



# Obsessive Co<sup>m</sup>pulsive Dis<sub>o</sub>rder and SLC6A4

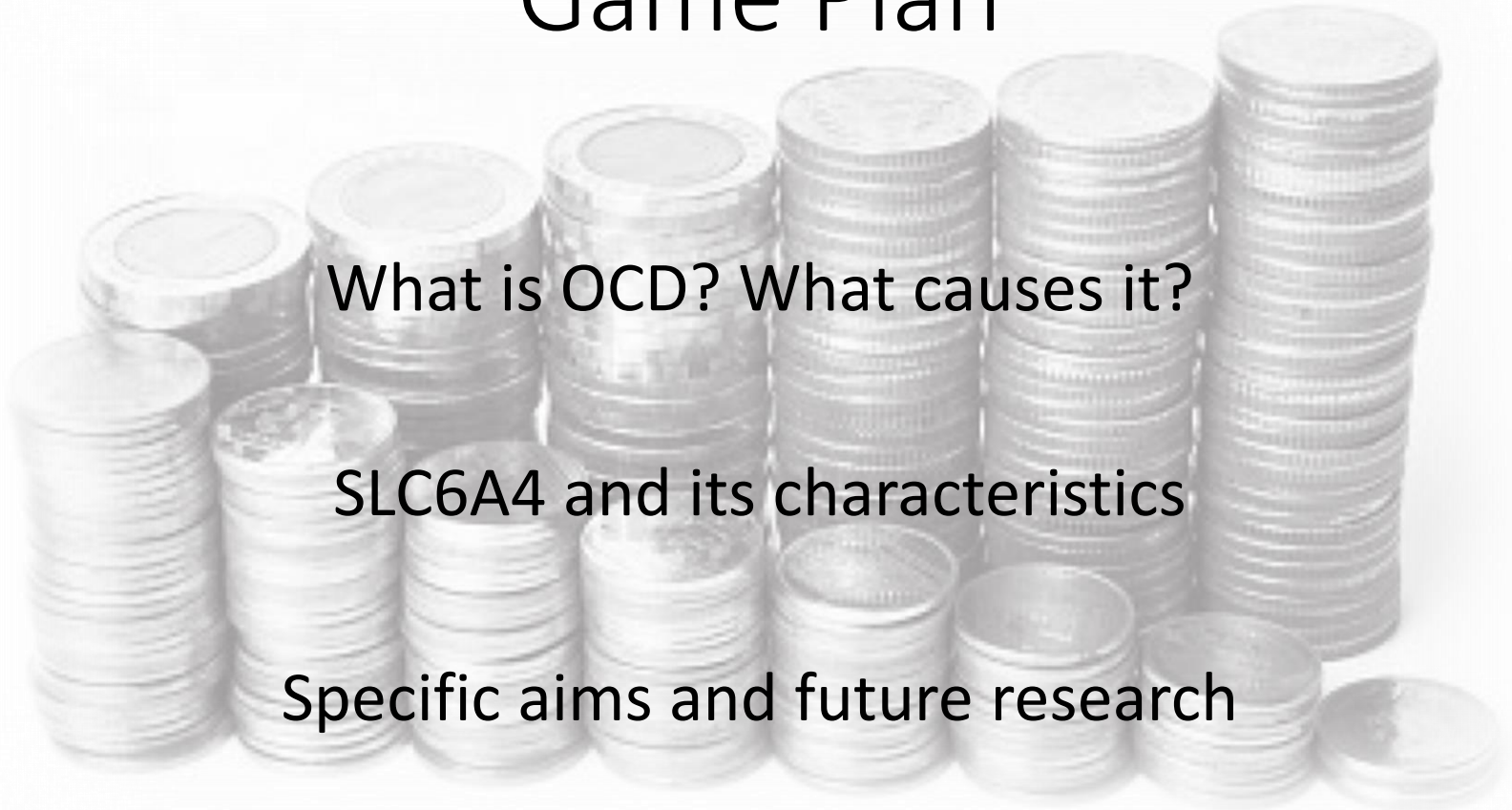
Maisie Steinbrink

# Game Plan

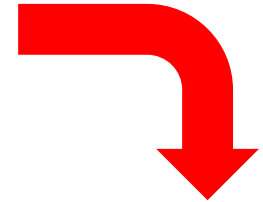
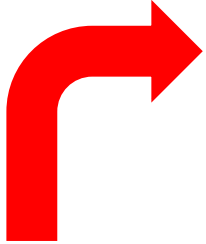
What is OCD? What causes it?

