2022 SISBID Clustering Demo

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Load packages

```
library(ggplot2)
library(ISLR)
library(kknn)
```

K-means Clustering

1. Data set 1 - Simulated Data

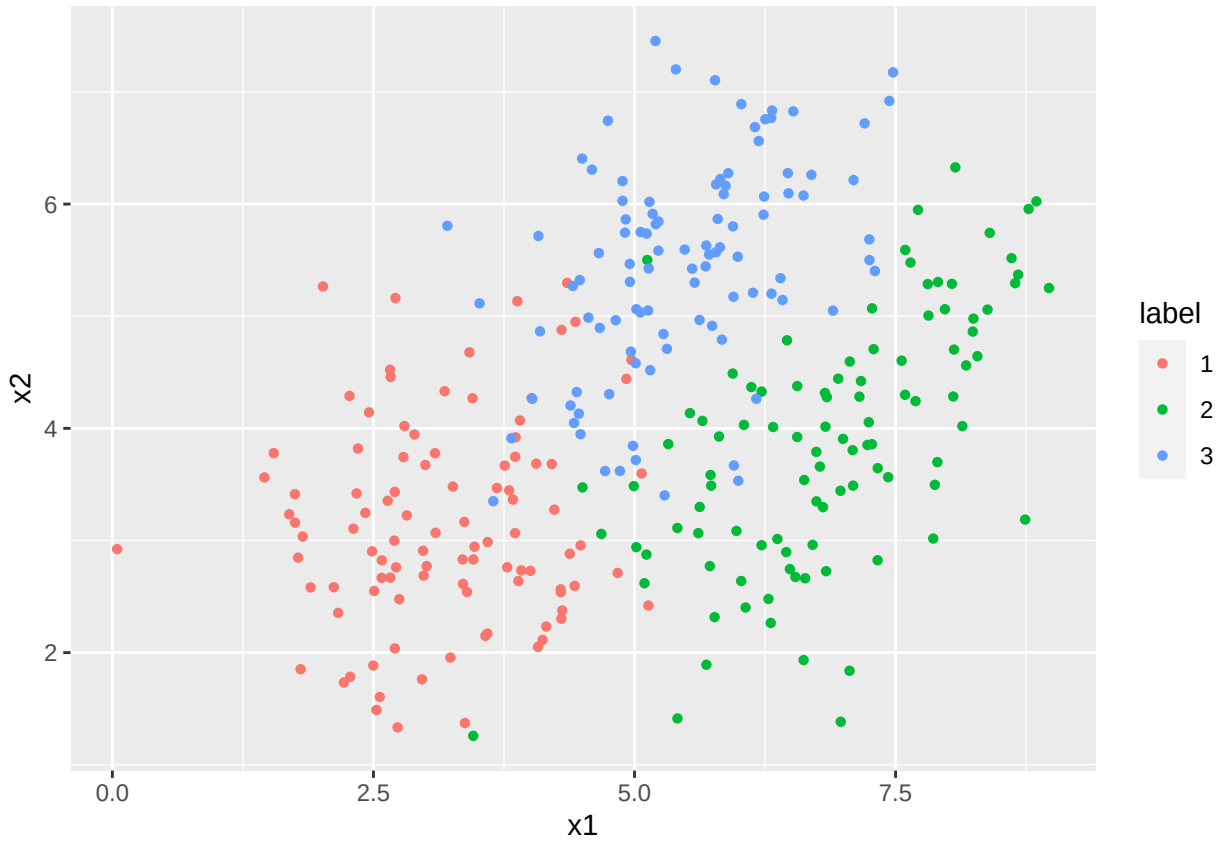
- small simulated data set to demonstrate concepts with k-means clustering

Simulate data: generate data from a mixture of three normal distribution

```
n = 300
mu1 = c(3,3)
mu2 = c(7,4)
mu3 = c(5.5,5.5)
Sig = matrix(c(1,.5,.5,1),2,2)
x1 = t(matrix(mu1,2,n/3)) + matrix(rnorm(n*2/3),n/3,2)
xx = matrix(rnorm(n*2/3),n/3,2)
x2 = t(matrix(mu2,2,n/3)) + xx%*%chol(Sig)
xx = matrix(rnorm(n*2/3),n/3,2)
x3 = t(matrix(mu3,2,n/3)) + xx%*%chol(Sig)
X = rbind(x1,x2,x3)
Y = c(rep(1,n/3),rep(2,n/3),rep(3,n/3))
Data = cbind(X,Y)
Data = data.frame(Data)
colnames(Data) = c("x1","x2","label")
Data$label = factor(Data$label)
```

