Chemviz_vignette

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Contents

1 Introduction

Scientists can have information about chemical compounds and then want a simple way to visualize the chemical structure and also the to understand the chemical similarity of compounds (Tanimoto similarity). This can be done in Cytoscape using the Chemviz plugin

In this vignette we will use the R package rcellminer to generate some data that we will use to look a some drug compounds. Then, in Cytoscape, we will then see how these drugs are chemically related, look at the 2-dimensional structures of these compounds and then colour the compounds by their mechanism of action to see if it is related to their similarity.

2 Required materials:

- Cytoscape (www.cytoscape.org)
- Chemviz - plugin for Cytoscape (http://www.cgl.ucsf.edu/cytoscape/chemViz2/index.shtml)
- Rpackages: RCy3, httr, JSONIO, rcellminer, RColorBrewer

3 Load the packages

```r
library(RCy3)
library(rcellminer)
library(RColorBrewer)
source("./functions_to_add_to_RCy3/working_with_namespaces.R")
```

4 Get data from rcellminer

```r
df <- getFeatureAnnot(rcellminerData::drugData)[["drug"]]
## smiles strings
## moa mechanism of action

moaToCompounds <- getMoaToCompounds()
Moa_names <- names(moaToCompounds)

df_knownMoaDrugs <- subset(df, MOA %in% Moa_names)

## use only those with greater than 3 experiments
df_with_knownMoaDrugs <- subset(df_knownMoaDrugs, TOTAL_EXPS > 10)
```

For display purposes we will chop off long names after 12 characters.

```r
long_names <- df_with_knownMoaDrugs$NAME[nchar(df_with_knownMoaDrugs$NAME) > 12]
chopped_long_names <- gsub("^(.{12})(.*)$", "\\1", long_names)
df_with_knownMoaDrugs$NAME[nchar(df_with_knownMoaDrugs$NAME) > 12 ] <- chopped_long_names
```

5 Set up connection between R and Cytoscape

```r
# first, delete existing windows to save memory:
deleteAllWindows(CytoscapeConnection())
cy <- CytoscapeConnection()
getCommandsWithinNamespace(cy,
                           "chemviz")
```

```
##  [1] "calculate mcss"           "create attributes"
##  [3] "create similarity"        "hide results"
##  [5] "paint structures"         "remove structures"
##  [7] "search"                   "settings"
##  [9] "show compound structures" "show compound table"
## [11] "show results"
```

6 Format dataframe from RCellMiner to format that can be sent to cytoscape

```r
g <- new("graphNEL",
         nodes = df_with_knownMoaDrugs$NAME,
         edgemode = "undirected")

cw <- CytoscapeWindow("vignette_for_chemviz",
                      graph = g,
                      overwrite = TRUE)
```

```r
displayGraph(cw)
```

```
## [1] "label"
```

```r
layoutNetwork(cw,
              layout.name = "grid")
showGraphicsDetails(cw, new.value)
```

```
## RCy3::showGraphicsDetails(), Switching between show and hide full graphics details.
```

```r
g <- cw@graph
g <- initNodeAttribute(graph = g,
                       "SMILES",
                       "char",
                       "none")
nodeData(g, nodes(g), "SMILES") <- df_with_knownMoaDrugs$SMILES

g <- initNodeAttribute(graph = g,
                       "NSC_from_df",
                       "char",
                       "none")
nodeData(g, nodes(g), "NSC_from_df") <- df_with_knownMoaDrugs$NSC

g <- initNodeAttribute(graph = g,
                       "MOA",
                       "char",
                       "none")
nodeData(g, nodes(g), "MOA") <- df_with_knownMoaDrugs$MOA
```

```r
cw <- setGraph(cw,
               g)
displayGraph(cw) # cw's graph is sent to Cytoscape
```

```
## [1] "label"
## [1] "SMILES"
## [1] "NSC_from_df"
## [1] "MOA"
```

Network successfully sent to Cytoscape. The node attributes have also been sent.

