



Abigail Jaquish



WISCONSIN
UNIVERSITY OF WISCONSIN-MADISON



Common symptoms



**Social
Challenges**



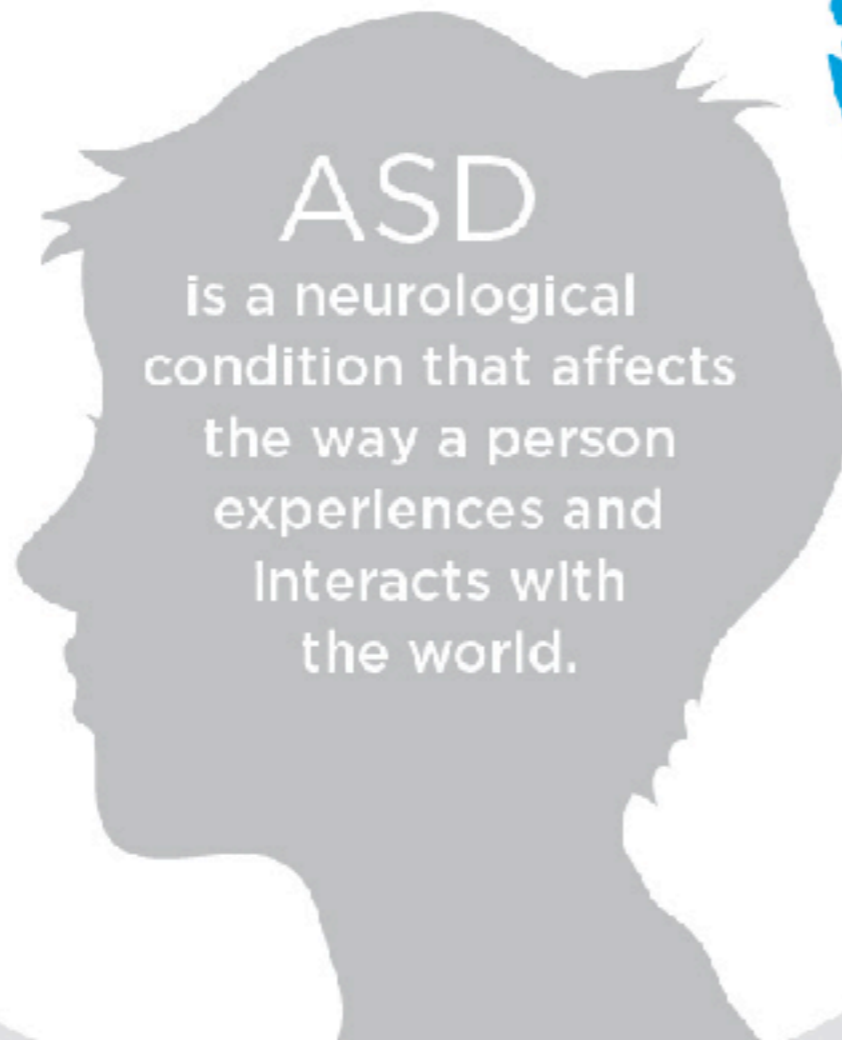
**Repetitive
Behaviors**



**Intellectual
Disability &
Epilepsy**



**Narrow
Interests**



Common symptoms



Social Challenges



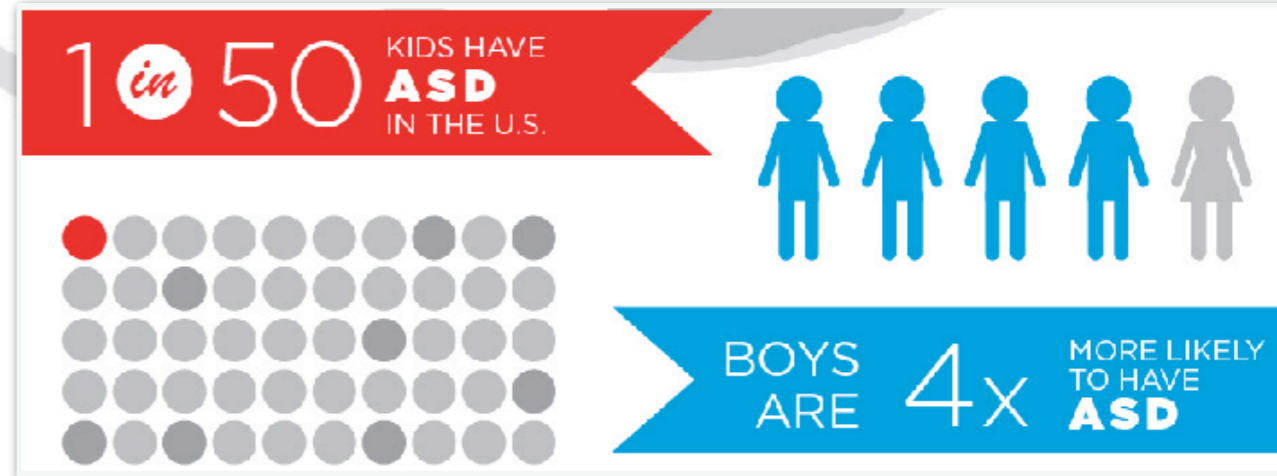
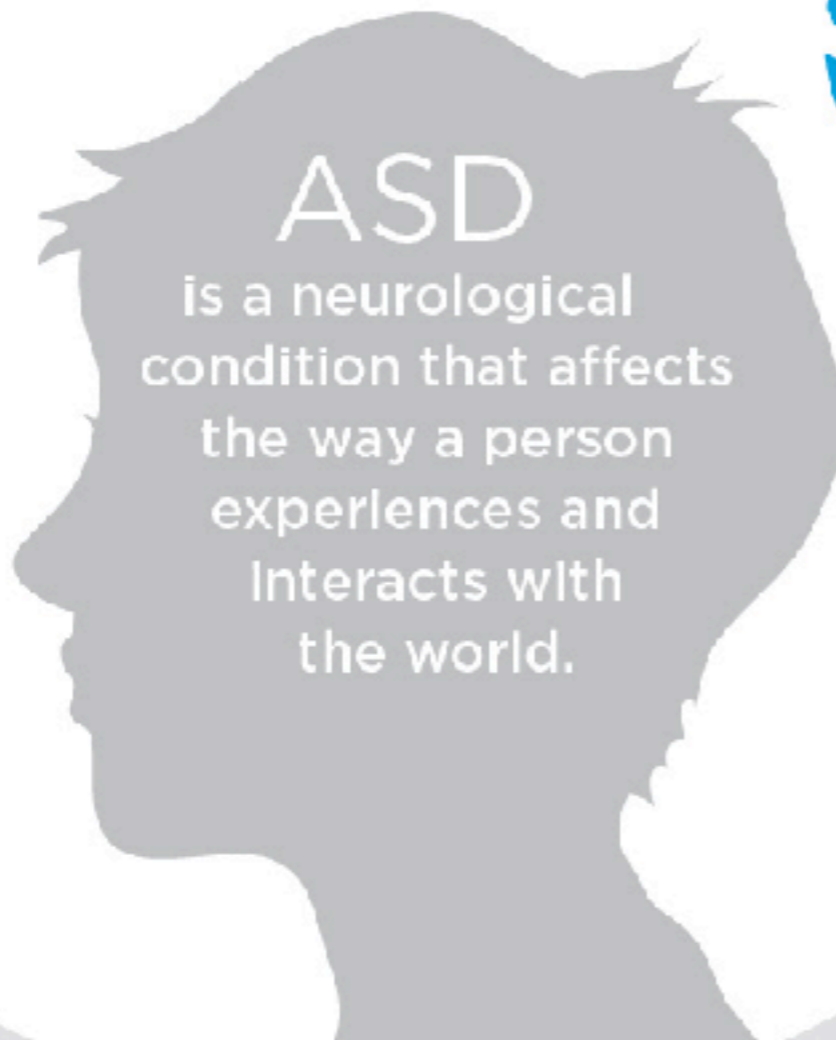
Repetitive Behaviors



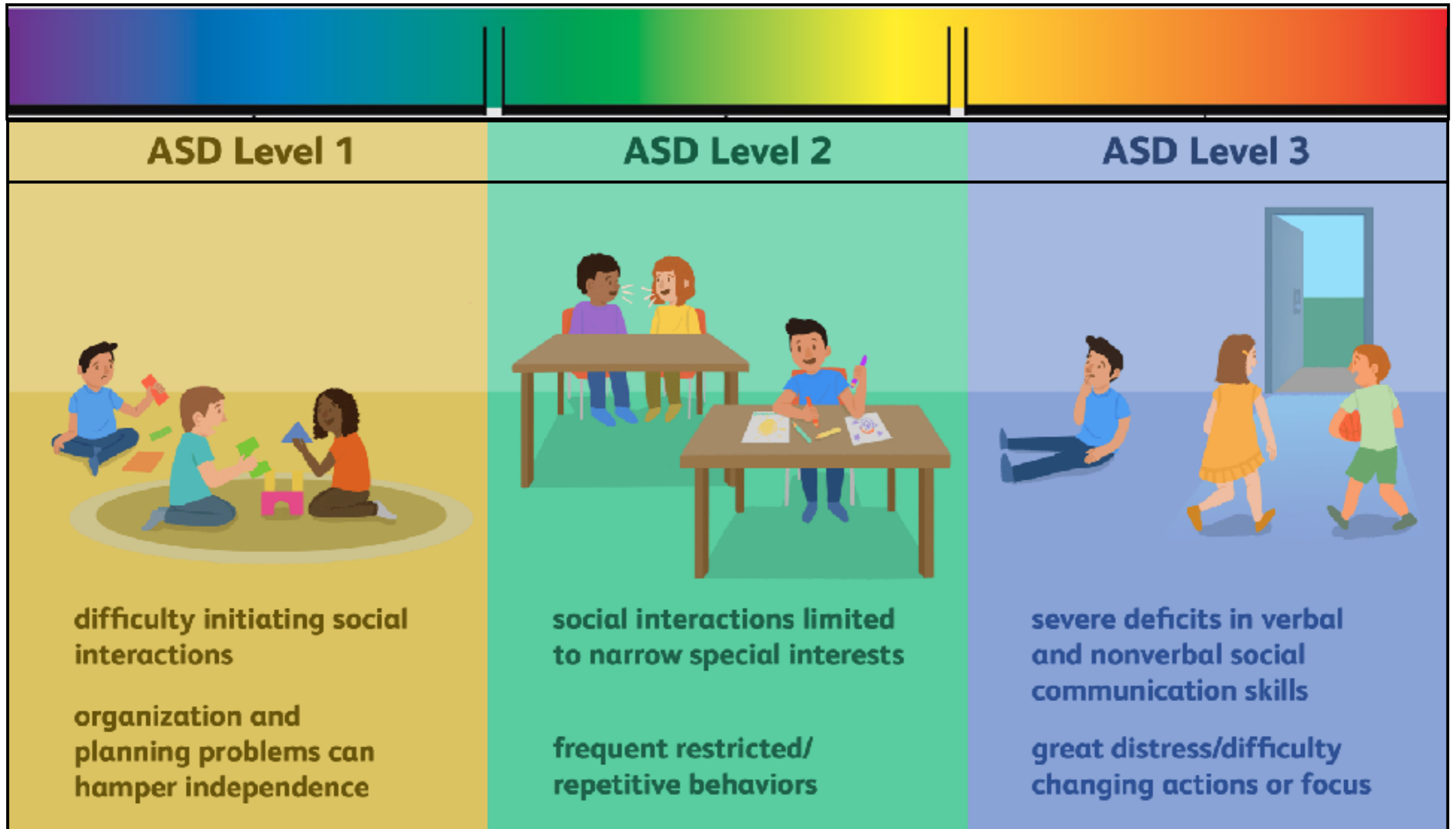
Intellectual Disability & Epilepsy



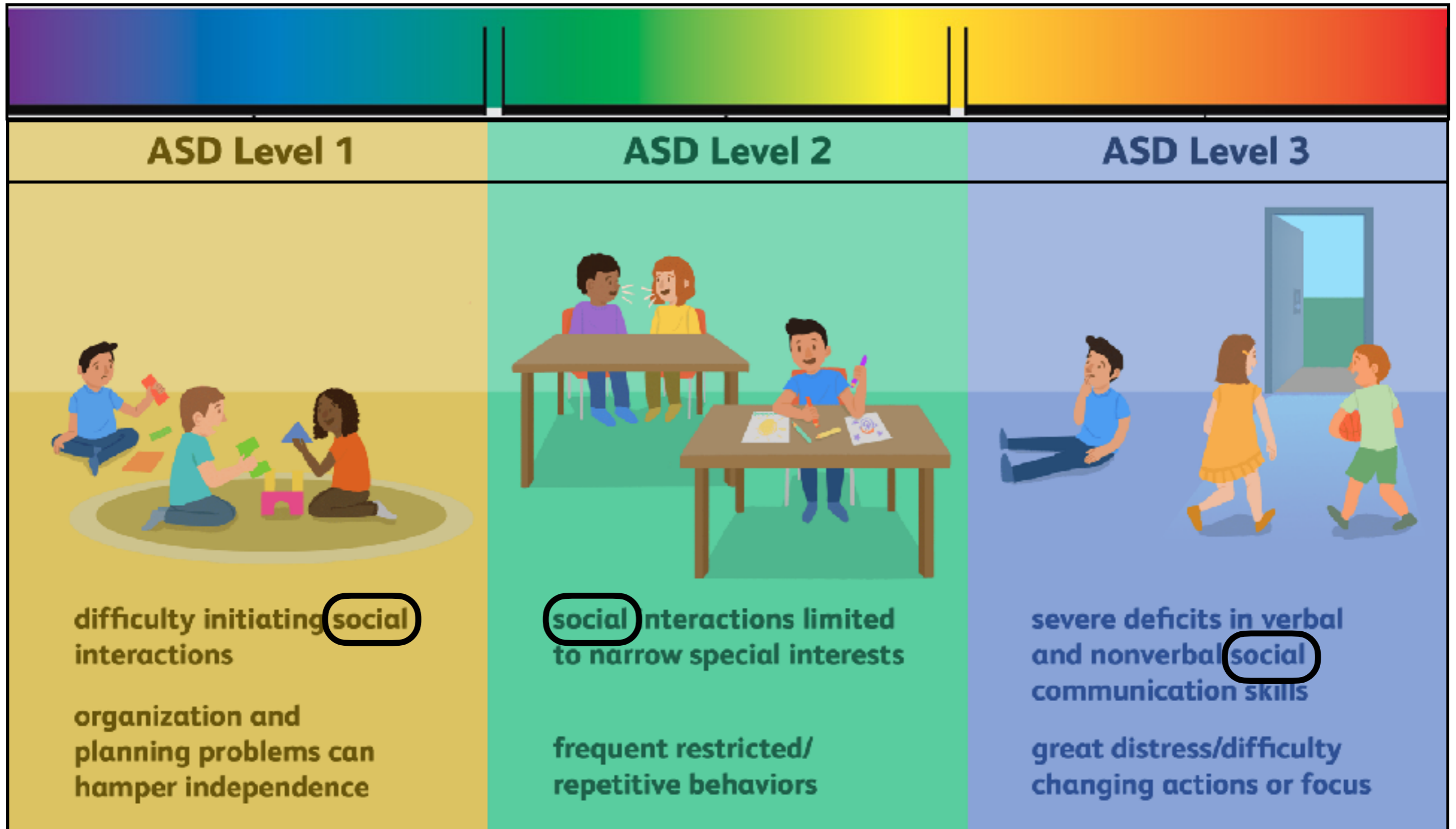
Narrow Interests



Autism as a “spectrum”



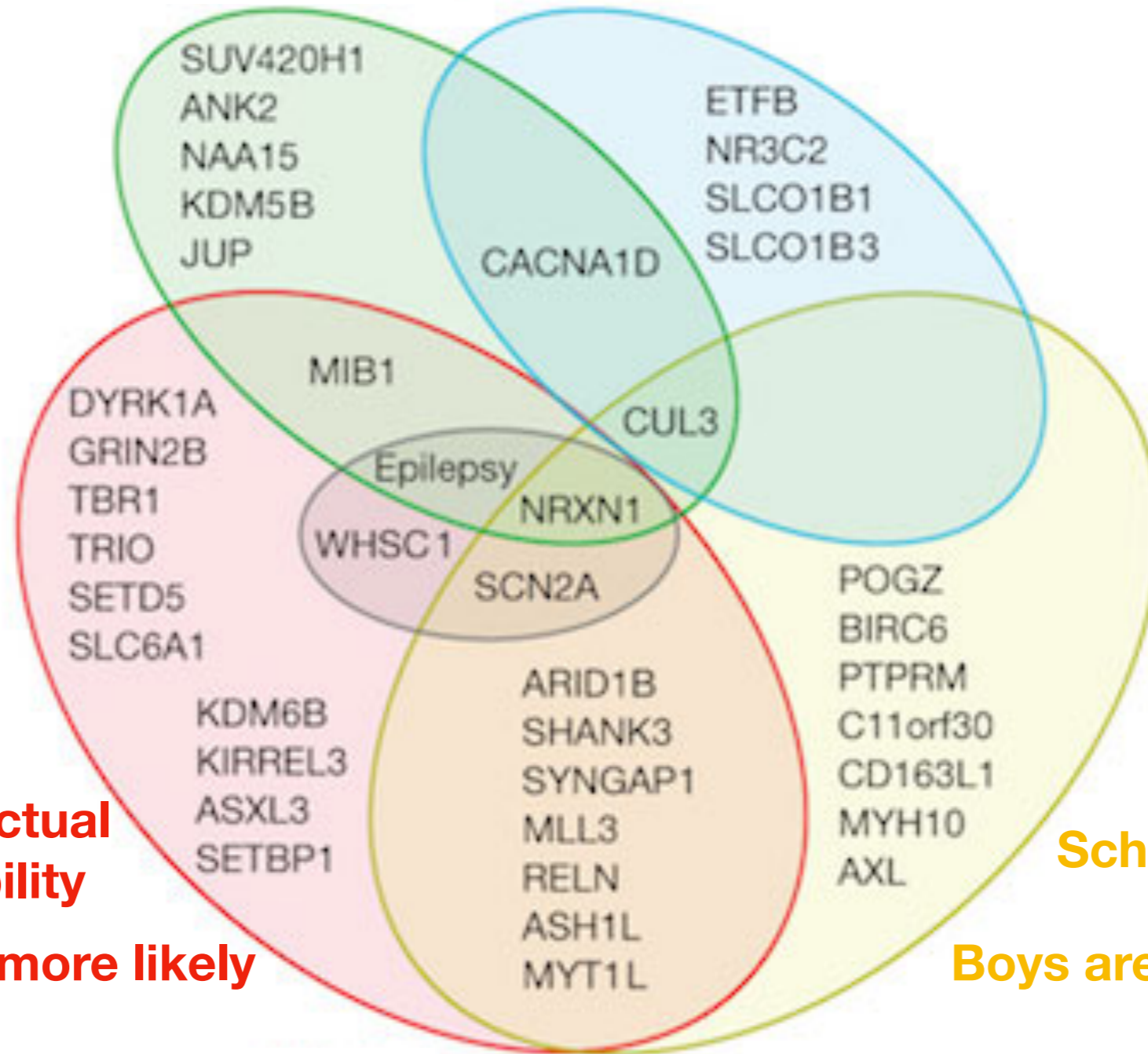
Autism as a “spectrum”