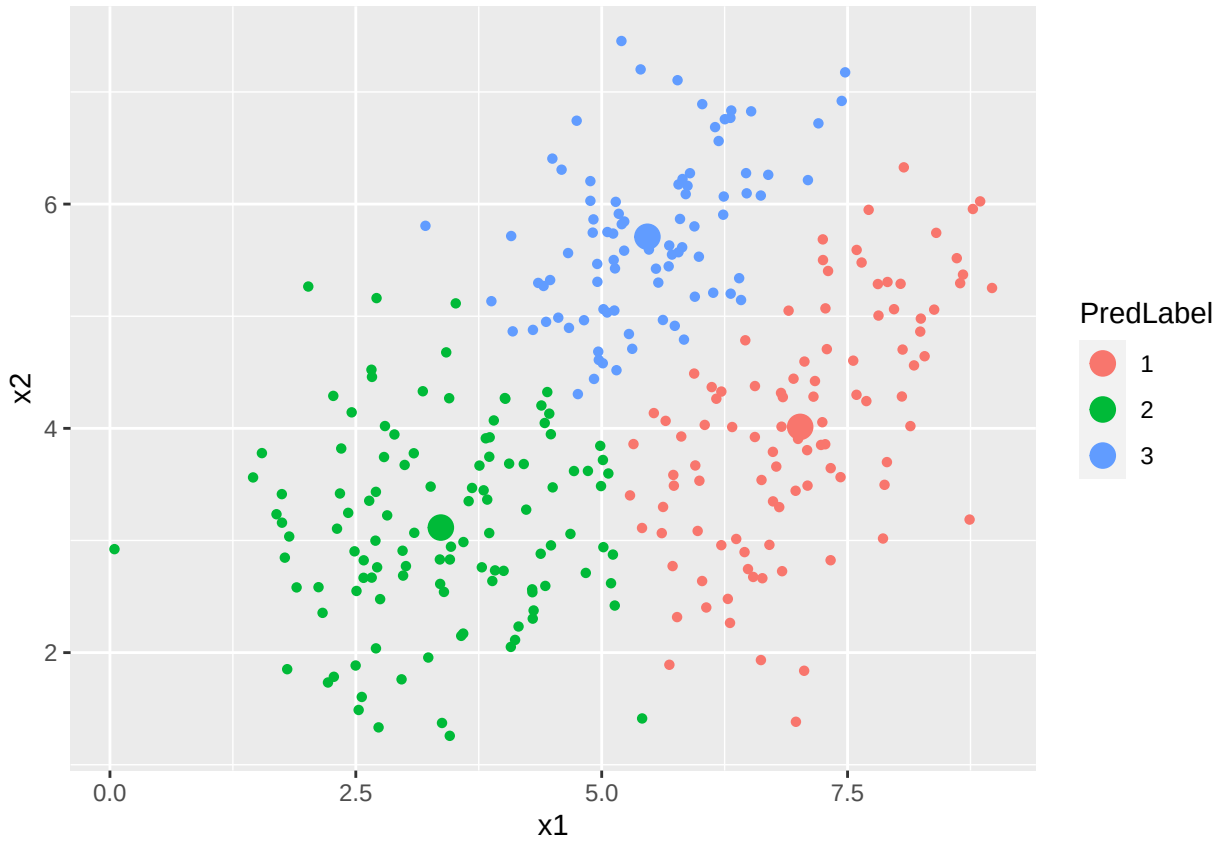
Plot with true labels

```
ggplot(data = Data) +
  geom_point(mapping = aes(x = x1,y = x2,color = label),pch = 16)
```



Apply k-means

```
k = 3
km = kmeans(X,centers=k)
gd = data.frame(km$centers)
gd$label = rownames(gd)
colnames(gd) = c("x1","x2","label")
Data$PredLabel = factor(km$cluster)
ggplot() +
    geom_point(data = Data,mapping = aes(x = x1,y = x2,color = PredLabel), pch = 16)  +
    geom_point(gd,mapping = aes(x = x1,y = x2,color= factor(label)),size = 4)
```



Code to understand K-means algorithm: raw code for k-means

```
par(mfrow=c(2,3))
k = 3
n = nrow(X)
cens = X[sample(1:n,k),]
plot(X[,1],X[,2],pch=16)
points(cens[,1],cens[,2],col=1:k,pch=16,cex=3)
for(i in 1:4){
    oldcen = cens
    km = kmeans(X,centers=cens,iter.max=1,nstart=1,algorithm="MacQueen")
    plot(X[,1],X[,2],col=km$cluster,pch=16)
    points(cens[,1],cens[,2],col=1:k,pch=16,cex=3)
    cens = km$centers
    plot(X[,1],X[,2],col=km$cluster,pch=16)
    points(cens[,1],cens[,2],col=1:k,pch=16,cex=3)
    ind = sum(diag((oldcen-cens)%*%t(oldcen-cens)))
    }
```

```
## Warning: did not converge in 1 iteration

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```
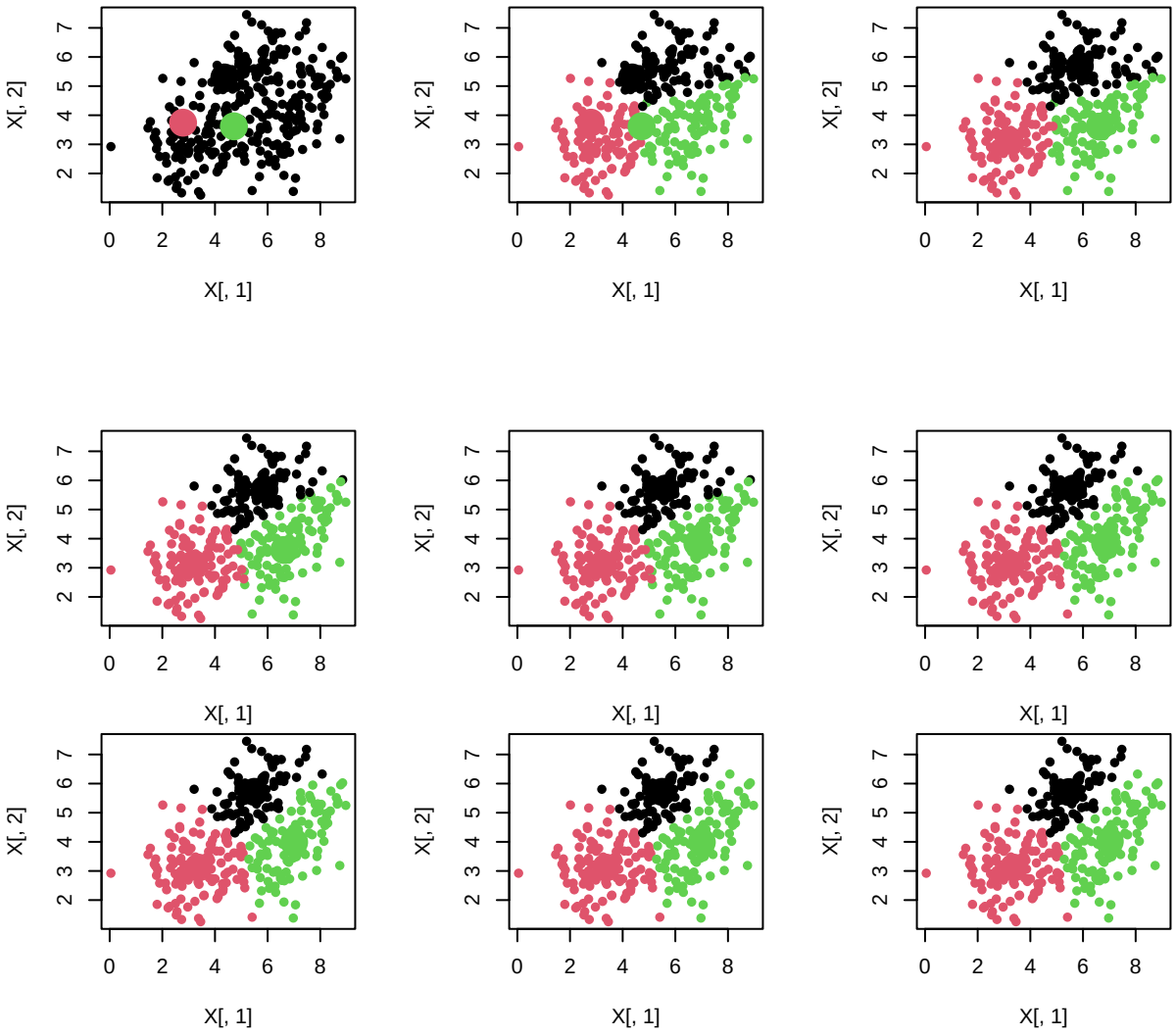



2. Data set 2 - NCI Microarray data: The data contains expression levels on 6830 genes from 64 cancer cell lines. Cancer type is also recorded.

- Apply K-means to cluster a high-dimensional data set.
- Apply hierarchical clustering & try out different linkages.
- Apply biclustering (Cluster heatmap) to visualize data.