SLC6A4 and its characteristics

Specific aims and future research



Obsessions

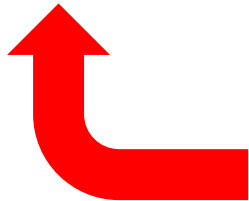


# The OCD Cycle

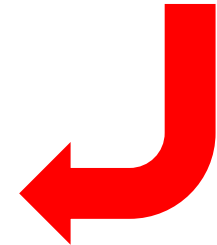


Anxiety

Relief



Compulsions



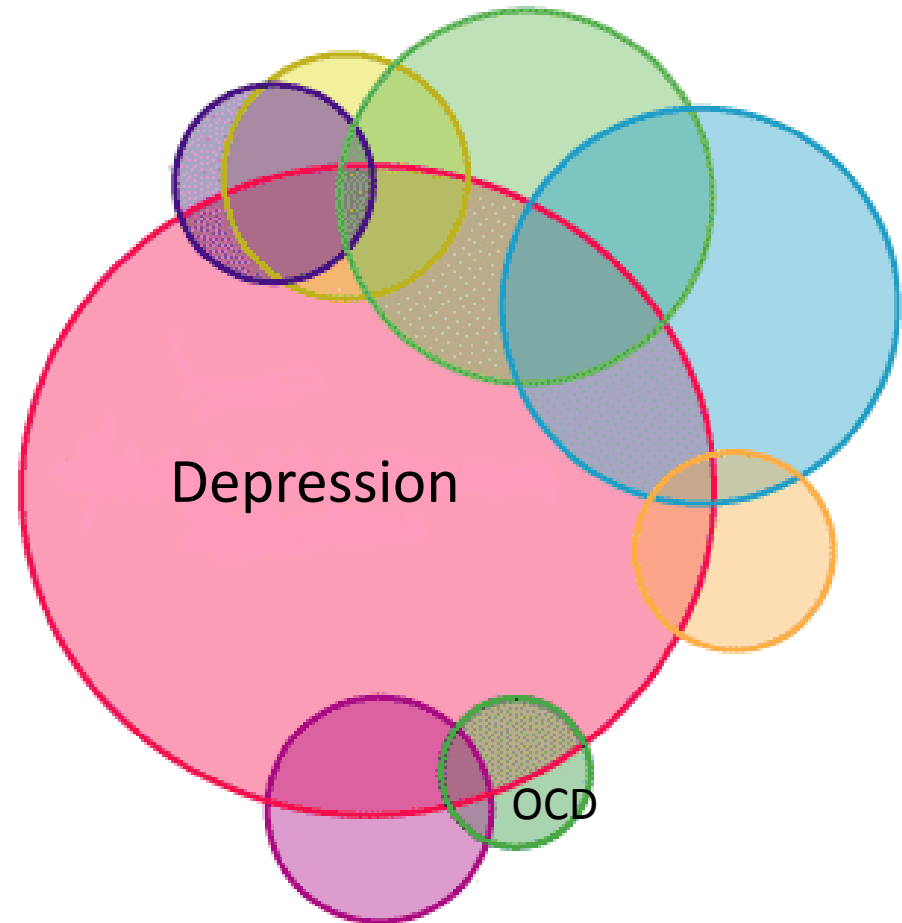
This obsession doesn't count 😊



# Why study OCD?

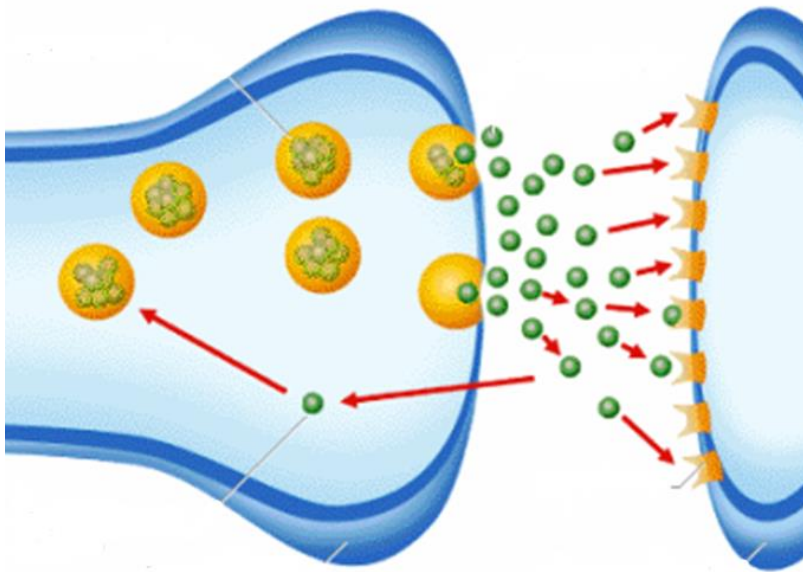
## Diagnoses

- Bipolar
- Conduct Disorder
- ADHD
- Anxiety Disorder
- Panic Disorder
- OCD
- Tourettes Syndrome

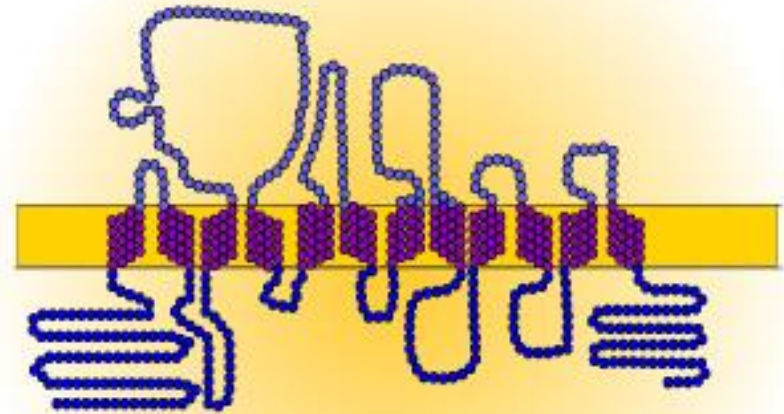


**Long-Term Goal:** Determine **complex interactions** between SLC6A4 and other proteins as they relate to development of OCD, because they will likely apply in related disorders as well.

# SLC6A4 and OCD



Extracellular

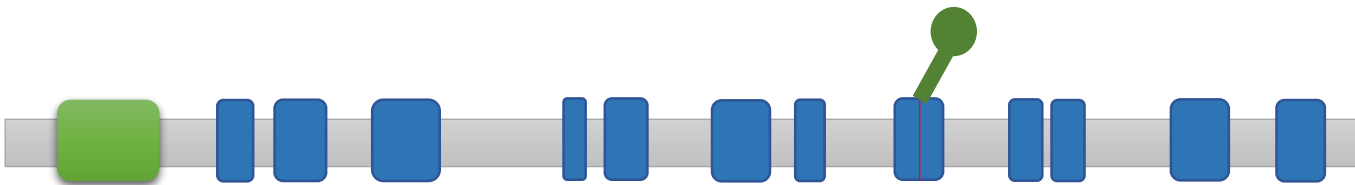
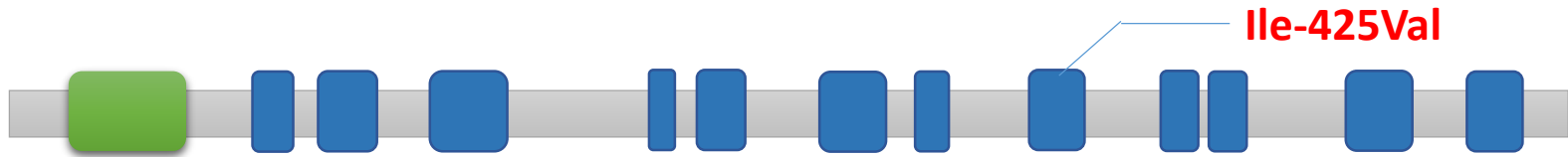


Cytoplasm

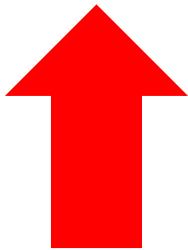
 5-HT Transport Domain

 Transmembrane Domain

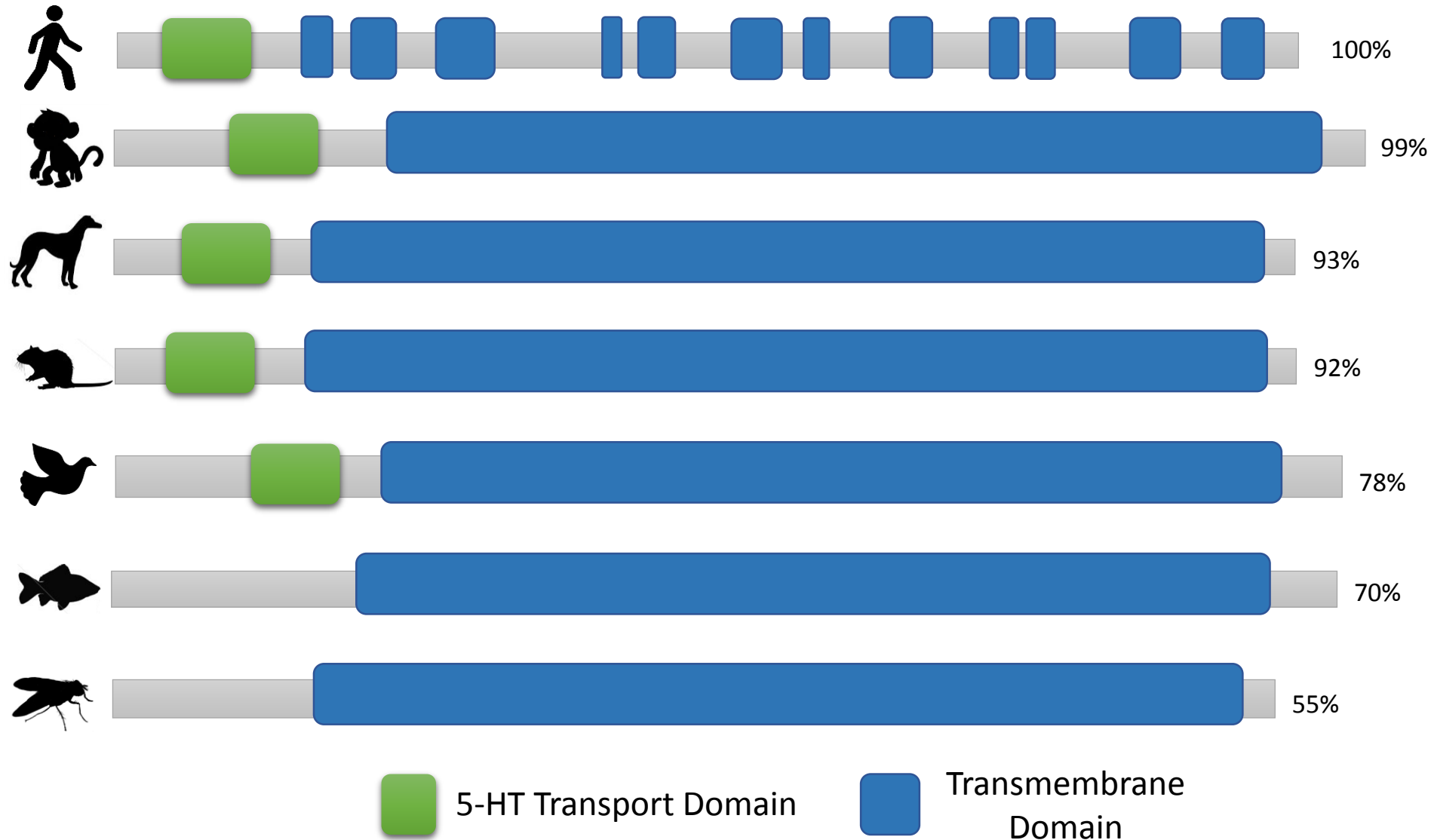
# Mutations in SLC6A4?