Genes related to ASD

Congenital heart disease

Metabolic disorders



Intellectual disability

Schizophrenia

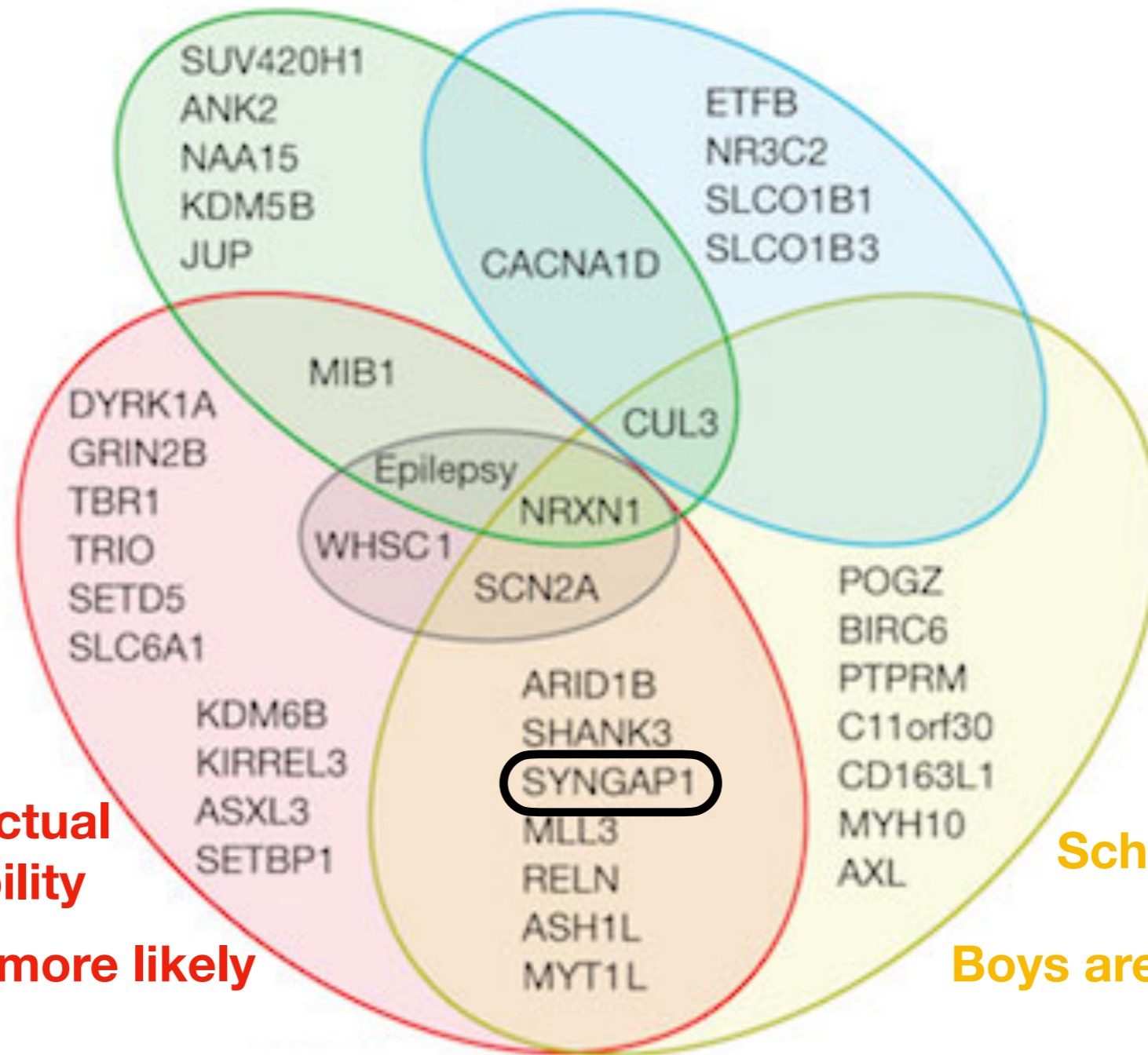
Boys are 3x more likely

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Genes related to ASD

Congenital heart disease

Metabolic disorders



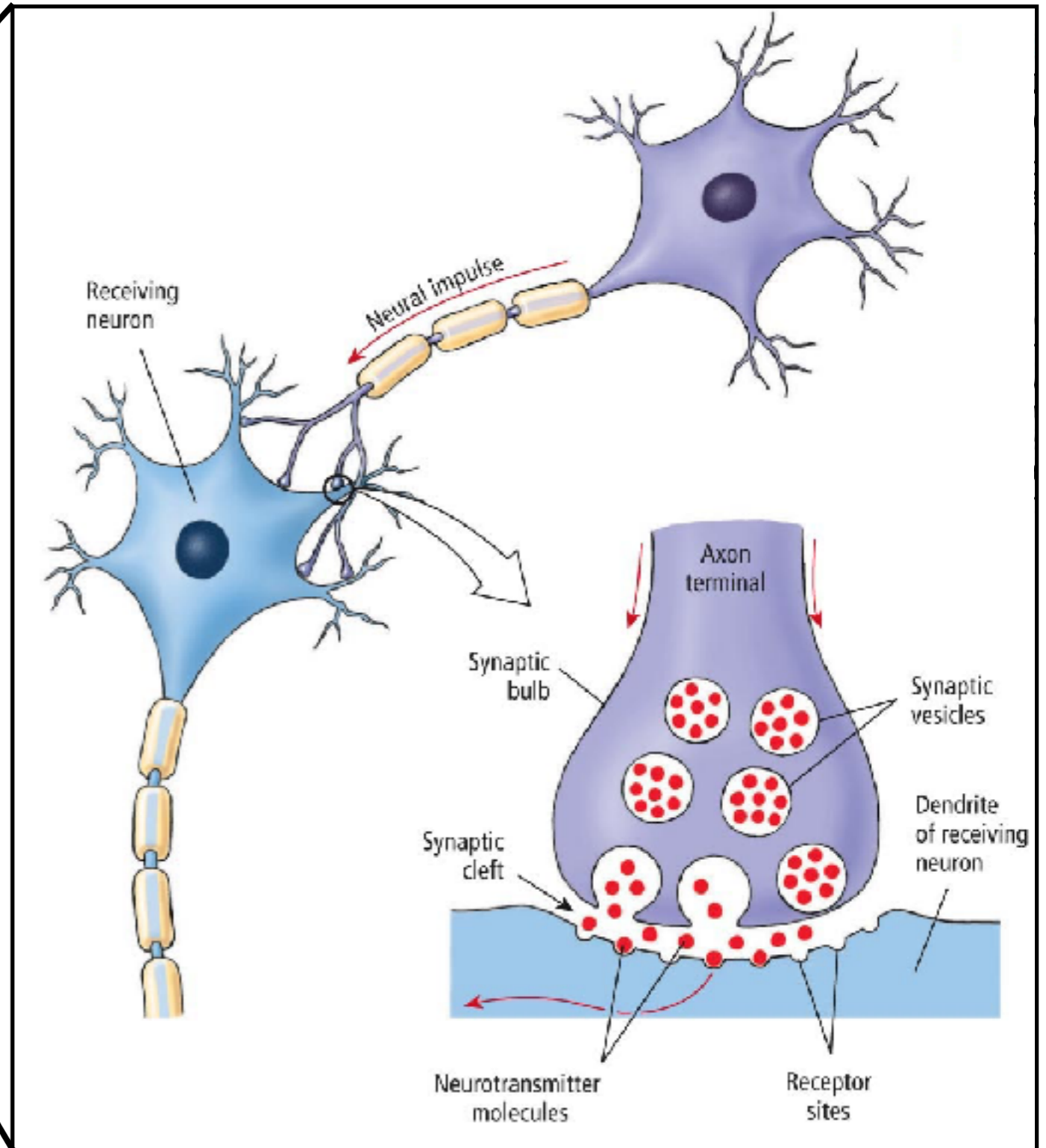
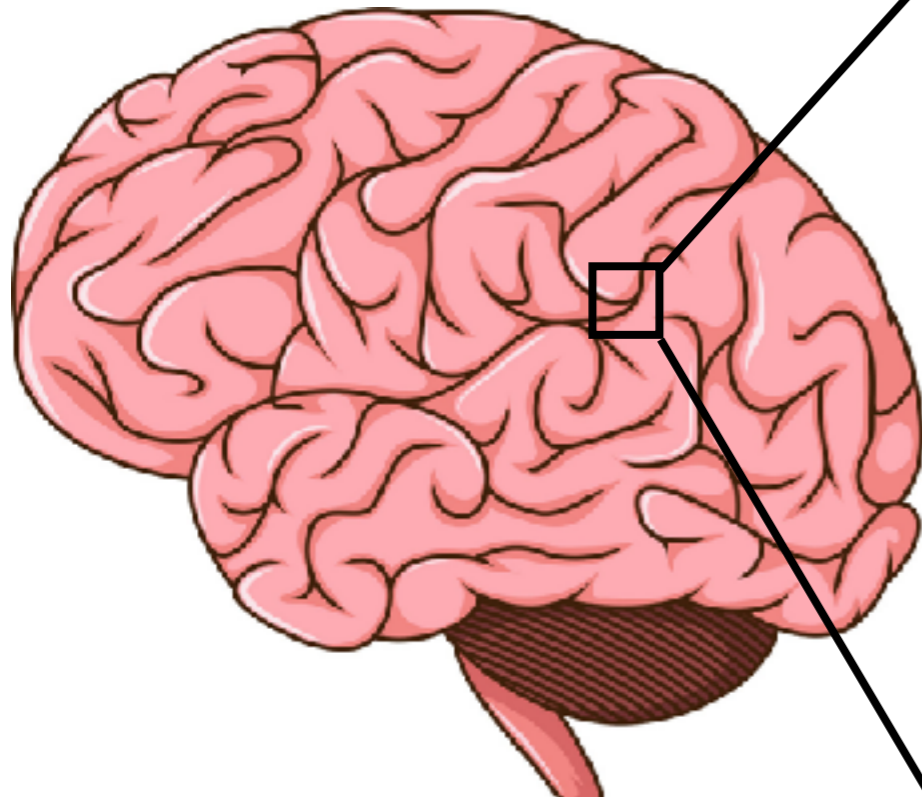
Intellectual disability

Schizophrenia

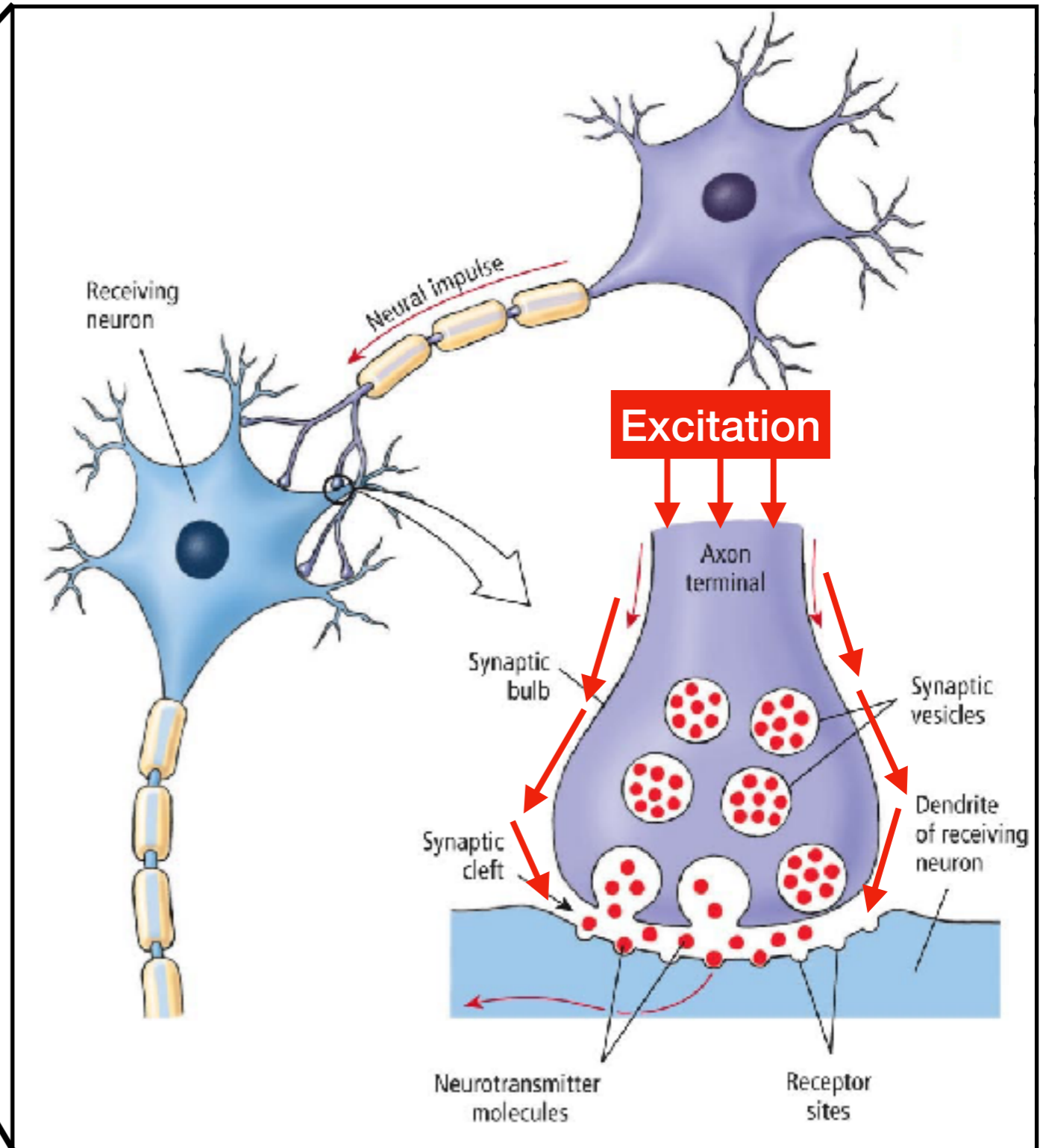
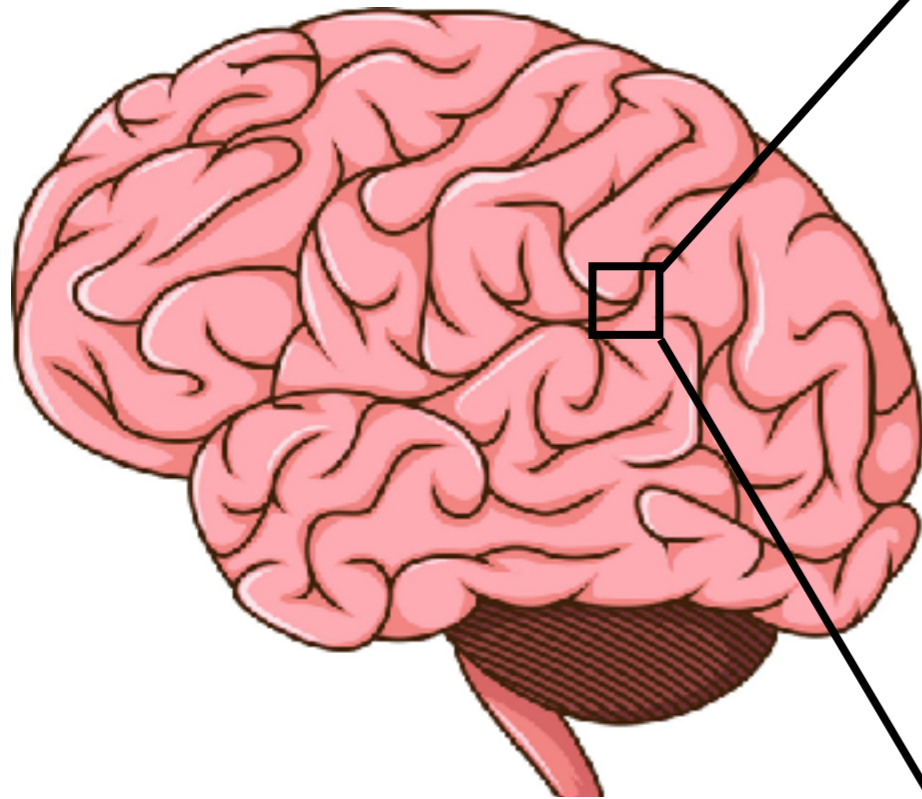
Boys are 3x more likely

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SYNGAP1 and ASD



SYNGAP1 and ASD



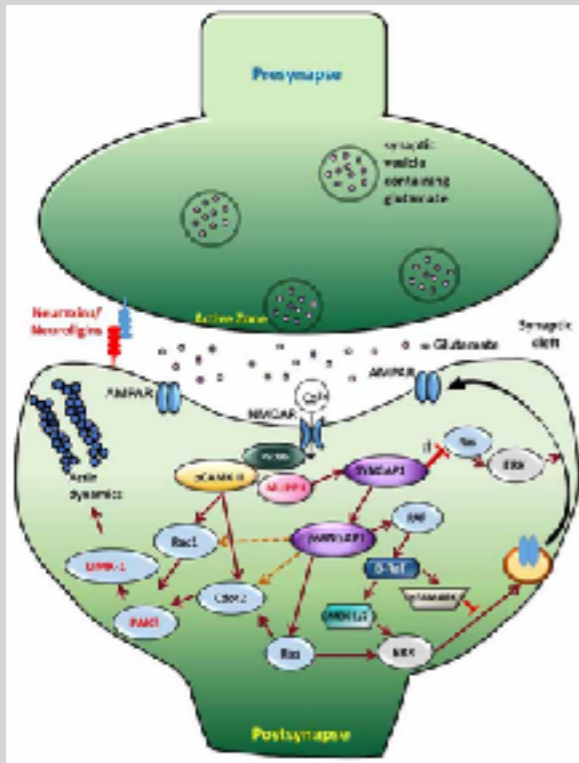
SYNGAP1 and ASD



SYNGAP1 and ASD



Cellular Component

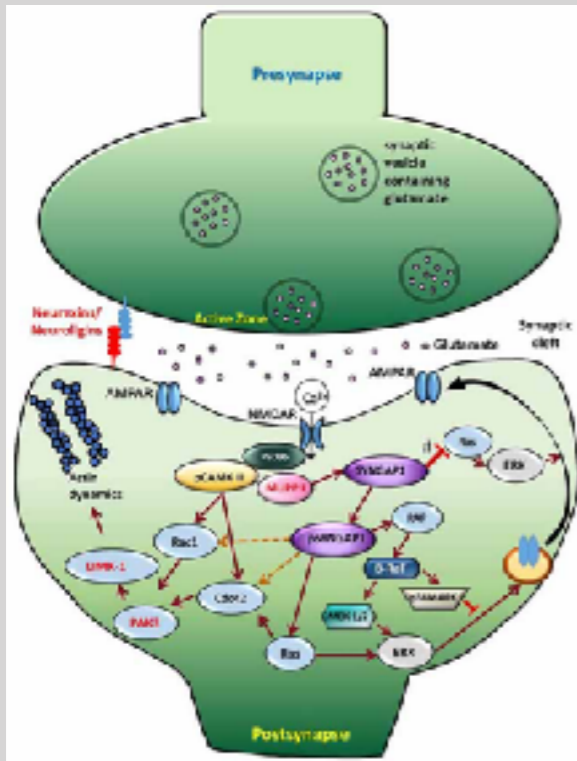


Synaptic function
Phosphorylation

SYNGAP1 and ASD

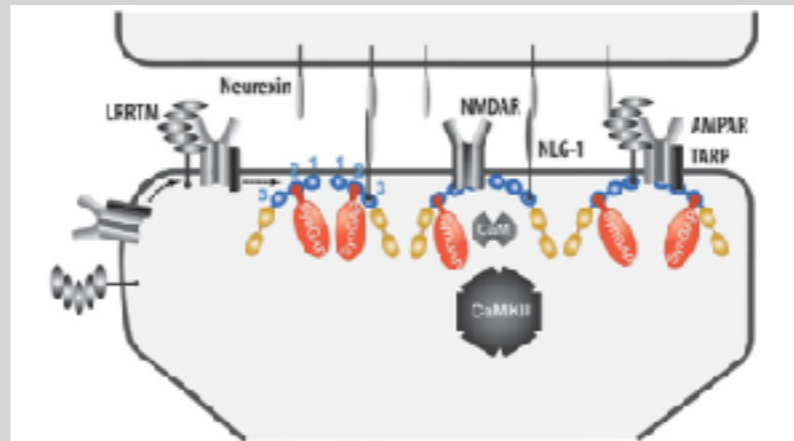


Cellular Component



Synaptic function
Phosphorylation

Molecular Function

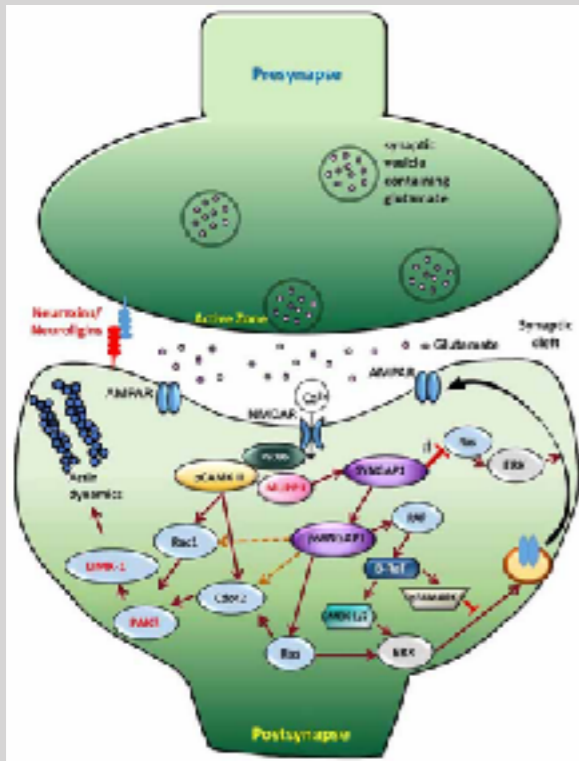


Inactivates GTPases
MAPK pathway
CAMK II interactions
AMPA exploitation

SYNGAP1 and ASD

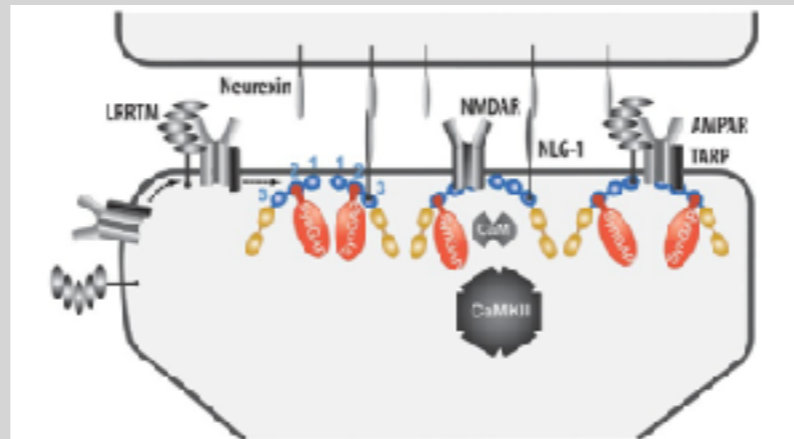


Cellular Component



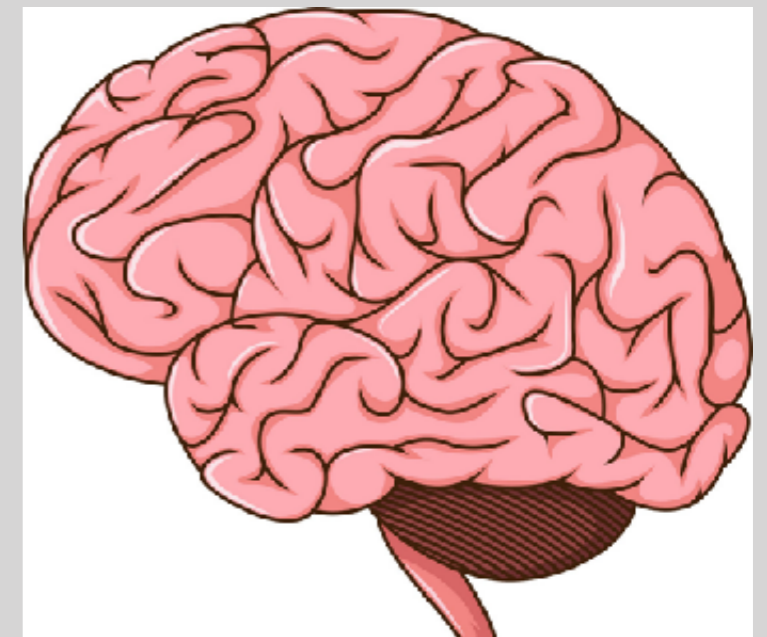
Synaptic function
Phosphorylation

Molecular Function



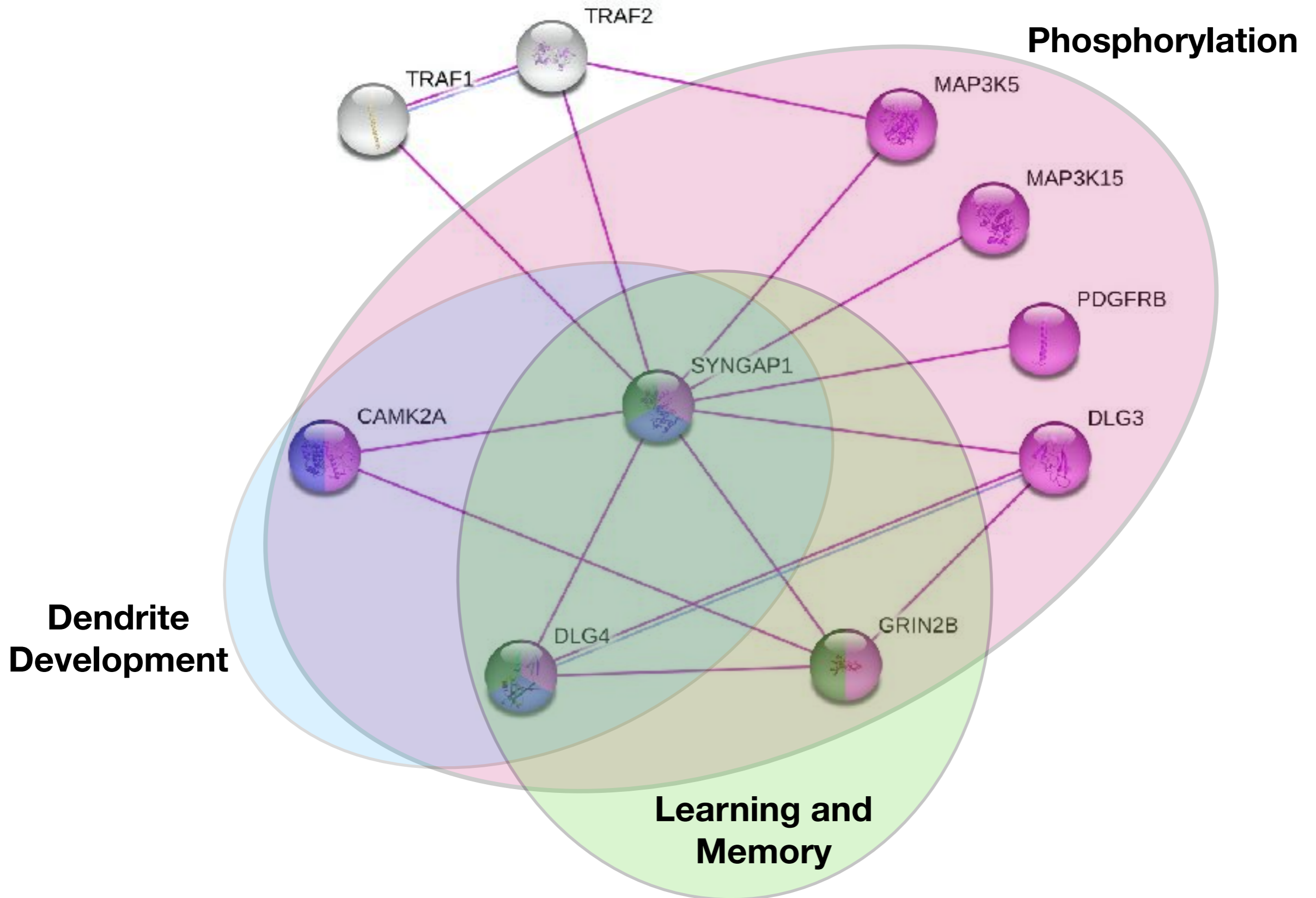
Inactivates GTPases
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Biological Process

