

# iLINCS API R Notebook

```
#Loading packages
#Setting default width option
```

## Display Signature Libraries

```
apiUrl <- "http://www.ilincs.org/api/SignatureLibraries"
req <- GET(apiUrl)
json <- httr::content(req, as = "text")
ilincs_libraries <- fromJSON(json)
ilincs_libraries[,c("libraryID", "libraryName")]
```

##	libraryID	libraryName
## 1	LIB_1	Disease related signatures
## 2	LIB_10	Cancer therapeutics response signatures
## 3	LIB_11	LINCS gene overexpression signatures
## 4	LIB_12	DrugMatrix signatures
## 5	LIB_13	Transcriptional signatures from EBI Expression Atlas
## 6	LIB_14	Pharmacogenomics transcriptional signatures
## 7	LIB_2	Connectivity Map signatures
## 8	LIB_3	ENCODE transcription factor binding signatures
## 9	LIB_5	LINCS chemical perturbagen signatures
## 10	LIB_6	LINCS consensus gene (CGS) knockdown signatures
## 11	LIB_8	LINCS RNA-Seq signatures
## 12	LIB_9	LINCS targeted proteomics signatures

## Searching for Everolimus chemical perturbation (CP) perturbation signatures in the MCF7 cell line

```
term <- "Everolimus"
ilincs_libId <- "LIB_5"
apiUrl <- paste("http://www.ilincs.org/api/SignatureMeta/findTermWithSynonyms?term=", term, "&library=", i
req <- GET(apiUrl)

everolimusCps <- fromJSON(httr::content(req, type = "text"))$data
```

```
## No encoding supplied: defaulting to UTF-8.
```

```
everolimusCpsMcf7 <- everolimusCps[intersect(grep("Everolimus", everolimusCps$compound), grep("MCF7", everol
everolimusCpsMcf7[,c("compound", "time", "concentration", "signatureid", "cellline")]
```

##	compound	time	concentration	signatureid	cellline
## 61	Everolimus	24h	10uM	LINCSCP_137886	MCF7
## 62	Everolimus	24h	3.33uM	LINCSCP_137887	MCF7
## 63	Everolimus	24h	1.11uM	LINCSCP_137888	MCF7
## 64	Everolimus	24h	0.37uM	LINCSCP_137889	MCF7

```
## 65 Everolimus 24h 0.12uM LINCSCP_137890 MCF7
## 66 Everolimus 24h 0.04uM LINCSCP_137891 MCF7
## 132 Everolimus 24h 10uM LINCSCP_32458 MCF7
## 133 Everolimus 6h 10uM LINCSCP_32655 MCF7
```

## Enrichr analysis of everolimus signature at 0.04uM concentration (LINCSCP\_137891) (Fig 2C)

```
ilincs_signatureId <- "LINCSCP_137891"

req <- POST("http://www.ilincs.org/api/ilincsR/downloadSignature", body = list(sigID = ilincs_signatureId,
ilincs_sessionId<-unlist(httr::content(req))
ilincs_sessionId

##                               data
## "sig_Sat_May__7_22_13_30_2022_27789"

signatureFileUrl=paste("http://www.ilincs.org/tmp/",ilincs_sessionId,".xls",sep="")
everolimusSignatureData<-read.table(signatureFileUrl,sep="\t",header=T,stringsAsFactors = F)
sigGenes100<-everolimusSignatureData$Name_GeneSymbol[order(everolimusSignatureData$Significance_pvalue)]

setEnrichrSite("Enrichr")

## Connection changed to https://maayanlab.cloud/Enrichr/
## Connection is Live!

enriched <- enrichr(genes=sigGenes100, databases="KEGG_2019_Human")

## Uploading data to Enrichr... Done.
## Querying KEGG_2019_Human... Done.
## Parsing results... Done.

enriched[["KEGG_2019_Human"]][1:5,]
```

