## **Introducing an Outstanding Publicly Available Data Set**

Zhang B, Gaiteri C, Bodea LG, Wang Z, McElwee J, Podtelezhnikov AA, Zhang C, Xie T, Tran L, Dobrin R, Fluder E, Clurman B, Melquist S, Narayanan M, Suver C, Shah H, Mahajan M, Gillis T, Mysore J, MacDonald ME, Lamb JR, Bennett DA, Molony C, Stone DJ, Gudnason V, Myers AJ, Schadt EE, Neumann H, Zhu J, Emilsson V. **Integrated** systems approach identifies genetic nodes and networks in late-onset Alzheimer's disease. Cell. 2013 Apr 25;153(3):707-20. doi: 10.1016/j.cell.2013.03.030. PMID: 23622250; PMCID: PMC3677161.

The genetics of complex disease produce alterations in the molecular interactions of cellular pathways whose collective effect may become clear through the organized structure of molecular networks. To characterize molecular systems associated with late-onset Alzheimer's disease (LOAD), we constructed gene-regulatory networks in 1,647 postmortem brain tissues from LOAD patients and nondemented subjects, and we demonstrate that LOAD reconfigures specific portions of the molecular interaction structure. Through an integrative network-based approach, we rank-ordered these network structures for relevance to LOAD pathology, highlighting an immune- and microglia-specific module that is dominated by genes involved in pathogen phagocytosis, contains TYROBP as a key regulator, and is upregulated in LOAD. Mouse microglia cells overexpressing intact or truncated TYROBP revealed expression changes that significantly overlapped the human brain TYROBP network. Thus the causal network structure is a useful predictor of response to gene perturbations and presents a framework to test models of disease mechanisms underlying LOAD.

## Check various visualization plots used in the article!

## Multi-tissue gene expression profiles of human brain



Zhang B, Gaiteri C, Bodea LG, Wang Z et al. Integrated systems approach identifies genetic nodes and networks in lateonset Alzheimer's disease. Cell 2013 Apr 25;153(3):707-20. PMID: 23622250

This SuperSeries is composed of the following SubSeries:

GSE44768 Multi-tissue gene expression profiles of human brain (CR)

Multi-tissue gene expression profiles of human brain (PFC)

GSE44771 Multi-tissue gene expression profiles of human brain (VC)

Samples (690) 

GSE44770

GSM1090267 1 CR

GSM1090268 2\_CR

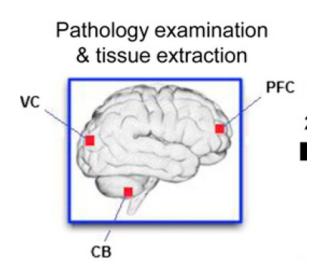
GSM1090269 3 CR

Samples:

230 CR

230 PFC

230 VC







#### Male

Four subpopulation for each tissue study

https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE44772

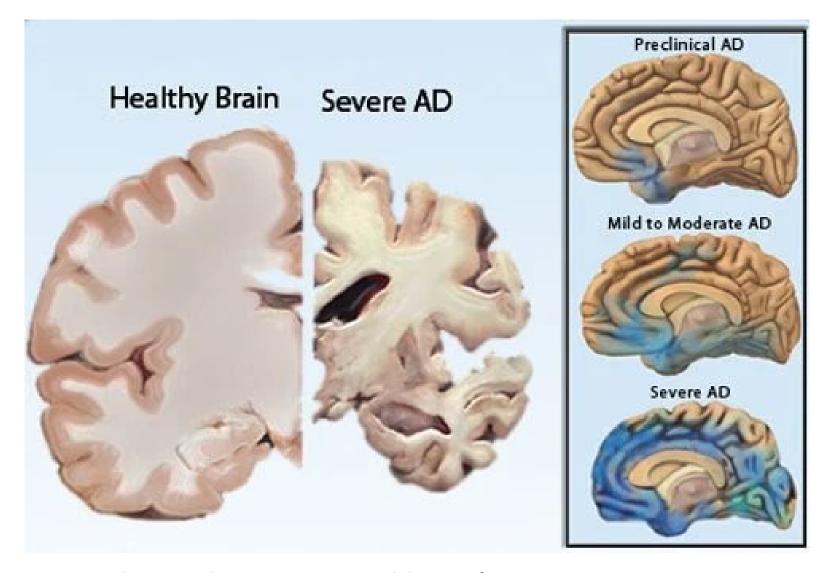
#### **Picture of Alzheimer's Disease**



Analyze mRNA gene expression data



Construct gene-regulatory networks



nd = non- disease

A = Alzheimer's





## **Quick Facts**

MORE THAN **6 MILLION**AMERICANS ARE LIVING
WITH ALZHEIMER'S. BY
2050, THIS NUMBER IS
PROJECTED TO RISE TO
NEARLY 13 MILLION.