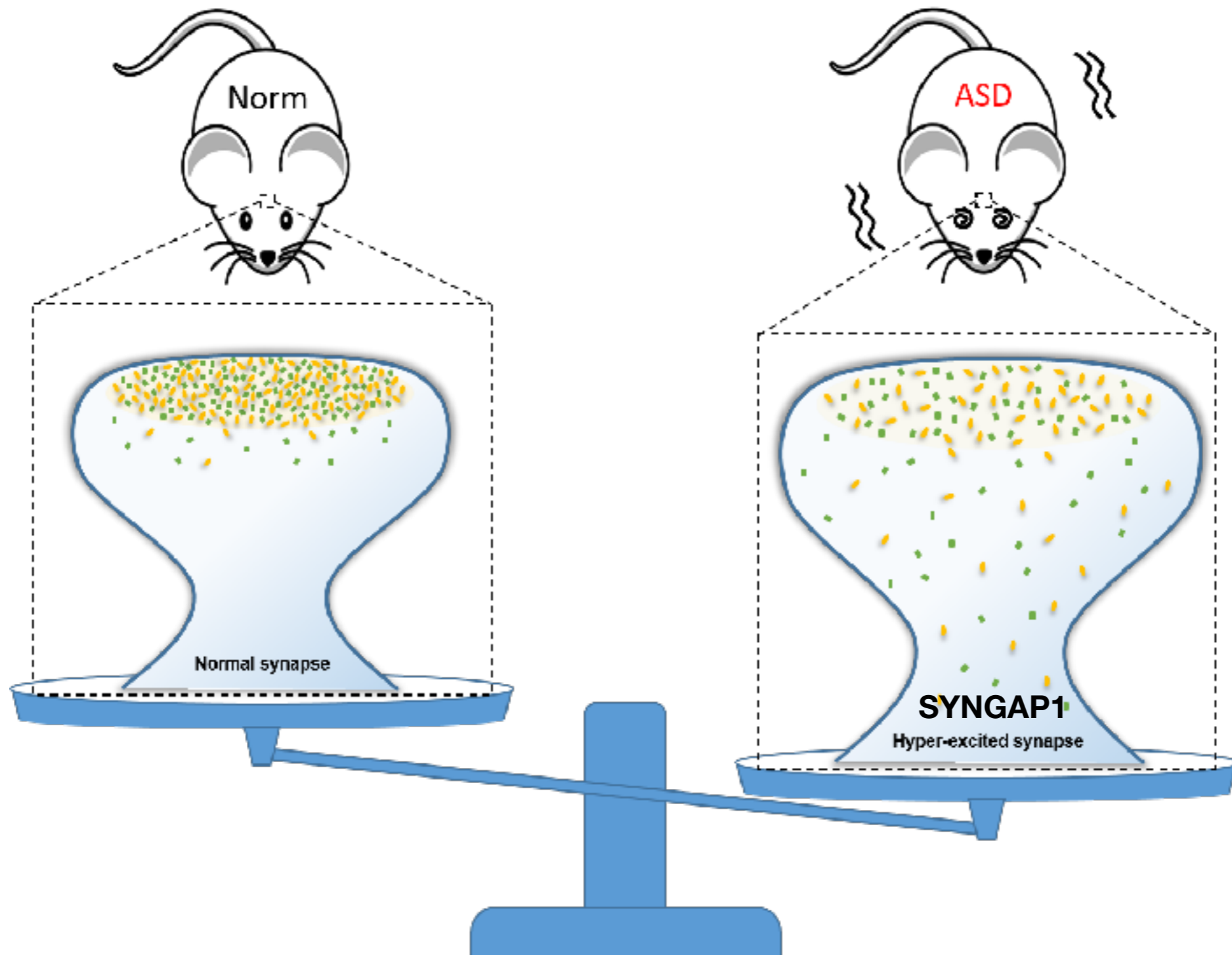


Brain Development
Intelligence
Social Behavior

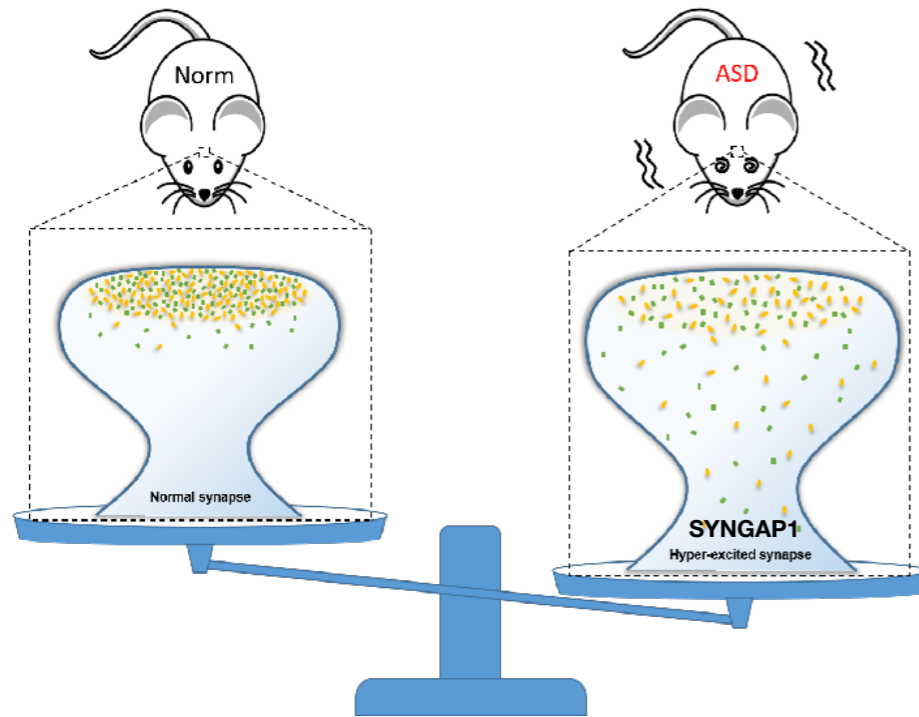
SYNGAP1 Interaction Network



Knowledge Gap

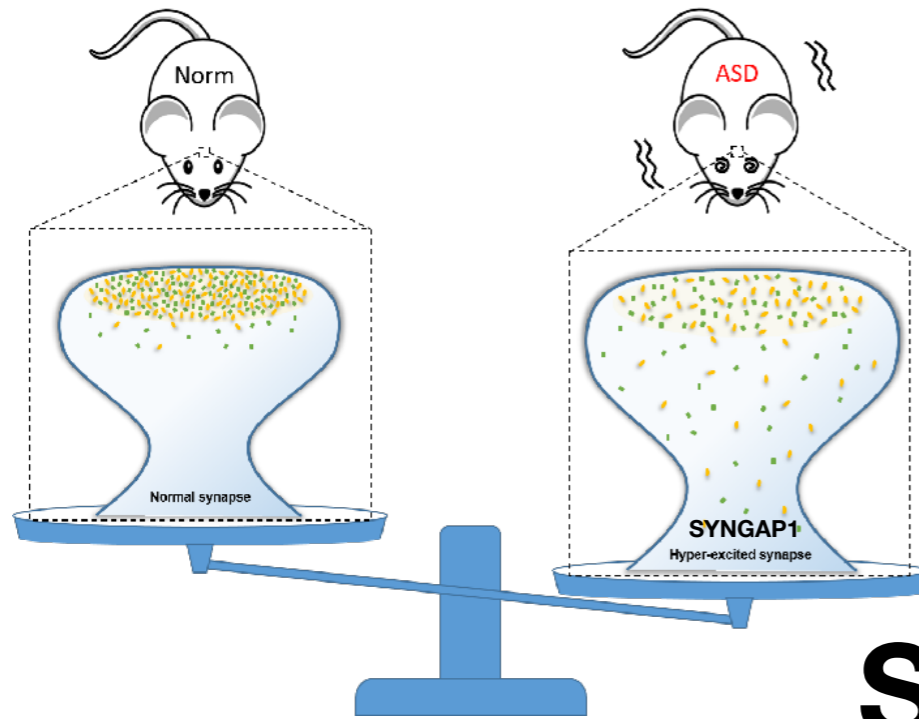


Knowledge Gap



Intellectual Disability
Epilepsy
Lack of Brain Development

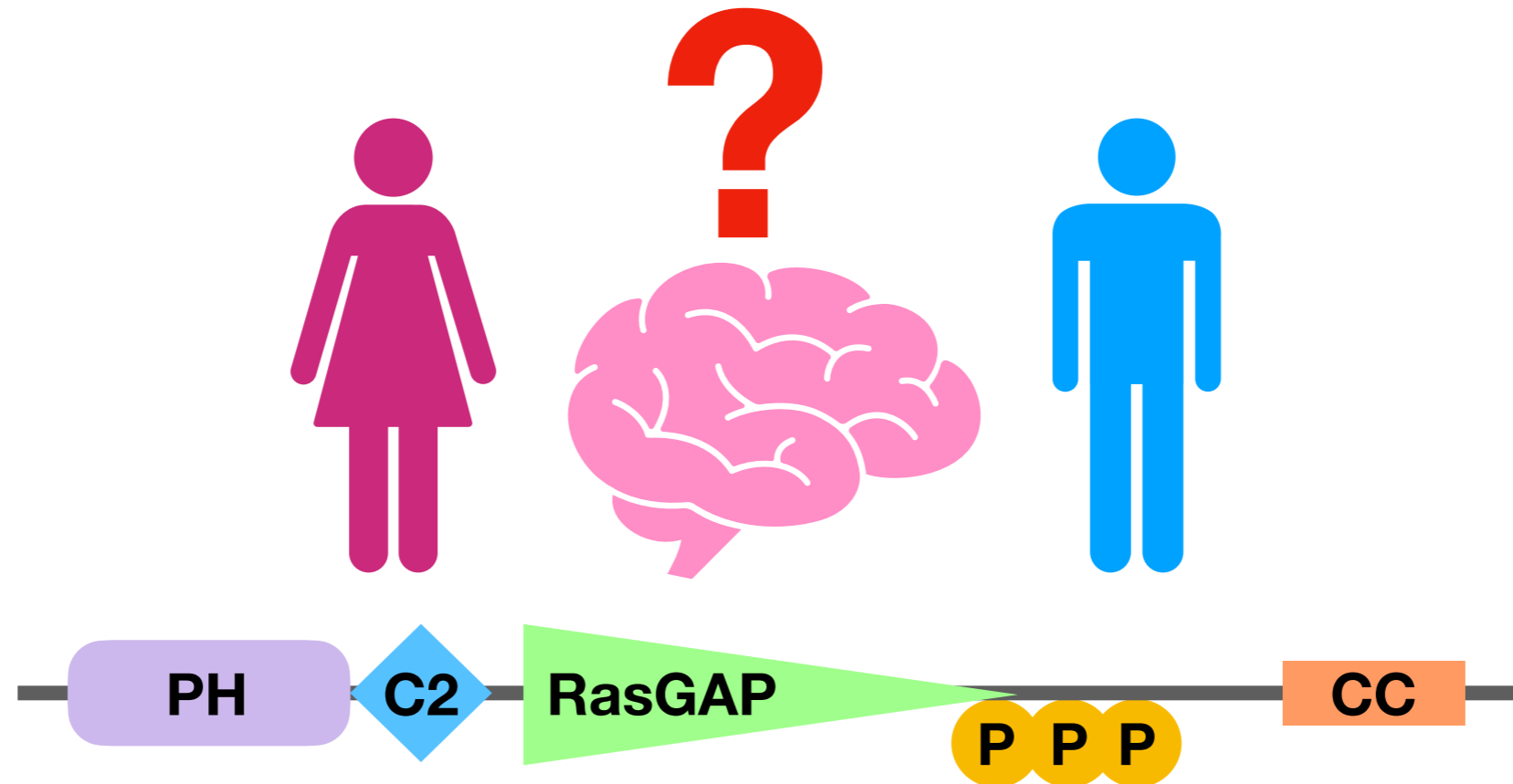
Knowledge Gap



Intellectual Disability
Epilepsy
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Social Behavior Impairments?

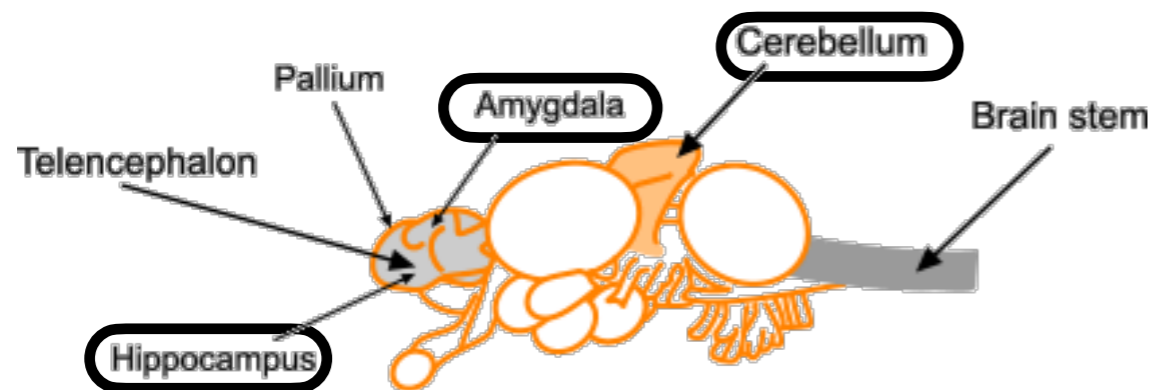
SYNGAP1



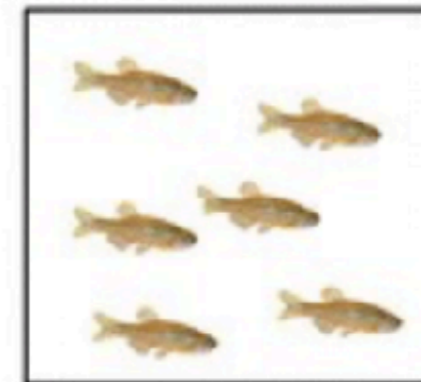
Zebrafish as a model organism for behavior



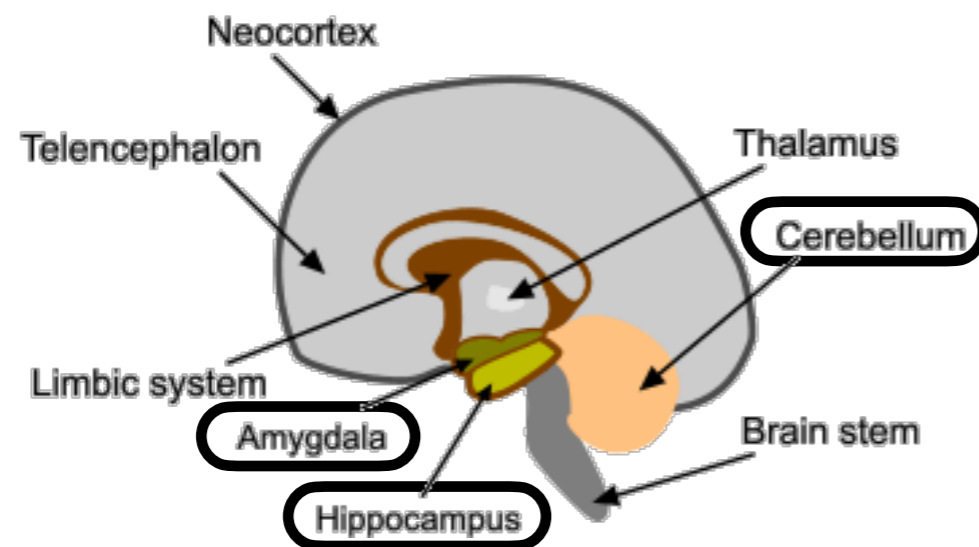
Danio rerio brain



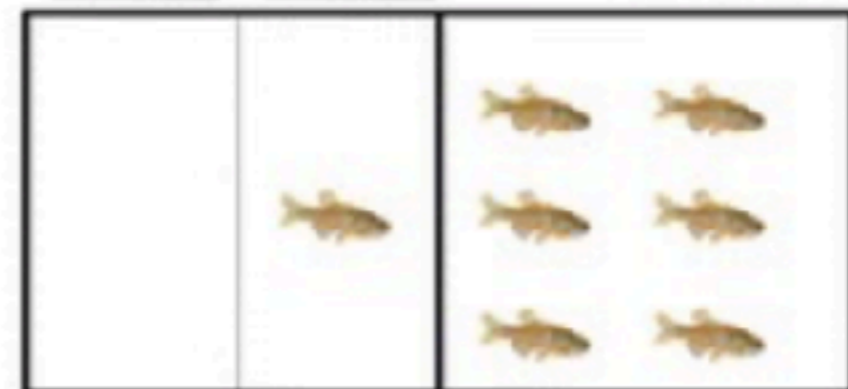
Shoaling



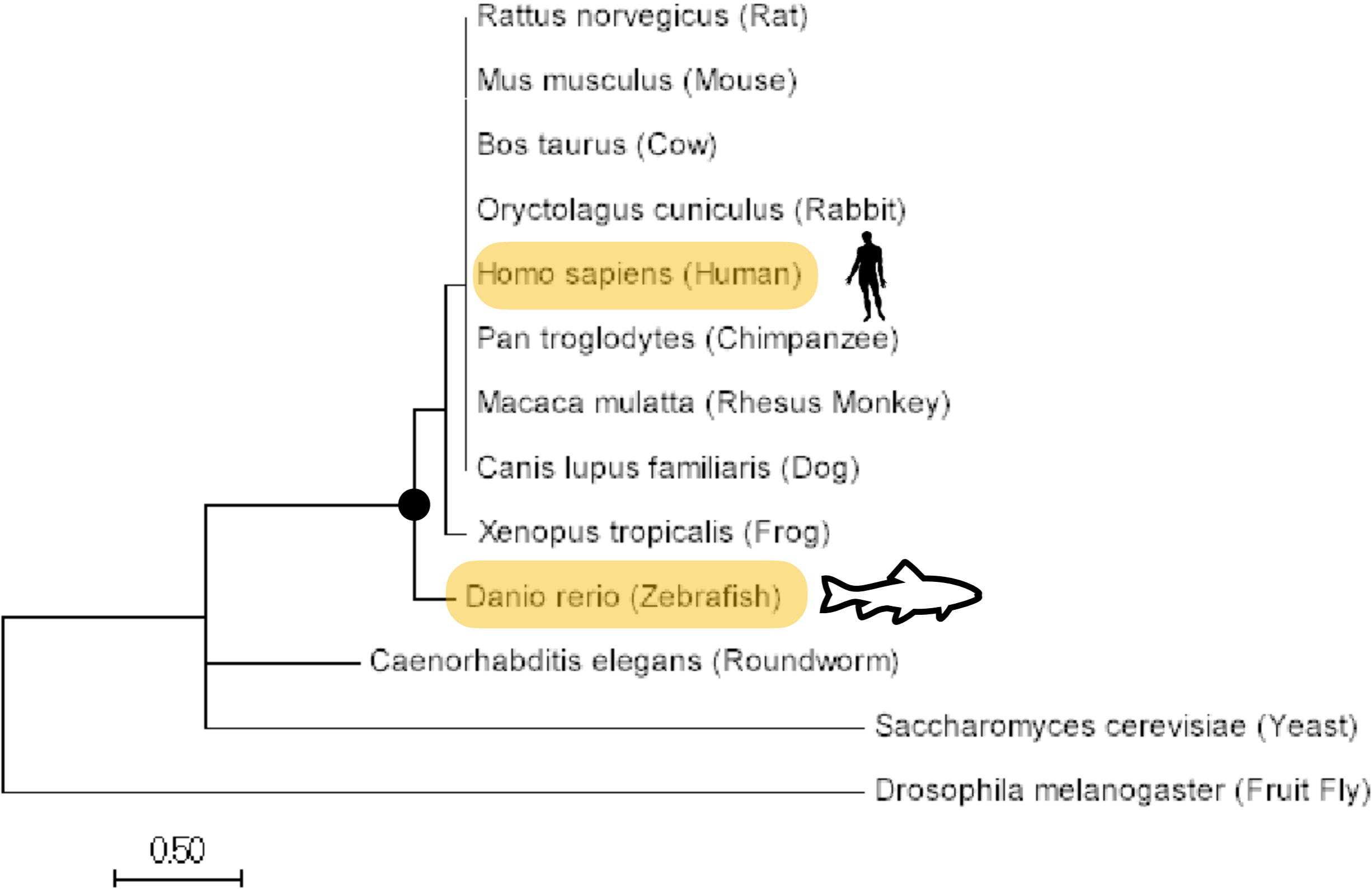
Homo sapien brain



Social Preference

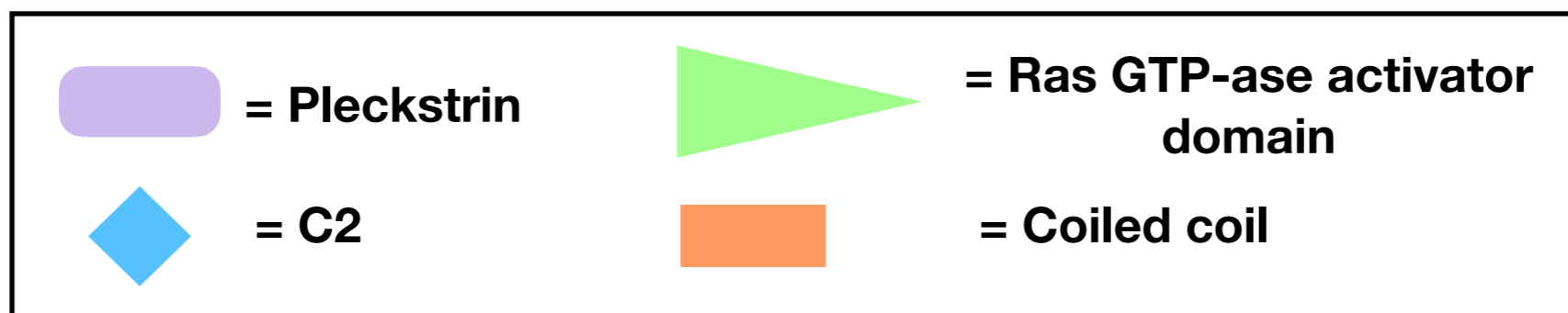
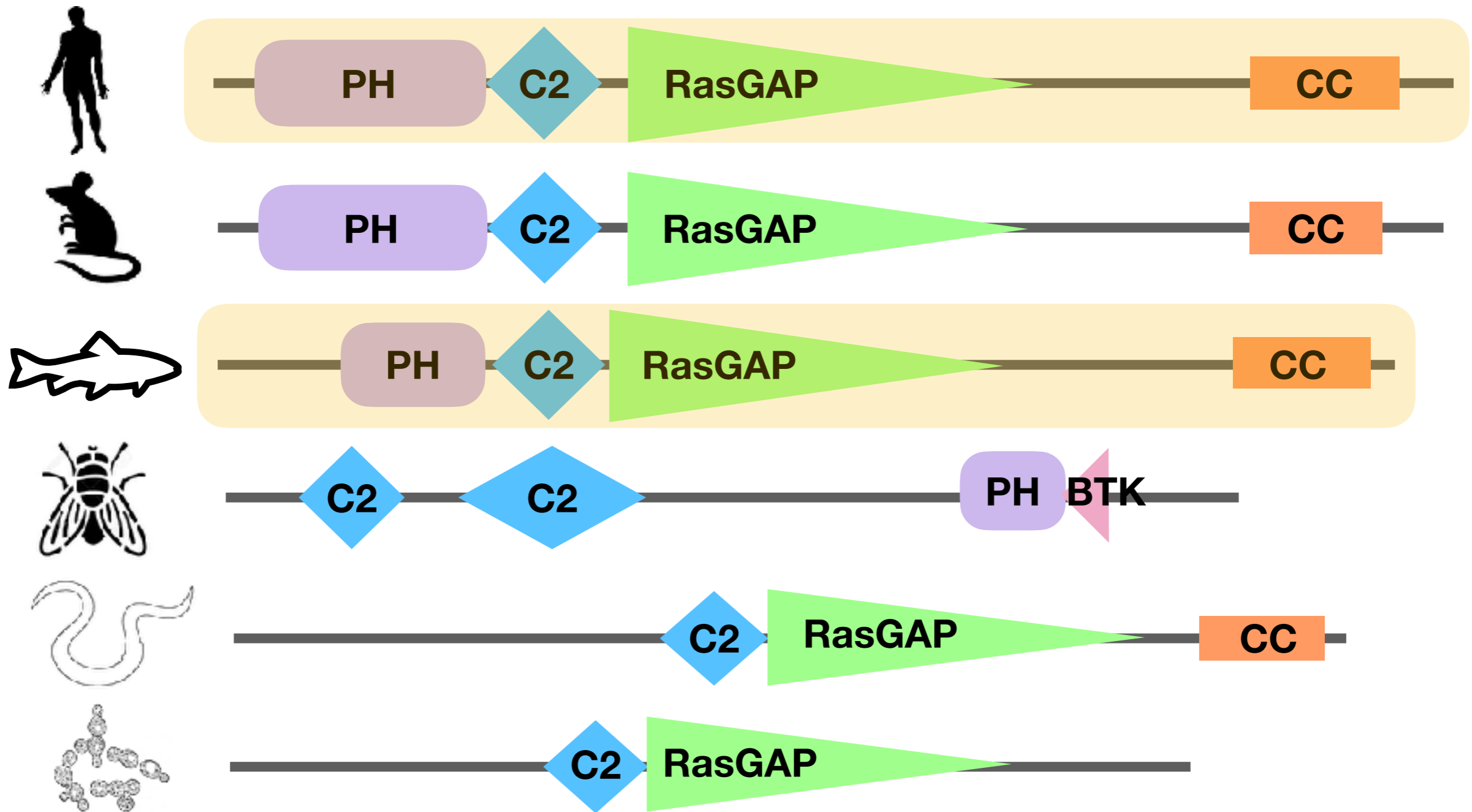


SYNGAP1 conserved across species



SYNGAP1 is fairly conserved across species.

SYNGAP1 conserved domains



The Primary Goal

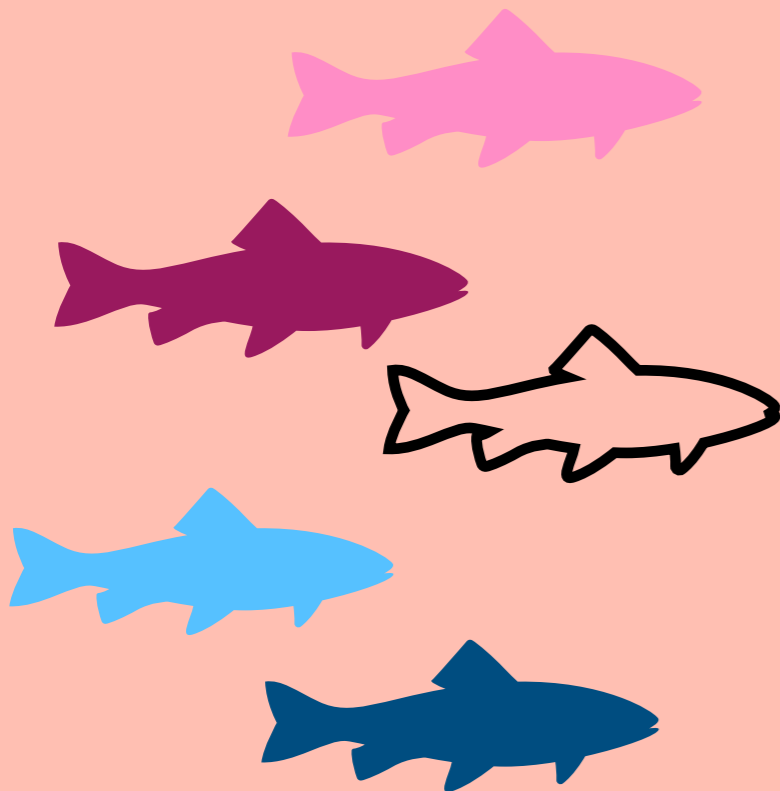
Elucidate the role of SYNGAP1 phosphorylation between males and females in social behavior.