```
ncidat = NCI60$data
rownames(ncidat) = NCI60$labs # cancer type
dim(ncidat)
```

```
## [1]   64 6830
```

```
table(NCI60$labs)
```

```
##
##      BREAST         CNS       COLON K562A-repro K562B-repro    LEUKEMIA
##           7           5           7           1           1           6
## MCF7A-repro MCF7D-repro    MELANOMA       NSCLC     OVARIAN    PROSTATE
##           1           1           8           9           6           2
```

```
##       RENAL     UNKNOWN
##           9           1
```

Apply K-means

```
K = 9
km = kmeans(ncidat,centers=K)
```

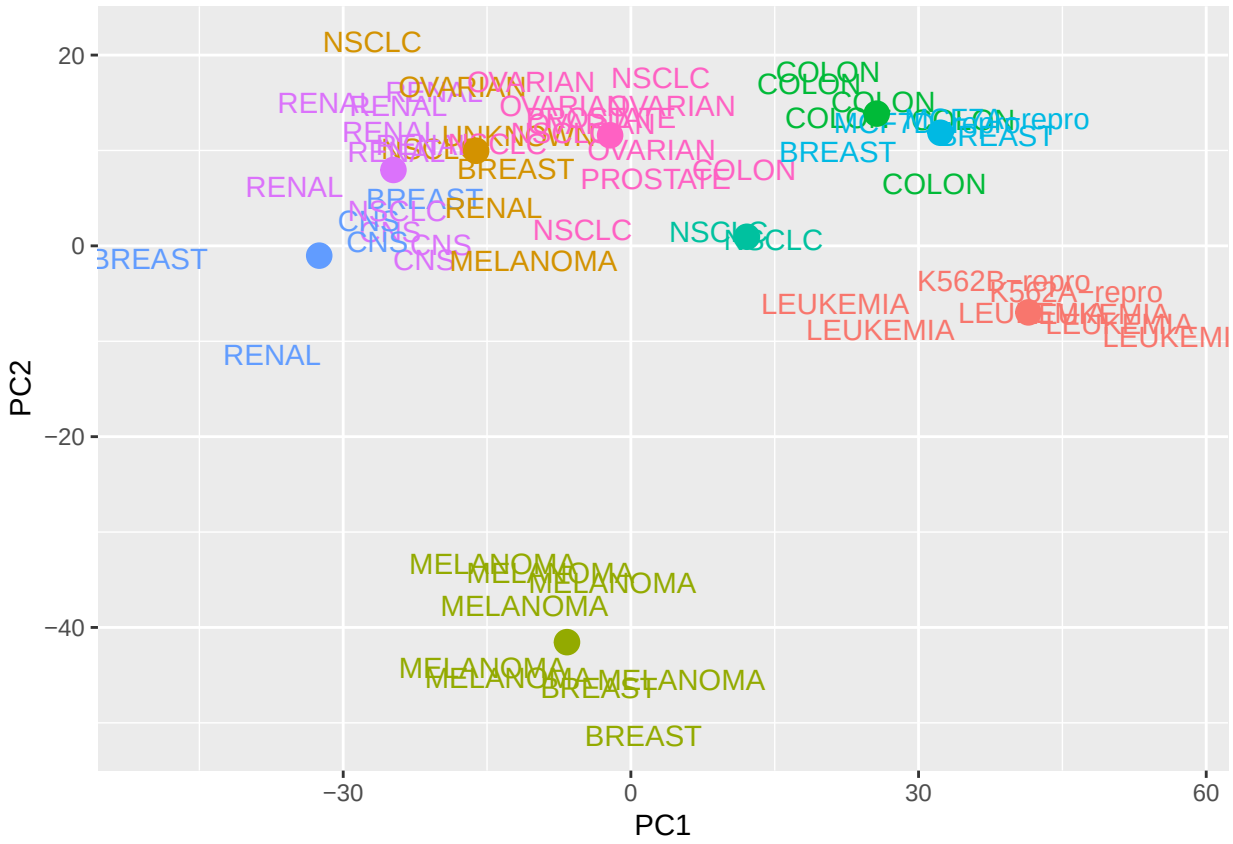
How do we visualize K-means results?
PCA - take SVD to get solution
Center genes, but don't scale