	Term	Overlap	P.value	Adjusted.P.value	Old.P.value	Old.A
## 1	Colorectal cancer	6/86	4.570116e-06	0.0007677795		0
## 2	Valine, leucine and isoleucine degradation	4/48	9.668983e-05	0.0081219461		0
## 3	Terpenoid backbone biosynthesis	3/22	1.743100e-04	0.0085224485		0
## 4	Endometrial cancer	4/58	2.029154e-04	0.0085224485		0
## 5	Cell cycle	5/124	3.974780e-04	0.0096239910		0

## Finding and summarizing connected CGSes with the Everolimus signature at 0.04uM concentration (LINCSCP\_137891)

### Finding connected CGSes

```
ilincs_libId<-"LIB_6"

apiUrl <- paste("http://www.ilincs.org/api/SignatureMeta/findConcordantSignatures?sigID=",ilincs_signatureId)
req <- GET(apiUrl)

connectedCgs<-fromJSON(httr::content(req,type="text"))

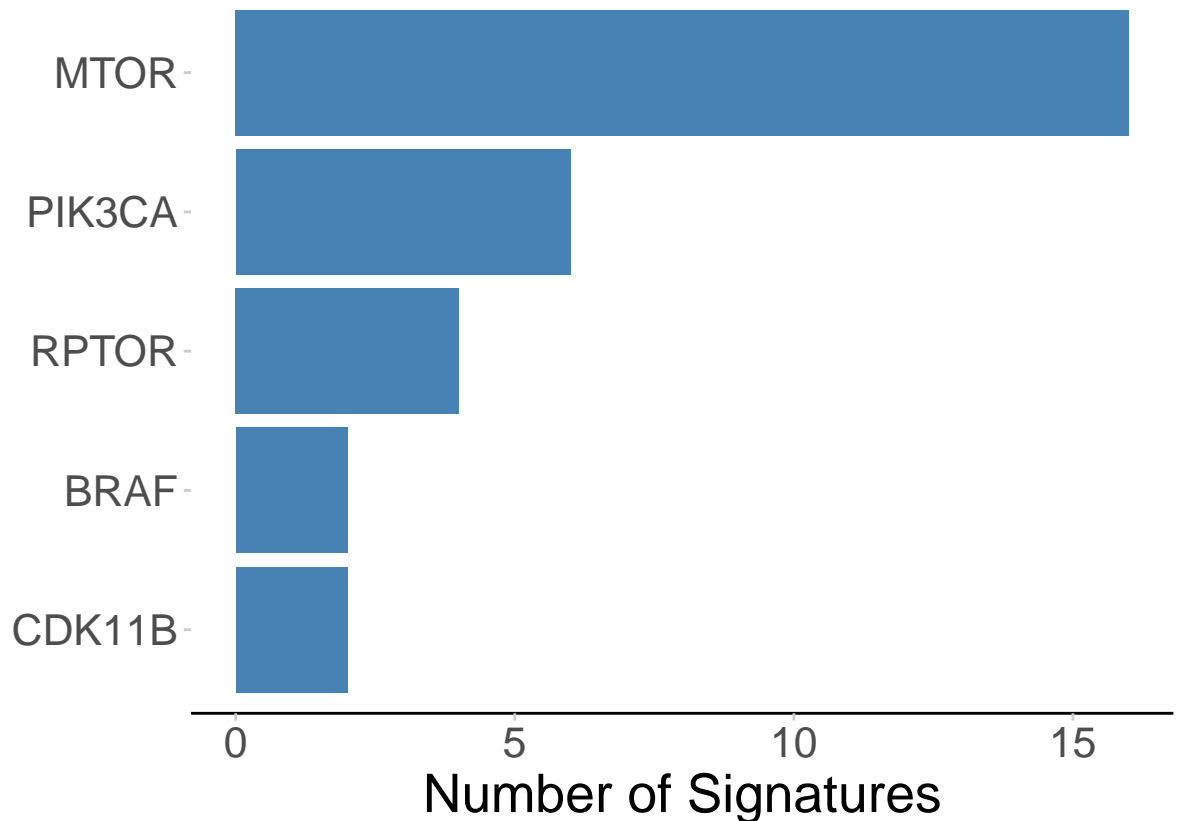
## No encoding supplied: defaulting to UTF-8.
```

```
head(connectedCgs[,c("signatureid", "similarity", "pValue", "cellline", "treatment")])
```

```
##      signatureid similarity      pValue cellline treatment
## 1 LINCSD_33816  0.355679 1.074249e-35 MCF7.311      MTOR
## 2 LINCSD_33763  0.319918 7.222069e-30 MCF7.101      MTOR
## 3 LINCSD_33922  0.304985 1.177066e-27 PC3.311       MTOR
## 4 LINCSD_33869  0.297908 1.189836e-26 PC3.101       MTOR
## 5 LINCSD_33710  0.297193 1.497679e-26 HT29.311      MTOR
## 6 LINCSD_33975  0.296891 1.649948e-26 YAPC.311      MTOR
```