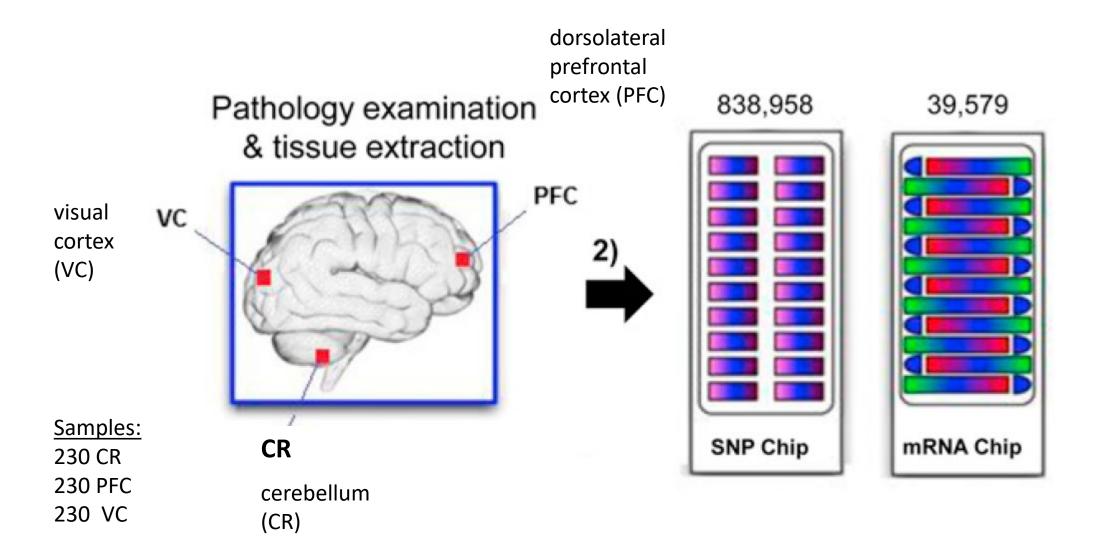
IN THE UNITED STATES,
ALZHEIMER'S AND
DEMENTIA DEATHS HAVE
INCREASED 16%
DURING THE COVID-19
PANDEMIC.

1 IN 3 SENIORS DIES
WITH ALZHEIMER'S OR
ANOTHER DEMENTIA. IT
KILLS MORE THAN BREAST
CANCER AND PROSTATE
CANCER COMBINED.

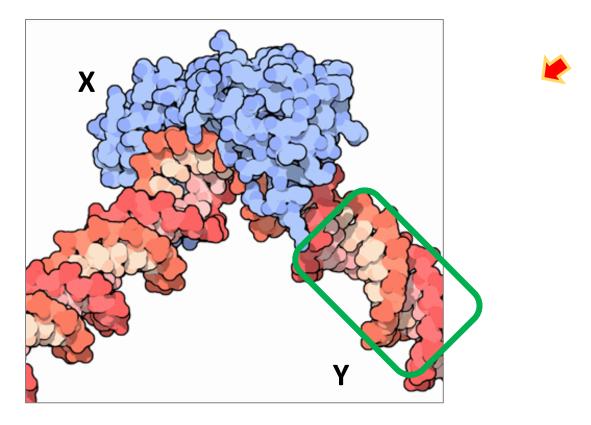
We are in the business of training next generation work force who can combat this and other human health related issues!

## Multi-tissue gene expression profiles of human brain (CR)





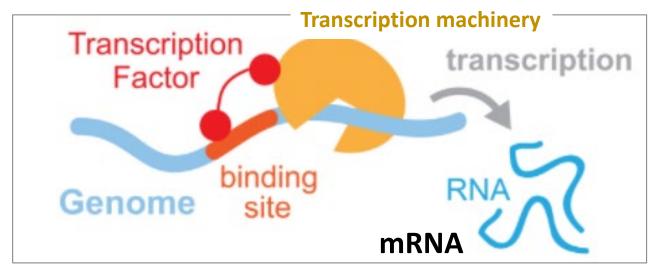
## Gene X may activate expression of gene Y. Gene X may inhibit expression of gene Y.



