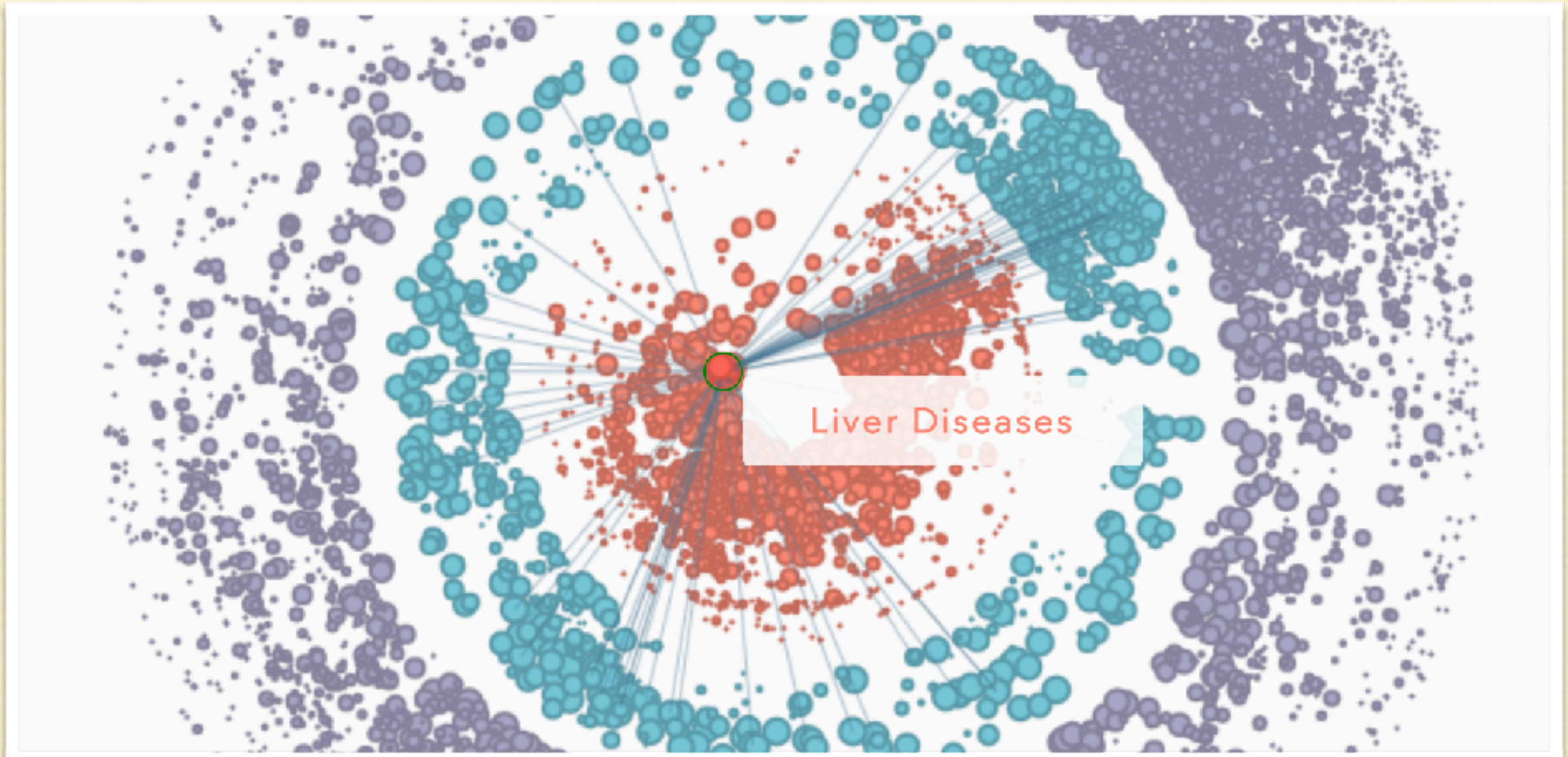
DISEASE-MIRNA RELATIONSHIPS

Alexander Liang & Matt Laws Under Dr. Nestoras Karathanasis

RStudio®



INTRODUCTION

GOAL

- Text-mining miR-Disease Relations

- Existing Models
  - HMDD (Manual)
  - miR2Disease (Manual)
  - miR2Cancer (Incomplete)