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Aim1

Identify conserved phosphorylation sites of SYNGAP1 that play a role in social behavior.

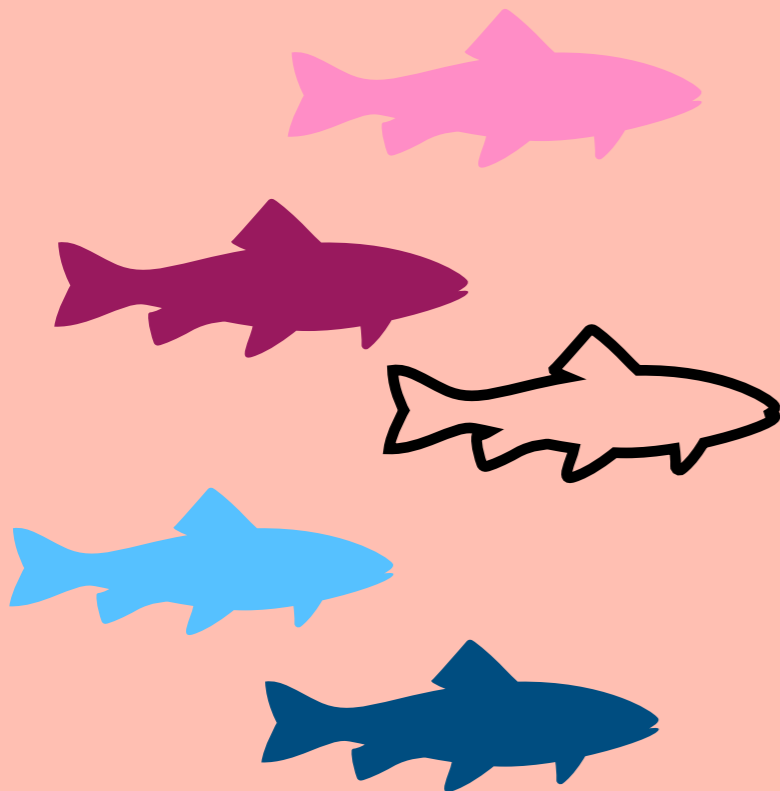


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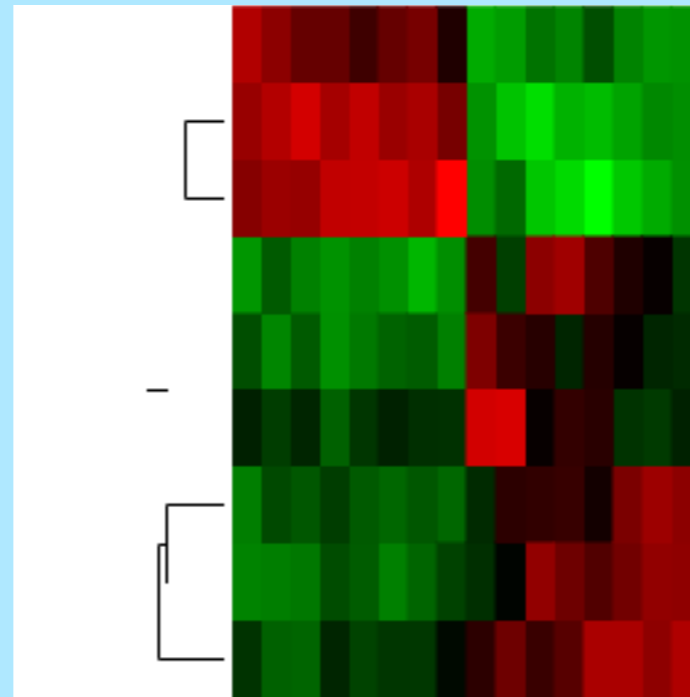
Aim1

Identify conserved phosphorylation sites of SYNGAP1 that play a role in social behavior.



Aim 2

Profile differentially expressed genes in social behavior mutant brains.

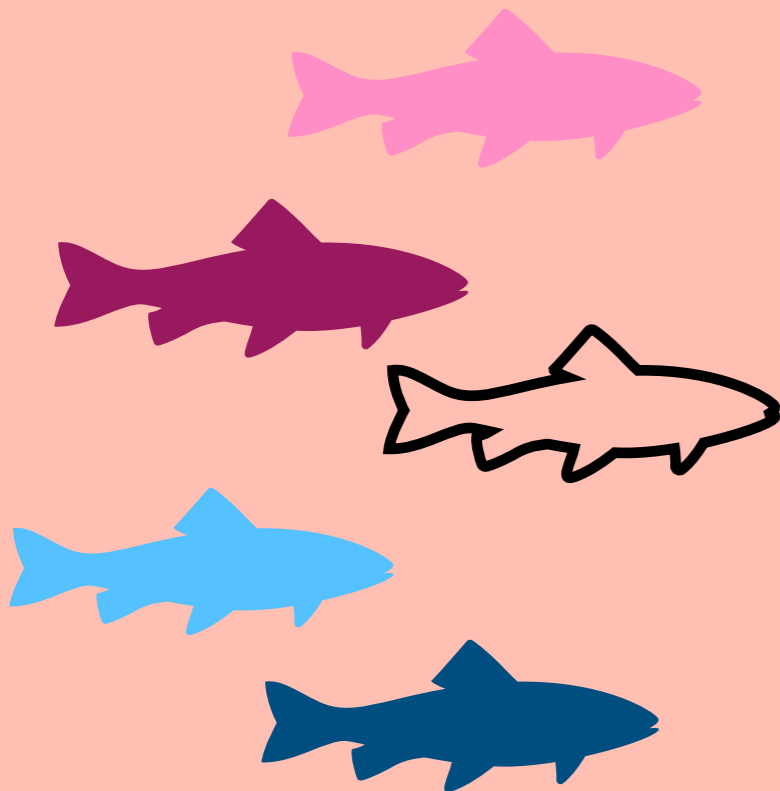


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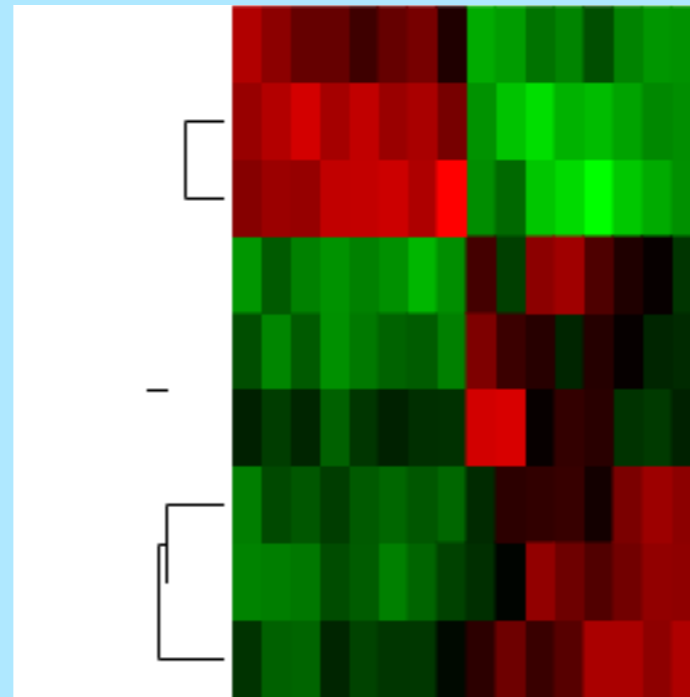
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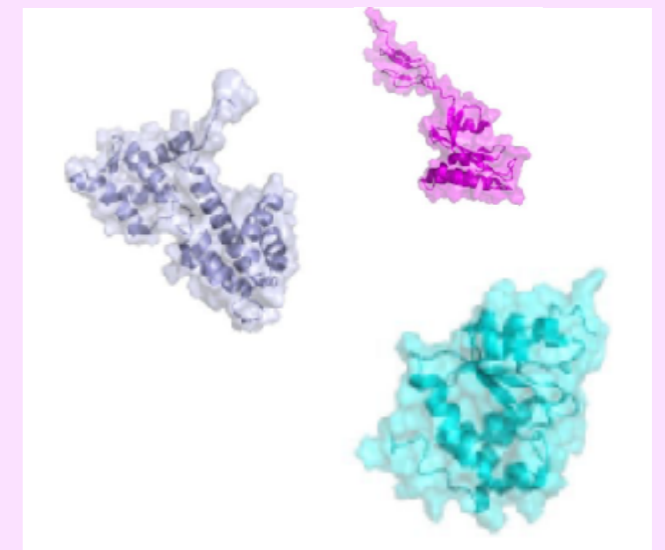
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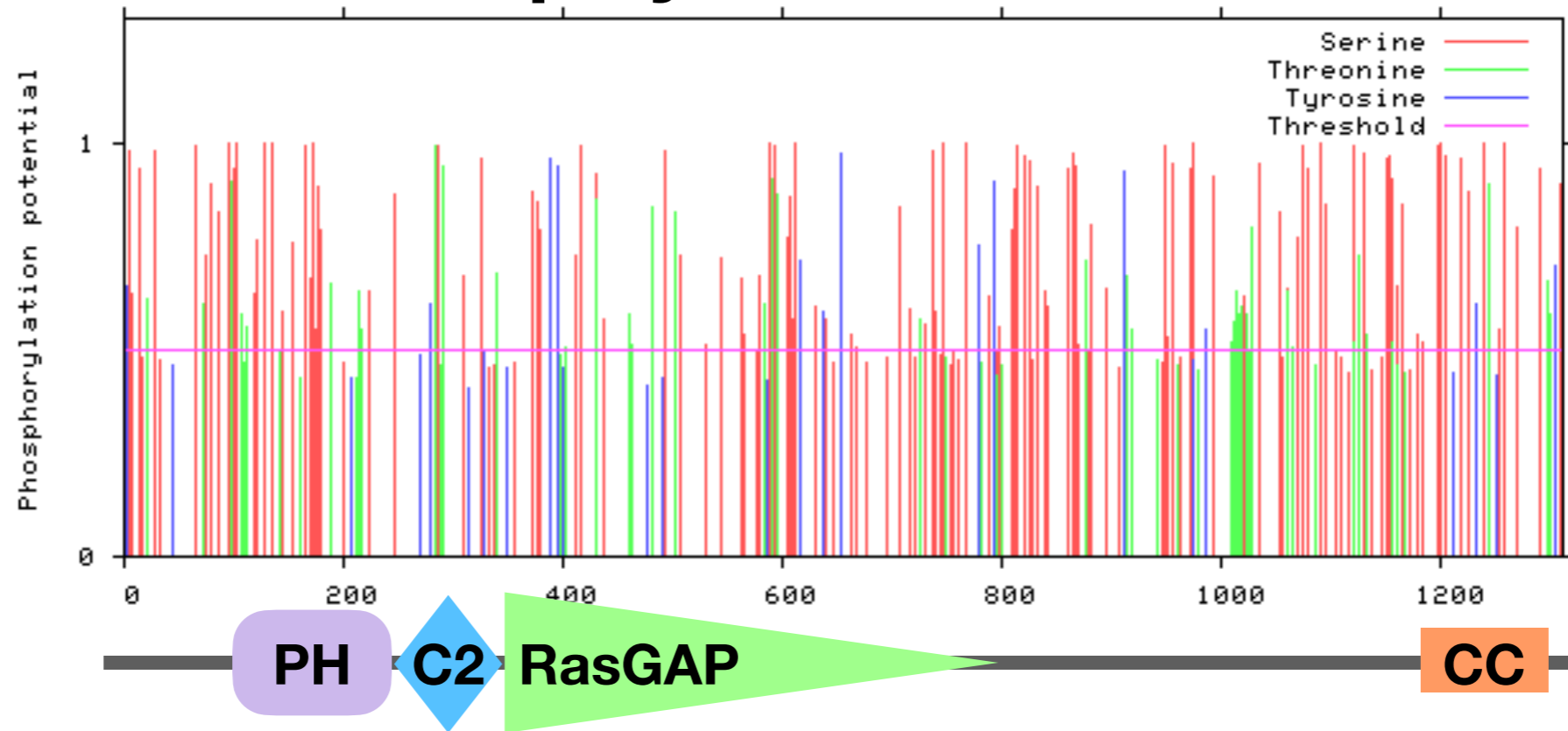


Aim 3

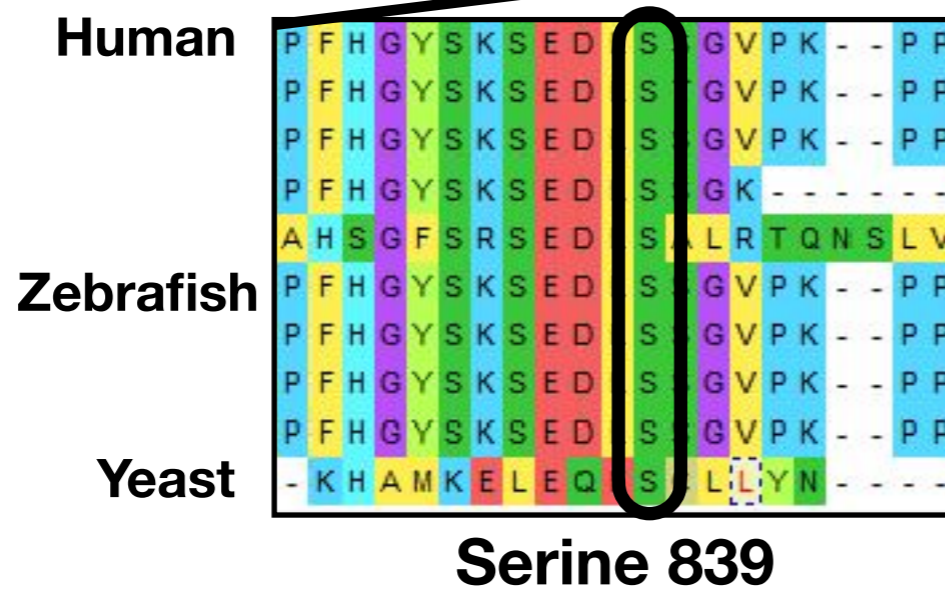
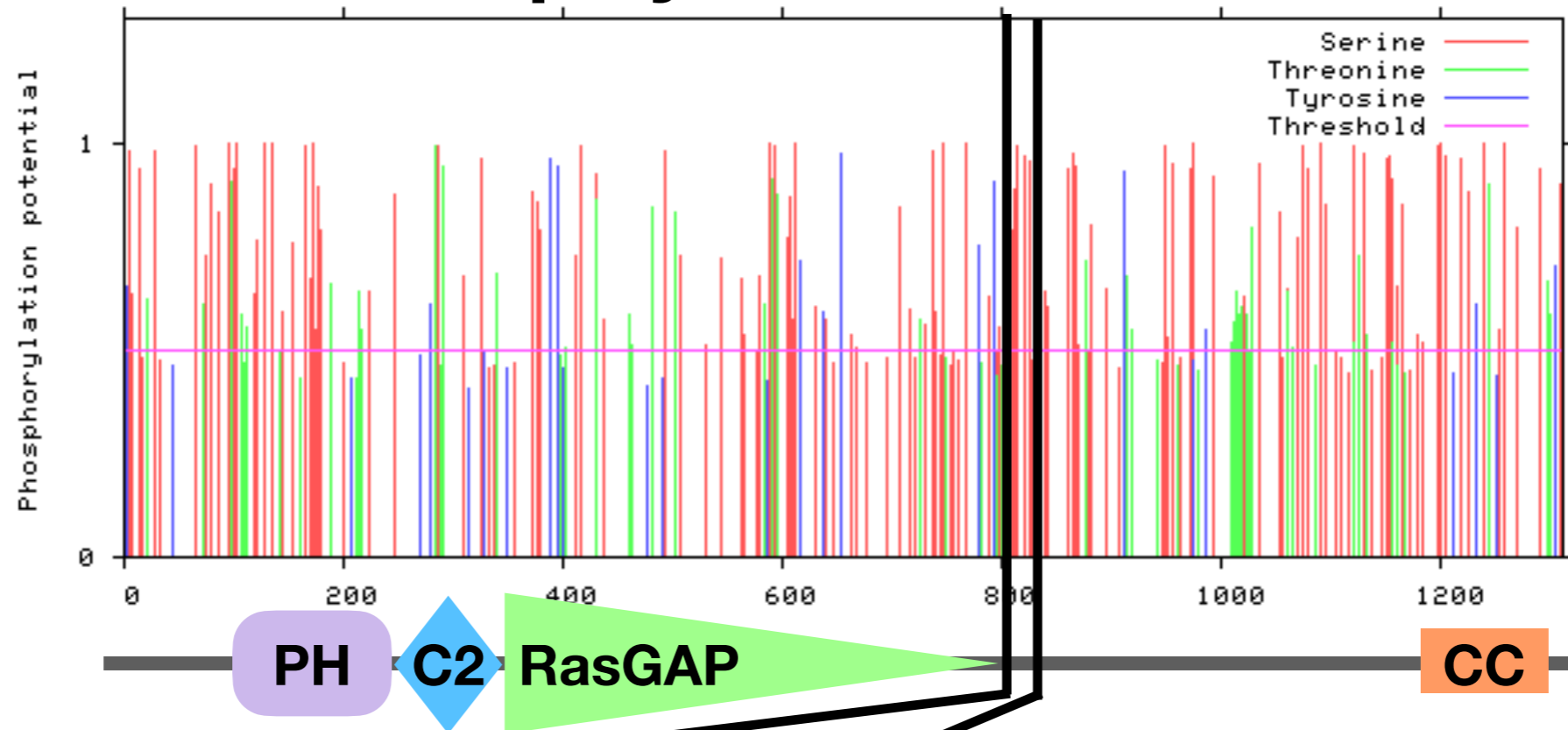
Identify SYNGAP1 interacting proteins that differentiate between gender and are associated with social behavior.



Aim 1: Identify conserved phosphorylation sites of SYNGAP1 that play a role in social behavior.

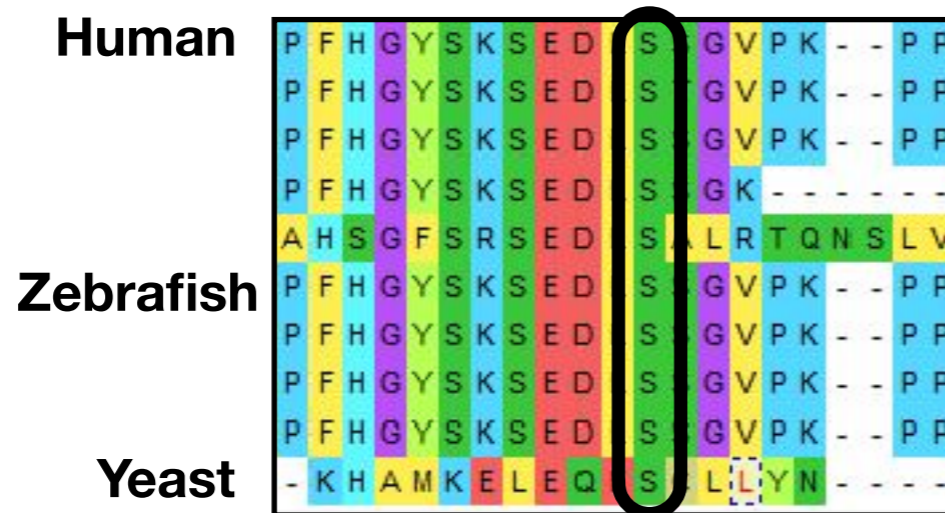
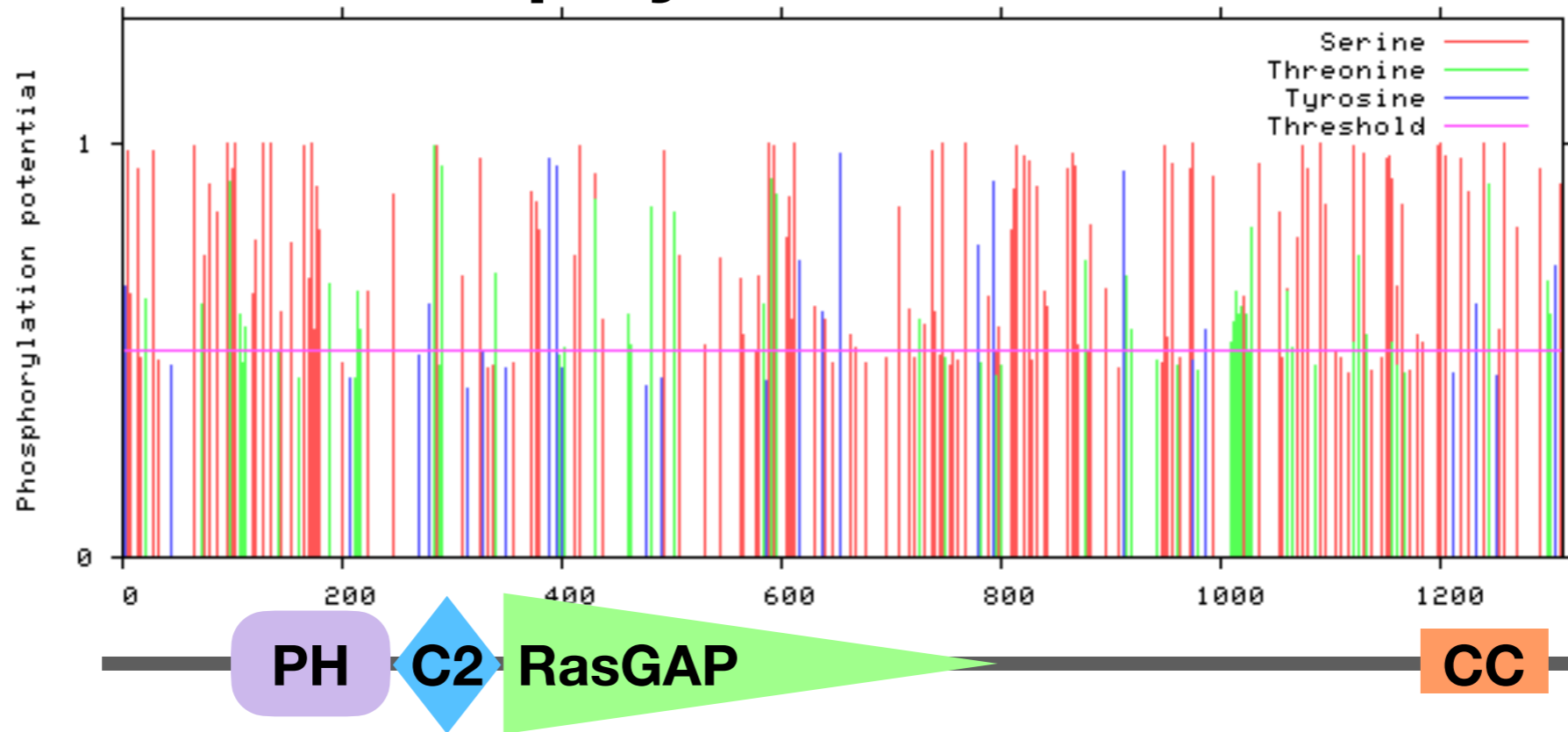


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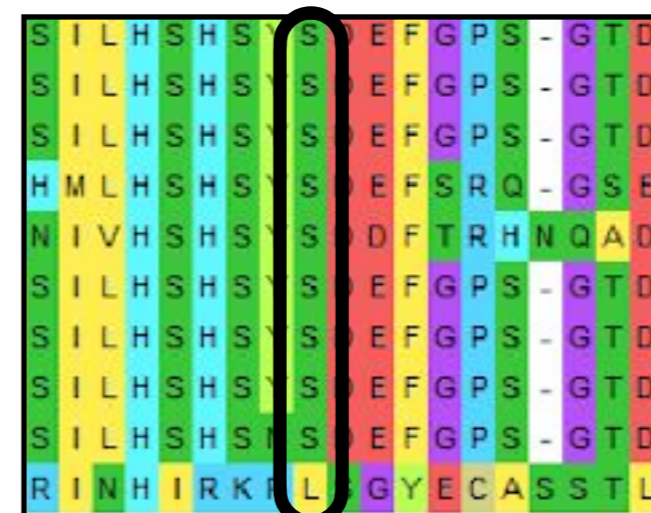


NetPhos and
ClustalOMEGA

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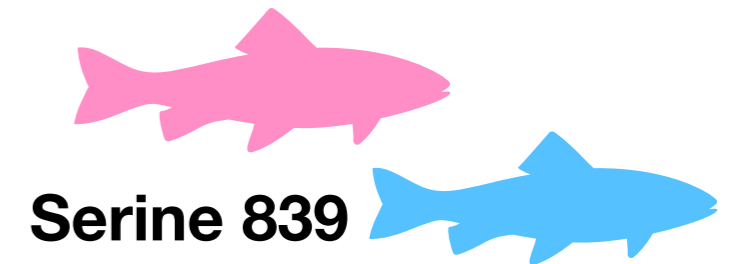
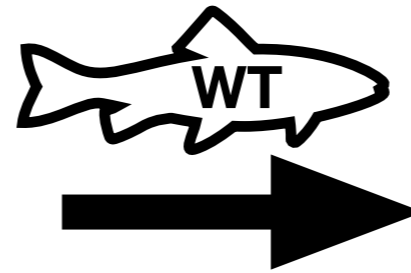
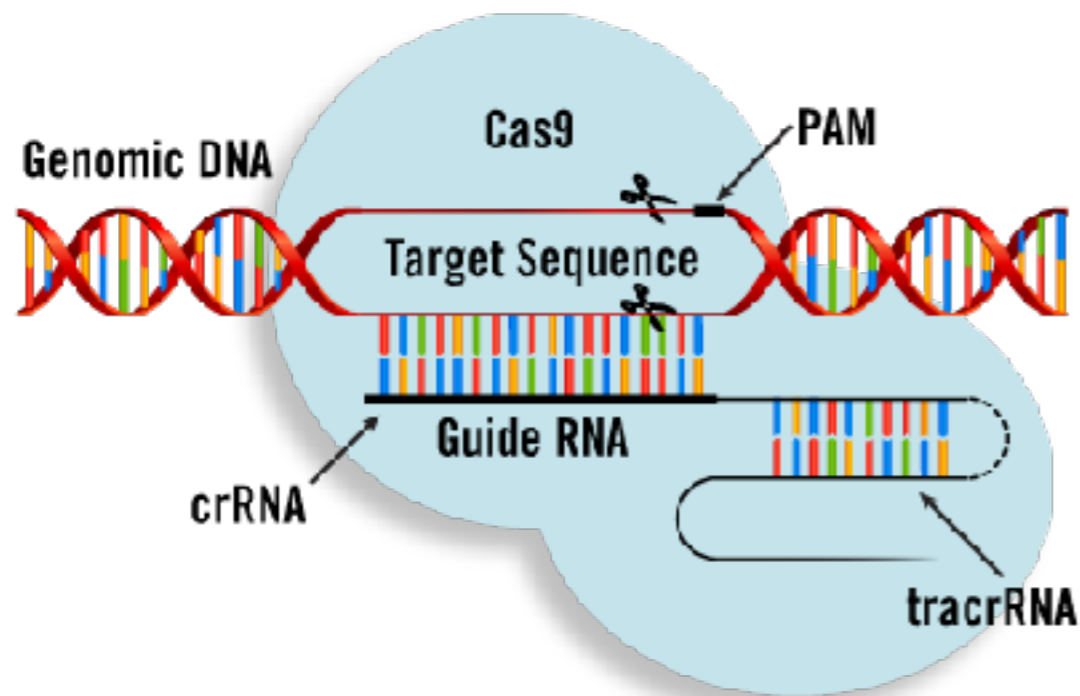
Serine 839



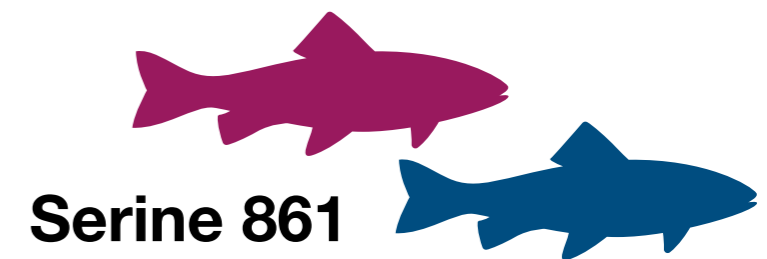
Serine 861

NetPhos and
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Aim 1: Identify conserved phosphorylation sites of SYNGAP1 that play a role in social behavior.