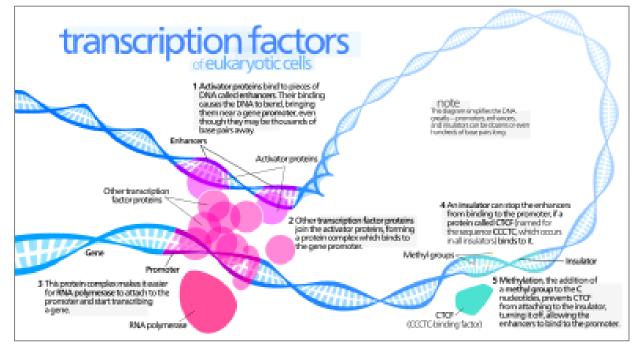
The transcription factor TATA binding protein (blue) bound to DNA (red).

Image by David S. Goodsell based on the crystal structure 1cdw from the Protein Data Bank.

http://en.wikipedia.org/wiki/Transcription\_factor



doi: https://doi.org/10.1371/journal.pcbi.1004891.g001



https://en.wikipedia.org/wiki/Transcription\_factor

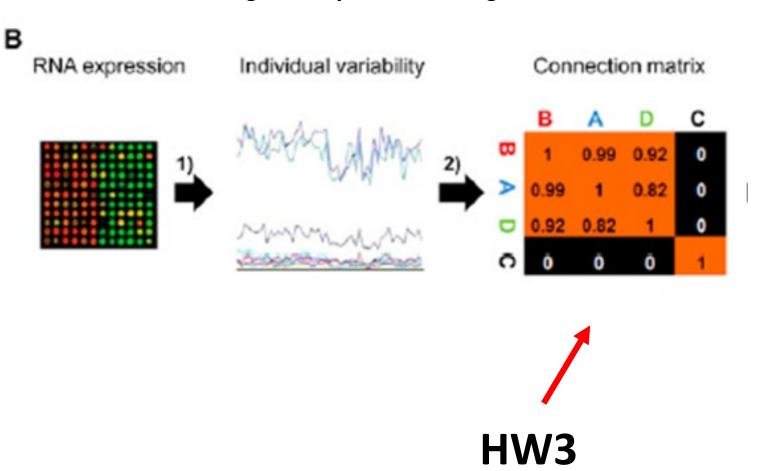
## First Step of Analysis



Construct Pearson Correlation coefficient matrix for the subset of genes of you are focusing.

#### **Example:**

node1	node2	r_val
TYROBP	DOCK2	0.927
TYROBP	FCER1G	0.885
TYROBP	GSTA4	-0.7
TYROBP	ABCC2	0.028
DOCK2	FCER1G	0.841
DOCK2	GSTA4	-0.647
DOCK2	ABCC2	0.071
FCER1G	GSTA4	0.841
FCER1G	ABCC2	0.206
GSTA4	ABCC2	-0.085