SLC6A4  
Activity

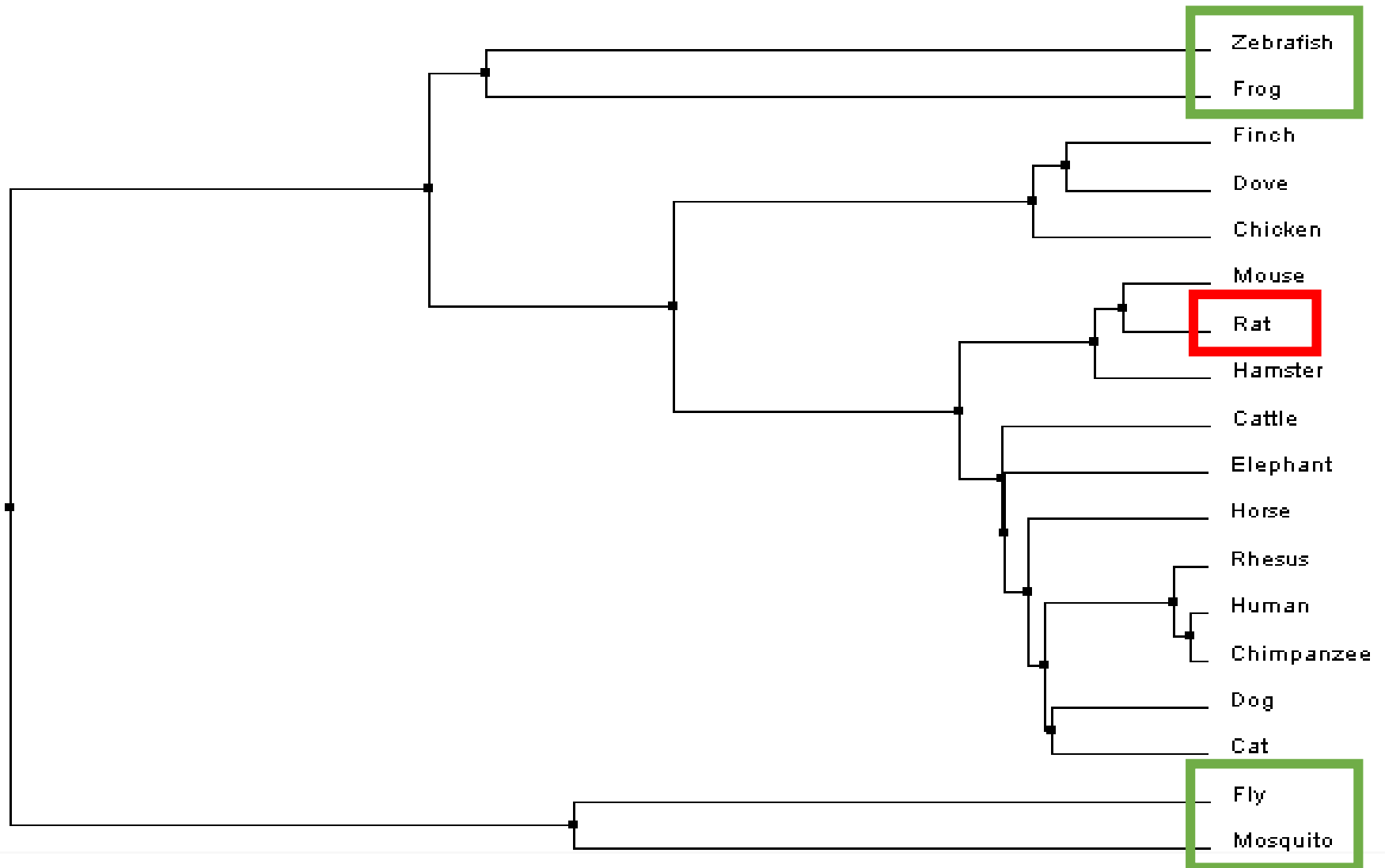


# How well is SLC6A4 conserved?

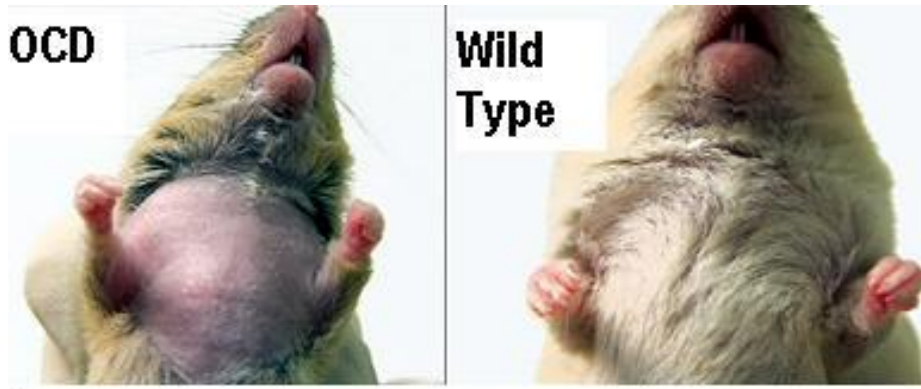
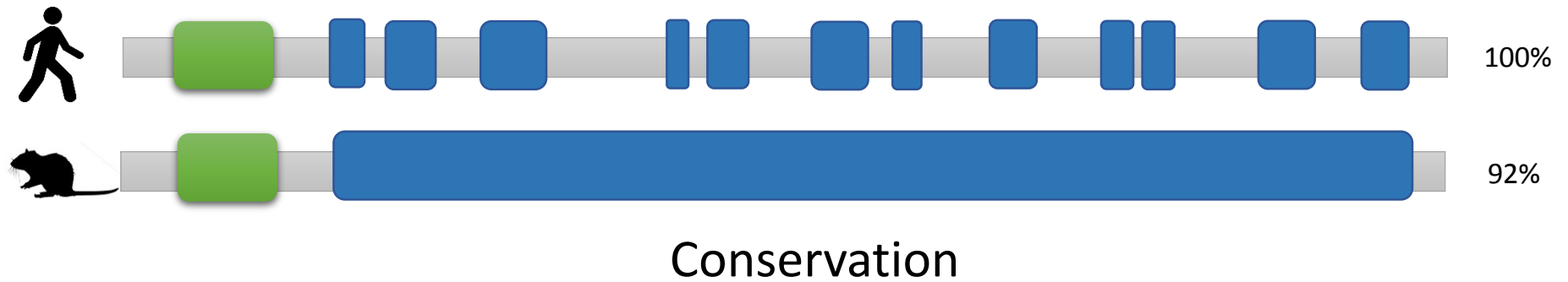