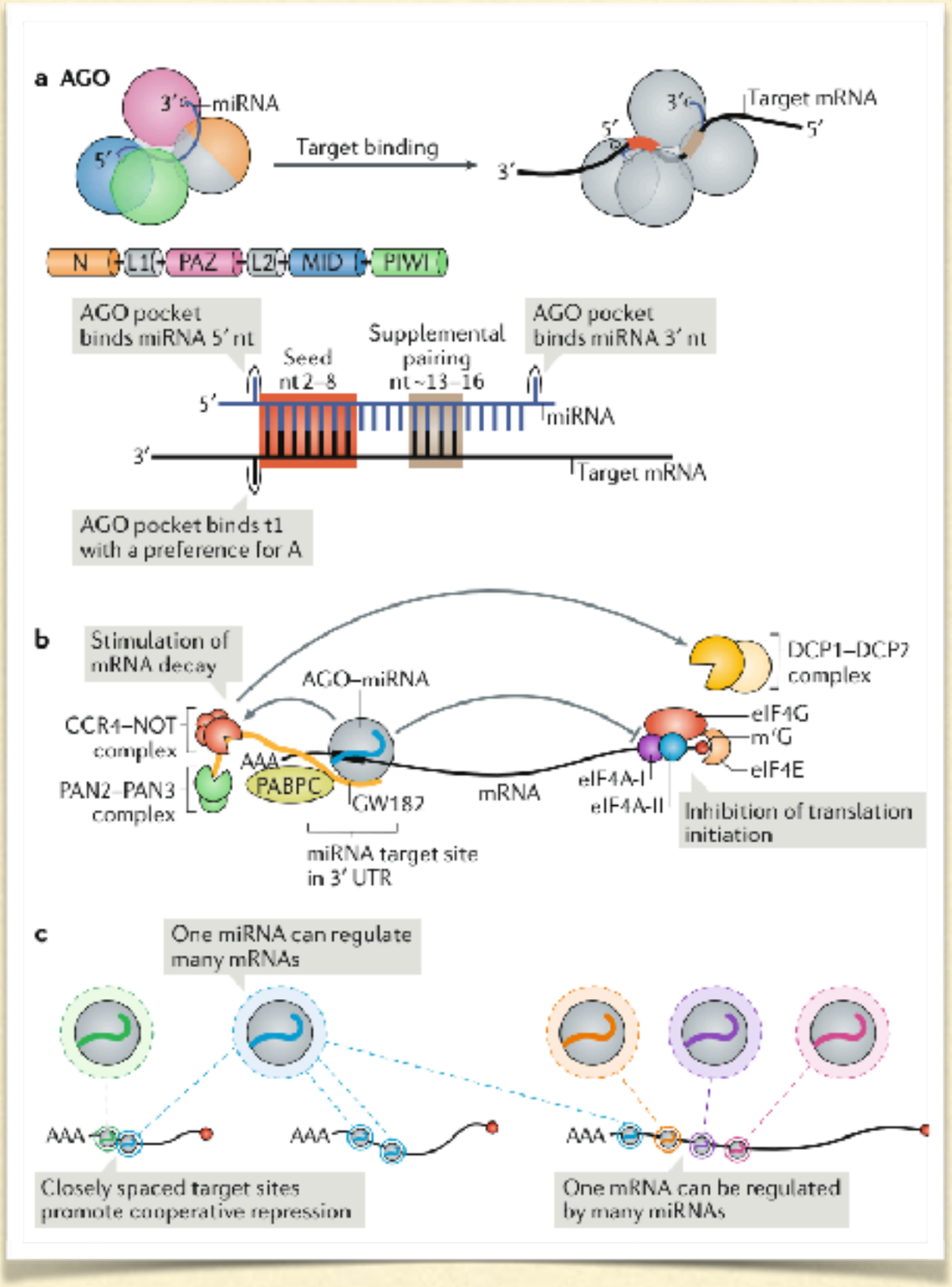
- Our Goal
  - Automatic, Efficient

PROCESS

- Understanding the Field
- Learning R
- Reading Literature
- Extracting miRNA
- Finding Relation Sentences
- Evaluating Our Findings
- Cleaning Code