Vinblastine	Chlorozotoci	Aphidicoline	Testolactone	Maytansine	Mitomycin	Rhizoxin	6-Thioguanin
6-Mercaptopu	5-HP	Paclitaxel	N,N-Dibenzyl	Asaley	Oxanthrazole	Amonafide	Streptozocin
Triciribine	Mitoxantrone	N-Phosphonac	M-AMSA	Vincristine	Trityl cyste	Dexrazoxane	Topotecan
Anthrapyrazo	Depsipeptide	PCNU	Bleomycin	Hepsulfam	Halichondrin	Daunorubicin	Acivicin
Menogaril	Dihydro-5-az	3-HP	Etoposide	ellipticine	Deoxydoxoru	Morpholinodo	Methyl CCNU
AZQ	Floxuridine	Colchicine	Doxorubicin	Actinomycin	Azacitidine	Buthionine s	A-TGdR
Dianhydroga	Cyanomorpho	2-methylellp	Spirohydanto	Trimetrexate	Mithramycin	Teniposide	Yoshi 864
Thiotepa	Cytarabine	Bisantrene h	Methotrexate	Beta-Thiogua	Fluorodopan	CHIP	Tamoxifen
Tegafur							

7 Create similarity network

Next based on the chemical properties of each node (which are associated using the SMILES strings (Simplified Molecular Input Line Entry System which are line representations of chemical structures) we will use chemviz to calculate the similarity of each drug based on its chemical properties (using Tanimoto similarity which is a distance-based measure of chemical similarity).

To begin let's look at some of the commands available to use in chemviz:

```
getCommandsWithinNamespace(cw, "chemviz")
```

```
##  [1] "calculate mcss"           "create attributes"
##  [3] "create similarity"        "hide results"
##  [5] "paint structures"         "remove structures"
##  [7] "search"                   "settings"
##  [9] "show compound structures" "show compound table"
## [11] "show results"
```

Now let's look at the arguments we can use for creating a similarity network:

```
getCommandsWithinNamespace(cw, "chemviz/create%20similarity")
```

```
## [1] "createNewNetwork" "network"          "nodeList"
```

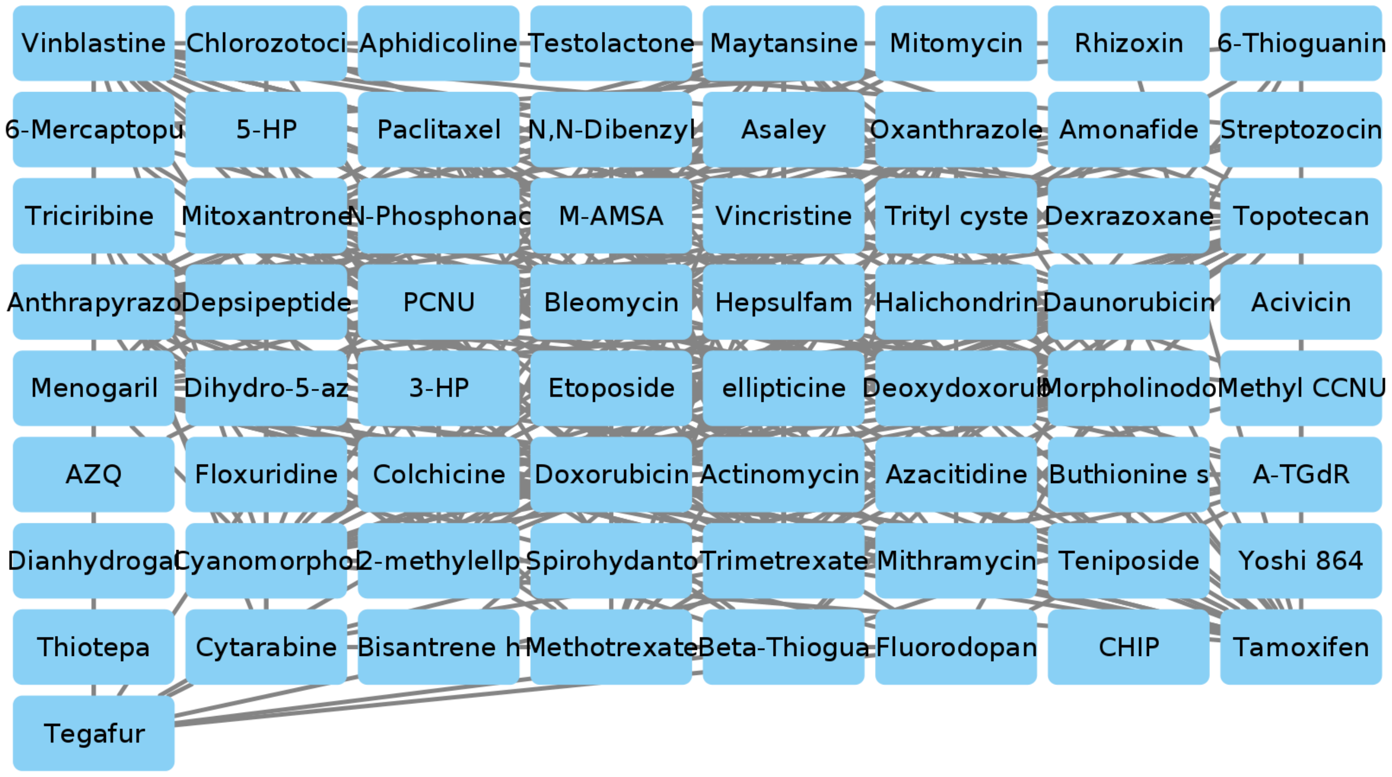
Set the properties that we would like to use

```
properties.list <- list(createNewNetwork = TRUE,
                        network = "current",
                        nodeList = "all")

command.name <- "chemviz/create%20similarity"

chemviz_cw <- setCommandProperties(cw,
                     command.name,
                     properties.list,
                     copy.graph.to.R = FALSE)
```

```
## [1] "Successfully built the EnrichmentMap."
## [1] "Cytoscape window vignette_for_chemviz copy successfully connected to R session."
```


