48%
HALLMARK_ADIPOGENESIS	184	0.2585026	1.2498535	0.06625259	0.31768975	754	6432	tags=38%, list=31%, signal=54%
HALLMARK_DNA_REPAIR	145	0.27045995	1.220323	0.25440314	0.37851238	844	6445	tags=34%, list=31%, signal=49%
HALLMARK_ESTROGEN_RESPONSE_EARLY	183	0.29162228	1.2086581	0.057494868	0.39013368	877	1687	tags=14%, list=8%, signal=15%
HALLMARK_PEROXISOME	98	0.26575372	1.2073532	0.115384616	0.36860234	881	6877	tags=38%, list=33%, signal=56%
HALLMARK_MYC_TARGETS_V1	173	0.481558	1.1877586	0.38492063	0.40412134	915	7998	tags=57%, list=39%, signal=92%
HALLMARK_ANDROGEN_RESPONSE	94	0.2428143	1.1861122	0.102713175	0.38849032	915	4883	tags=31%, list=24%, signal=40%
HALLMARK_WNT_BETA_CATENIN_SIGNALING	40	0.34349075	1.1845423	0.15767635	0.37267235	916	4889	tags=38%, list=24%, signal=49%
HALLMARK_HEDGEHOG_SIGNALING	35	0.3436916	1.183618	0.18837675	0.35571563	916	1072	tags=17%, list=5%, signal=18%
HALLMARK_CHOLESTEROL_HOMEOSTASIS	71	0.33077985	1.1479423	0.17760618	0.42038524	0.95	2256	tags=18%, list=11%, signal=20%
HALLMARK_PROTEIN_SECRETION	88	0.35464782	1.1016811	0.42352942	0.5150438	972	6980	tags=42%, list=34%, signal=63%
HALLMARK_OXIDATIVE_PHOSPHORYLATION	188	0.32158187	1.0274464	0.5450902	0.69437057	986	7107	tags=34%, list=34%, signal=51%
HALLMARK_IL2_STAT5_SIGNALING	182	0.3837396	0.99643314	0.5445545	0.75440615	989	2494	tags=24%, list=12%, signal=27%
HALLMARK_ALLOGRAFT_REJECTION	191	0.3501197	0.9865181	0.5752577	0.7505662	989	4113	tags=28%, list=20%, signal=34%
HALLMARK_APICAL_SURFACE	42	0.30094463	0.95951355	0.57715434	0.7958004	993	4367	tags=31%, list=21%, signal=39%
HALLMARK_TGF_BETA_SIGNALING	50	0.286461	0.8809257	0.72745097	0.96194637	995	4256	tags=30%, list=21%, signal=38%
HALLMARK_TNFA_SIGNALING_VIA_NFKB	185	0.25158665	0.8724303	0.70178926	0.9456293	995	3627	tags=23%, list=18%, signal=27%
HALLMARK_COMPLEMENT	192	0.25019673	0.86665404	0.68937874	0.9242008	995	3369	tags=20%, list=16%, signal=24%
HALLMARK_HEME_METABOLISM	184	0.19858962	0.85600936	0.8579882	0.91439253	999	6128	tags=30%, list=30%, signal=43%
HALLMARK_INTERFERON_GAMMA_RESPONSE	187	0.29006875	0.8416879	0.63842976	0.90728647	1.0	4763	tags=33%, list=23%, signal=42%
HALLMARK_APICAL_JUNCTION	193	0.21188706	0.8365217	0.87649405	0.8868689	1.0	6030	tags=33%, list=29%, signal=46%
HALLMARK_MITOTIC_SPINDLE	185	0.31453067	0.8285555	0.678501	0.8730112	1.0	4322	tags=28%, list=21%, signal=35%
HALLMARK_MYOGENESIS	196	0.20663904	0.7016324	0.9665971	0.9819069	1.0	2350	tags=15%, list=11%, signal=17%
HALLMARK_INFLAMMATORY_RESPONSE	189	0.25482258	0.6774285	0.79761904	0.969574	1.0	1679	tags=15%, list=8%, signal=17%
HALLMARK_G2M_CHECKPOINT	178	0.19088042	0.601792	0.8170974	0.9818409	1.0	4846	tags=24%, list=24%, signal=31%
HALLMARK_E2F_TARGETS	173	0.17057835	0.59205115	0.85265225	0.9589176	1.0	7214	tags=34%, list=35%, signal=52%