```
X = scale(ncidat,center=TRUE,scale=FALSE)
sv = svd(X)
U = sv$u
V = sv$v
D = sv$d
Z = X%*%V
```

Visualization

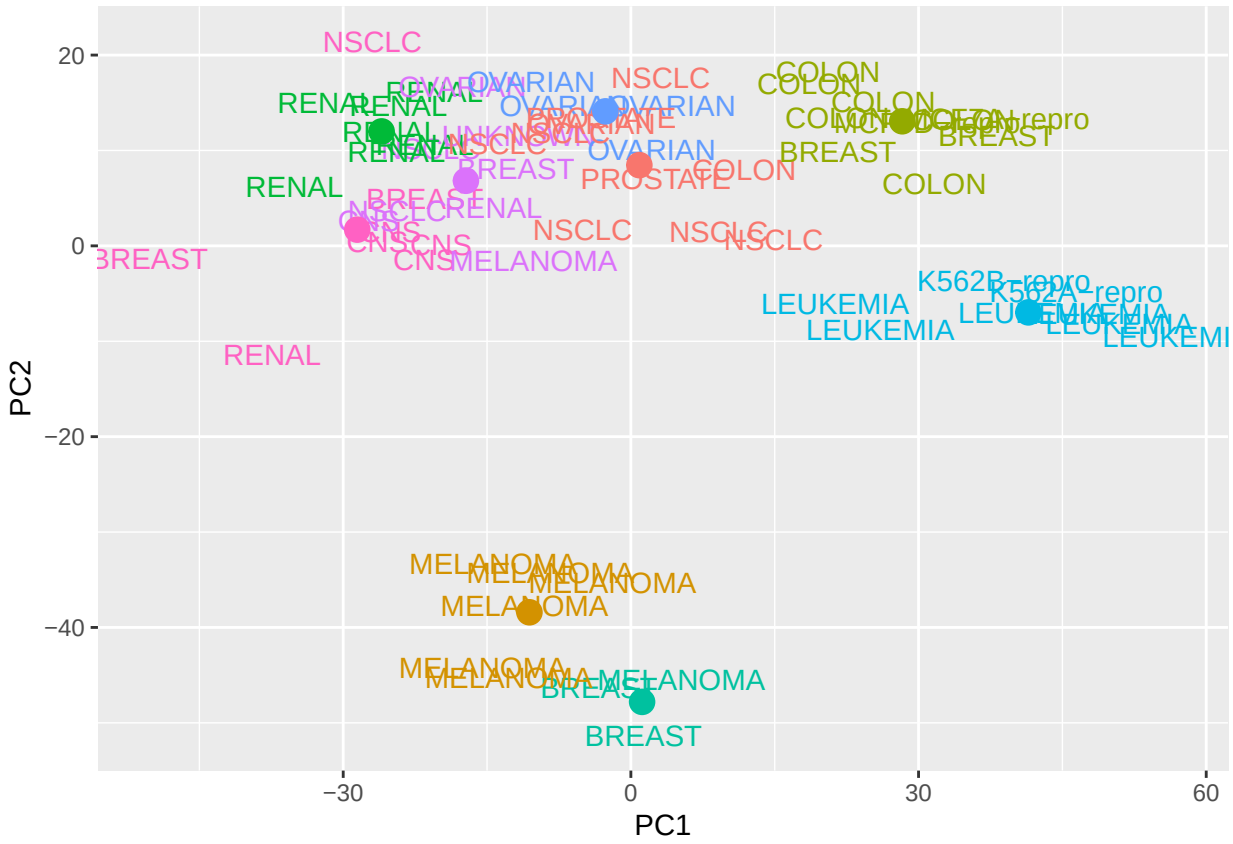
```
# projected data
PCData = data.frame(cbind(Z[,1],Z[,2],km$cluster,NCI60$labs),stringsAsFactors = FALSE)
colnames(PCData) = c("PC1","PC2","PredLabel","CancerType")
PCData$PC1 = as.numeric(PCData$PC1)
PCData$PC2 = as.numeric(PCData$PC2)
# projected k-means centers
GroupData = data.frame(km$centers%*%V[,1:2])
GroupData$label = rownames(GroupData)
colnames(GroupData) = c("PC1","PC2","PredLabel")
```

```
ggplot(PCData,mapping=aes(x = PC1,y= PC2,color = PredLabel)) +
  geom_text(mapping=aes(label = CancerType)) +
  geom_point(data = GroupData,size = 4) +
  theme(legend.position="none")
```



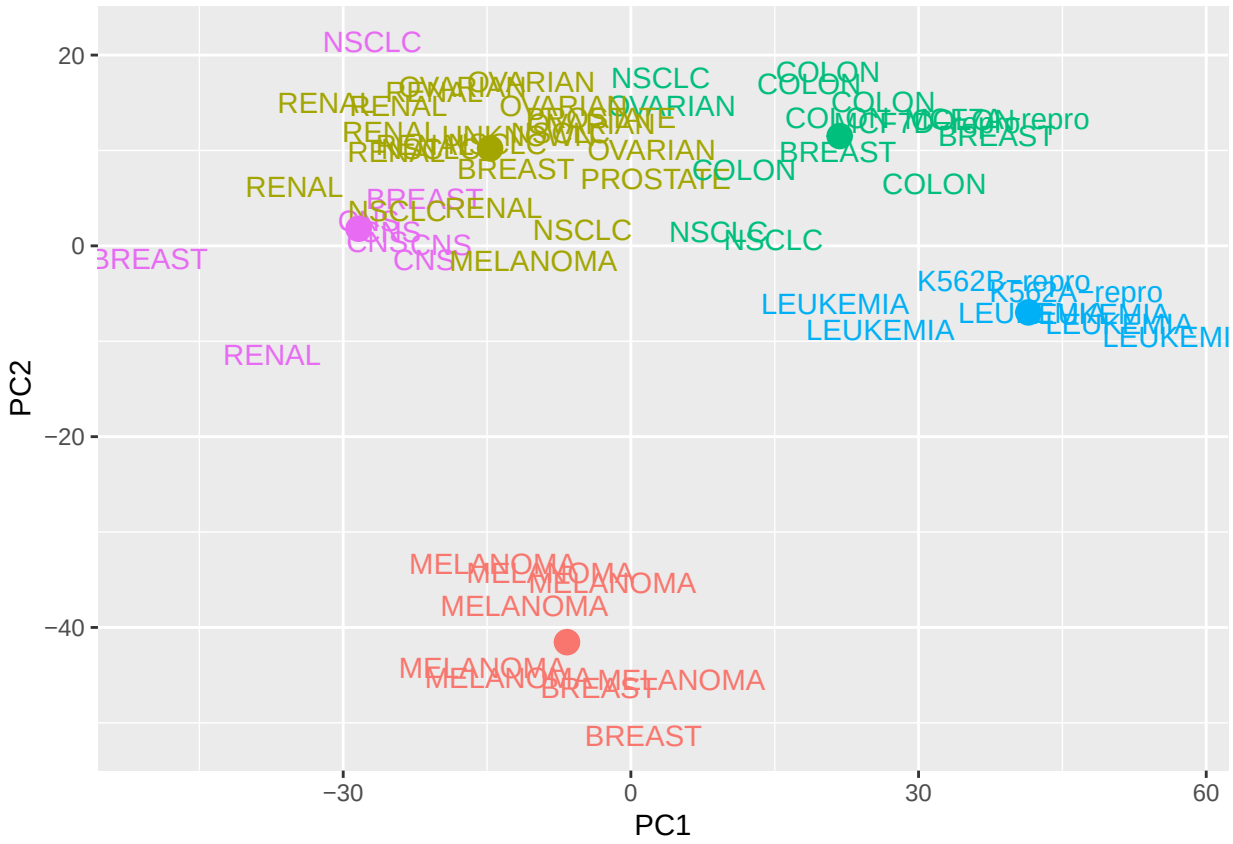
Re-run and see if solution changes