Vinblastine
Chlorozotoci
Aphidicoline
Testolactone
Maytansine
Mitomycin
Rhizoxin
6-Thioguanin
6-Mercaptopu
5-HP
Paclitaxel
N,N-Dibenzyl
Asaley
Oxanthrazole
Amonafide
Streptozocin
Triciribine
Mitoxantrone
N-Phosphonac
M-AMSA
Vincristine
Trityl cyste
Dexrazoxane
Topotecan
Anthrapyrazo
Depsipeptide
PCNU
Bleomycin
Hepsulfam
Halichondrin
Daunorubicin
Acivicin
Menogaril
Dihydro-5-az
3-HP
Etoposide
ellipticine
Deoxydoxorub
Morpholinodo
Methyl CCNU
AZQ
Floxuridine
Colchicine
Doxorubicin
Actinomycin
Azacitidine
Buthionine s
A-TGdR
Dianhydroga
Cyanomorpho
2-methylellp
Spirohydanto
Trimetrexate
Mithramycin
Teniposide
Yoshi 864
Thiotepa
Cytarabine
Bisantrene h
Methotrexate
Beta-Thiogua
Fluorodopan
CHIP
Tamoxifen
Tegafur

We currently just have the network in the grid format, but now with edges connecting the nodes we can do a layout that can help us visualize the connections.

Since we made a new network that is in Cytoscape, but not yet connected to our R session we will first need to connect to this window and then we can apply a layout.