Figure 5: Gene sets enriched in phenotype DMSO(Cell Lines: HPB-ALL KOPT-K1)

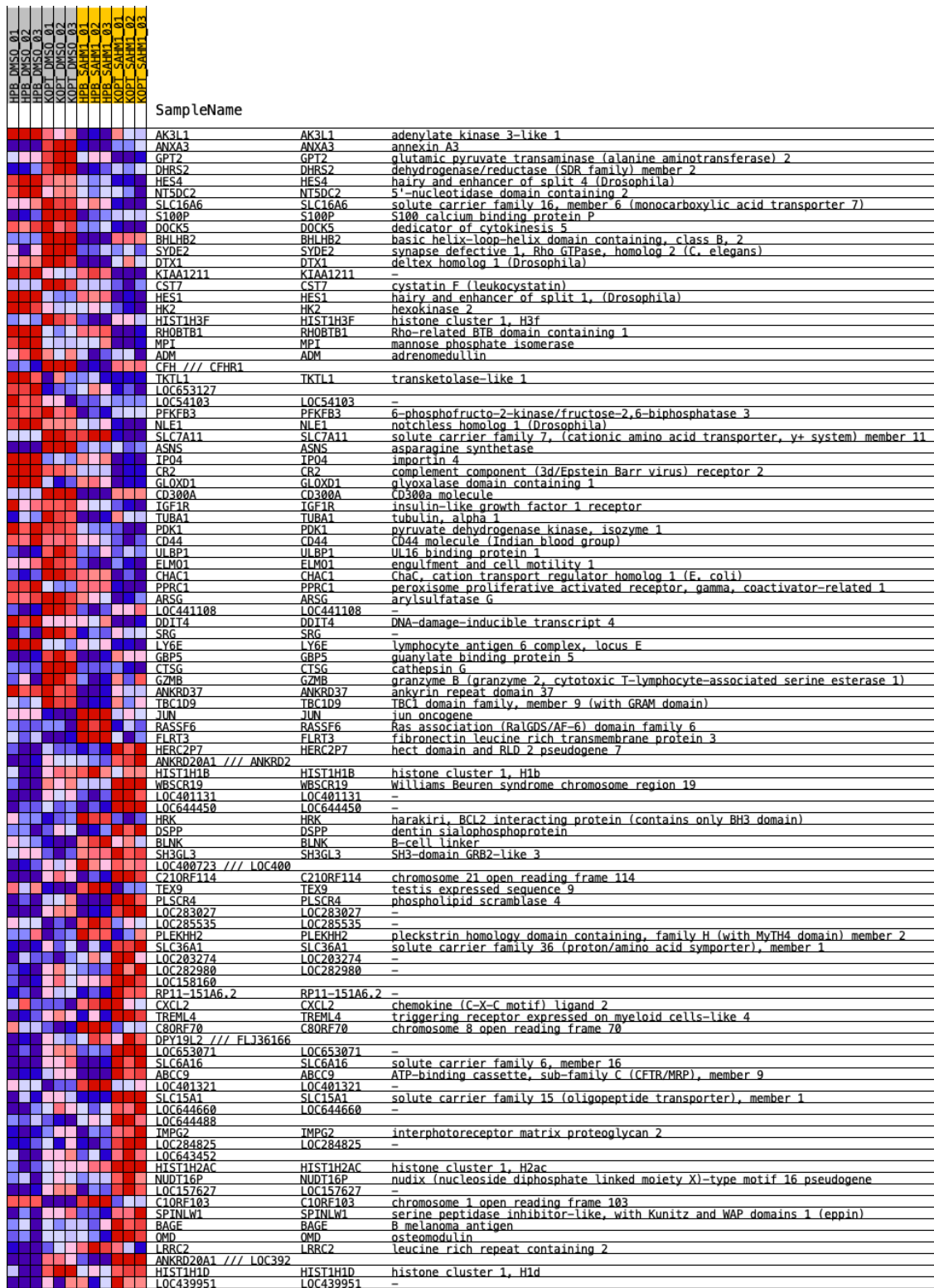