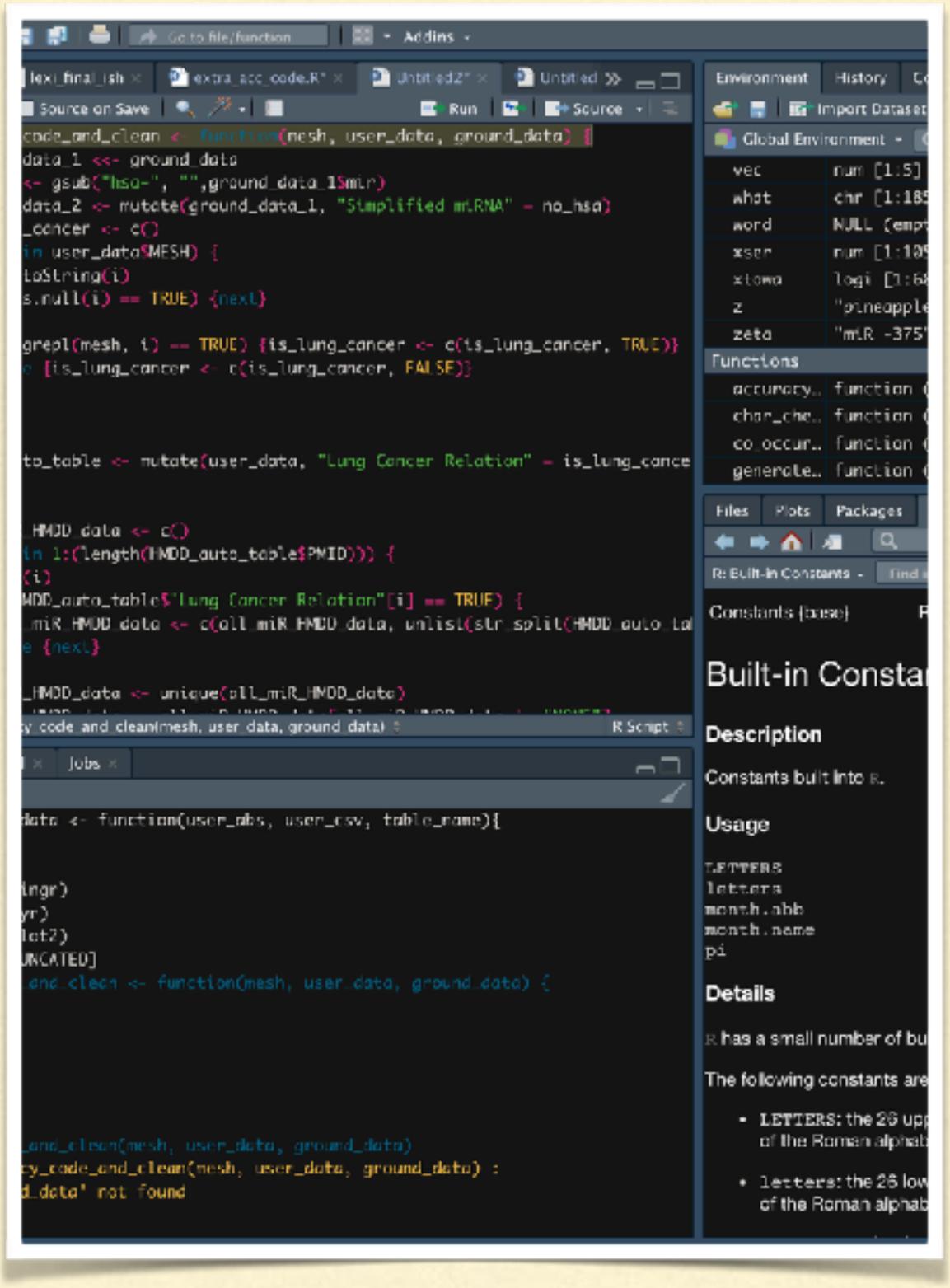
MIRNA

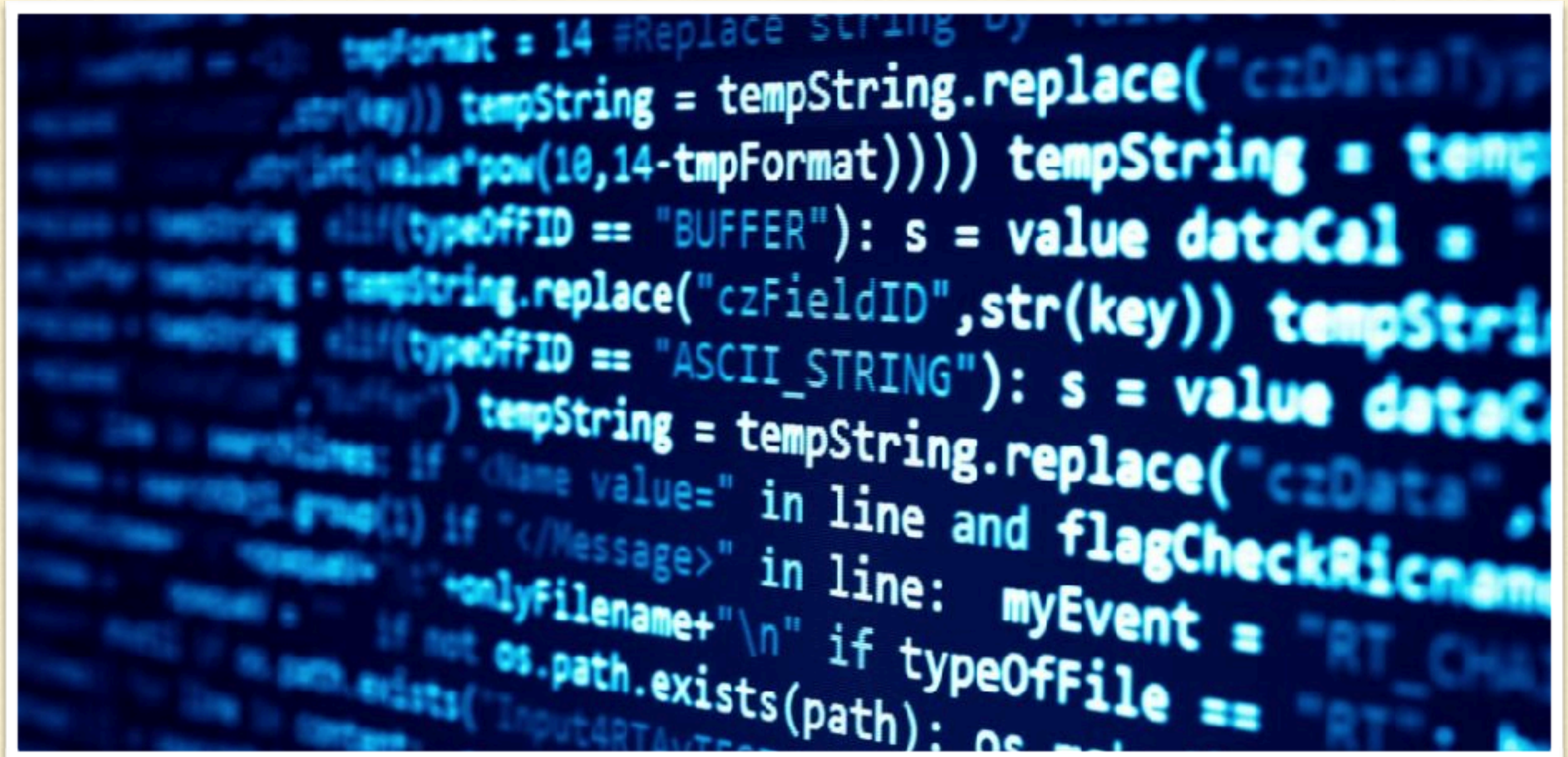
- Non-Coding Strand
- Roughly 18-28 Nucleotides Long
- Controls Gene Expression
- Dynamic Relationship With mRNAs