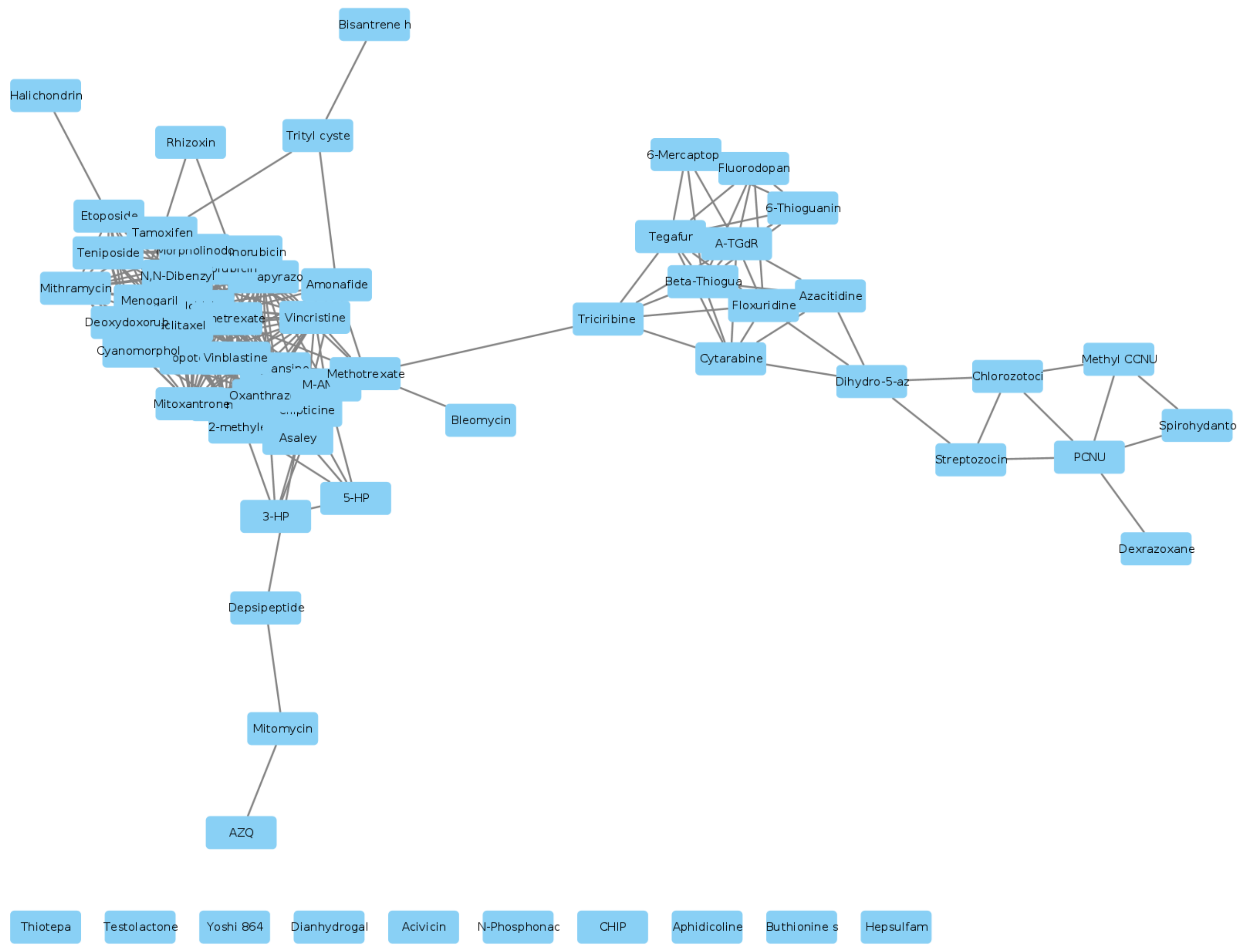
```
connectToNewestCyWindow <- function(obj,
                                    copyToR = FALSE) {
  resource.uri <- paste(obj@uri,
                        pluginVersion(obj),
                        "networks",
                        sep = "/")
  request.res <- GET(resource.uri)
  # SUIDs list of the existing Cytoscape networks
  cy.networks.SUIDs <- fromJSON(rawToChar(request.res$content))
  # most recently made enrichment map will have the highest SUID
  cy.networks.SUIDs.last <- max(cy.networks.SUIDs)

  res.uri.last <- paste(obj@uri,
                        pluginVersion(obj),
                        "networks",
                        as.character(cy.networks.SUIDs.last),
                        sep = "/")
  result <- GET(res.uri.last)
  net.name <- fromJSON(rawToChar(result$content))$data$name

  ## to get edges request.res$elements$edges
  newest_CyWindow <- existing.CytoscapeWindow(net.name,
                                     copy.graph.from.cytoscape.to.R = copyToR)
  return(newest_CyWindow)
}

new_cw <- connectToNewestCyWindow(chemviz_cw)
```

```
layoutNetwork(new_cw, "force-directed")
```