Serine 839



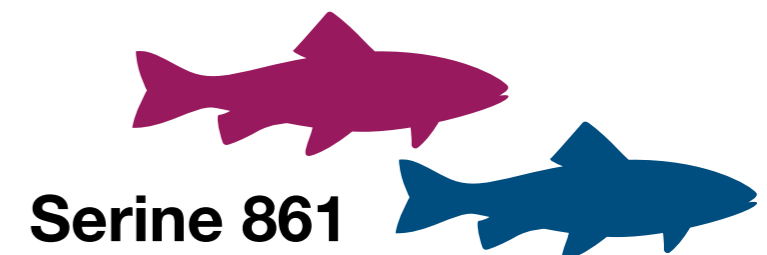
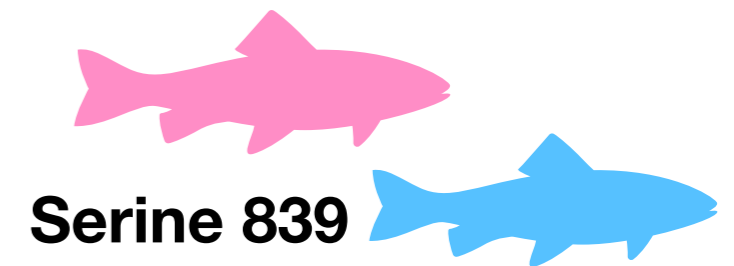
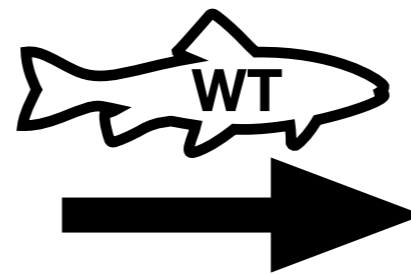
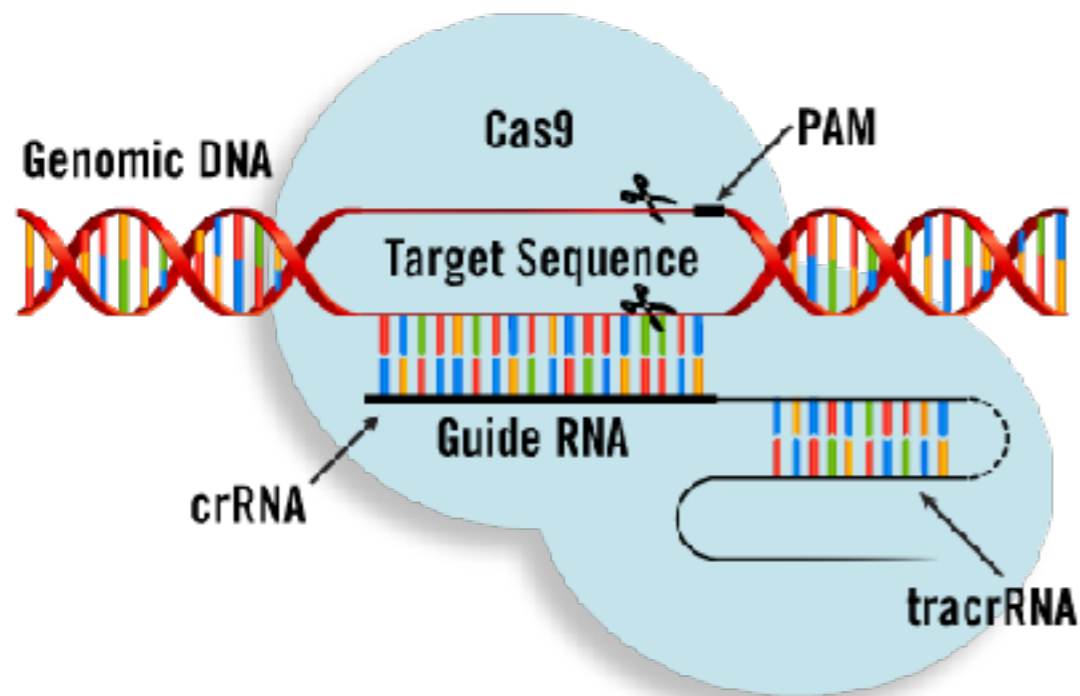
Serine 861

Heterozygous Mutants

NetPhos and
ClustalOMEGA

CRISPR/Cas9

Aim 1: Identify conserved phosphorylation sites of SYNGAP1 that play a role in social behavior.

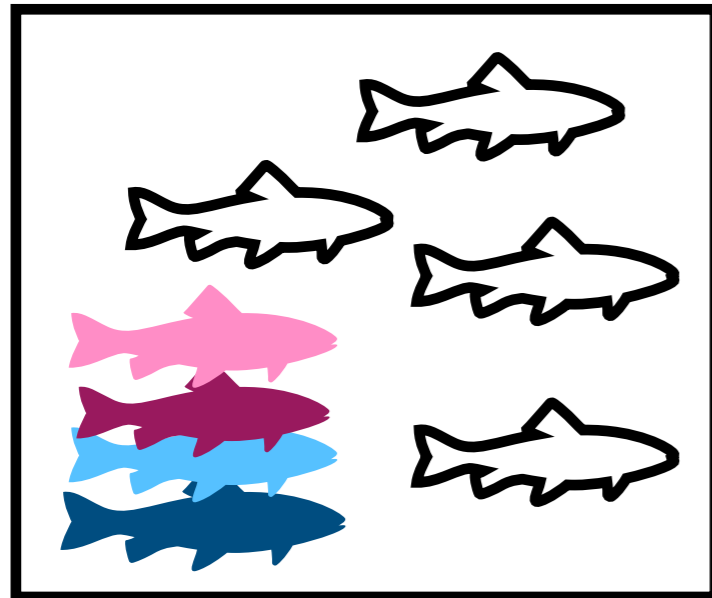
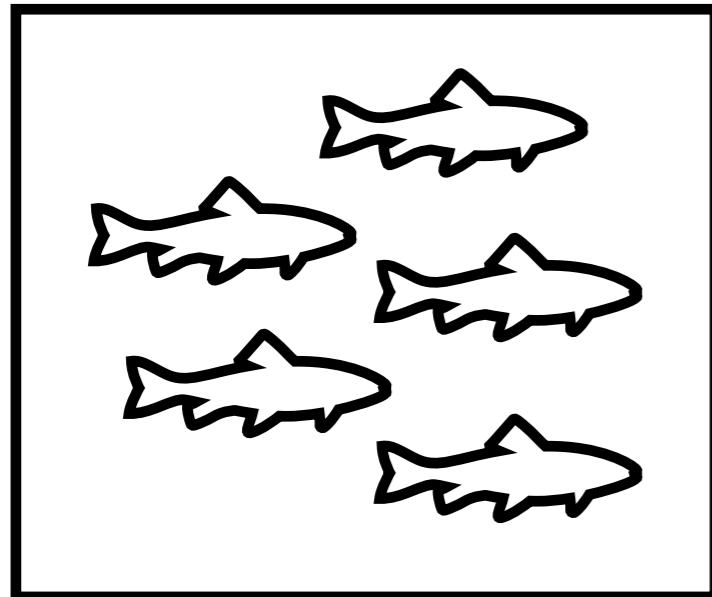


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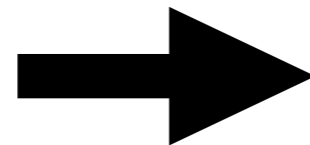
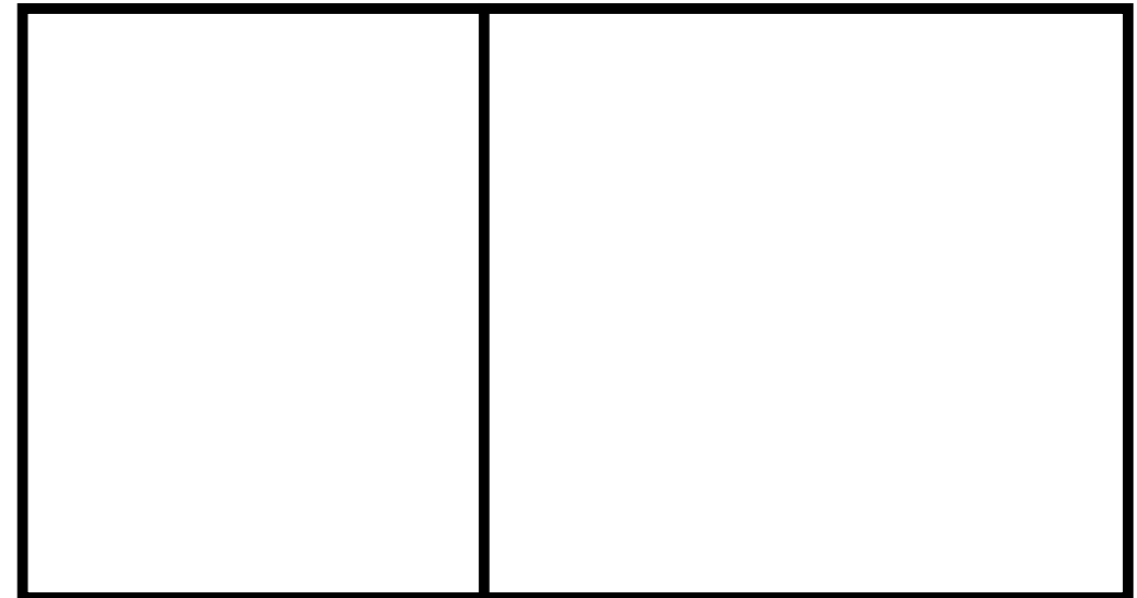
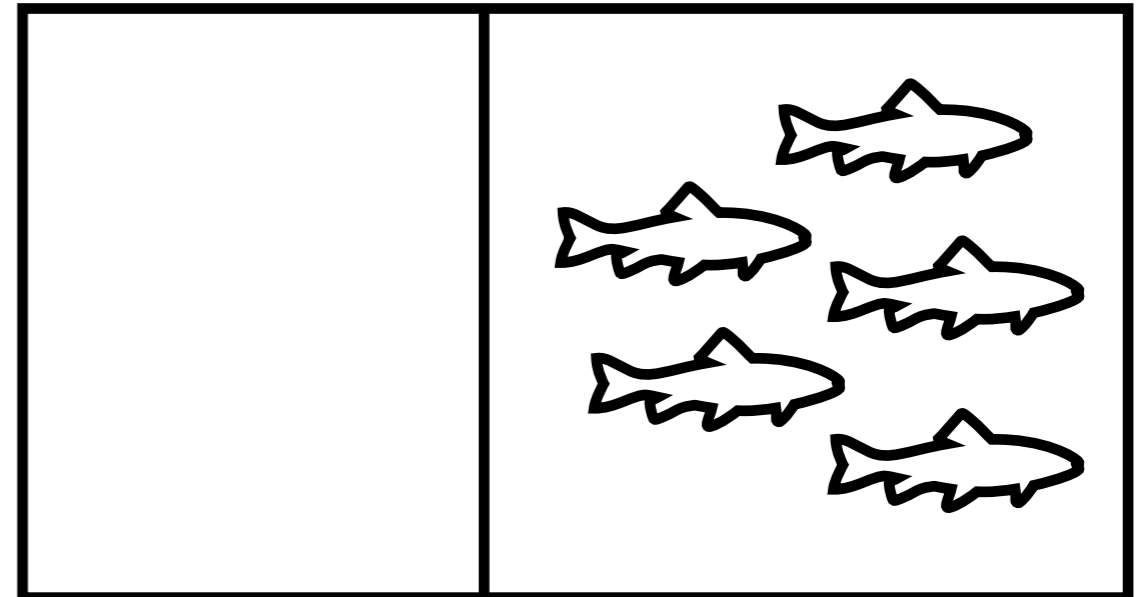


Aim 1: Identify conserved phosphorylation sites of SYNGAP1 that play a role in social behavior.

Shoaling



Social Preference



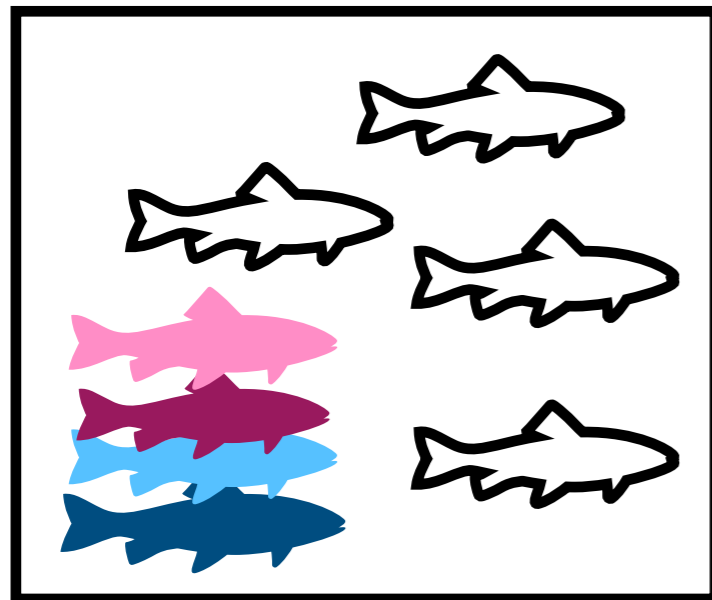
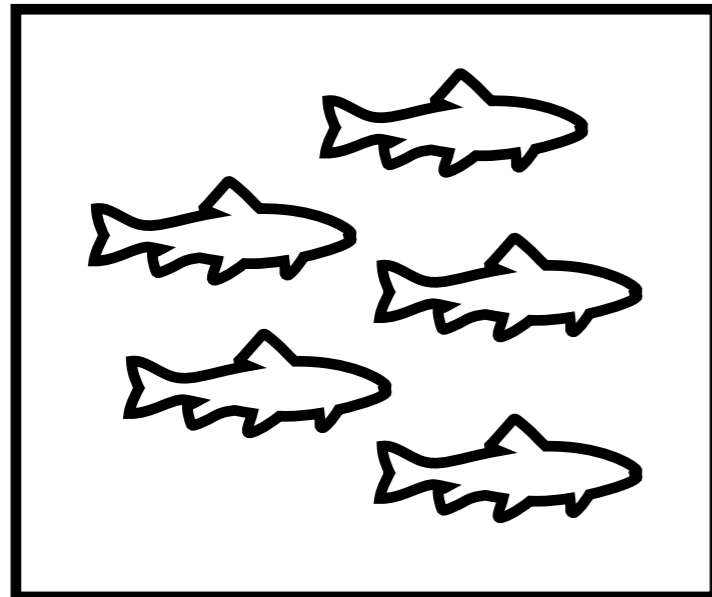
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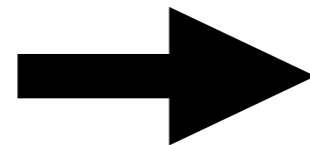
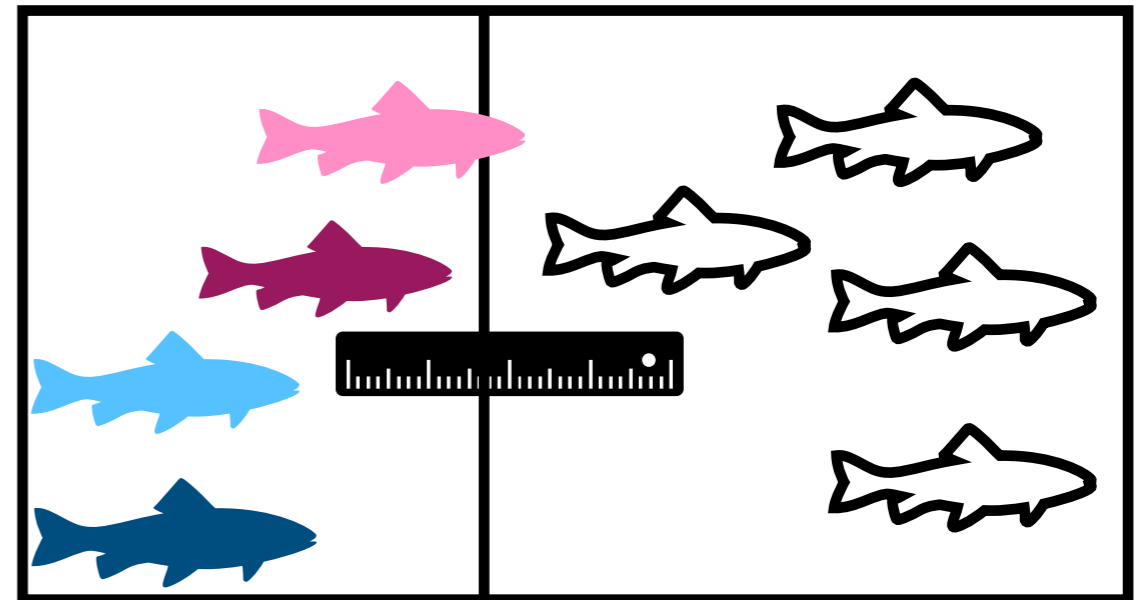
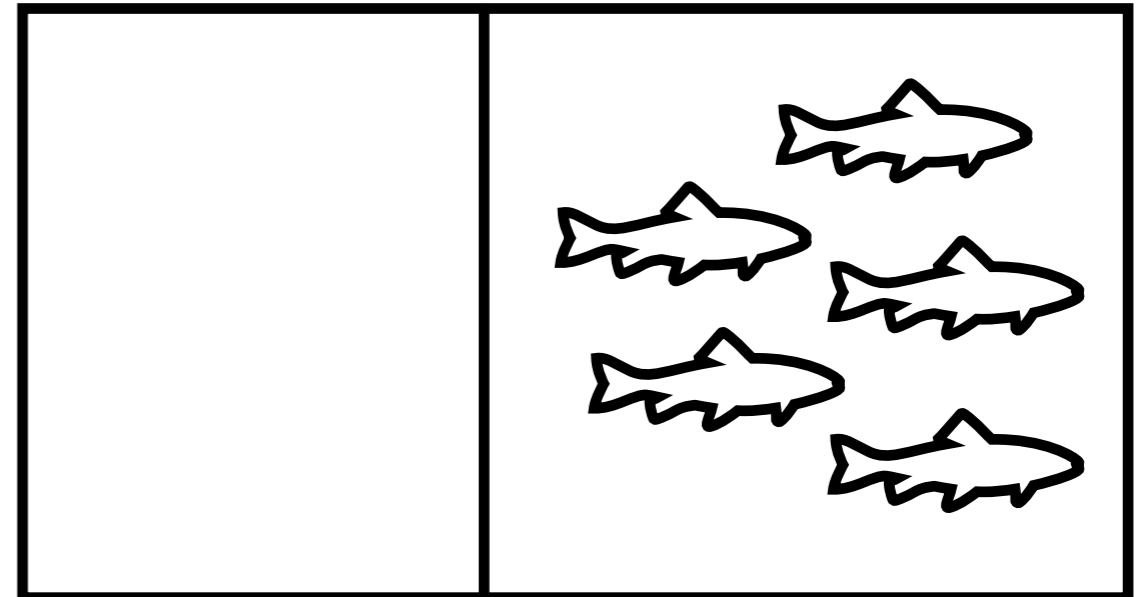
Screen for
Behavior Mutants