R Language

- Functional Oriented Language
- Data Analysis Program
- Useful Packages
- Widely Used for Bioinformatics





PROGRAMMING

PROGRAMMING

- pubmed.mineR package
- miRNA
- Disease/MeSH ID
- Relation
- Organism, Country, PMID

miRNA	Disease	Relationship
miR-21	lung cancer	CONCLUSIONS: MiR-21 expression levels in
miR-21	cancer	CONCLUSIONS: MiR-21 expression levels in
MiR-21	lung cancer	CONCLUSIONS: MiR-21 expression levels in
MiR-21	cancer	CONCLUSIONS: MiR-21 expression levels in
miR-21	lung carcinoma	*NA*
miR-21	cancer	In summary, our results suggest that miR-2
miR-21	lung cancer	In summary, our results suggest that miR-2
miR-24	lung carcinoma	*NA*
miR-24	cancer	In summary, our results suggest that miR-2
miR-24	lung cancer	In summary, our results suggest that miR-2
miR-30d	lung carcinoma	*NA*
miR-30d	cancer	In summary, our results suggest that miR-2
miR-30d	lung cancer	In summary, our results suggest that miR-2
miR-205	lung carcinoma	*NA*
miR-205	cancer	In summary, our results suggest that miR-2
miR-205	lung cancer	In summary, our results suggest that miR-2
miR-21	tumor	Our results suggest that tumor miR-21, mi
miR-21	lung cancer	*NA*
miR-21	cancer	While the level of serum miR-21 was increas
miR-21	NSCLC	Our results suggest that tumor miR-21, mi
miR-21	lymph node metastasis	Overexpression of serum miR-21 was stron
miR-200c	tumor	In addition, this study, for the first time, ide
miR-200c	lung cancer	*NA*
miR-200c	cancer	While the level of serum miR-21 was increas
miR-200c	NSCLC	In addition, this study, for the first time, ide
miR-141	tumor	Our results suggest that tumor miR-21, mi

MIRNA EXTRACTION

```
contextSearch(subsetabs(liverCancer,a), c("miRNA","mir","m
if (file.exists("companion.txt")==FALSE) {
  next #if no miRNA found, next
} else {
  rnasearch <- read_file("companion.txt")
  rnasearch <- strsplit(rnasearch," ")[[1]]
  mir <- grep("miR", ignore.case = TRUE, rnasearch, value
  mir <- paste(c(mir,grep("let", ignore.case = TRUE, rnase
```

- Extract Sentences: contextSearch()
- Extract miRs: grep()
- Clean miR List

Slashed	mir-21/mir-22	mir-21/22
Attached	mir-21-overexpressed	
Numberless	mir, miRNA, antimiR, oncomiR	
Special characters	miR-21,	(miR-21)

RELATION EXTRACTION

```
for (i in 1:length(mir)) { #for loop within fo
  for (j in 1:length(diseases)) { #for loop al
    unlink("testco_occurrence.txt")
    #search for co-occurence between one disea
    diseaseTerm <- substr(x=diseases[j], start
                          stop=which(strsplit(
    #extract MESH of disease, sometimes is "No
    if (grepl(pattern = "[[:digit:]]", disease
      MESH <- "No Data"
    } else {
      MESH <- substr(x=diseases[j], start=whic
                     stop=nchar(diseases[j]))
    }
    co_occurrence_fn(mir[i], subsetabs(liverCa
```

- Nested for loops
- Extract Sentences: co_occurrence_fn()
- Filter Sentences:
  - read_lines()
  - strsplit()
  - grep()