# Phylogeny



# Why use rats?

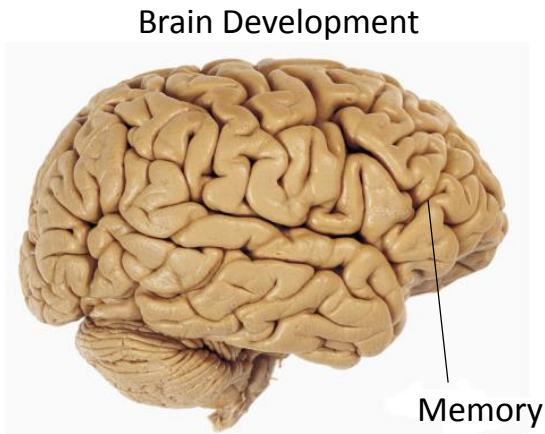


Ritualistic Grooming



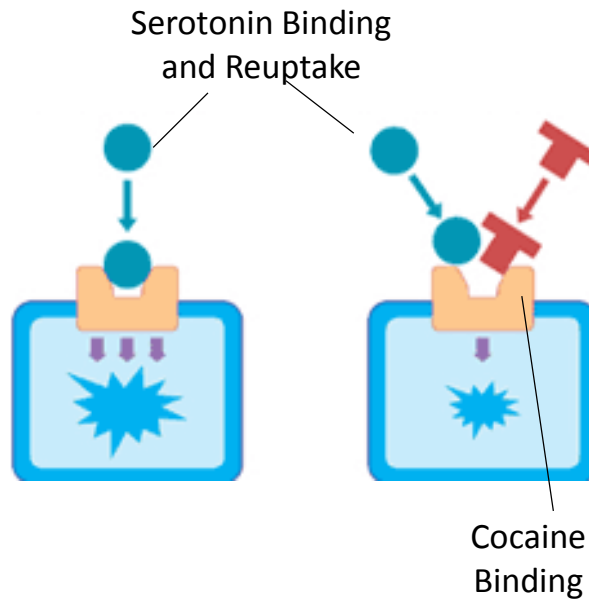
Anxiety-like Behaviors

# Characteristics of SLC6A4

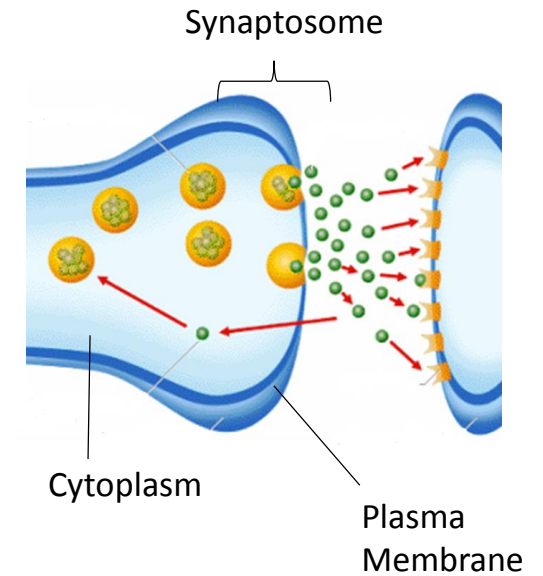


Circadian Rhythm

Biological Process

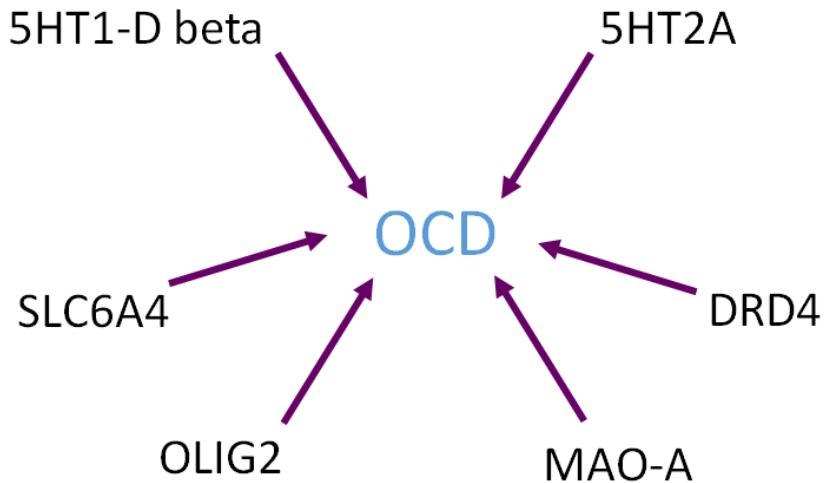


Molecular Function



Cellular Component

# But there is still a long way to go...

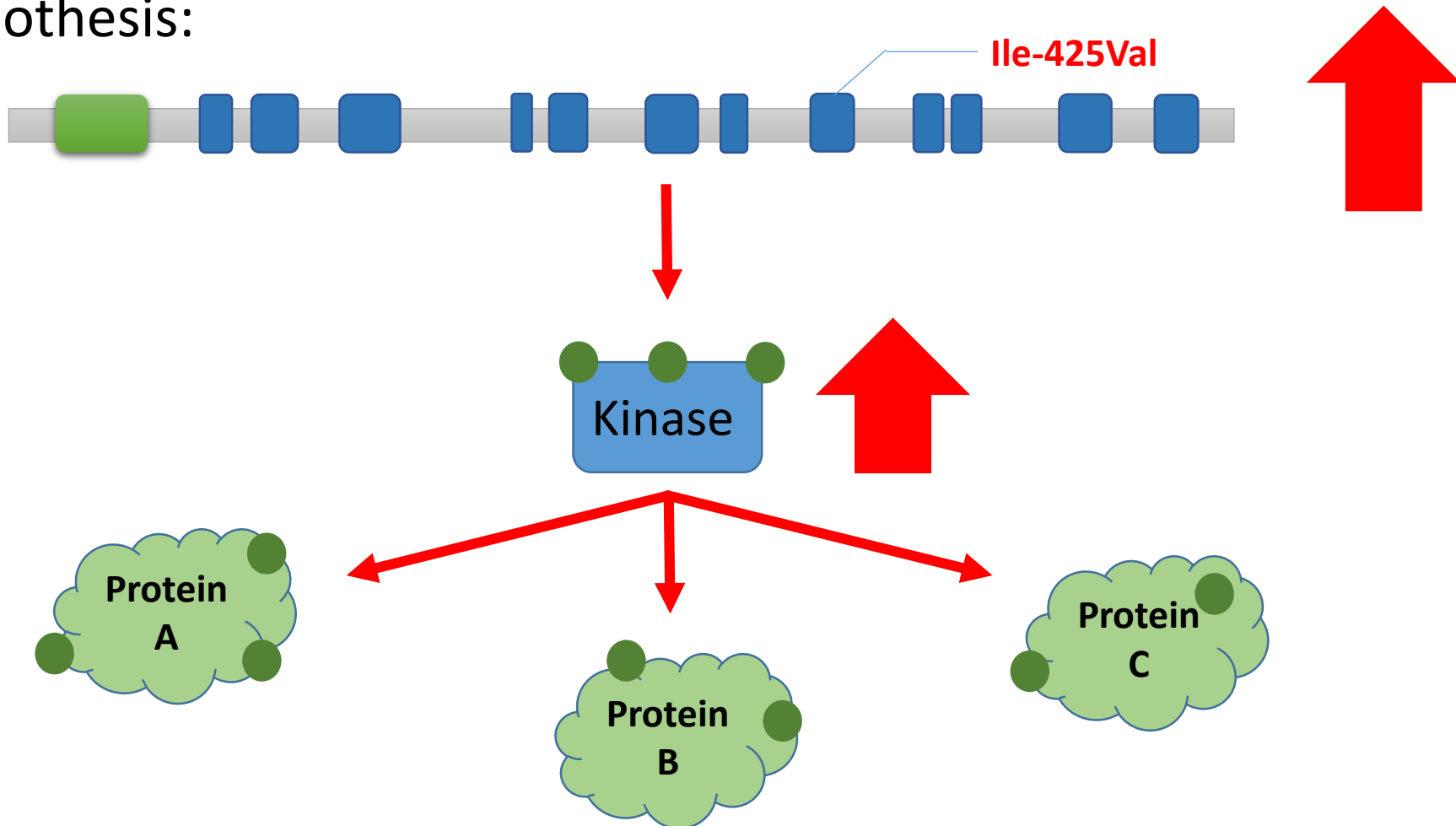


OCD is **polygenic**