```
K = 9
km = kmeans(ncidat,centers=K)
PCData$PredLabel = as.factor(km$cluster)

# projected k-means centers
GroupData = data.frame(km$centers%*%V[,1:2])
GroupData$label = rownames(GroupData)
colnames(GroupData) = c("PC1","PC2","PredLabel")

# plot
ggplot(PCData,mapping=aes(x = PC1,y= PC2,color = PredLabel)) +
  geom_text(mapping=aes(label = CancerType)) +
    geom_point(data = GroupData,size = 4) +
  theme(legend.position="none")
```



Try different K

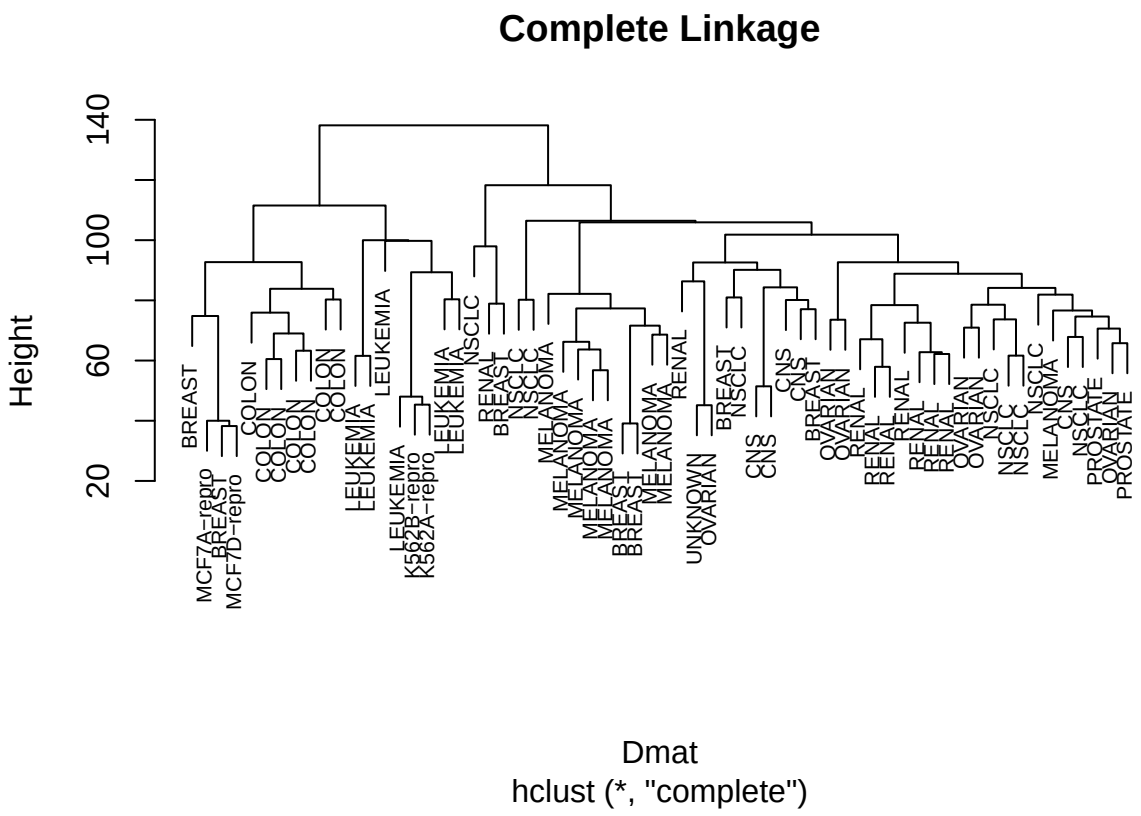
```
K = 5
km = kmeans(ncidat,centers=K)
PCData$PredLabel = as.factor(km$cluster)

# projected k-means centers
GroupData = data.frame(km$centers%*%V[,1:2])
GroupData$label = rownames(GroupData)
colnames(GroupData) = c("PC1","PC2","PredLabel")