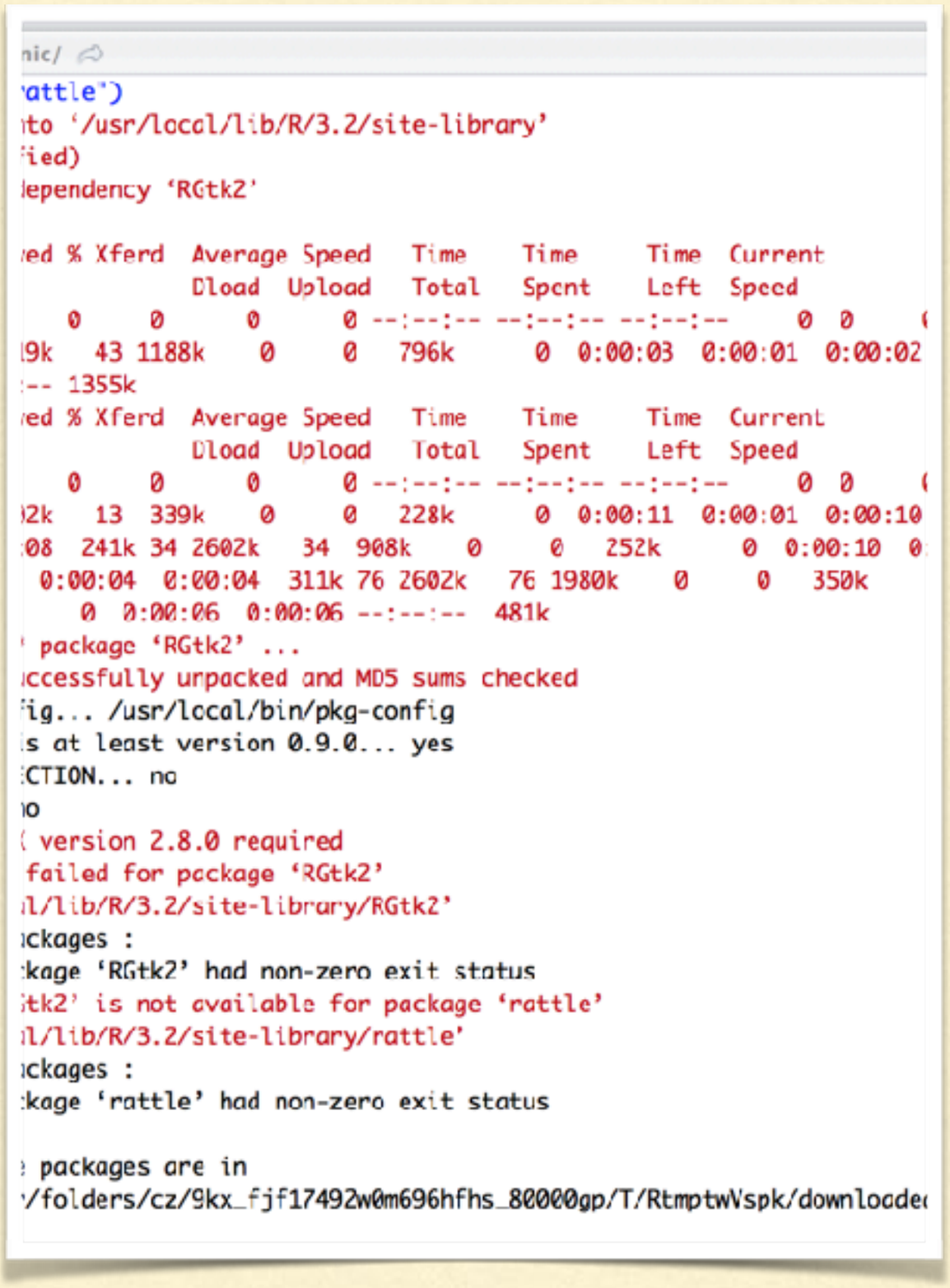
RESULTS

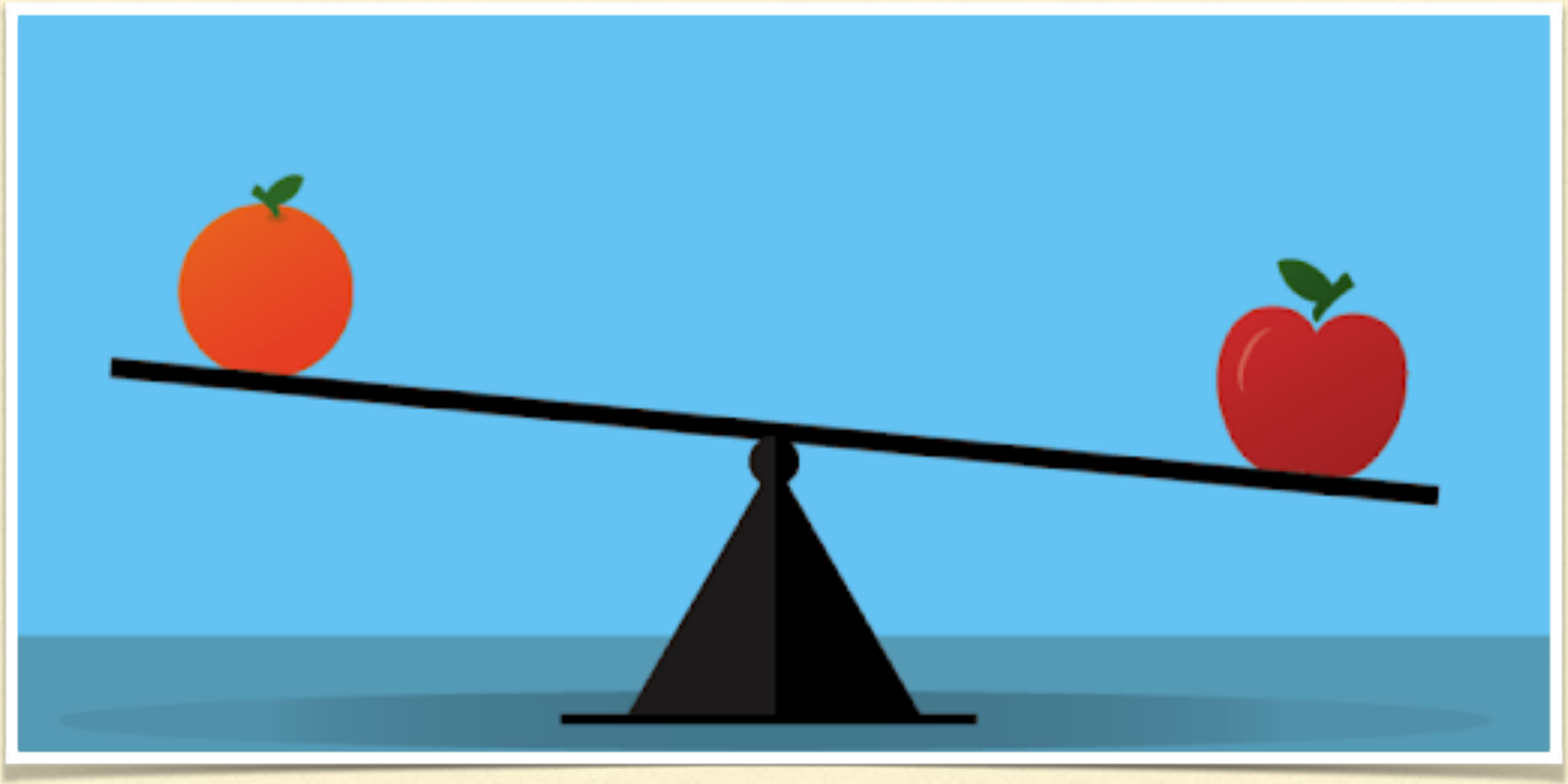
PMID	Disease	MESH	miRNA	Relation	Organism	Country
30256056	chronic hepatitis	D056487	miR-34a	So both miR-34a and miR-183 were suit...	Human	India
30256056	Cirrhosis	D005355	miR-34a	So both miR-34a and miR-183 were suit...	Human	India
30256056	chronic hepatitis	D056487	miR-183	So both miR-34a and miR-183 were suit...	Human	India
30256056	Cirrhosis	D005355	miR-183	So both miR-34a and miR-183 were suit...	Human	India
30127924	hepatocellular carcinoma	D006528	miR-122	Exosomal microRNAs (miRNAs) have bee...	Human	Japan
30127924	HCC	D006528	miR-122	Exosomal microRNAs (miRNAs) have bee...	Human	Japan
30127924	HCC	D006528	miR-122	Taken together, our results demonstrate ...	Human	Japan
30127924	tumor	D009369	miR-122	The expression levels of exosomal miR-...	Human	Japan
30127924	liver cirrhosis	D008103	miR-122	According to the median relative expres...	Human	Japan
30127924	liver cirrhosis	D008103	miR-122	Taken together, our results demonstrate ...	Human	Japan
30127924	hepatocellular carcinoma	D006528	miR-21	Exosomal microRNAs (miRNAs) have bee...	Human	Japan
30127924	HCC	D006528	miR-21	Exosomal microRNAs (miRNAs) have bee...	Human	Japan
30065664	Hepatocellular Carcinoma	D006528	mir-21	Extracellular Vesicle-Associated mir-21 ...	Human	China/Au...