Environmental factors  
- heritability 0.5

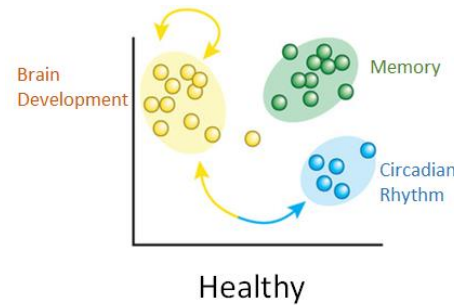
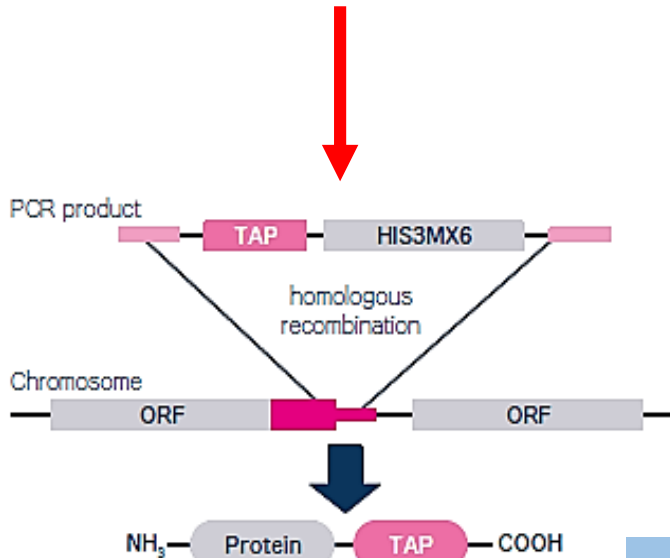
**Primary Goal:** Determine how **over-expression of SLC6A4** affects other proteins involved in the development of OCD.

Hypothesis:



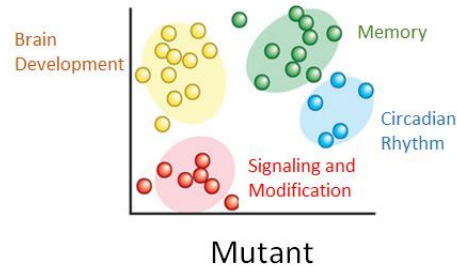
# Aims roadmap

**Aim 1:** Identify novel and conserved SLC6A4 interacting proteins



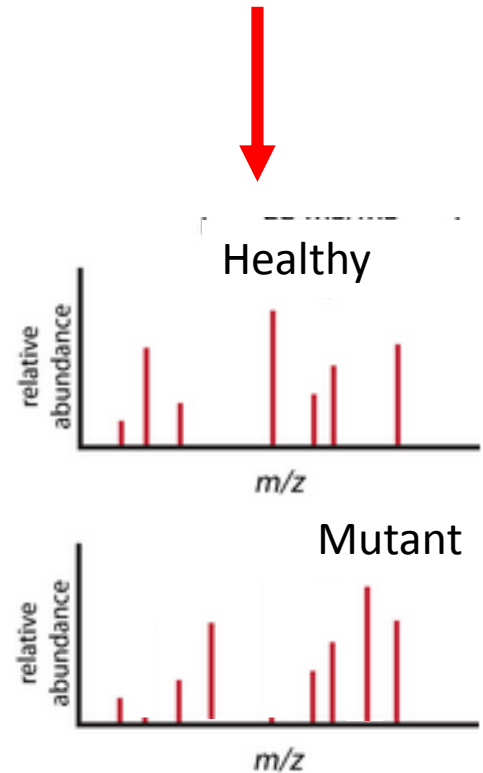
Healthy

Vs.