Summary boxplot, Figure 2D in the manuscript

```
geneFreq <- sort(table(connectedCgs$treatment[1:100]),decreasing=TRUE)[5:1]
geneFreqDf<-data.frame(gene=factor(names(geneFreq),levels=names(geneFreq),ordered=T),geneFreq=as.vector
tp100cgs<-ggplot(data=geneFreqDf,aes(x=gene,y=geneFreq)) +
  geom_bar(stat="identity",fill="steelblue") +
  coord_flip() + theme_bw() +
  theme(axis.ticks=element_line(color="grey80"),text=element_text(size=20),legend.key.size=unit(1,"cm"))
  labs(x="",y="Number of Signatures")
tp100cgs
```



## Enrichr analysis of connected CGSes (Fig 2D)

```
setEnrichrSite("Enrichr")

## Connection changed to https://maayanlab.cloud/Enrichr/
## Connection is Live!

enrichedCgsTargets <- enrichr(genes=unique(connectedCgs$treatment), databases="KEGG_2019_Human")

## Uploading data to Enrichr... Done.
## Querying KEGG_2019_Human... Done.
## Parsing results... Done.

enrichedCgsTargets[["KEGG_2019_Human"]][1:5,]

##              Term Overlap      P.value Adjusted.P.value Old.P.value Old.Adjusted.P
## 1      mTOR signaling pathway 14/152 3.917992e-15      7.169925e-13      0
## 2      Colorectal cancer      9/86 1.276902e-10      9.035277e-09      0
## 3      Endometrial cancer      8/58 1.481193e-10      9.035277e-09      0
## 4      Autophagy              10/128 2.129479e-10      9.742369e-09      0
## 5 Thyroid hormone signaling pathway 9/116 1.904802e-09      6.971575e-08      0
##                                     Genes
## 1 MAP2K1;FZD5;PDPK1;FZD4;STRADB;MAPKAP1;BRAF;MTOR;RPTOR;PIK3CA;RHEB;AKT1;RICTOR;EIF4E
## 2 MAP2K1;PIK3CA;MYC;AKT1;PMAIP1;BRAF;TP53;MTOR;BBC3
## 3 MAP2K1;PIK3CA;PDPK1;MYC;ILK;AKT1;BRAF;TP53
## 4 RPTOR;BECN1;MAP2K1;PIK3CA;PDPK1;RHEB;AKT1;PIK3C3;ATG7;MTOR
## 5 MAP2K1;PIK3CA;PDPK1;RHEB;MYC;AKT1;ATP1A3;TP53;MTOR
```

## Finding and summarizing connected chemical perturbation (CP) signatures with the Everolimus signature at 0.04uM concentration (LINCSCP\_137891)