- Comprehensive Data Frame
- Applicable to Multiple Diseases
- Relation & Non-Relation Versions
- Time-efficient

DIFFICULTIES

- Finding the correct package
- Filtering out smaller problems
- Combining major parts of code
- Formatting miRNAs to match HMDD





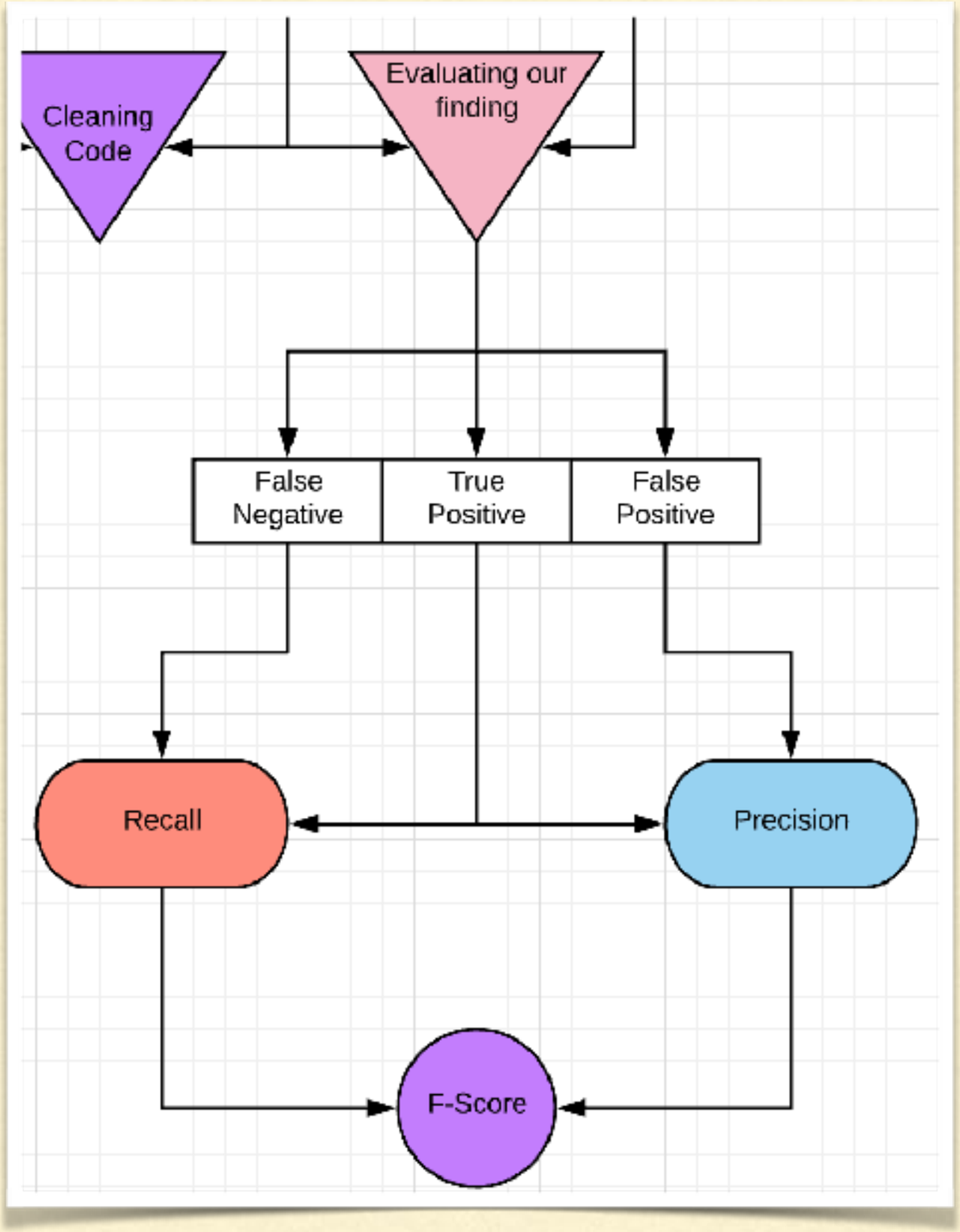
EVALUATION

METHODOLOGY

- Evaluate the significance of the findings

- Compare to existing databases

- Conclude if the data is reliable enough for use



COMPARISON

- Baseline: HMDD Abstracts
- Official **mirList** and our **mymirList**
- Expected Systematic Error

Examples of TP, FN, FP

TP: “mir-21“ in both mirList & mymirList

FN: “mir-26a” only in mirList

FP: “let-7e” only in mymirList

```
for (check in 1:length(mi
  if (any(grepl(pattern =
    TP = TP+1
    tpositive <- append(x
    next
  }
  if (all(grepl(pattern =
    FN=FN+1
    fnegative <- append(x
    next
  }
}
FP=length(mymirList)-TP
```

STATISTICS