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Social Preference



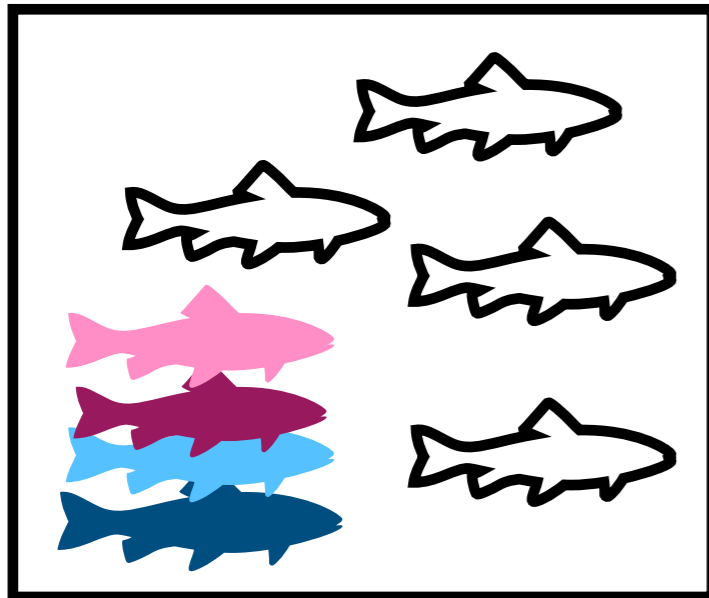
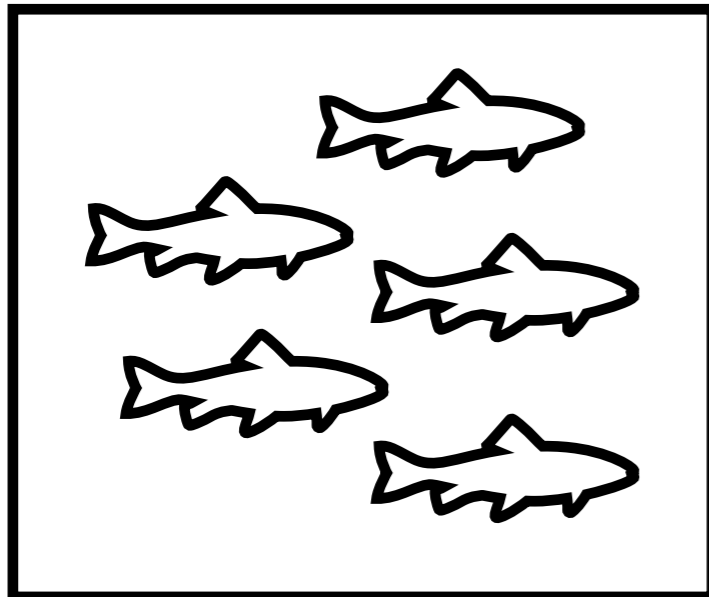
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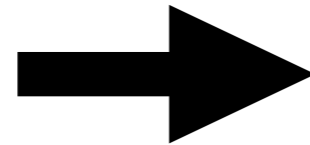
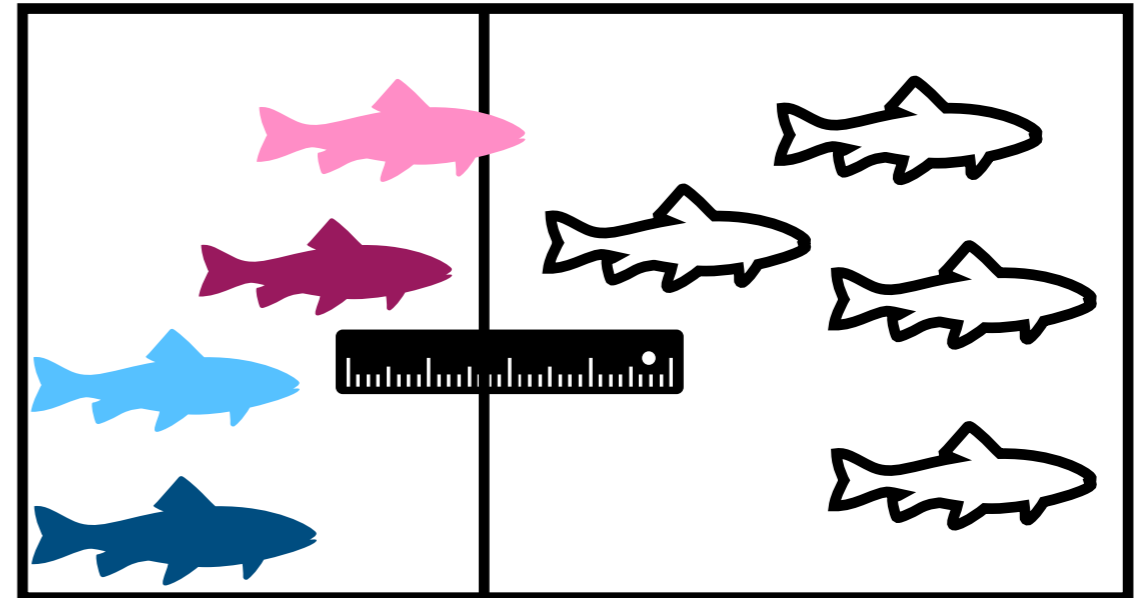
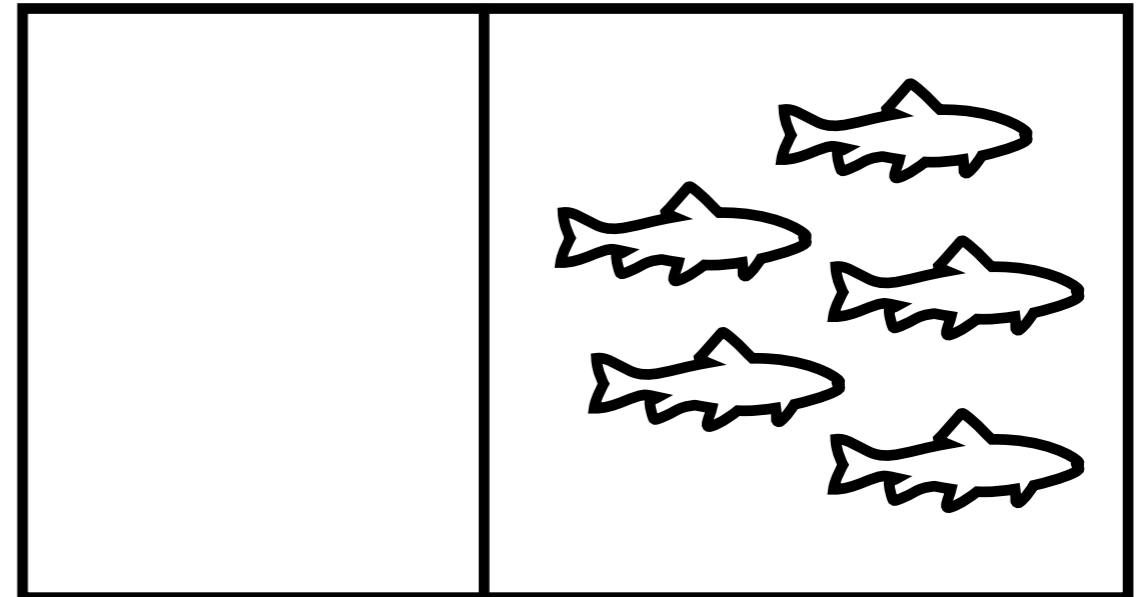
Screen for
Behavior Mutants

Hypothesis: Males will show a larger social deficit than females, but both males and females with phosphorylation mutations will show a phenotype.

Shoaling



Social Preference



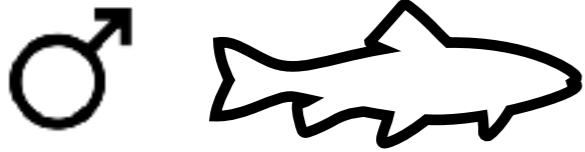
**NetPhos and
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CRISPR/Cas9

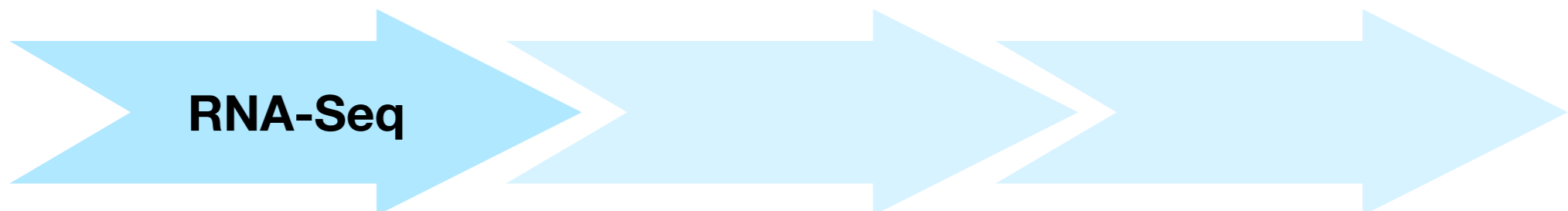
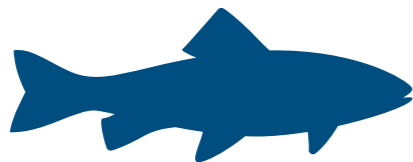
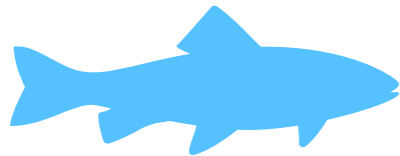
**Screen for
Behavior Mutants**

Aim 2: Profile differentially expressed genes in social behavior mutant brains.

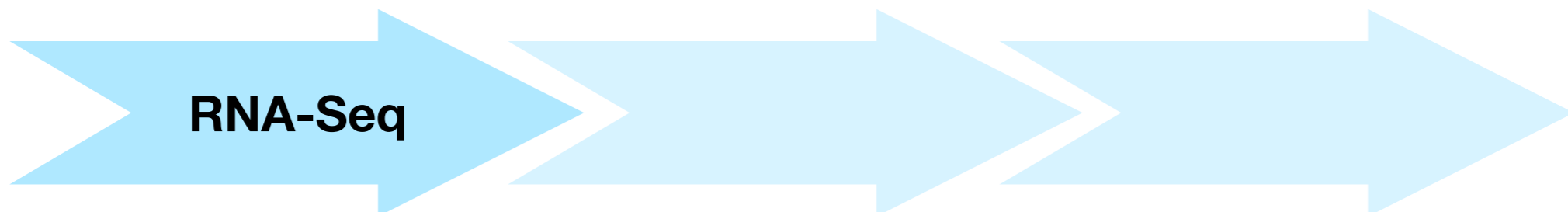
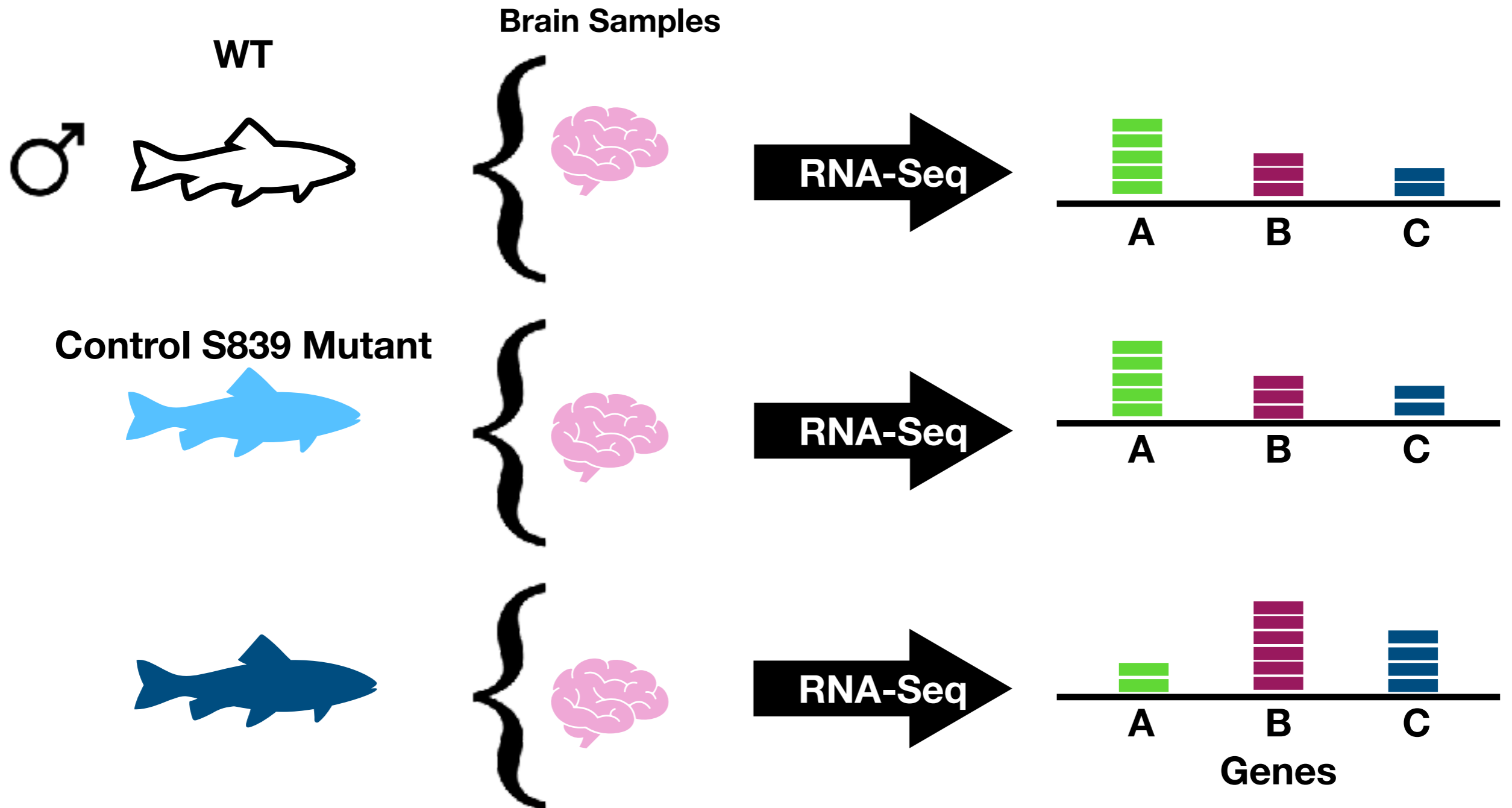
WT



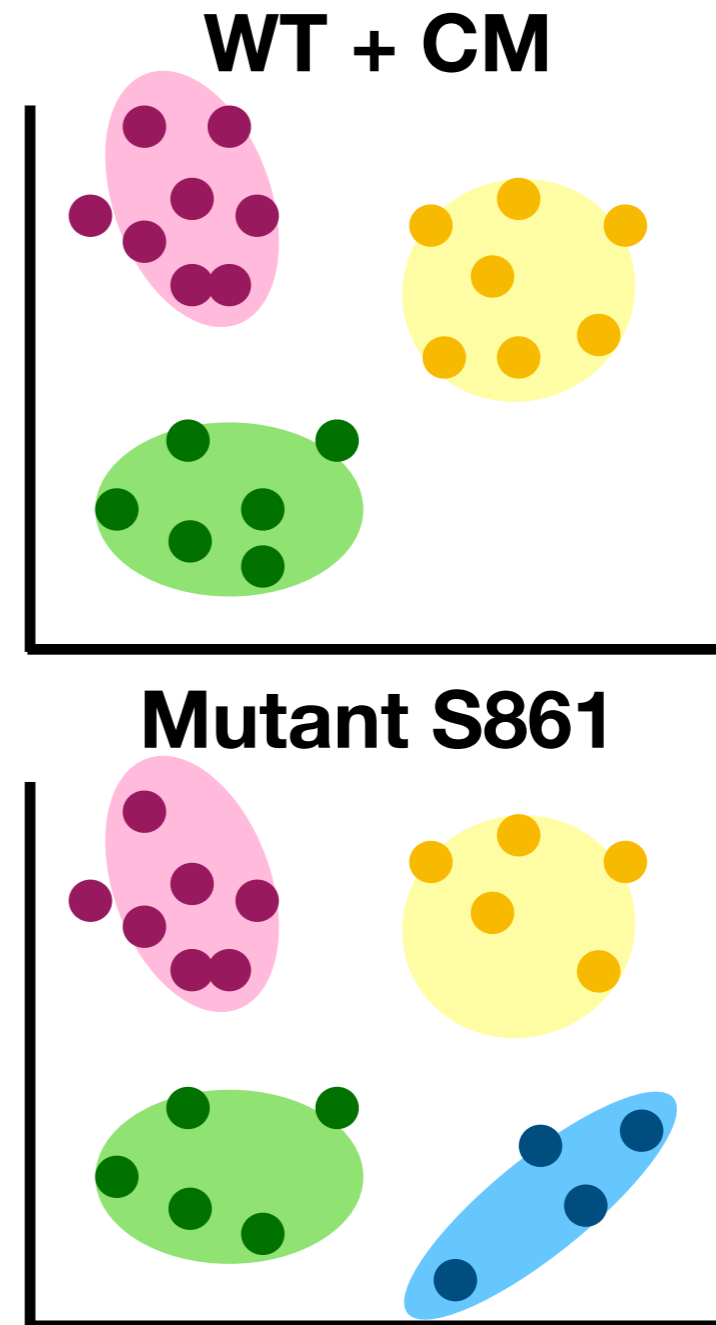
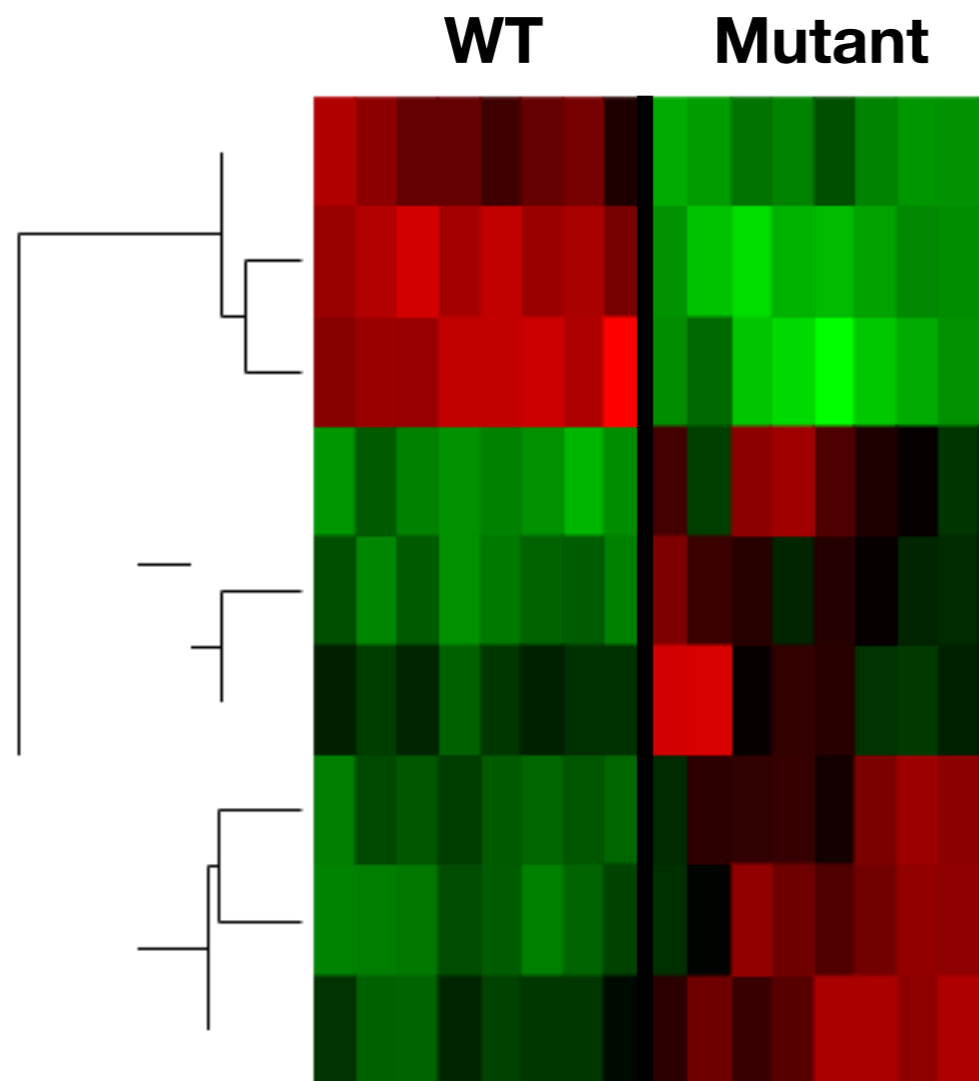
Control S839 Mutant



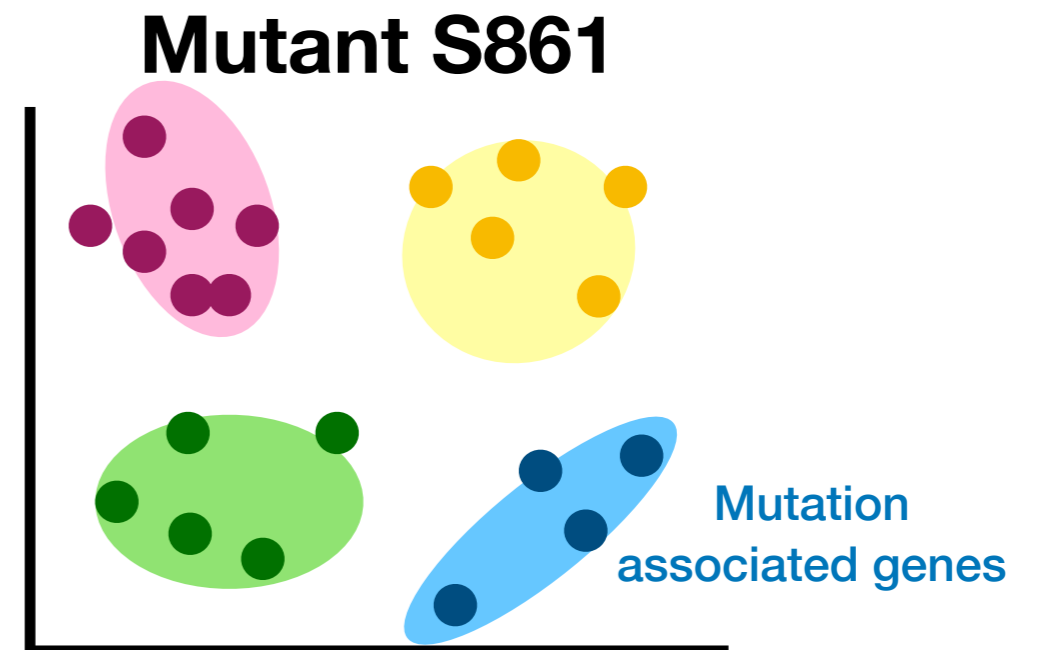
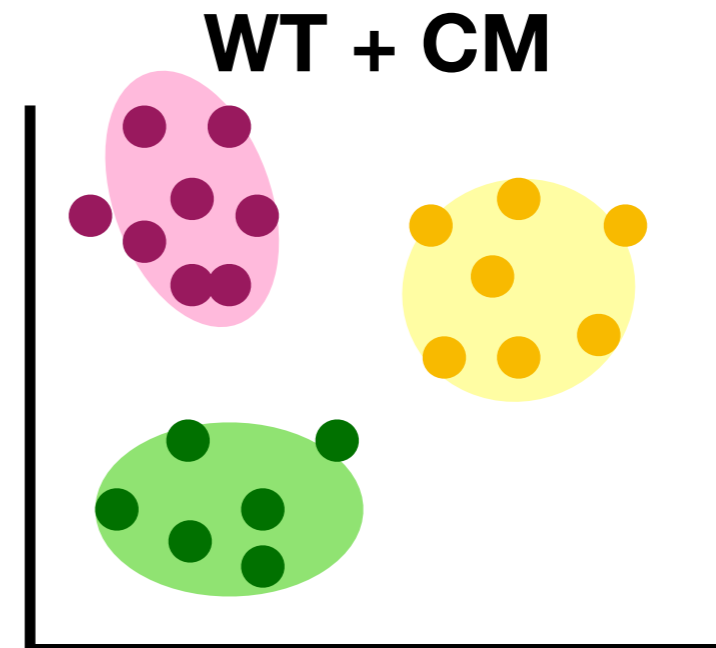
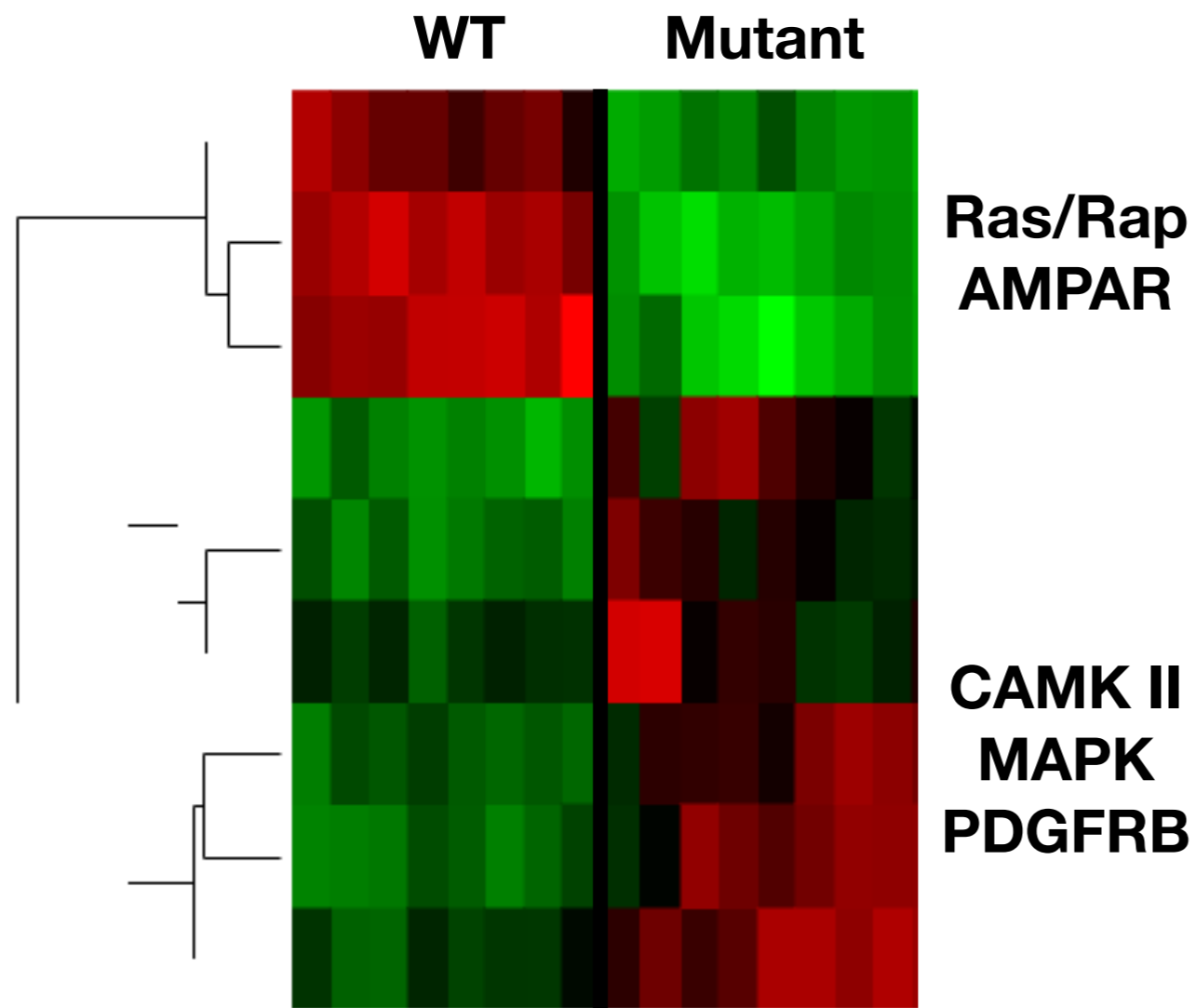
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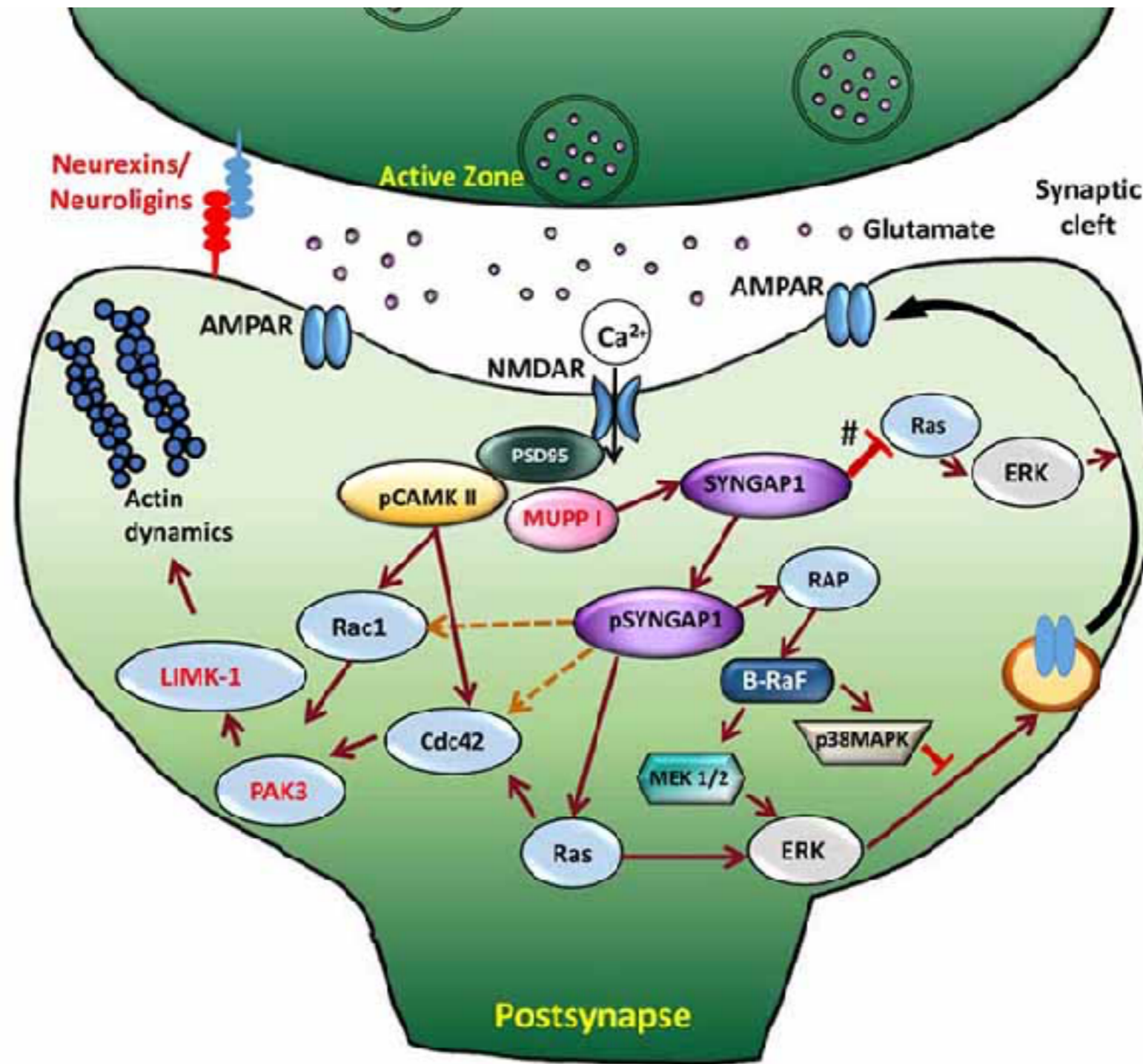
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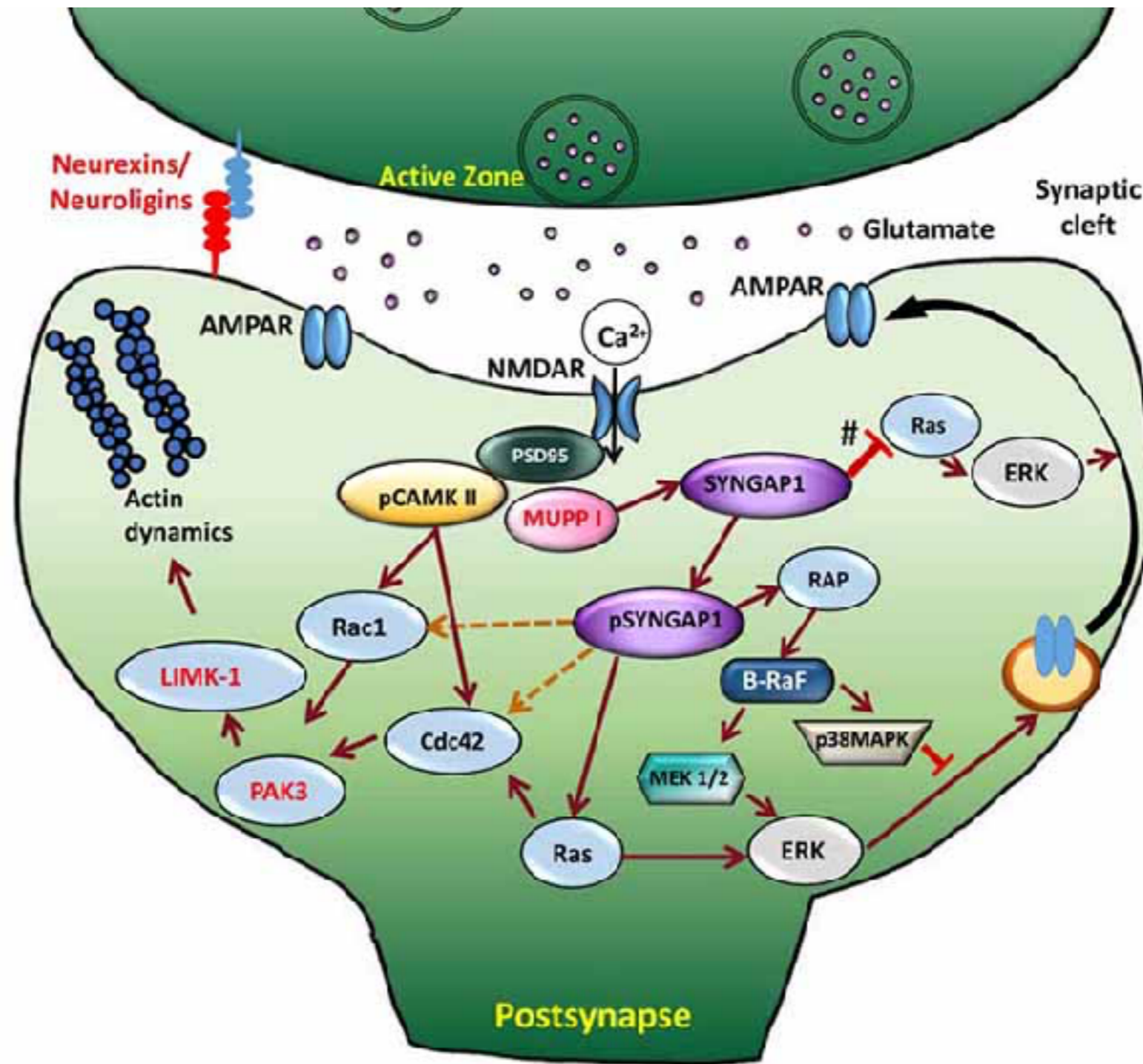