### Finding connected CPs

```
ilincs_libId<-"LIB_5"

apiUrl <- paste("http://www.ilincs.org/api/SignatureMeta/findConcordantSignatures?sigID=",ilincs_signame)
req <- GET(apiUrl)

connectedCps<-fromJSON(httr::content(req,type="text"))

## No encoding supplied: defaulting to UTF-8.

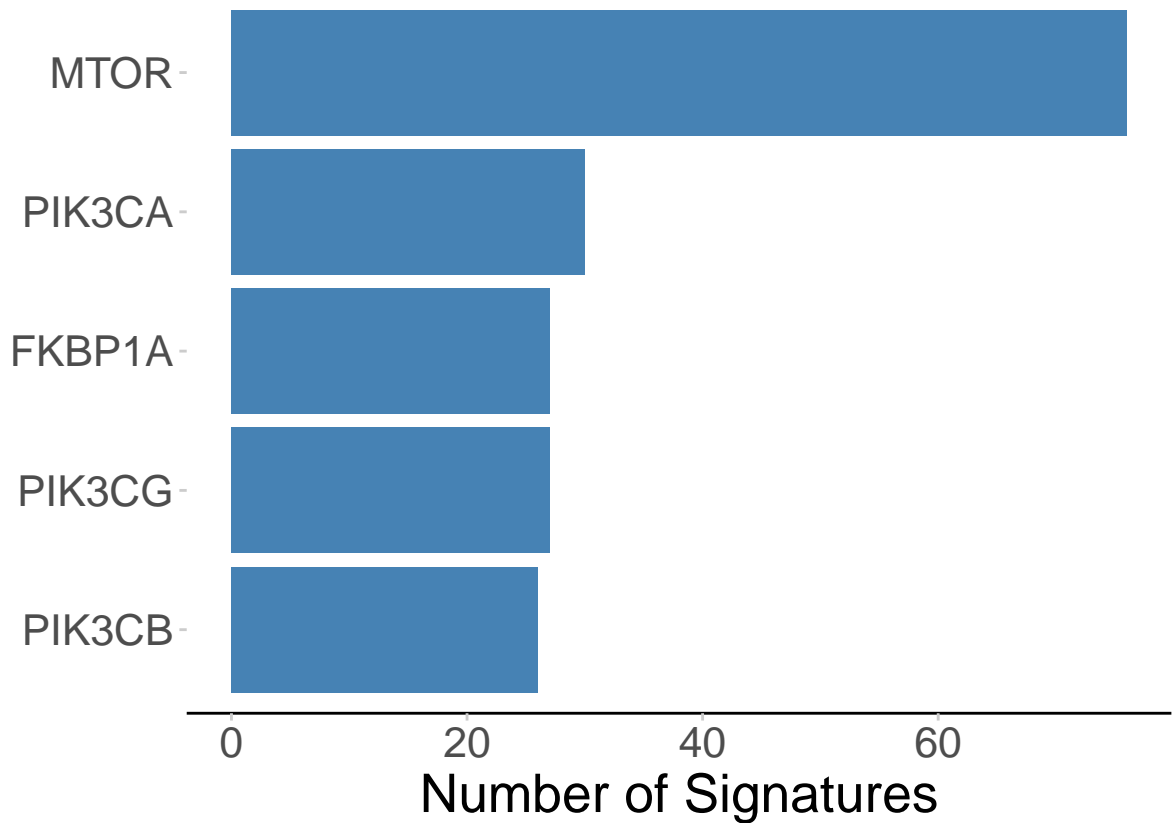
head(connectedCps)

##      signatureid similarity significance      pValue nGenes factor  compound concentration celllin
## 1 LINCSCP_137889  0.691327    144.3390 4.580566e-145    978    NA Everolimus      0.37uM    MCF
## 2 LINCSCP_137888  0.671113    133.4310 3.705507e-134    978    NA Everolimus      1.11uM    MCF
## 3 LINCSCP_137886  0.619745    109.2560 5.550003e-110    978    NA Everolimus      10uM    MCF
## 4 LINCSCP_143132  0.606843    103.8700 1.348646e-104    978    NA Sirolimus      0.37uM    MCF
## 5 LINCSCP_143130  0.594678     99.0135 9.692821e-100    978    NA Sirolimus      3.33uM    MCF
## 6 LINCSCP_143133  0.574759     91.4952 3.197302e-92     978    NA Sirolimus      0.12uM    MCF
##      is_exemplar GeneTargets
## 1      NA FKBP1A|MTOR
```

```
## 2      NA FKBP1A|MTOR
## 3      NA FKBP1A|MTOR
## 4      NA FKBP1A|MTOR
## 5      NA FKBP1A|MTOR
## 6      NA FKBP1A|MTOR
```