Figure 6: Heatmap(Cell Lines: HPB-ALL KOPT-K1)

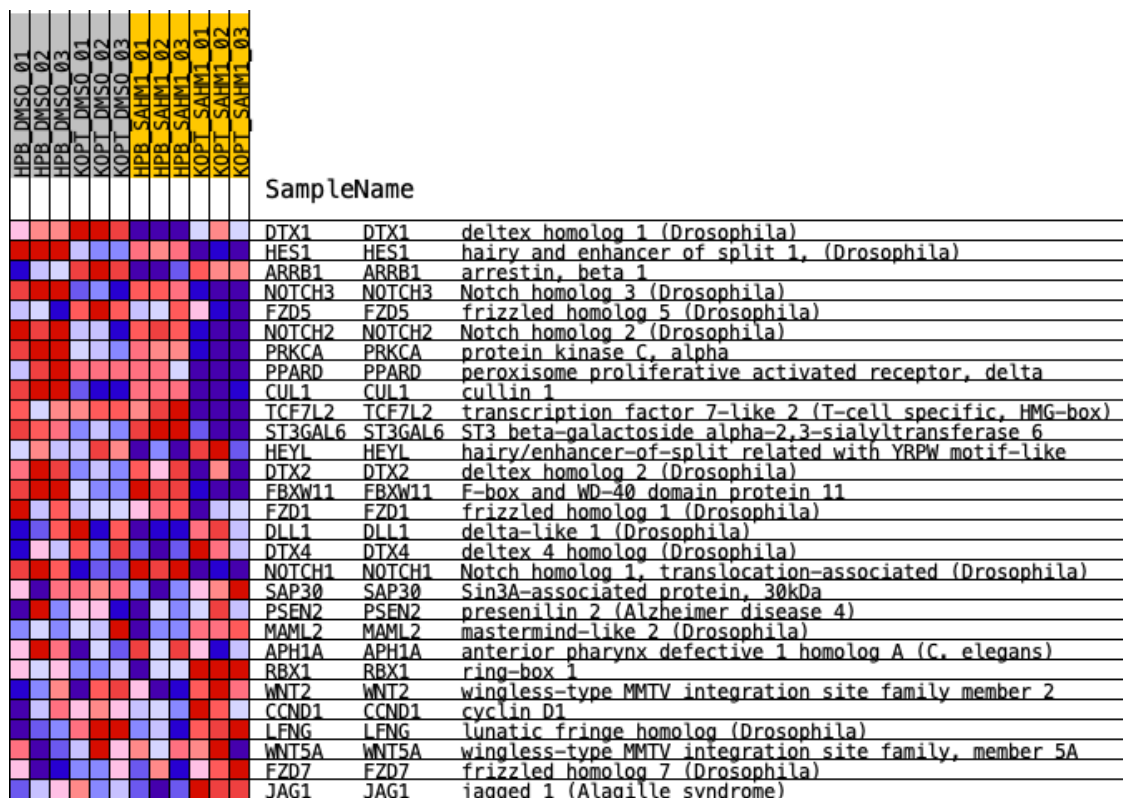


Figure 7: Heatmap(NOTCH signaling pathway)