Bisantrene h
Halichondrin
Rhizoxin
Trityl cyste
Etoposide
Tamoxifen
Teniposide
Morpholinodo
morubicin
N,N-Dibenzyl
rubicin
apyrazo
Amonafide
Mithramycin
Menogaril
Deoxydoxorub
clitaxel
etrexate
Vincristine
Cyanomorphol
opot
Vinblastine
ansine
Methotrexate
M-AM
Oxanthraz
Mitoxantrone
lipticine
2-methyle
Asaley
Bleomycin
5-HP
3-HP
Depsipeptide
Mitomycin
AZQ
6-Mercaptop
Fluorodopan
6-Thioguanin
Tegafur
A-TGdR
Beta-Thiogua
Azacitidine
Floxuridine
Triciribine
Cytarabine
Dihydro-5-az
Chlorozotoci
Methyl CCNU
Spirohydanto
Streptozocin
PCNU
Dexrazoxane
Thiotepa
Testolactone
Yoshi 864
Dianhydrogal
Acivicin
N-Phosphonac
CHIP
Aphidicoline
Buthionine s
Hepsulfam

8 Add 2D chemical structures to nodes

Another thing we can do with chemviz is to add the two dimensional chemical structure on to the nodes of our networks.

Let's look again at the commands available in Chemviz:

```
getCommandsWithinNamespace(new_cw, "chemviz")
```

```
##  [1] "calculate mcss"            "create attributes"
##  [3] "create similarity"         "hide results"
##  [5] "paint structures"          "remove structures"
##  [7] "search"                    "settings"
##  [9] "show compound structures" "show compound table"
## [11] "show results"
```

And the arguments needed for the command we want to use: "paint structures"

```
getCommandsWithinNamespace(new_cw, "chemviz/paint%20structures")
```

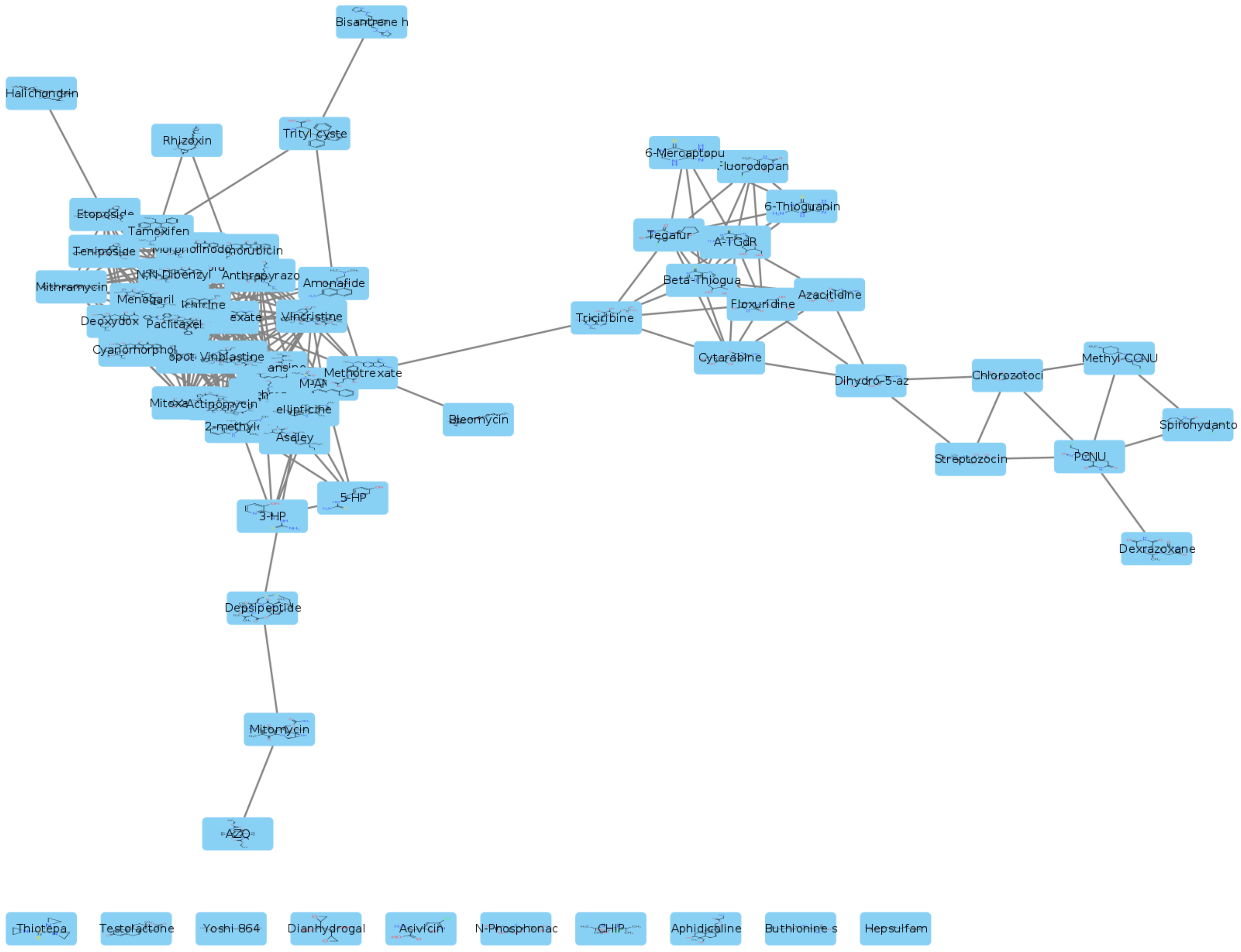
```
## [1] "nodeList"
```

```
properties.list <- list(nodeList = "all")

command.name <- "chemviz/paint%20structures"

setCommandProperties(new_cw,
                     command.name,
                     properties.list,
                     copy.graph.to.R = FALSE)
```