Summary boxplot, Figure 2E in the manuscript

```
top100GeneTargets<-unlist(strsplit.connectedCps$GeneTargets[1:100],split="\\|")
geneFreq <- sort(table(top100GeneTargets),decreasing=TRUE)[5:1]
geneFreqDf<-data.frame(gene=factor(names(geneFreq),levels=names(geneFreq),ordered=T),geneFreq=as.vector
tp100cp<-ggplot(data=geneFreqDf,aes(x=gene,y=geneFreq)) +
  geom_bar(stat="identity",fill="steelblue") +
  coord_flip() + theme_bw() +
  theme(axis.ticks=element_line(color="grey80"),text=element_text(size=20),legend.key.size=unit(1,"cm"))
  labs(x="",y="Number of Signatures")
tp100cp
```



Enrichr analysis of connected CGSes (Fig 2E)

```
setEnrichrSite("Enrichr")

## Connection changed to https://maayanlab.cloud/Enrichr/
## Connection is Live!
```

```
enrichedCgsTargets <- enrichr(genes=unique(top100GeneTargets), databases="KEGG_2019_Human")
```

```
## Uploading data to Enrichr... Done.
## Querying KEGG_2019_Human... Done.
## Parsing results... Done.
```

```
enrichedCgsTargets[["KEGG_2019_Human"]][1:5,]
```

##		Term	Overlap	P.value	Adjusted.P.value	Old.P.value	Old.Adjusted.P
## 1		HIF-1 signaling pathway	14/100	1.858086e-27	1.497395e-25	0	
## 2		Phospholipase D signaling pathway	15/148	2.454745e-27	1.497395e-25	0	
## 3		Glioma	13/75	1.072013e-26	4.359521e-25	0	
## 4		PI3K-Akt signaling pathway	17/354	1.024631e-25	2.772415e-24	0	
## 5		FoxO signaling pathway	14/132	1.136236e-25	2.772415e-24	0	
##							
## 1		INSR;PIK3CD;PIK3R3;PIK3R2;PIK3CB;PIK3R1;MTOR;EGFR;IGF1R;PIK3CA;AKT2;AKT3;MKNK2;A					Gen
## 2		INSR;PIK3CD;PIK3R3;PIK3R2;PIK3CB;PIK3R1;MTOR;PIK3CG;EGFR;PIK3R5;PIK3CA;AKT2;AKT3;AKT1;R					
## 3		PIK3CD;PIK3R3;PIK3R2;PIK3CB;PIK3R1;MTOR;EGFR;IGF1R;PIK3CA;AKT2;AKT3;AKT1;R					
## 4		INSR;PIK3CD;PIK3R3;PIK3R2;PIK3CB;PIK3R1;MTOR;PIK3CG;EGFR;PIK3R5;IGF1R;PIK3CA;AKT2;AKT3;AKT1;RAF1;J					
## 5		INSR;PLK1;PIK3CD;PIK3R3;PIK3R2;PIK3CB;PIK3R1;EGFR;IGF1R;PIK3CA;AKT2;AKT3;AKT1;R					