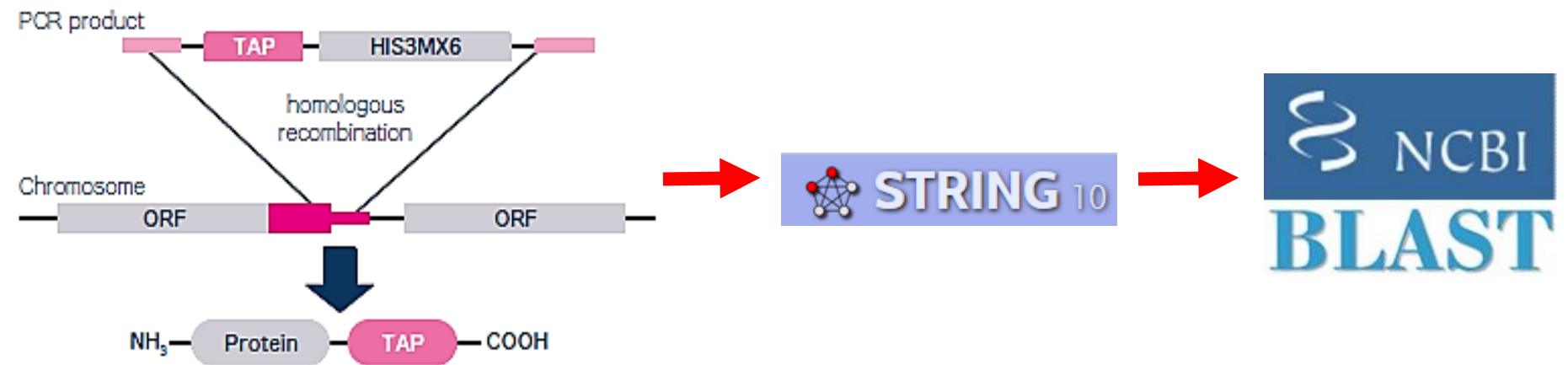
Mutant

**Aim 3:** Identify alternatively phosphorylated proteins due to interactions with kinases



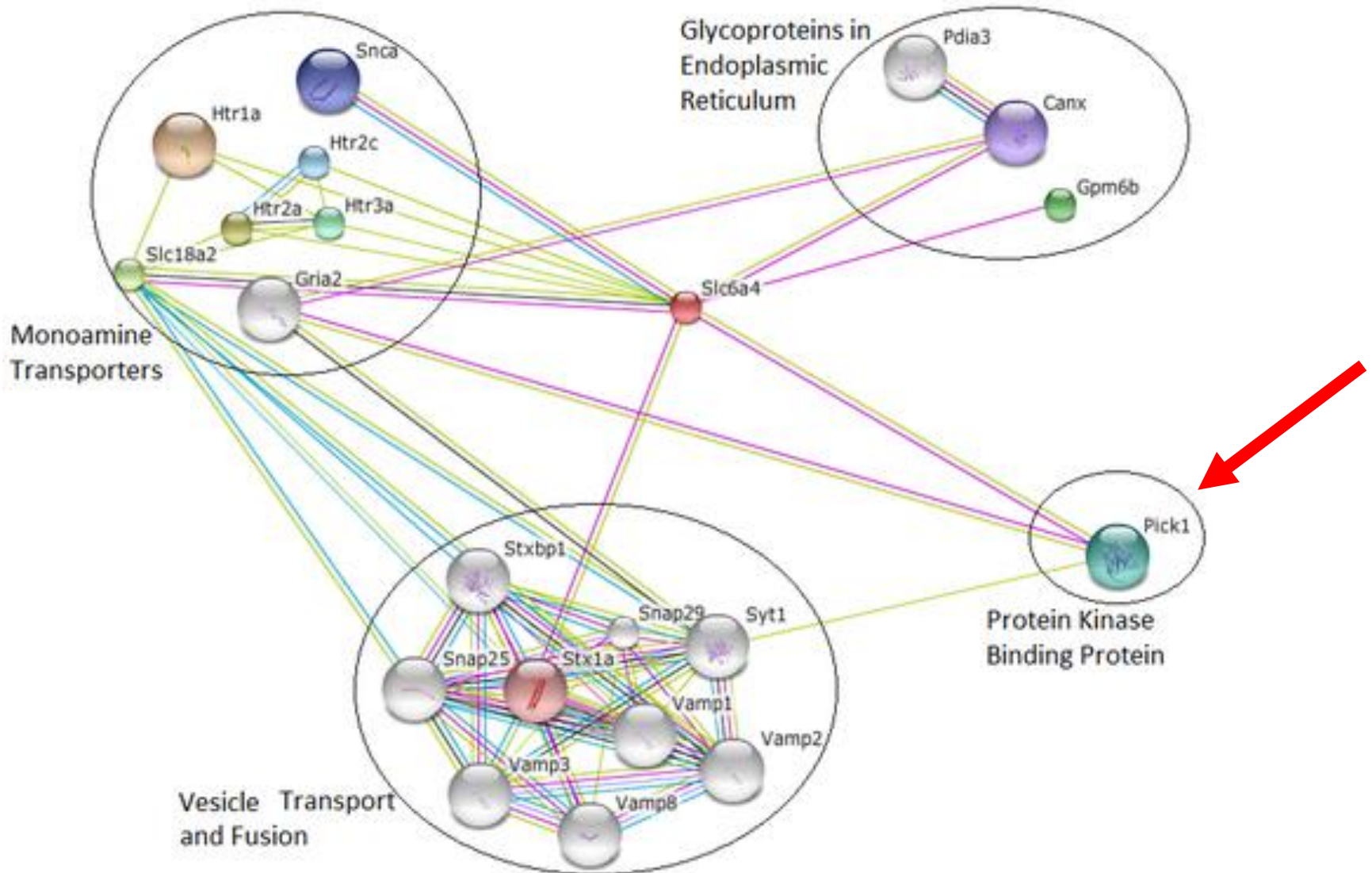
**Aim 2:** Identify genes that are misregulated in SLC6A4 mutant rats

# Aim 1: Identify novel and conserved SLC6A4 interacting proteins



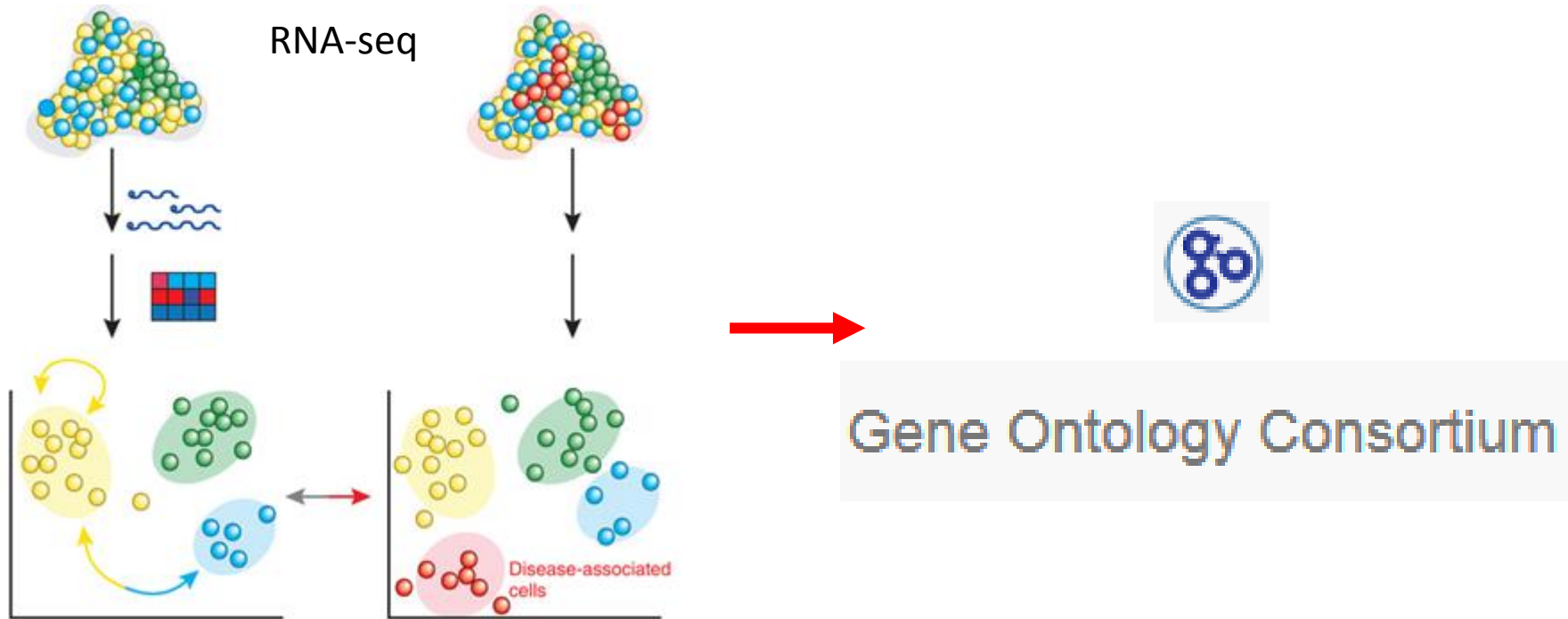
**Hypothesis:** New interactions found will add several protein kinases to the rat STRING network