RNA-Seq

GO

Pathway
Analysis

Hypothesis: Many new gene/protein interactions with SYNGAP1 will be identified and a large amount of these will involve kinases.

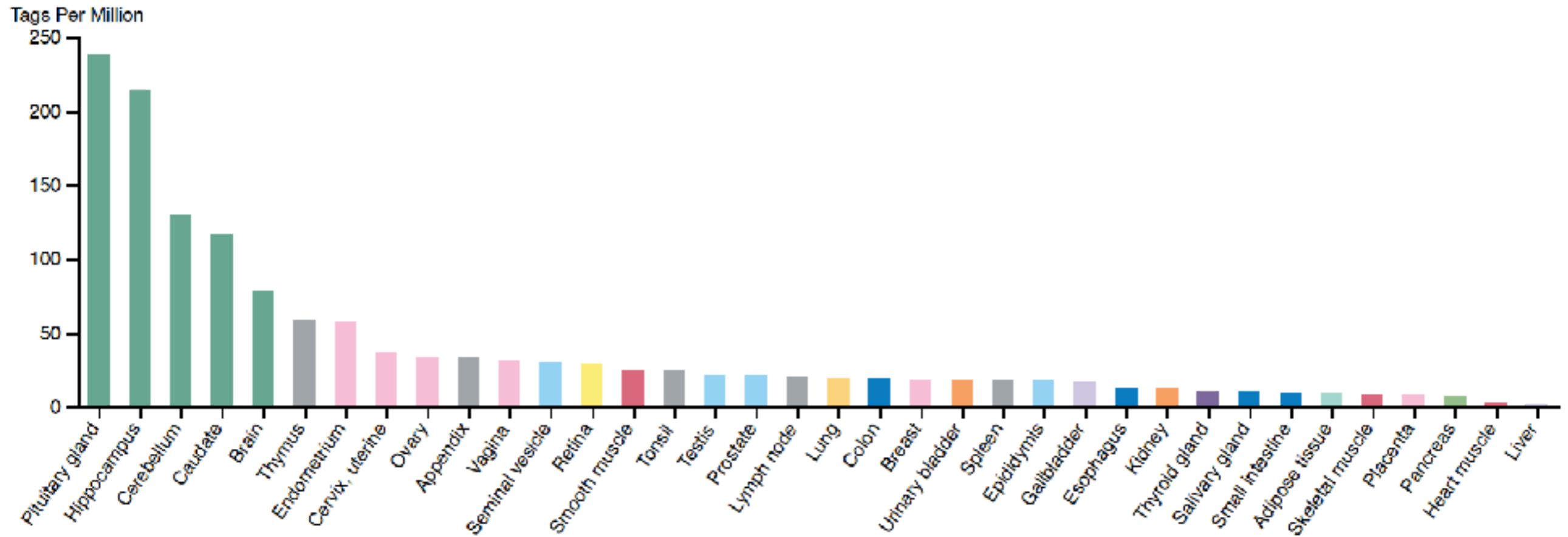


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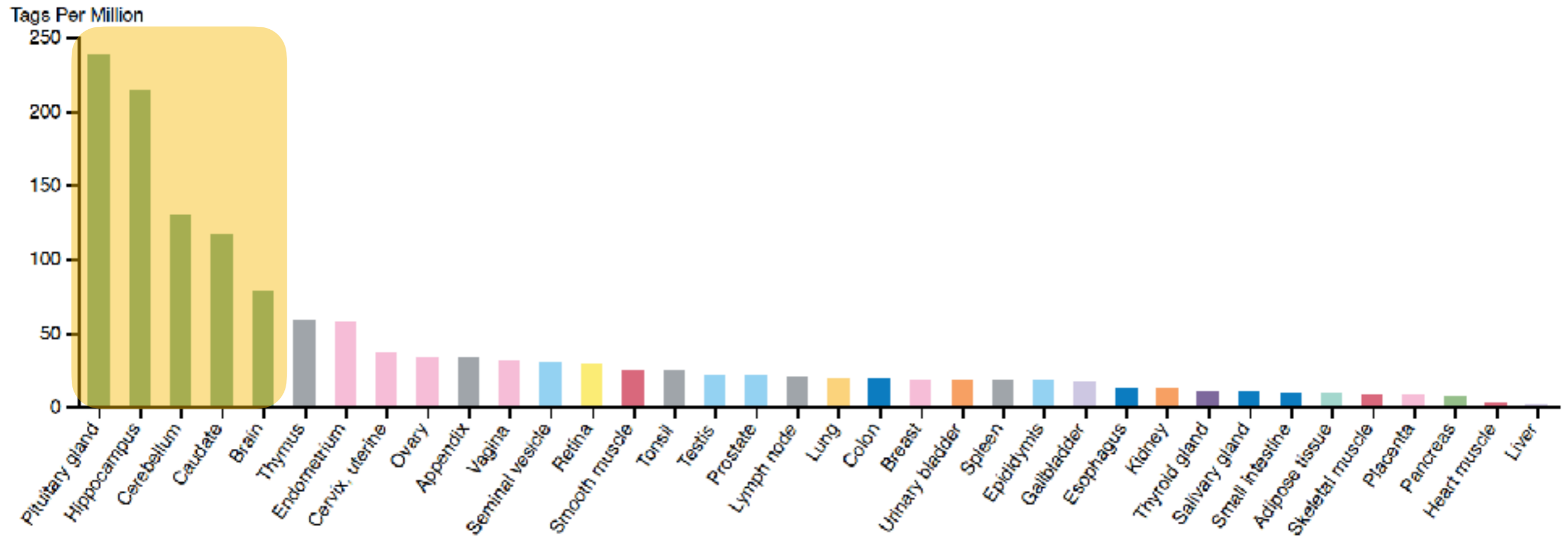
GO

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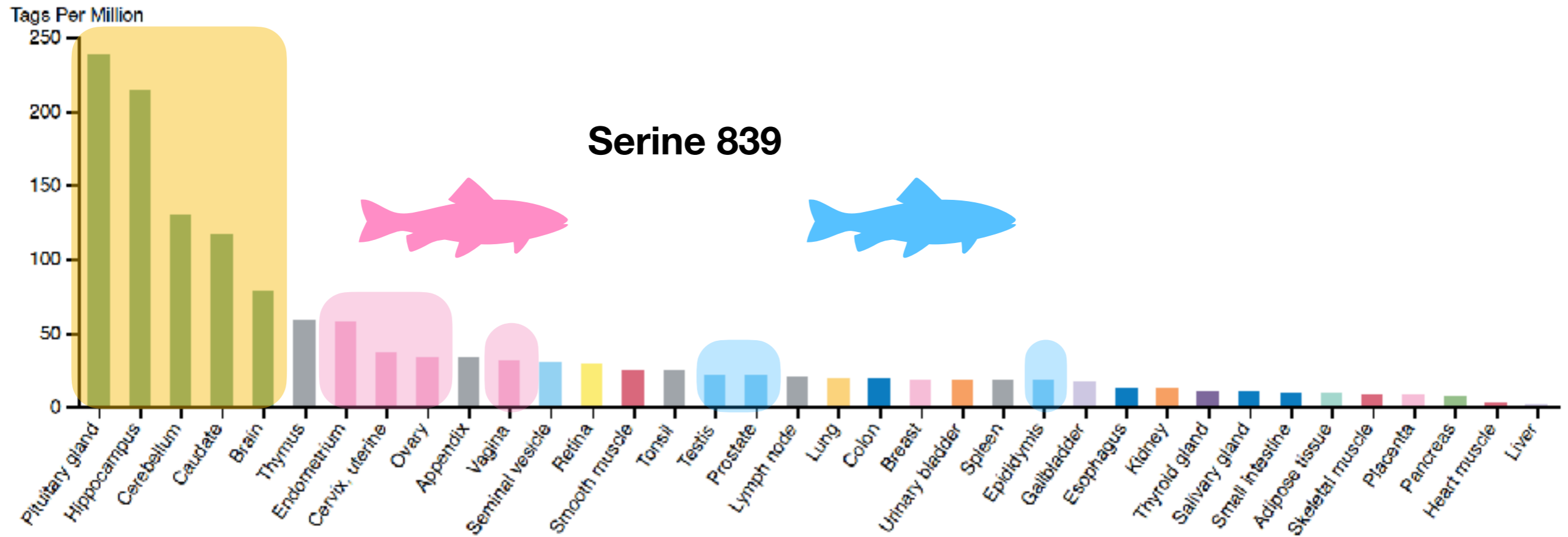
Aim 3: Identify SYNGAP1 interacting proteins that differentiate between gender and are associated with social behavior.



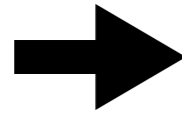
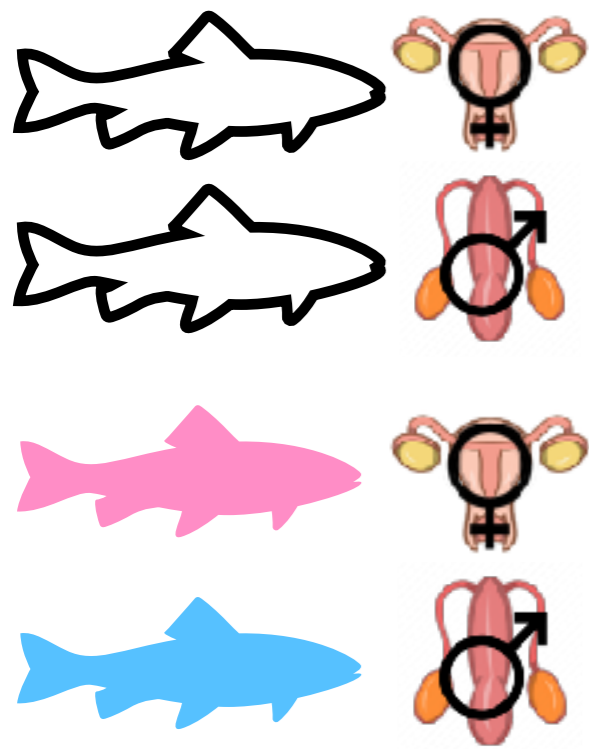
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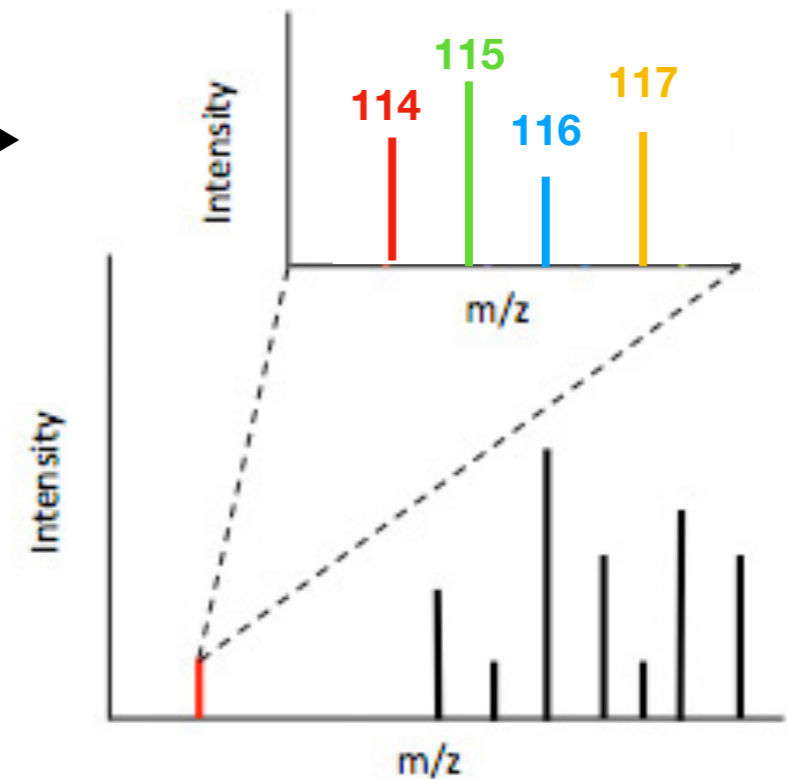
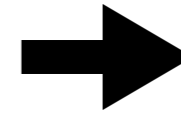


iTRAQ- 114

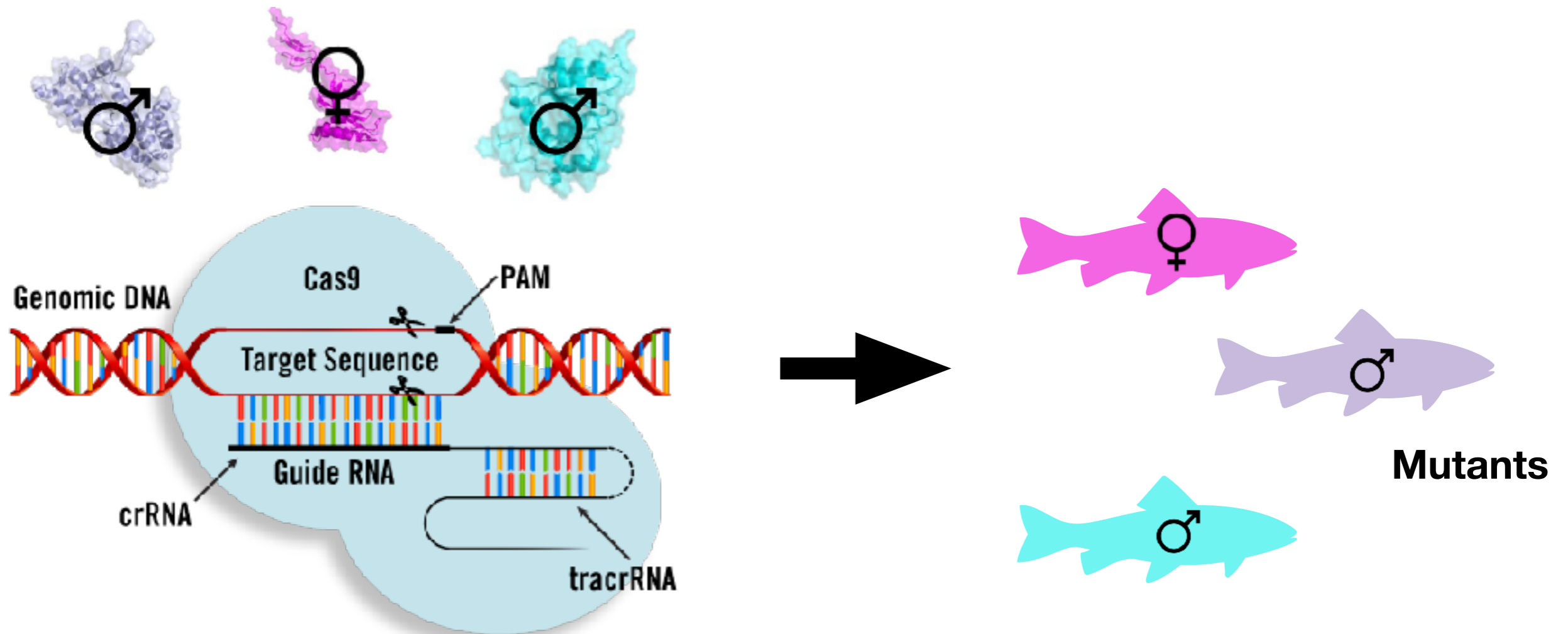
iTRAQ- 115

iTRAQ- 116

iTRAQ- 117

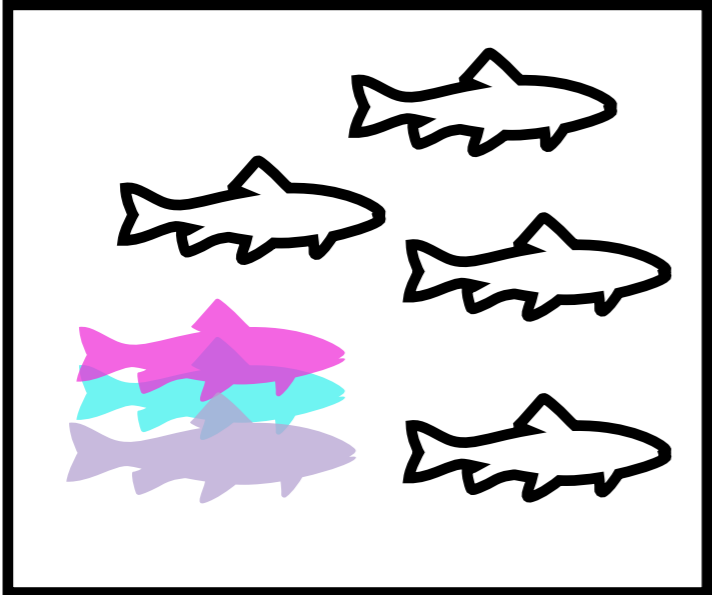
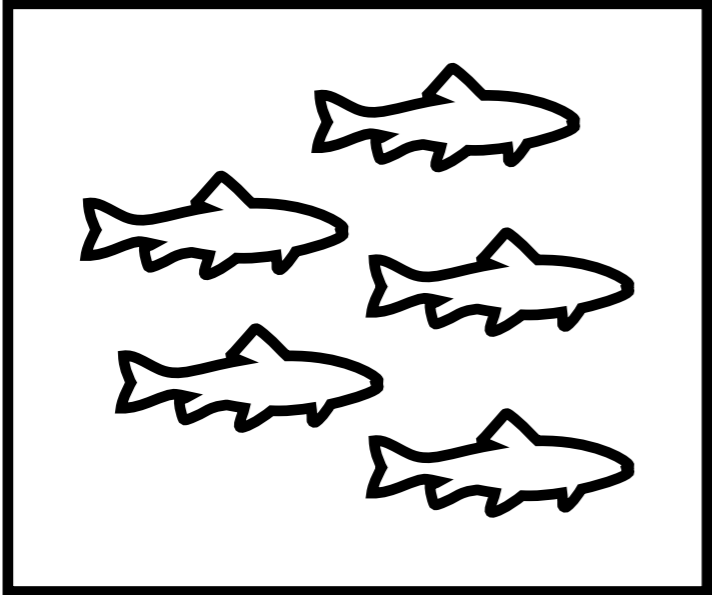