Now we have all of the chemical structures displayed on the nodes of our network.


Bisantrene h
Halichondrin
Rhizoxin
Trityl cyste
Etoposide
Tamoxifen
Teniposide
Morpholinodo
norubicin
N,N-Dibenzyl
Anthrapyrazo
Mithramycin
Amonafide
Menogaril
ichrine
Deoxydox
Paclitaxel
exate
Vincristine
Cyanomorphol
Vinblastine
Methotrexate
M-AM
MitoxaActinomycin
ellipticine
2-methyl
Asaley
Bleomycin
5-HP
3-HP
Depsipeptide
Mitomycin
AZQ
6-Mercaptopu
Fluorodopan
6-Thioguanin
Tegafur
A-TGdR
Beta-Thiogua
Azacitidine
Floxuridine
Triciribine
Cytarabine
Dihydro-5-az
Chlorozotoci
Methyl-CCNU
Spirohydanto
Streptozocin
PCNU
Dexrazoxane
Thiotepa
Testolactone
Yoshi-864
Dianhydrogal
Acivicin
N-Phosphonac
CHIP
Aphidicoline
Buthionine s
Hepsulfam

# Colour nodes by mechanism of action (MOA)

The nodes that we are examining have mechanisms of action (MOA) associated with them. We can then colour these nodes by their MOA.

```
MOA_classes <- unique(df_with_knownMoaDrugs$MOA)
number_of_unique_MOA <- length(MOA_classes)
colours_for_MOA_classes <- colorRampPalette(brewer.pal(12, "Set3"))(number_of_unique_MOA)
```

We have 14 different MOA classes and have used RColorBrewer to generate different colours for the different classes.

```
setNodeColorRule(new_cw,
                 "MOA",
                 MOA_classes,
                 colours_for_MOA_classes,
                 "lookup",
                 default.color = "#000000")
```

```
## Successfully set rule.
```

```
## node font looks ugly, let's turn it off for now
setDefaultNodeFontSize(new_cw,
                       0)
```

We have coloured the nodes nicely, but we do not know which ones are associated with which classes. To know more about this we will print out the legend from Cytoscape. At the moment there is no automated way to do this so we need to go into Cytoscape, click on the “Style” tab and then click on the little arrow (that has a mouseover text of “Options”). Once the menu opens there you will find a dialogue that lets you export a legend (in gif, svg, or pdf formats). Once exported we will look at the legend beside our new coloured network.