# plot
ggplot(PCData,mapping=aes(x = PC1,y= PC2,color = PredLabel)) +
  geom_text(mapping=aes(label = CancerType)) +
    geom_point(data = GroupData,size = 4) +
  theme(legend.position="none")
```



Hierarchical clustering

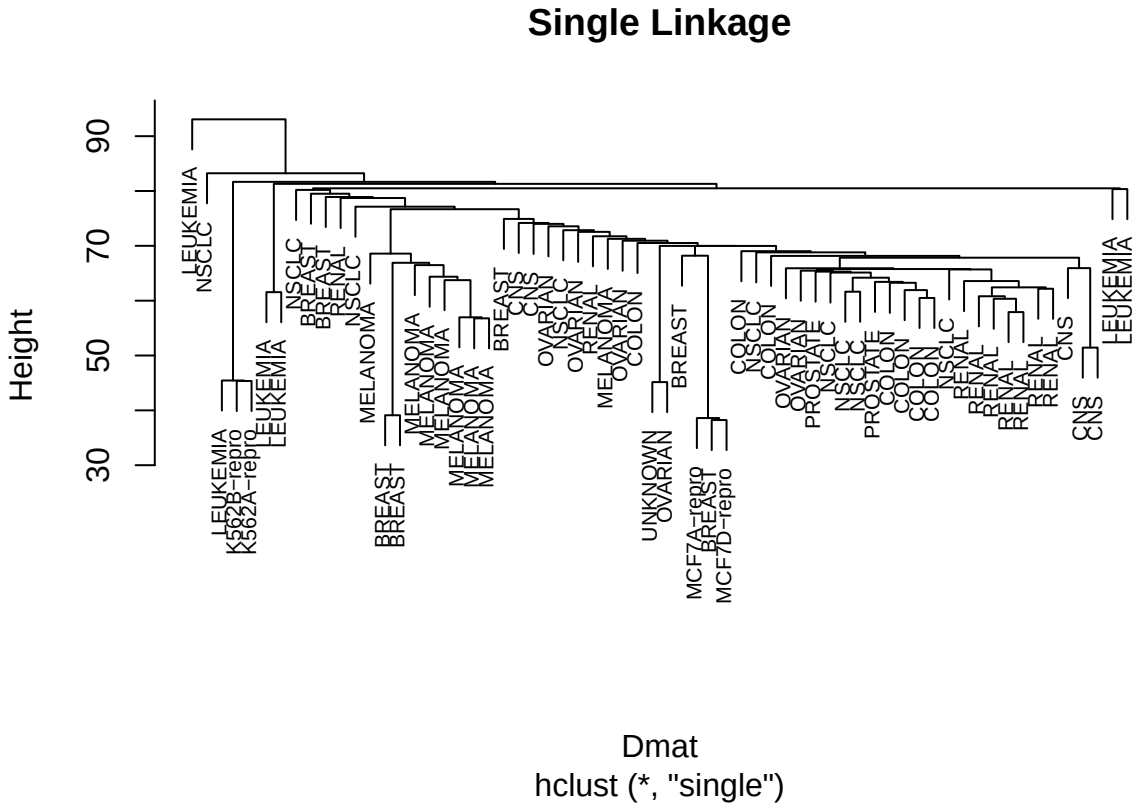
Real Data: NCI 60 data in ISLR package
Complete linakge - Euclidean distance

```
cols = as.numeric(as.factor(rownames(ncidat)))
Dmat = dist(ncidat)
com.hclust = hclust(Dmat,method="complete")
plot(com.hclust,cex=.7,main="Complete Linkage")
```



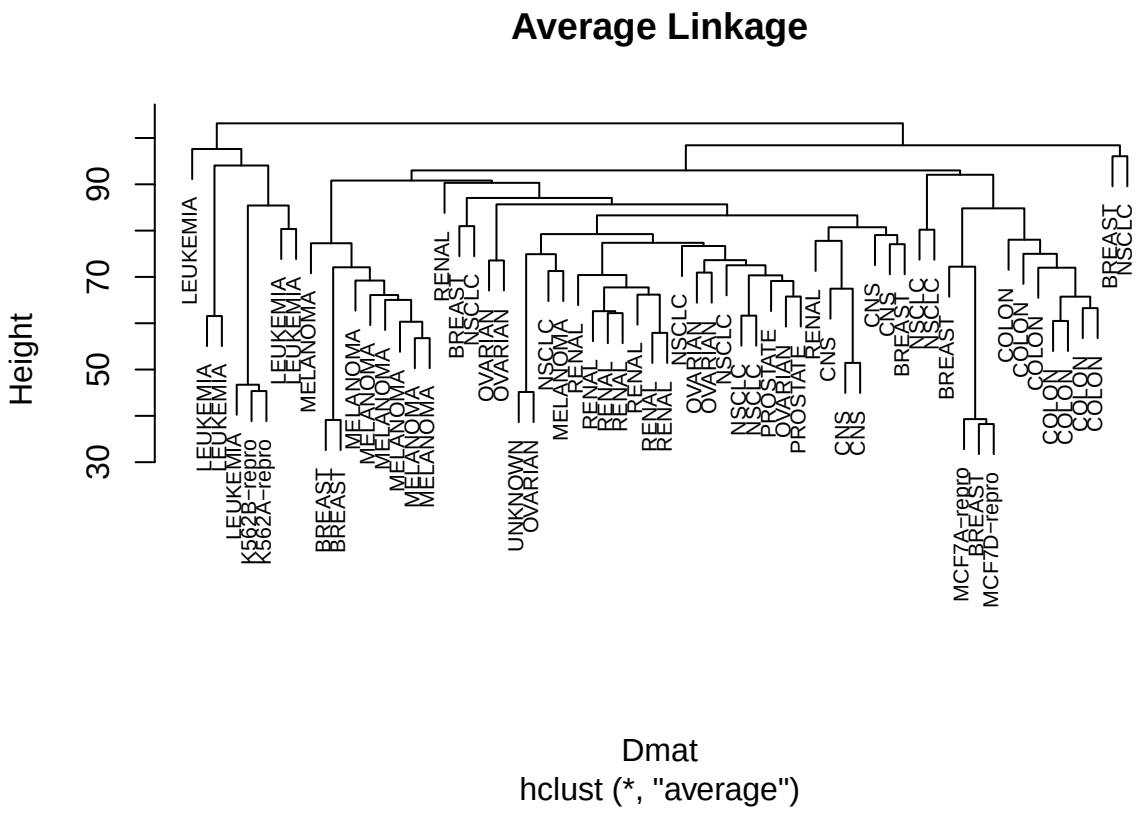
Single linakge