	TP	FN	FP	RECALL	PRECISION	FSCORE
Alex Liver	**71**	**10**	**46**	**0.877**	**0.607**	**0.717**
Matt Liver	**50**	**39**	**18**	**0.562**	**0.735**	**0.634**
Alex Lung	**38**	**14**	**6**	**0.731**	**0.864**	**0.792**
Matt Lung	**31**	**25**	**12**	**0.554**	**0.721**	**0.626**

IMPROVEMENTS

PROGRAMMING

- Difficult miR keywords
  - “miR-29c/DNMTs/miR-34c\
    \449a”
  - “miR-106a/b”
- let- miR terms
- Difficult Abstracts
  - Language
- Disease & MeSH ID Matching

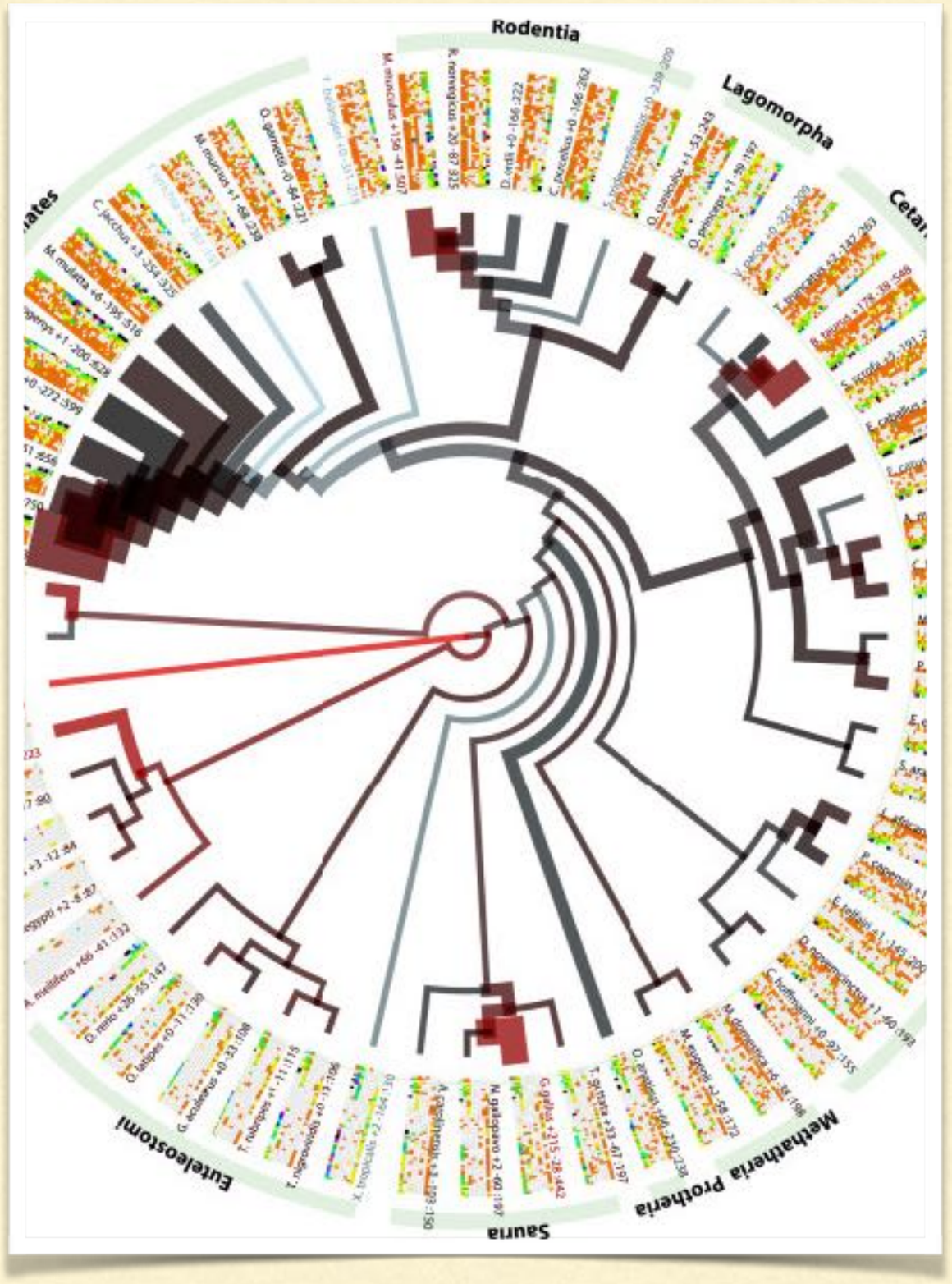
```
_check_fn <-
nction(x){allcheck <- c(letters[1:26], (
y1 <- allcheck != 'r'
_check <- allcheck[key1]

v_test <- c()
rd <- c()
r (i in x){
mirstring_split <- strsplit(i, "")[[1]]
for (j in mirstring_split){
 logic <- j == allcheck
 if (any(logic) == FALSE) {
   if (j =="r"){j="R"}
   else {j=""}}
 word <- paste(word, j, sep="")
}
new_test <- append(new_test, word)
word <- c()

v_test <- unique(new_test)
turn(new_test)
```