# Potential outcomes Aim 1?



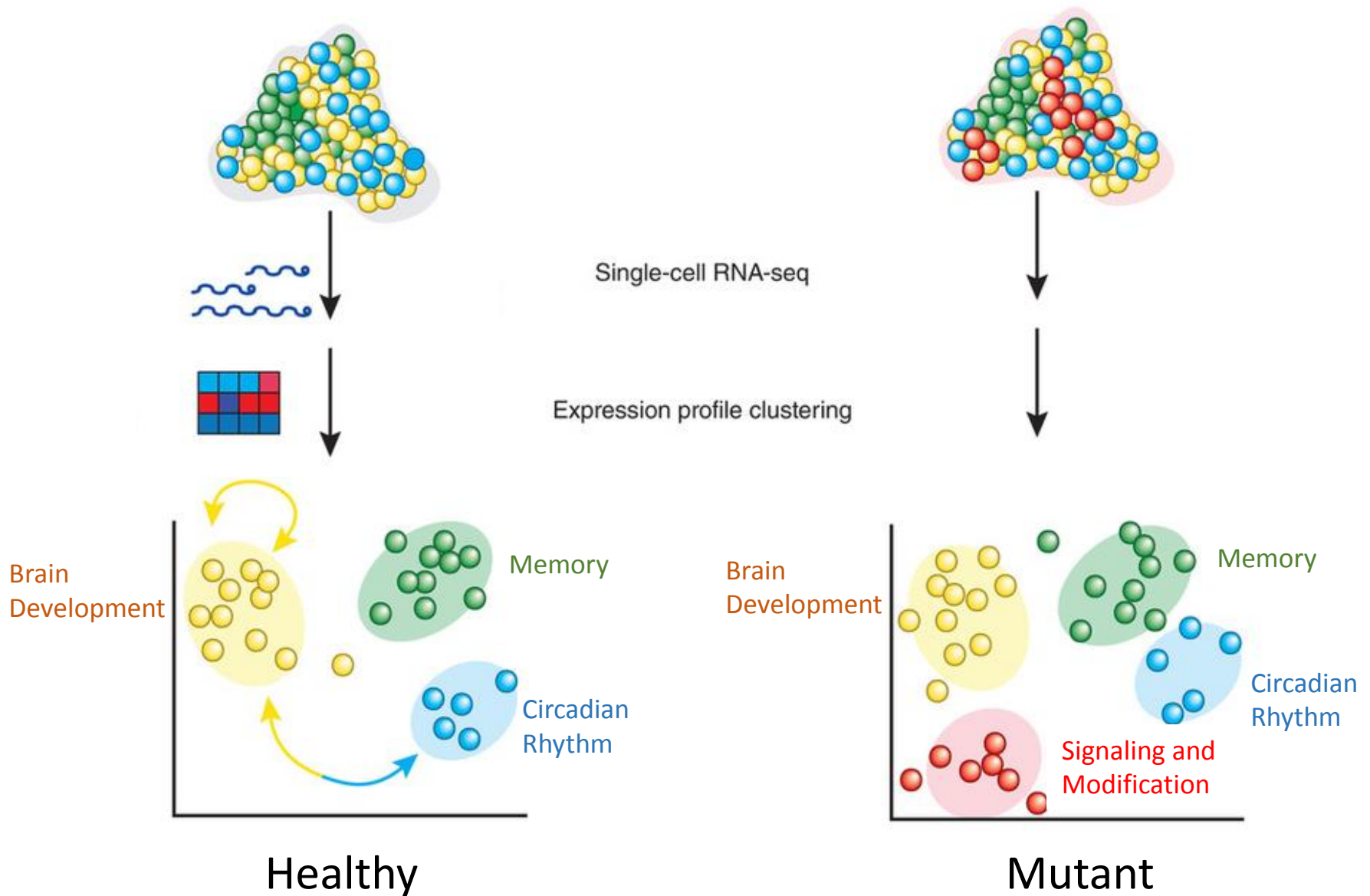


## Aim 2: Identify genes that are misregulated in SLC6A4 mutant rats

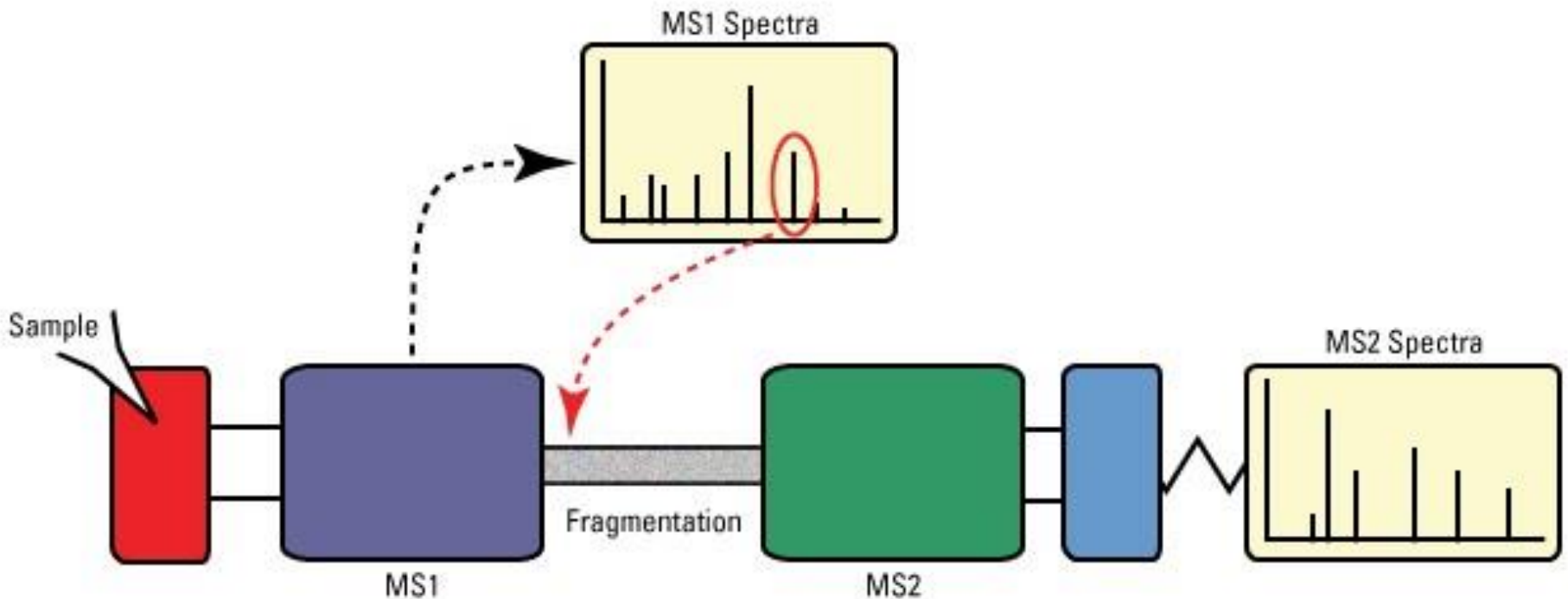


**Hypothesis:** Genes linked to signaling and modification GO terms will be over-expressed in SLC6A4 mutant rats

# Potential outcomes of Aim 2?

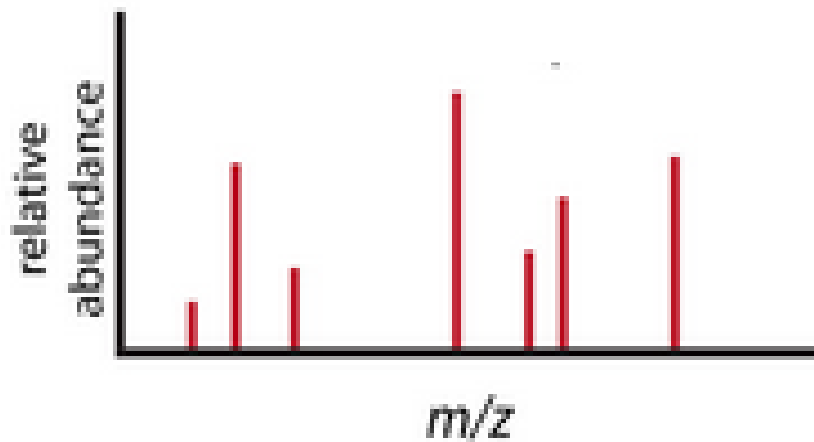


# Aim 3: Identify alternatively phosphorylated proteins due to interactions with kinases

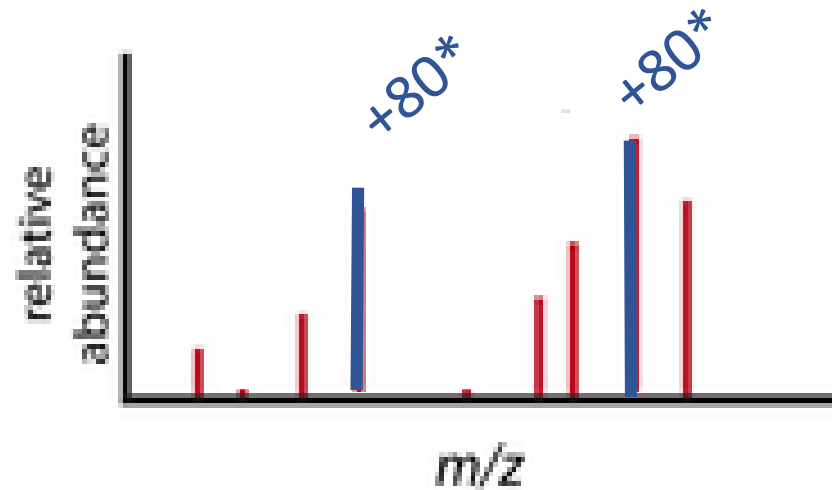


**Hypothesis:** Several proteins that interact with the kinases from Aim 2 will exhibit over-phosphorylation in the mutant sample

# Potential outcomes of Aim 3?



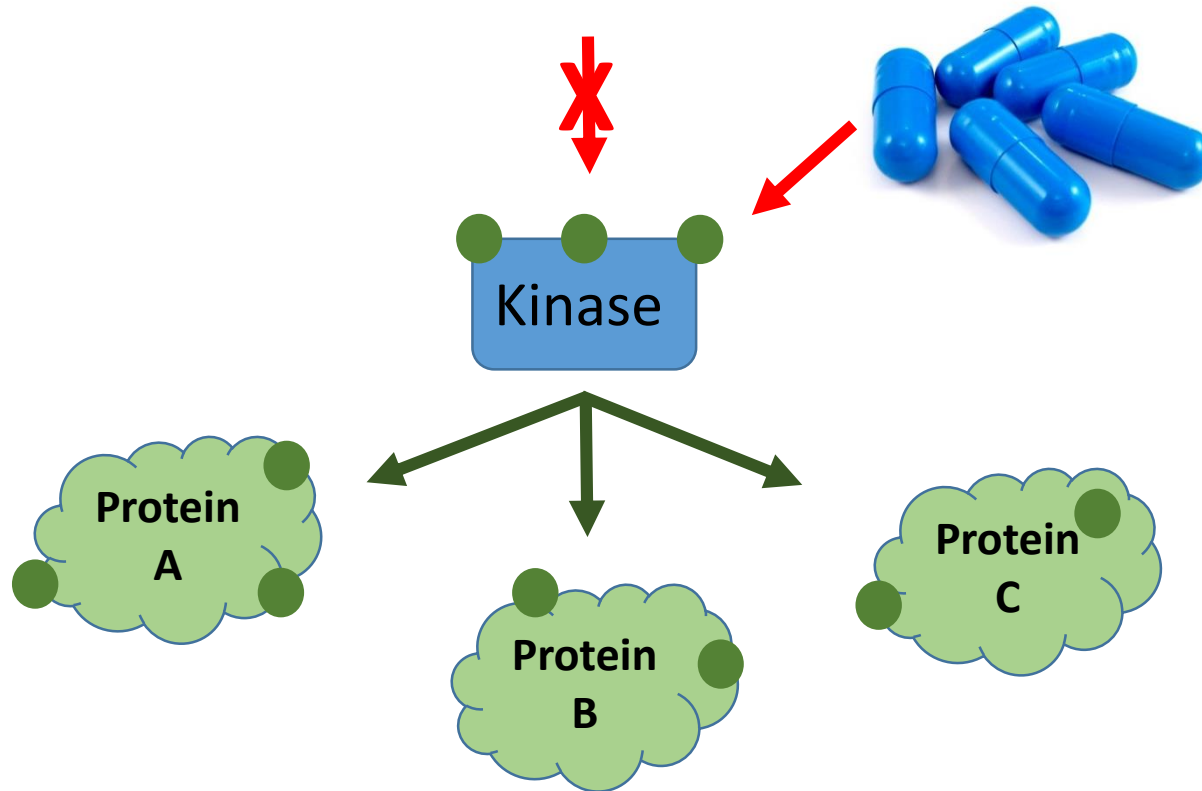