```
sing.hclust = hclust(Dmat,method="single")
plot(sing.hclust,cex=.7,main="Single Linkage")
```



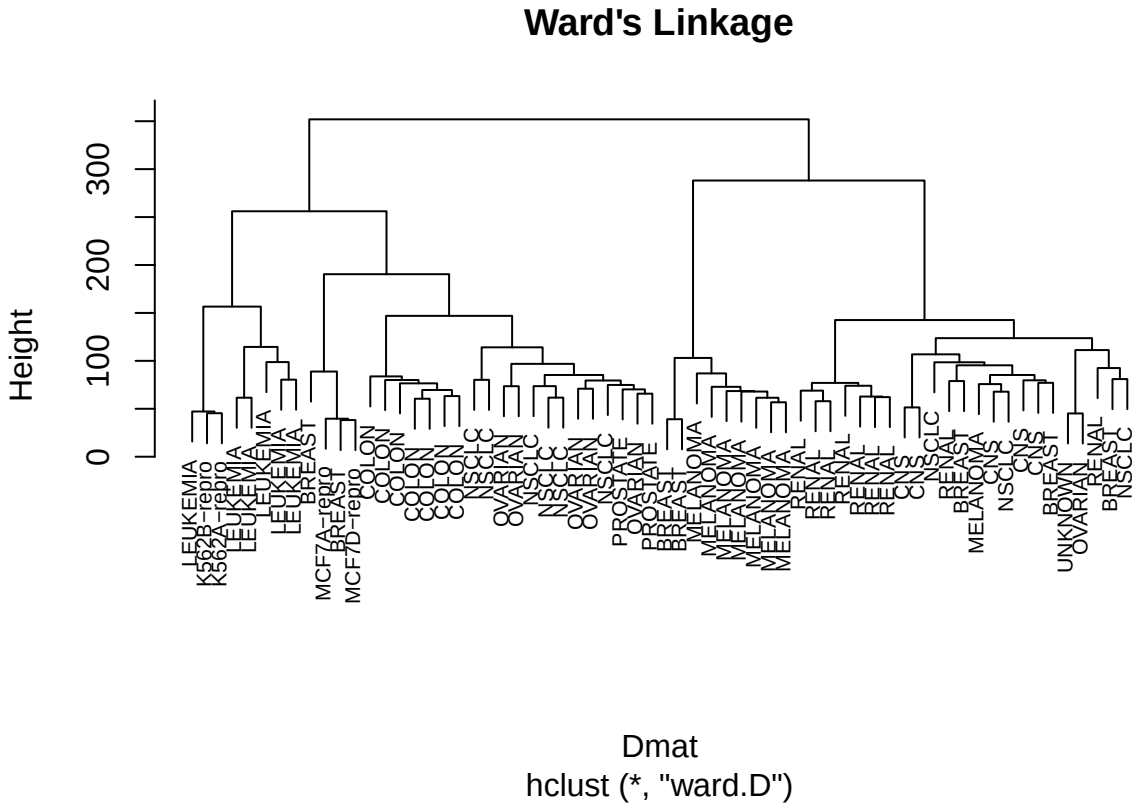
Average linakge

```
ave.hclust = hclust(Dmat,method="average")
plot(ave.hclust,cex=.7,main="Average Linkage")
```



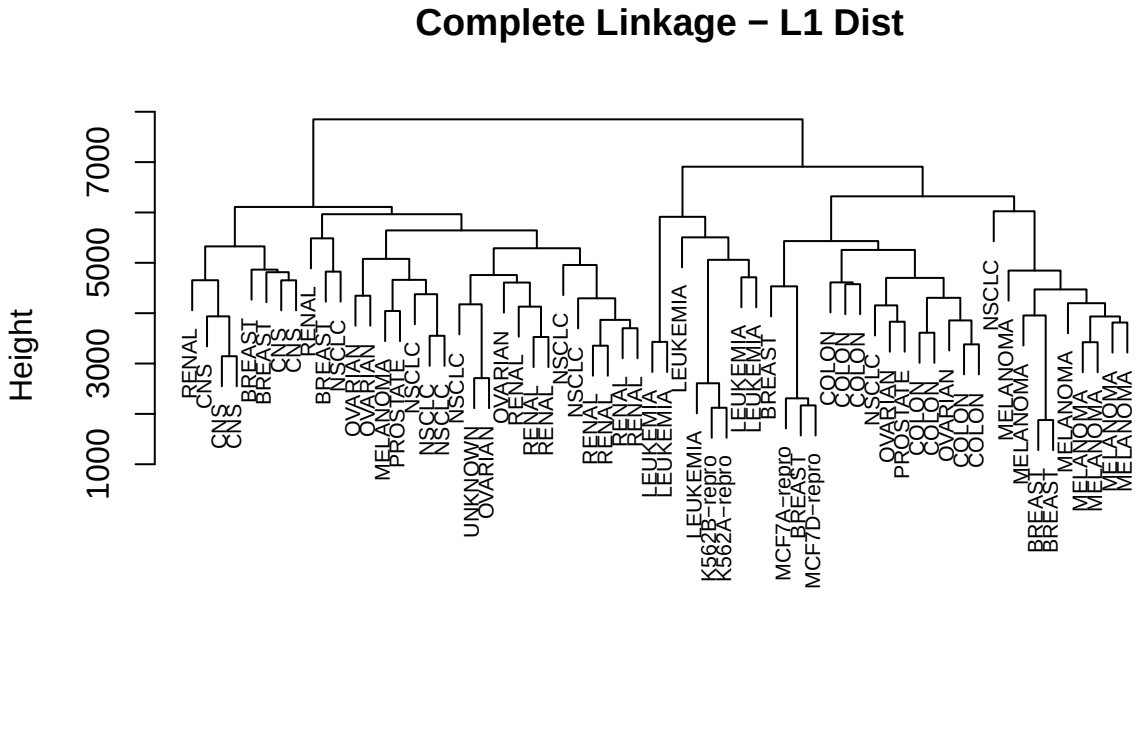
Ward's linakge

```
ward.hclust = hclust(Dmat,method="ward.D")
plot(ward.hclust,cex=.7,main="Ward's Linkage")
```



Complete linkage with different distances - L1 distance

```
Dmat = dist(ncidat,method="manhattan") #L1 distance
com.hclust = hclust(Dmat,method="complete")
plot(com.hclust,cex=.7,main="Complete Linkage - L1 Dist")
```



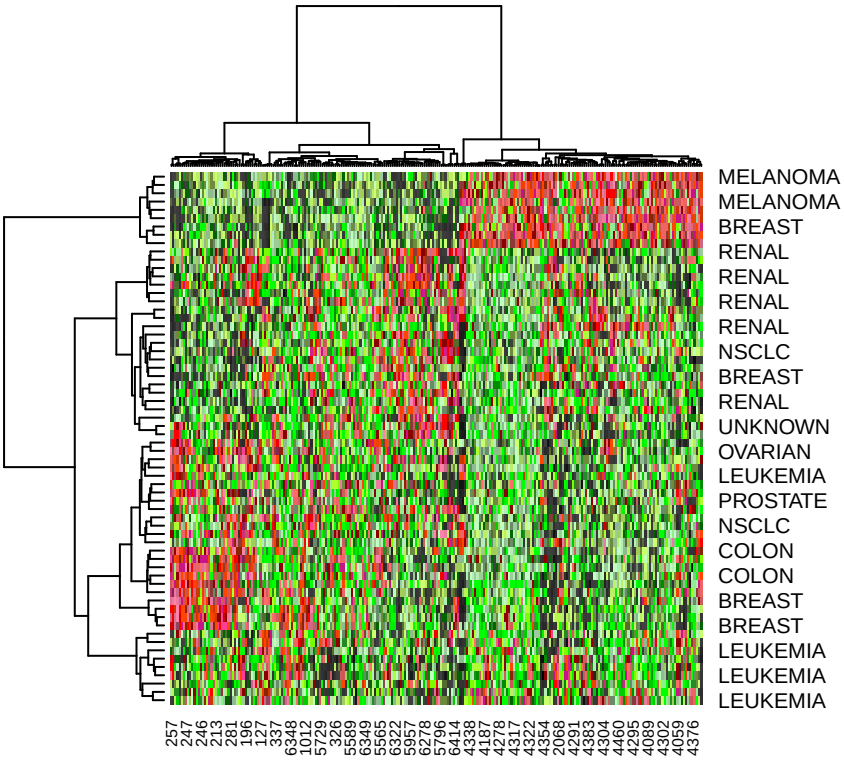
Biclustering - Cluster Heatmap

Filter genes using PCA
PC loadings - visualize data by limiting to top genes in magnitude in the PC loadings