#### Available at HuskyCT Data\_Files folder.

#### mRNA intensity values in log10



4	Α	В	С	D	Е	F	G	Н	1	J	K	L	М	N	0	Р	Q	R	
1	GSM_ID	disease	age	gender	pmi	рН	rin	pres	batch	tissue	XIST	TYROBP	DOCK2	FCER1G	GSTA4	ABCC2	TIMELESS	ACBD5	LM
2	GSM1090268	Α	90	F	12.6	6.164	6.3	LNV	1	brain	0.301474	0.209515	0.161961	0.310937	-0.17929	-0.00925	0.027849	0.057428	-0
3	GSM1090271	Α	90	F	9.25	6.057	6.7	LNV	1	brain	0.460495	-0.16217	-0.0896	-0.13201	-0.01009	0.02753	-0.00782	-0.00669	-(
4	GSM1090272	Α	77	F	6.86	6.793	7.2	LNV	1	brain	0.238641	0.280428	0.313562	0.267188	-0.10473	0.130515	0.228776	-0.0761	-(
5	GSM1090274	Α	100	F	24.28	6.576	7.1	LNV	1	brain	0.276038	0.400028	0.251573	0.275051	-0.33018	0.137491	0.105215	-0.09633	-(
6	GSM1090276	Α	89	F	13.8	6.145	6.4	LNV	1	brain	0.435775	-0.29332	-0.2628	-0.13867	-0.01655	0.013355	-0.00629	-0.25949	-(
7	GSM1090277	Α	61	F	14.1	6.115	7.5	LNV	1	brain	0.245945	-0.42066	-0.35032	-0.31697	-0.14612	0.10048	0.095884	0.024655	-(
8	GSM1090282	Α	77	F	10.75	6.58	6.4	LNV	1	brain	0.440187	0.199408	-0.09561	0.384826	-0.11276	0.163864	-0.19778	-0.1274	-(
9	GSM1090284	Α	76	F	21.83	6.388	6.3	LNV	1	brain	0.366115	-0.03379	-0.09254	0.150413	0.099431	-0.01735	-0.10217	-0.04408	0.
10	GSM1090285	Α	66	F	17.58	6.452	6.4	LNV	1	brain	0.342604	-0.19143	-0.16528	-0.04182	-0.31651	0.122101	-0.02727	-0.18149	0.
11	GSM1090291	Α	89	F	7.66	6.689	7.2	LNV	1	brain	0.497142	-0.29836	-0.22498	-0.23675	0.108094	-0.0842	0.028409	-0.1799	-(
12	GSM1090292	Α	85	F	6.25	6.654	6.5	LNV	1	brain	0.346257	0.147478	0.16301	0.221962	-0.14166	0.063308	0.114311	-0.07164	-(
13	GSM1090293	Α	87	F	13.83	6.86	5.9	Dry-Ice	3	brain	0.256477	-0.05275	-0.12644	0.165657	-0.03902	0.148996	-0.00269	-0.28127	-(
14	GSM1090296	Α	90	F	6.58	6.386	6.5	LNV	1	brain	0.373623	-0.18457	-0.14394	-0.10204	-0.04138	0.090129	0.018457	-0.17351	-(
15	GSM1090297	Α	92	F	7.08	5.838	6.7	LNV	1	brain	0.44892	-0.2411	-0.17966	-0.15971	-0.06525	0.161733	0.098187	-0.09937	-(
16	GSM1090298	Α	91	F	9.58	6.29	6.1	Dry-Ice	2	brain	0.335216	-0.31143	-0.27651	-0.15292	-0.03993	0.014787	0.024292	-0.28976	-(
17	GSM1090300	Α	70	F	20	6.058	6.2	Dry-Ice	2	brain	0.245378	-0.5246	-0.44006	-0.24046	0.041687	0.021471	0.082919	-0.39599	-(
18	GSM1090301	Α	83	F	13	5.667	6.4	LNV	1	brain	0.383436	-0.20521	-0.21682	-0.07422	-0.08448	0.039032	0.033073	-0.04243	-(
19	GSM1090302	Α	75	F	10.62	6.764	6.6	LNV	1	brain	0.251072	0.151106	0.042112	0.025138	-0.25303	0.087672	-0.03997	-0.00613	-0
20	GSM1090305	Α	87	F	20.58	6.77	6.9	LNV	1	brain	0.308346	0.100023	0.103067	0.347627	0.016947	-0.01039	0.041217	-0.12216	-(
21	GSM1090307	Α	74	F	34.25	6.449	6.3	LNV	1	brain	0.508474	-0.2744	-0.27189	0.079182	-0.01166	0.086366	-0.1255	-0.31437	-(
22	GSM1090309	Δ	83	F	19 25	6 707	69	INV	1	hrain	0 354007	0 075023	n n72999	0 160714	-0 05104	-0 096	0 086144	-0 02192	n