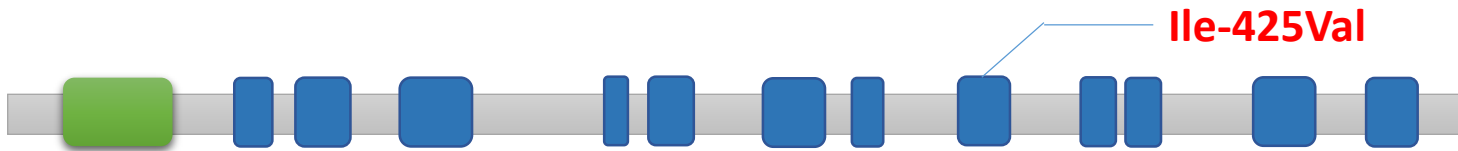
Healthy



Mutant

\*Molecular Weight of Phosphate Group = 80 g/mol

# Future Directions?



# References

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- [6] Ramamoorthy, S., Shippenberg, T., & Jayanthi, L. (2011). Regulation of monoamine transporters: Role of transporter phosphorylation. *Pharmacology & Therapeutics*, 129(2), 220-238. Retrieved April 14, 2015, from <http://www.sciencedirect.com/science/article/pii/S0163725810001932>
- [6] STRING: <http://string-db.org/>
- [7] BLAST: <http://blast.ncbi.nlm.nih.gov/Blast.cgi>
- [8] Gene Ontology Consortium: <http://geneontology.org/>

## Pictures:

<http://painmuse.org/?p=345>  
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