```
aa = grep("grey",colors())
bb = grep("green",colors())
cc = grep("red",colors())
gcol2 = colors()[c(aa[1:30],bb[1:20],rep(cc,2))]

j = 2
ord = order(abs(V[,j]),decreasing=TRUE)
x = as.matrix(X[,ord[1:250]])
```

#cluster heatmap - uses Ward's linkage (complete is default)

```
heatmap(x,col=gcol2,hclustfun=function(x) hclust(x,method="ward.D"))
```

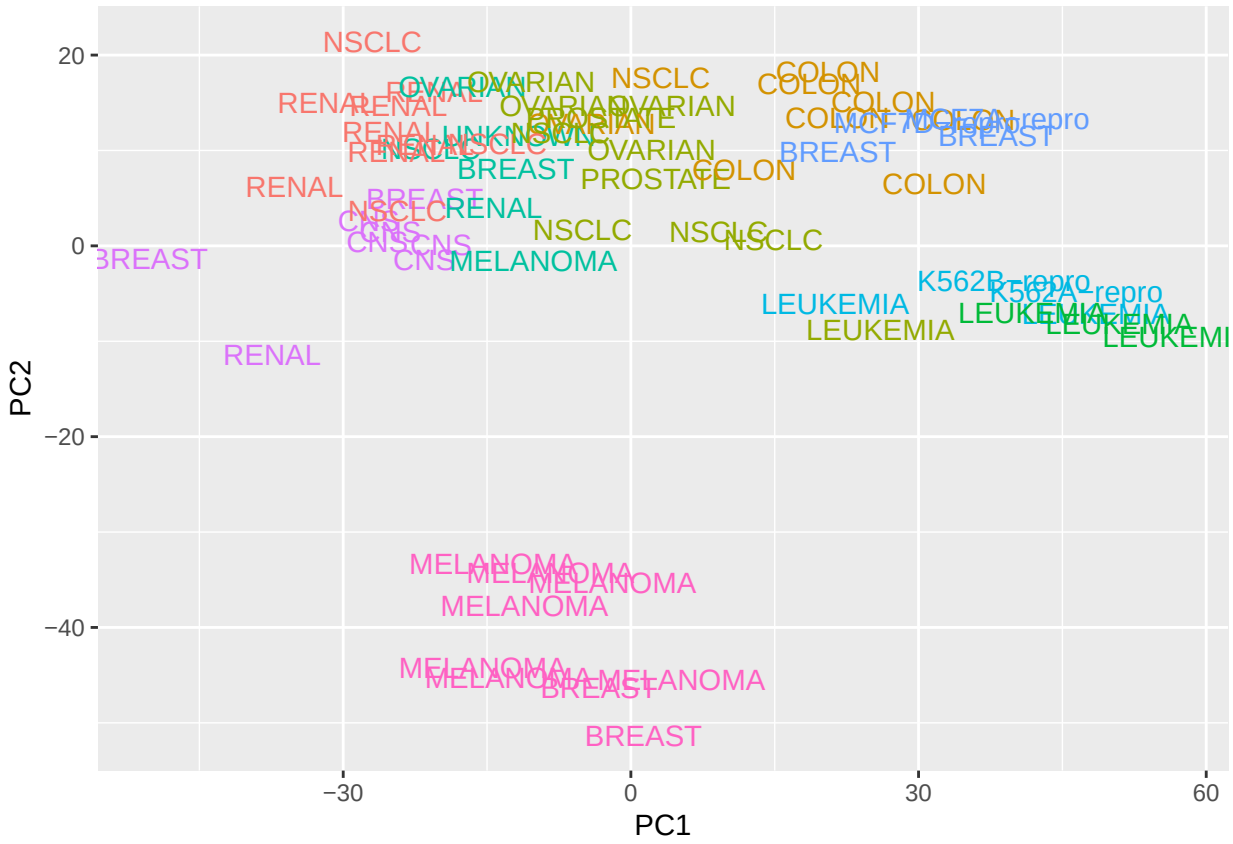


Spectral clustering

```
K = 9
SC_NCI = specClust(ncidat, centers=K, nn = 7, method = "symmetric", gmax=NULL)
```

Visualization

```
X = scale(ncidat,center=TRUE,scale=FALSE)
sv = svd(X)
U = sv$u
V = sv$v
D = sv$d
Z = X%*%V

# projected data
SCData = data.frame(cbind(Z[,1],Z[,2],SC_NCI$cluster,NCI60$labs),stringsAsFactors = FALSE)
colnames(SCData) = c("PC1","PC2","PredLabel","CancerType")
SCData$PC1 = as.numeric(SCData$PC1)
SCData$PC2 = as.numeric(SCData$PC2)
# plot
ggplot(SCData,mapping=aes(x = PC1,y= PC2,color = PredLabel)) +
  geom_text(mapping=aes(label = CancerType)) +
  theme(legend.position="none")
```


PC2
PC1
20
0
−20
−40
−30
0
30
60
NSCLC
RENAL
OVARIAN
BREAST
MELANOMA
COLON
PROSTATE
LEUKEMIA
K562B-repro
K562A-repro
MCF7D-repro
MCF7A-repro
UNKNOWN
CNS