Samples

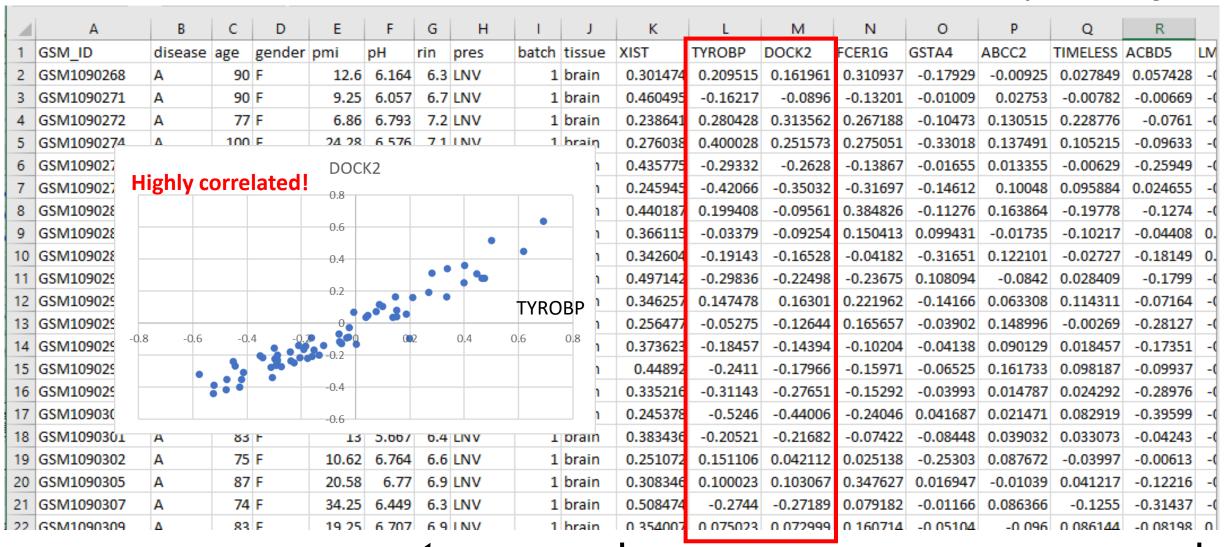
**Total 67 patients** 

RNA quality measure



#### Available at HuskyCT Data\_Files folder.

#### mRNA intensity values in log10



**Samples** 

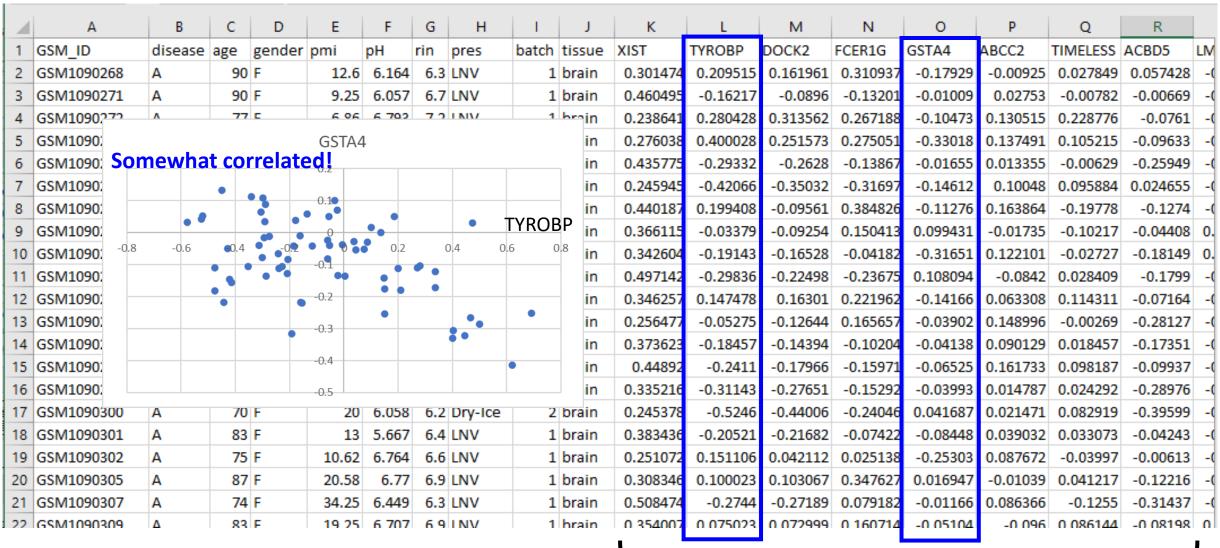
**Total 67 patients** 

**RNA** quality measure



#### Available at HuskyCT Data\_Files folder.

#### mRNA intensity values in log10



**Samples** 

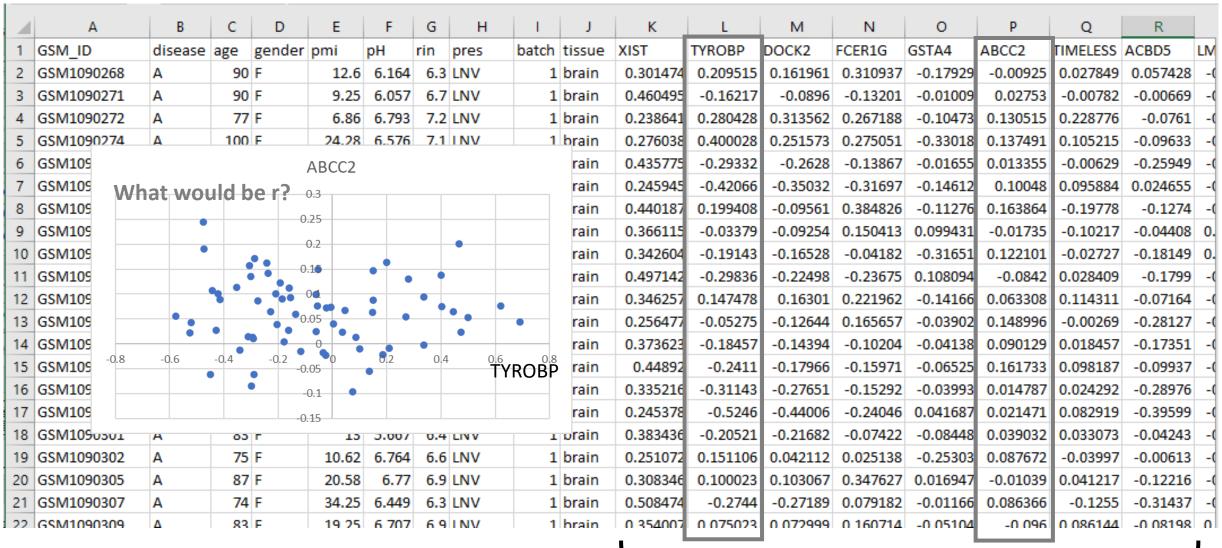
What would be r?