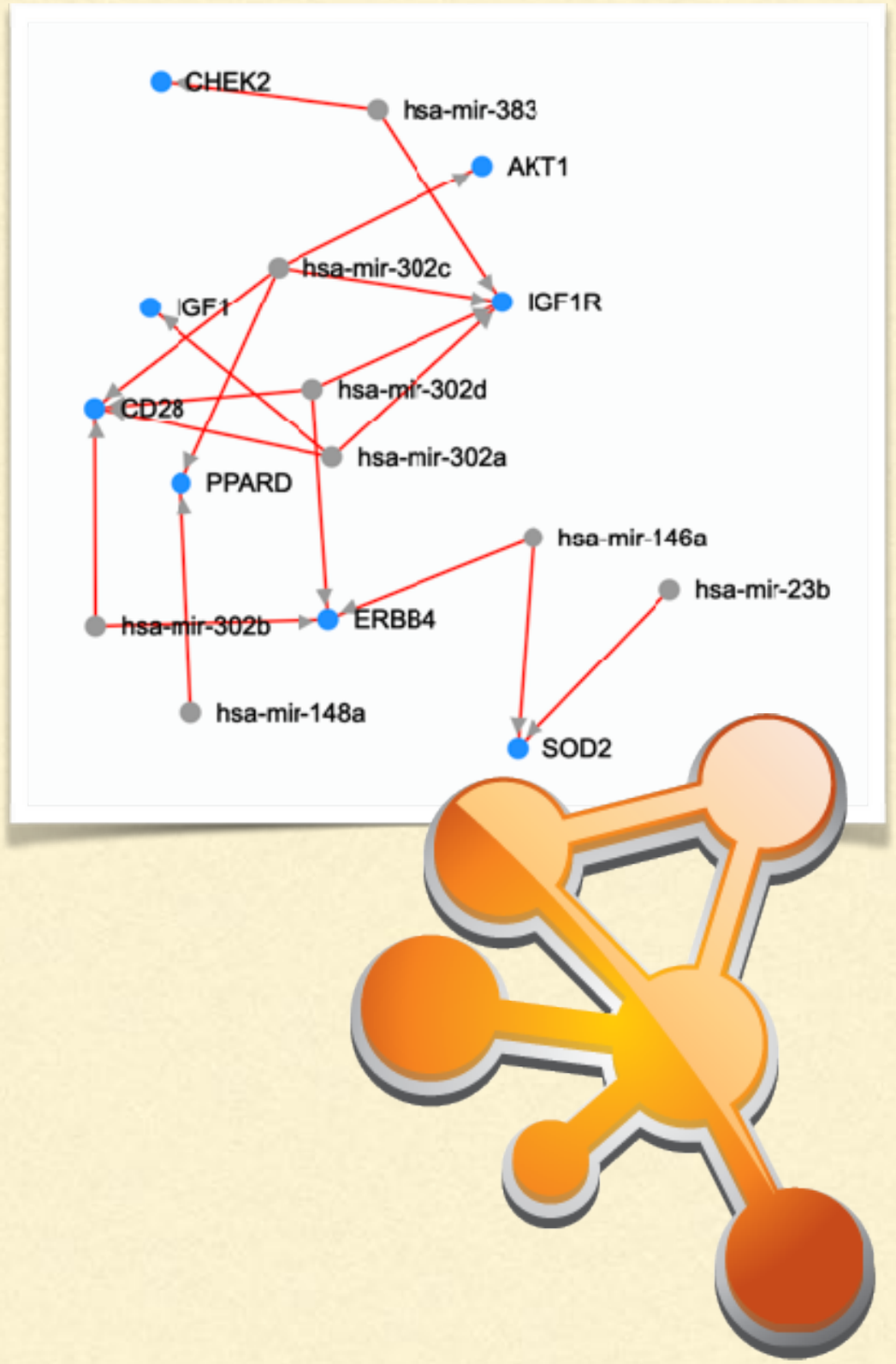
EVALUATION

- Source of False Negative
  - Paper Access
- Crosscheck Databases
- Family miRNA terms
  - “mir-1” & “mir-1-1”
  - “mir-200” & “mir-200a”
  - “mir-26a” & “mir-26a-1”



GENERAL

- Data Visualization via Cytoscape
- Online Database (HMDD)
- Relevant Data Table Features
  - Positive/Negative Relation
  - Relation Extraction Methodology



Thank you Dr. Karathanasis and the rest of the Jefferson Computational Medicine Center!

–Matt Laws & Alex Liang