**Total 67 patients** 



#### Available at HuskyCT Data\_Files folder.

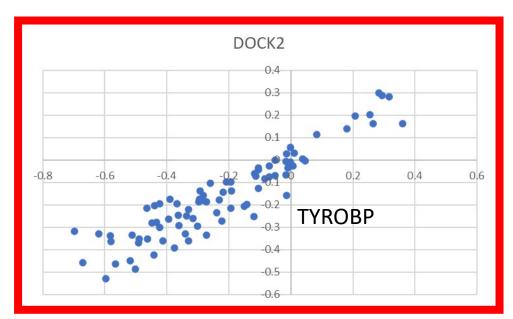
#### mRNA intensity values in log10

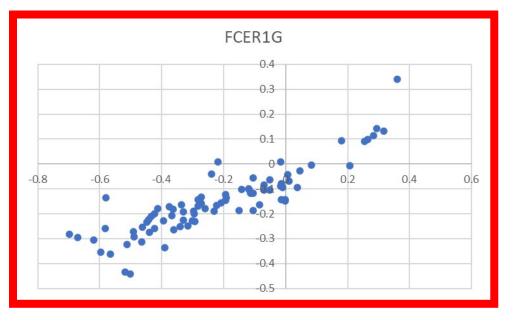


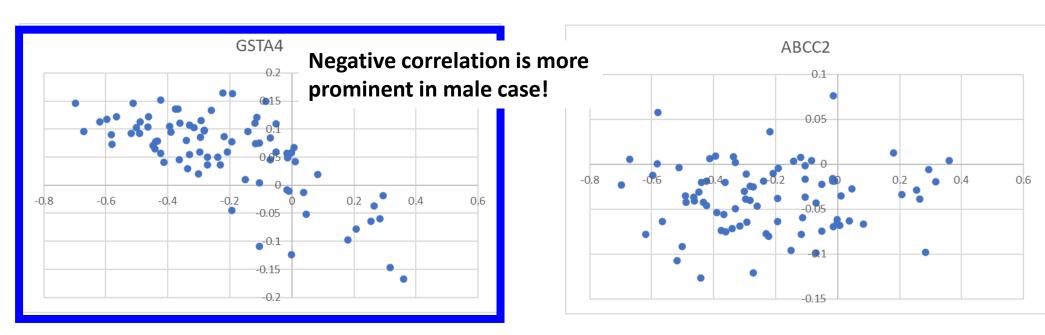
Samples

**Total 67 patients** 









## **Analysis outcome from CR nd Male** nd = non- disease Analysis outcome from CR alz female DOCK2 DOCK2 0.3 -0.8 -0.6 0.4 **TYROBP** 0.6 -0.6 GSTA4 GSTA4 -0.15 **Negative correlation is more** -0.5 prominent in male nd case!

### **Producing Heatmap from Correlation Matrix**



```
import pandas as pd
import matplotlib.pyplot as plt
import seaborn as sn

gene_names = ['XIST', 'TYROBP', 'DOCK2', ... ] # pick genes to compare.

mylist_corr_matrix = mylist.loc[:,gene_names].corr()

sn.heatmap(mylist corr matrix, annot=False)
```

Alzheimer's Female

XIST TYROBP DOCK2

XIST 1.000000 -0.222890 -0.194223 -0.202658 -0.168652 -0.162335 0.154905

TYROBP -0.222890 1.000000 0.959502 0.919214 0.746210 0.758362 -0.036335

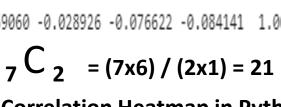
DOCK2 -0.194223 0.959502 1.000000 0.871248 0.769880 0.748357 -0.069060

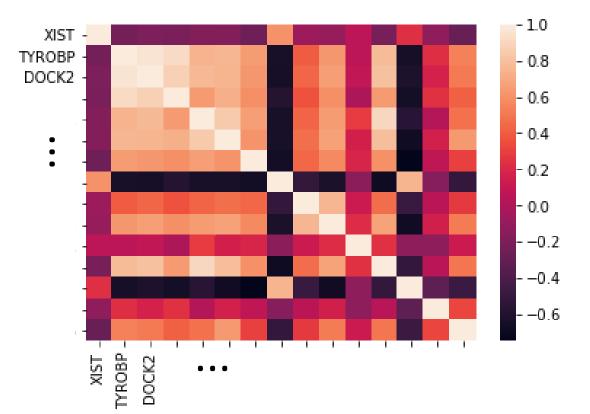
-0.202658 0.919214 0.871248 1.000000 0.644477 0.727700 -0.028926

-0.168652 0.746210 0.769880 0.644477 1.000000 0.844514 -0.076622

-0.162335 0.758362 0.748357 0.727700 0.844514 1.000000 -0.084141 0.154905 -0.036335 -0.069060 -0.028926 -0.076622 -0.084141 1.000000

plt.show()



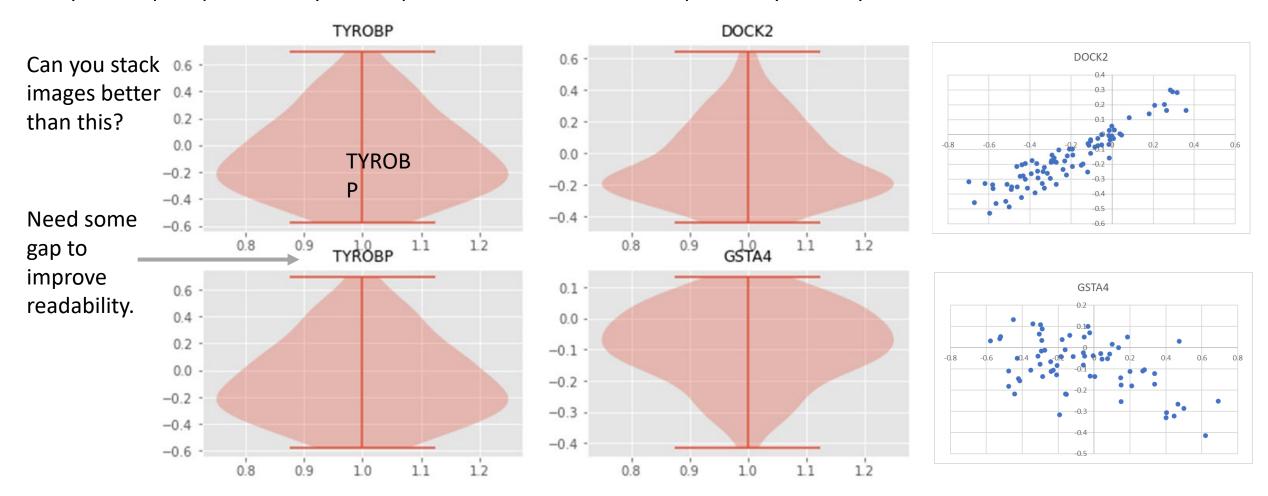


**How to Create a Seaborn Correlation Heatmap in Python?** 

## Combining multiple plots in a meaningful way.



Can you compare plots side by side, top to bottom to enhance interpretability of analysis outcome?



 $\mu$  and  $\sigma$  should be included somewhere in the plot (possibly in the title)

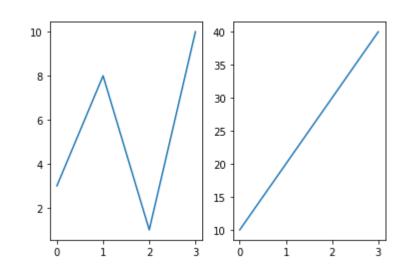
## **Display Multiple Plots**



With the subplots() function you can draw multiple plots in one figure:

#### **Example Draw 2 plots side by side:**

```
import matplotlib.pyplot as plt
import numpy as np
#plot 1:
x = np.array([0, 1, 2, 3])
y = np.array([3, 8, 1, 10])
plt.subplot(1, 2, 1)
plt.plot(x,y)
#plot 2:
x = np.array([0, 1, 2, 3])
y = np.array([10, 20, 30, 40])
plt.subplot(1, 2, 2)
plt.plot(x,y)
plt.show()
```





subplots() allows you to draw multiple plots in one figure:

```
Example Draw 2 plots:
import matplotlib.pyplot as plt
import numpy as np

#plot 1:
x = np.array([0, 1, 2, 3])
```

plt.subplot(1, 2, 1) plt.plot(x,y)

y = np.array([3, 8, 1, 10])

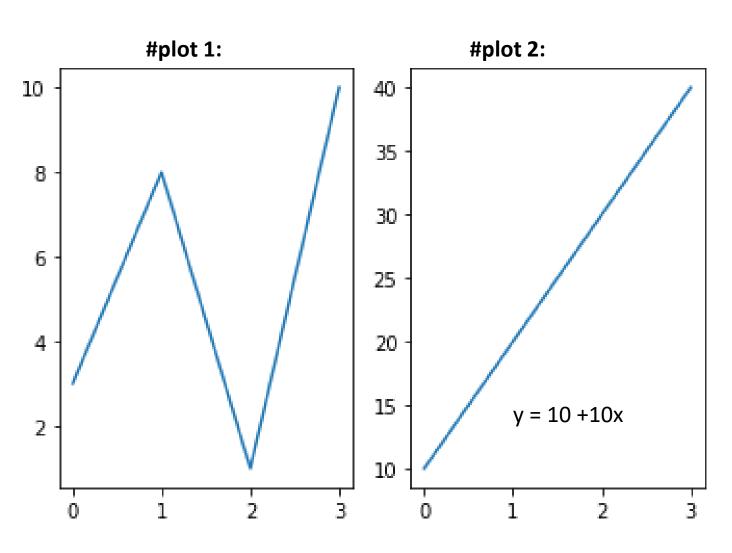
#plot 2:

x = np.array([0, 1, 2, 3])y = np.array([10, 20, 30, 40])

plt.subplot(1, 2, 2) plt.plot(x,y)

plt.show()

First two defines number of rows and columns and the third represents the index of the current plot.



#### The subplots() Function

#### What would be the plot in each case?

# plot 1:
x = np.array([0, 1, 2, 3])
y = np.array([3, 8, 1, 10])

# QUIZ??

## Can you merge related histograms in a meaningful way?

210

200

flipper\_length\_mm

220

230



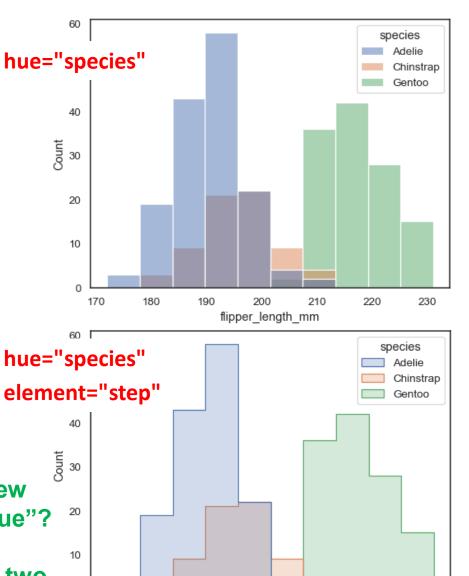
How many colors do you see in each plot?

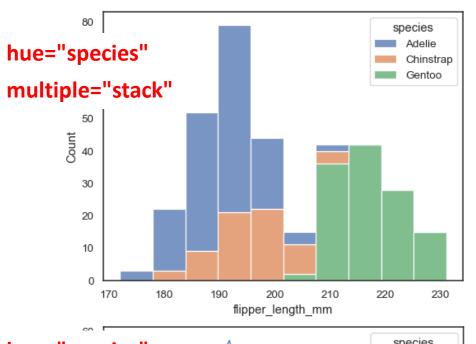
Is anyone plot more meaningful than others?

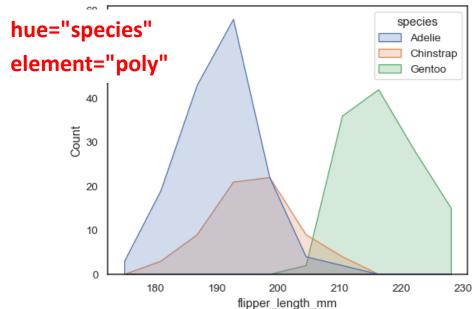
"hue" is designed to add semantics.

Should you create a new data frame and use "hue"?

Or can you just merge two histograms in one plot?



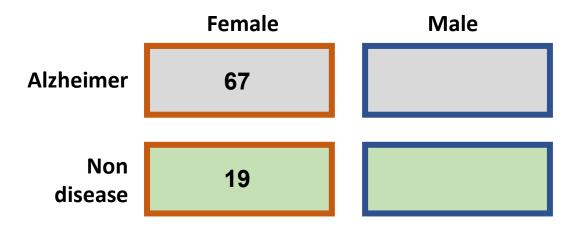




170

# Can you merge TYROBP histograms from alz female and nd female? If you do, would that comparison tell you anything?





Would you say Gene X is possibly involved in the development of Alzheimer's Disease?