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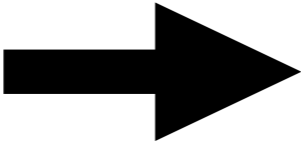
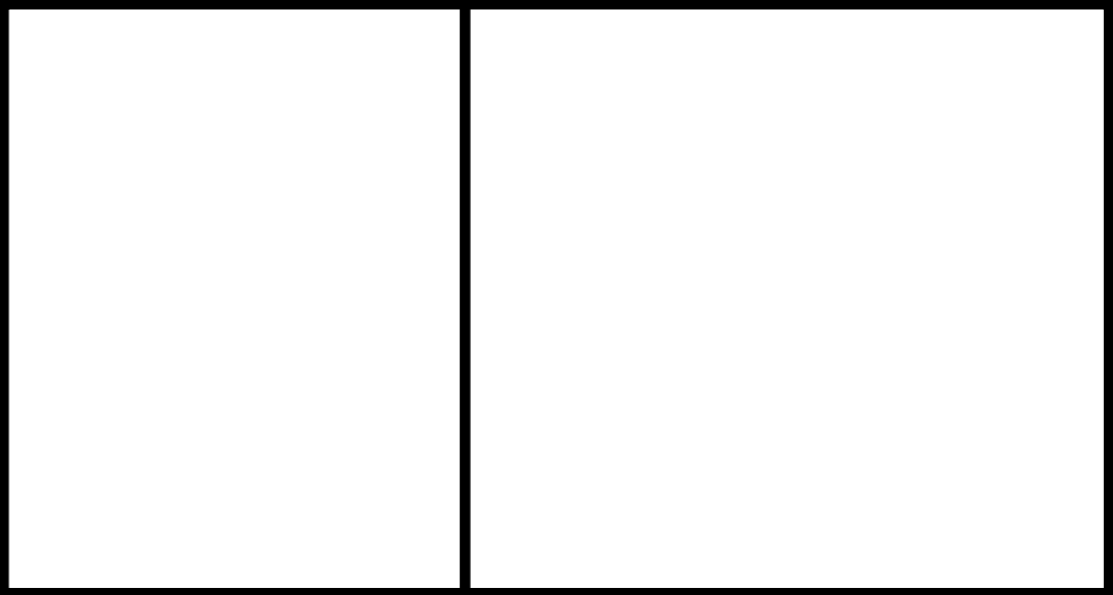
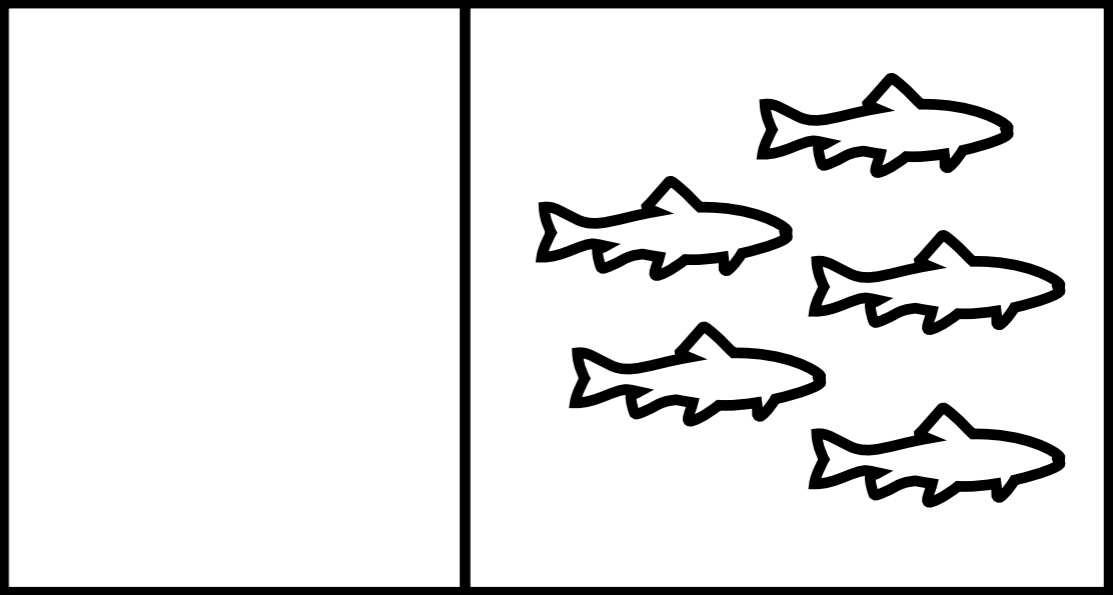


Aim 3: Identify SYNGAP1 interacting proteins that differentiate between gender and are associated with social behavior.

Shoaling

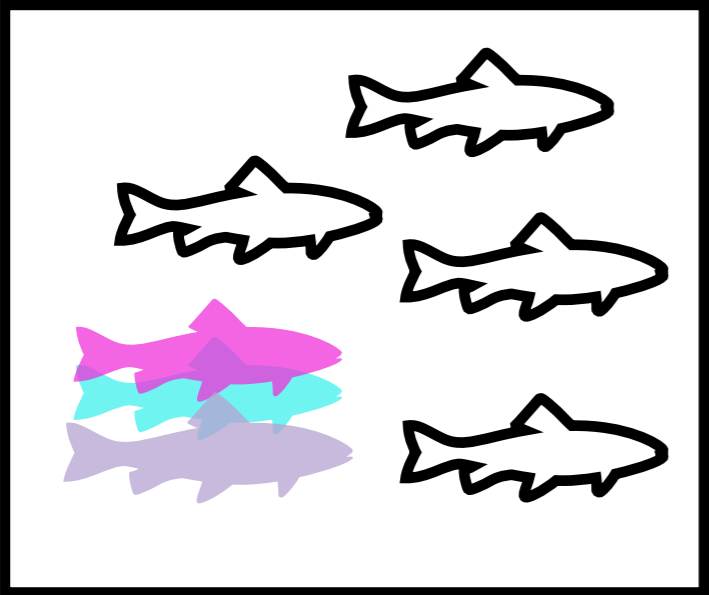
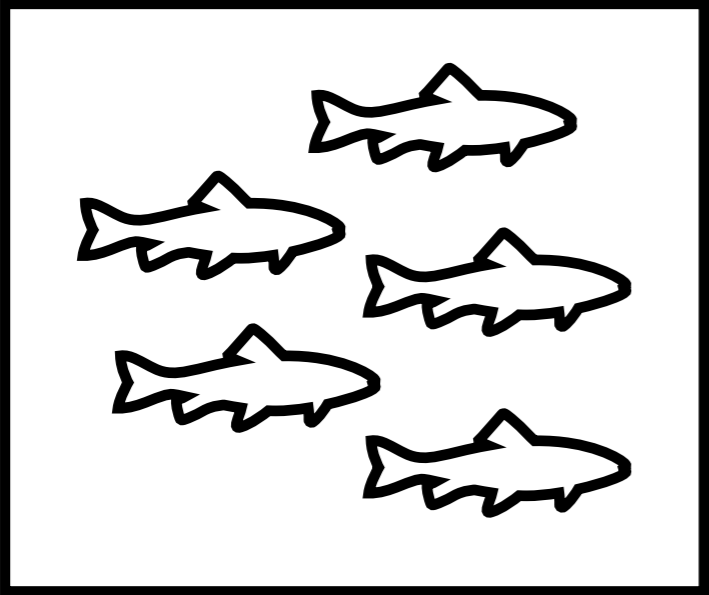


Social Preference

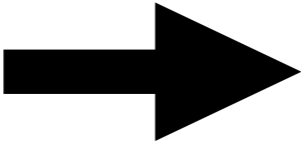
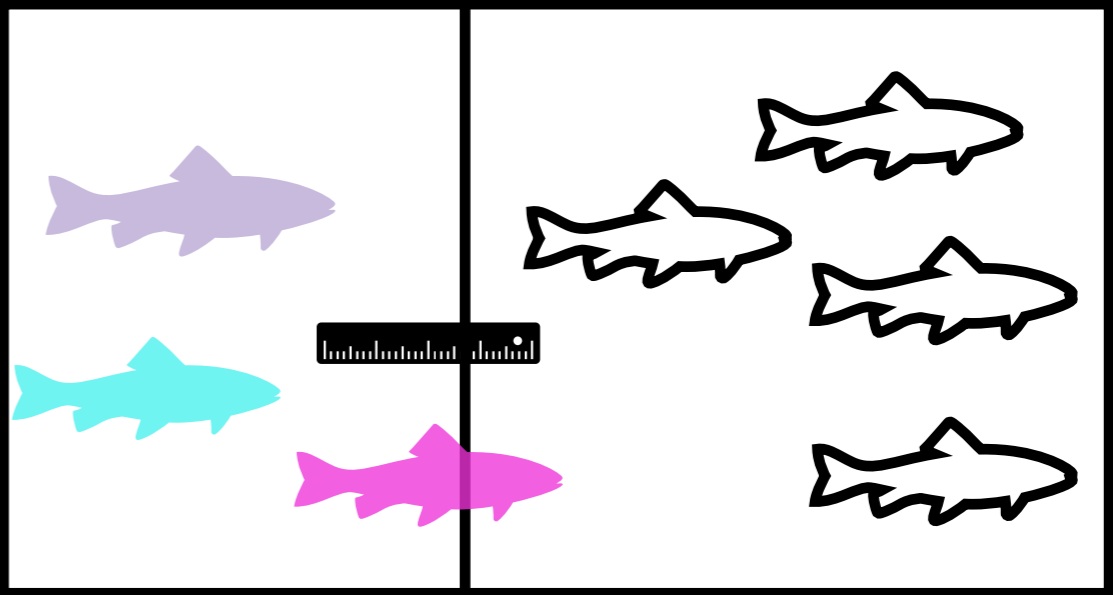
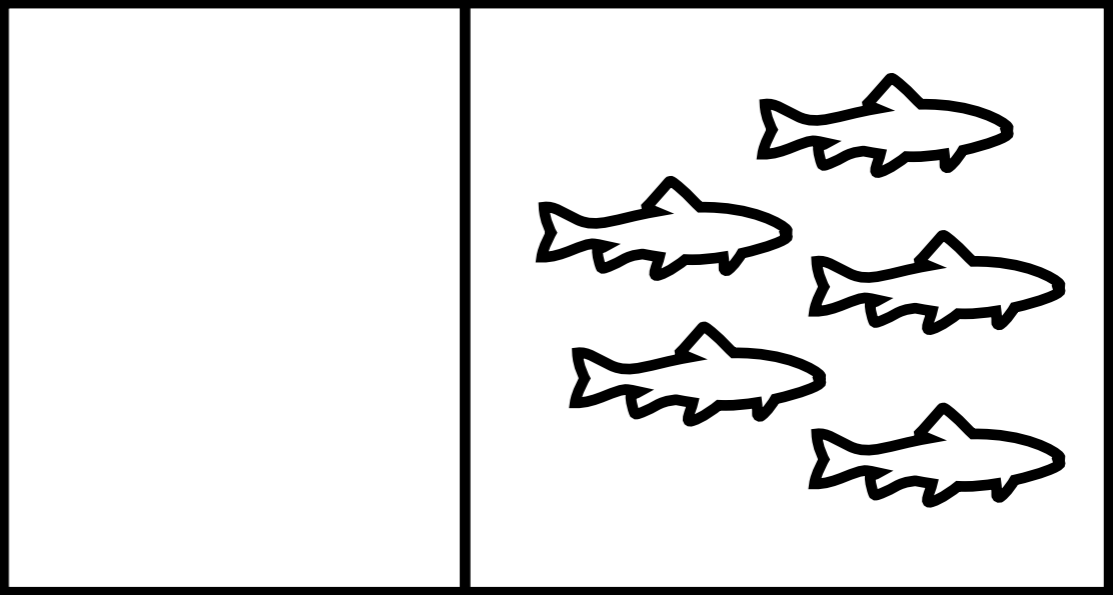


Aim 3: Identify SYNGAP1 interacting proteins that differentiate between gender and are associated with social behavior.

Shoaling



Social Preference

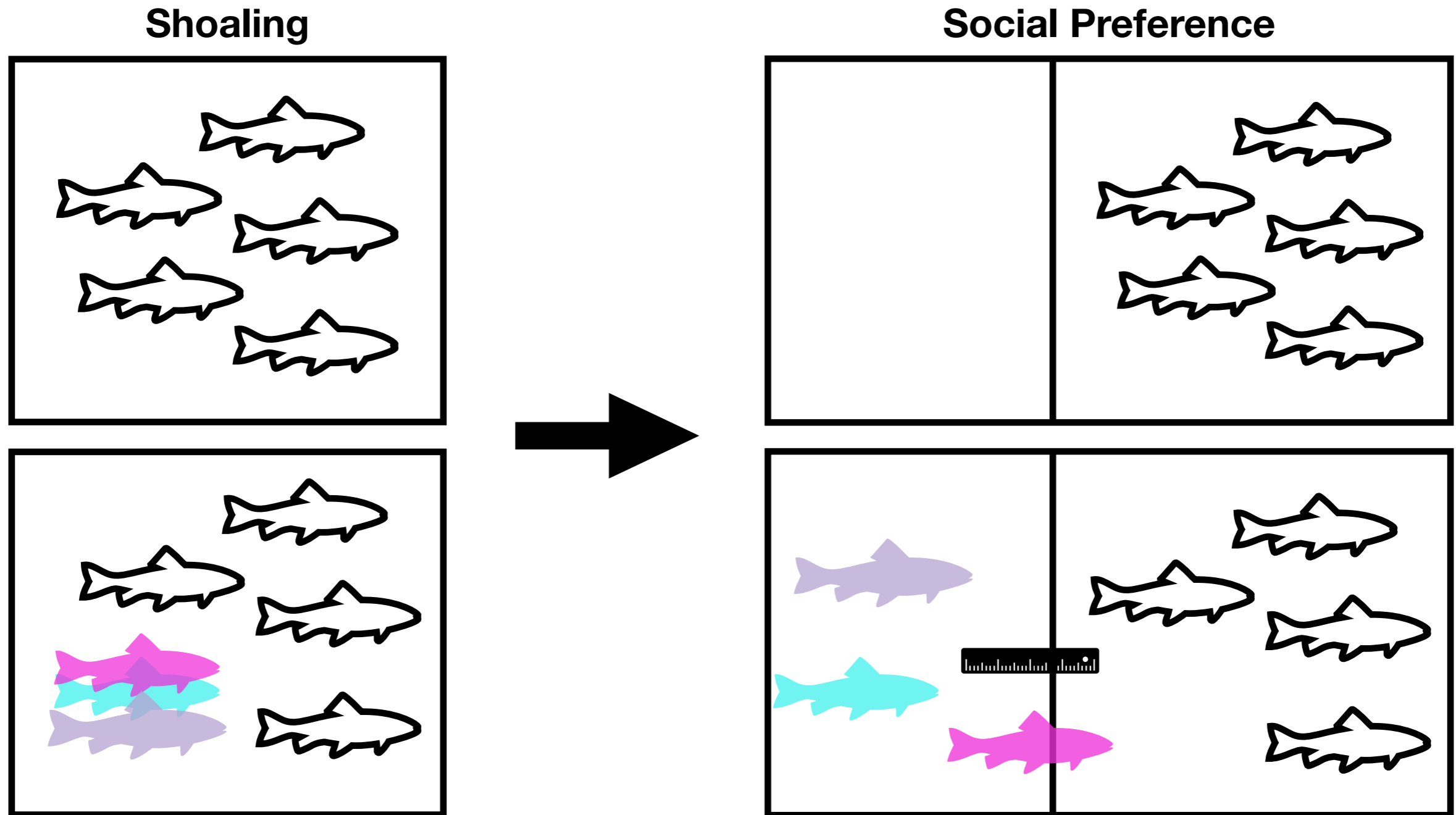


iTRAQ

CRISPR/Cas9

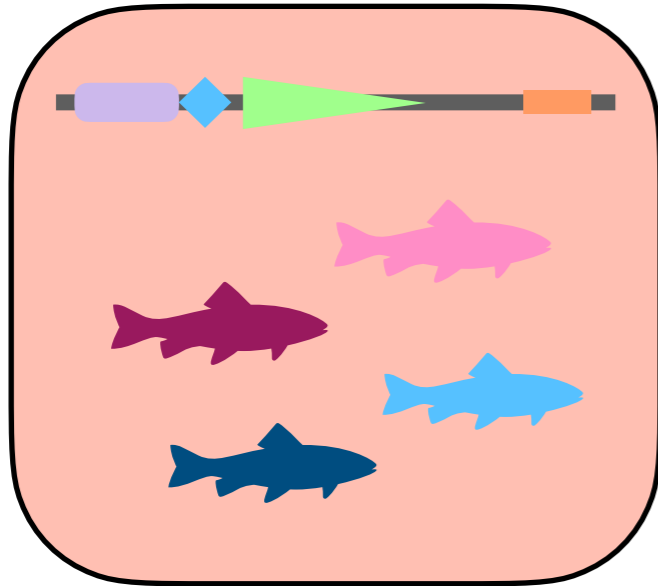
Screen for Behavior Mutants

Hypothesis: Kinases will interact with WT SYNGAP1 but not mutant. Males have more kinase interacting proteins than females that when mutated can lead to social deficits.



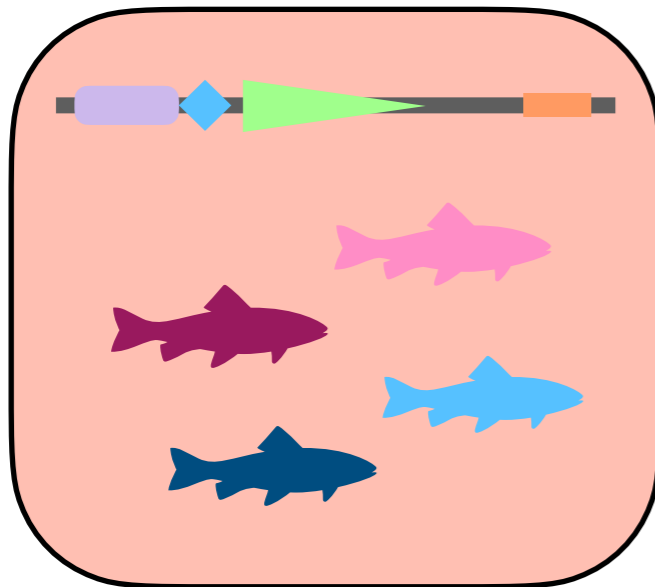
Conclusions

Conclusions

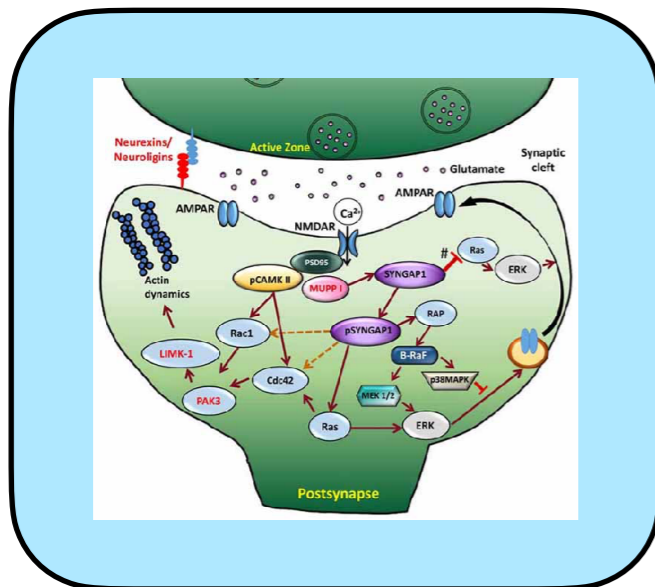


Specific conserved phosphorylation sites within SYNGAP1 play a role in social behavior.

Conclusions

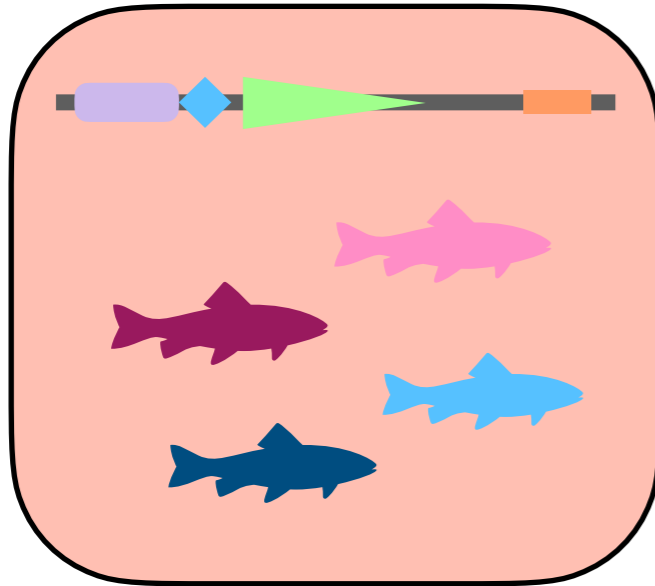


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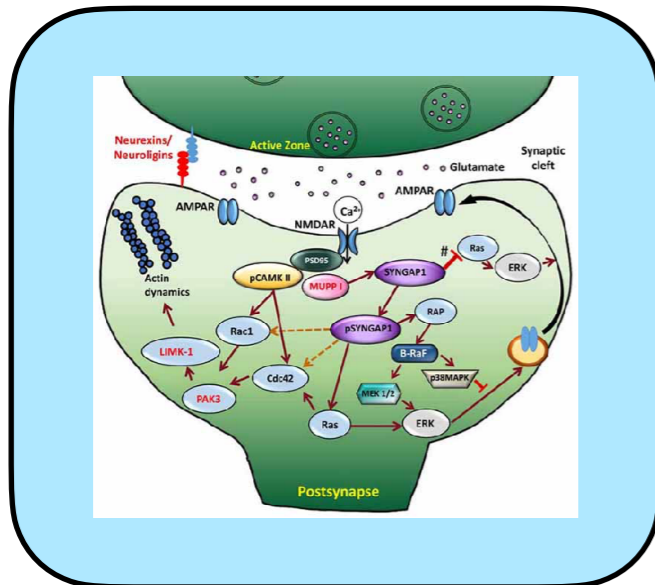


SYNGAP1 is up- and down regulated with other genes that correlate to social behavior.

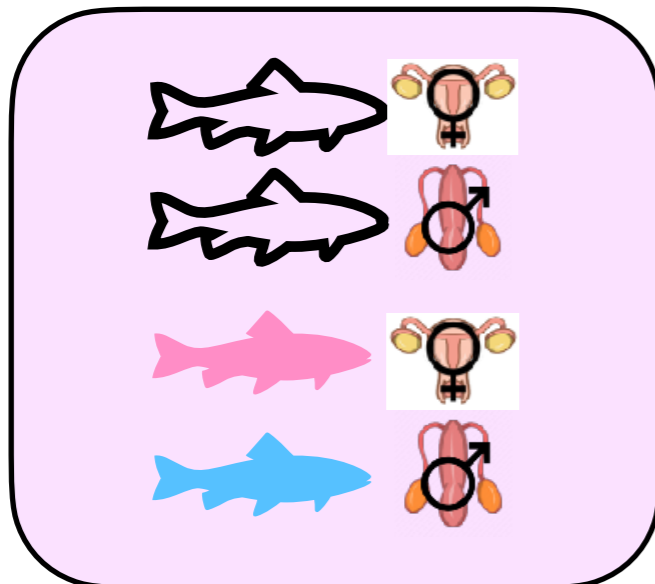
Conclusions



Specific conserved phosphorylation sites within SYNGAP1 play a role in social behavior.

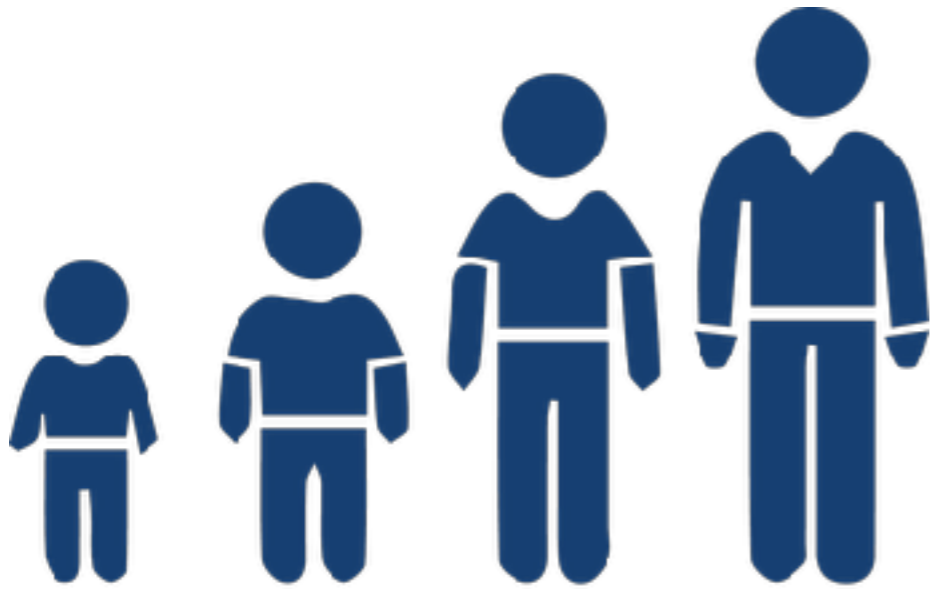


SYNGAP1 is up- and down regulated with other genes that correlate to social behavior.

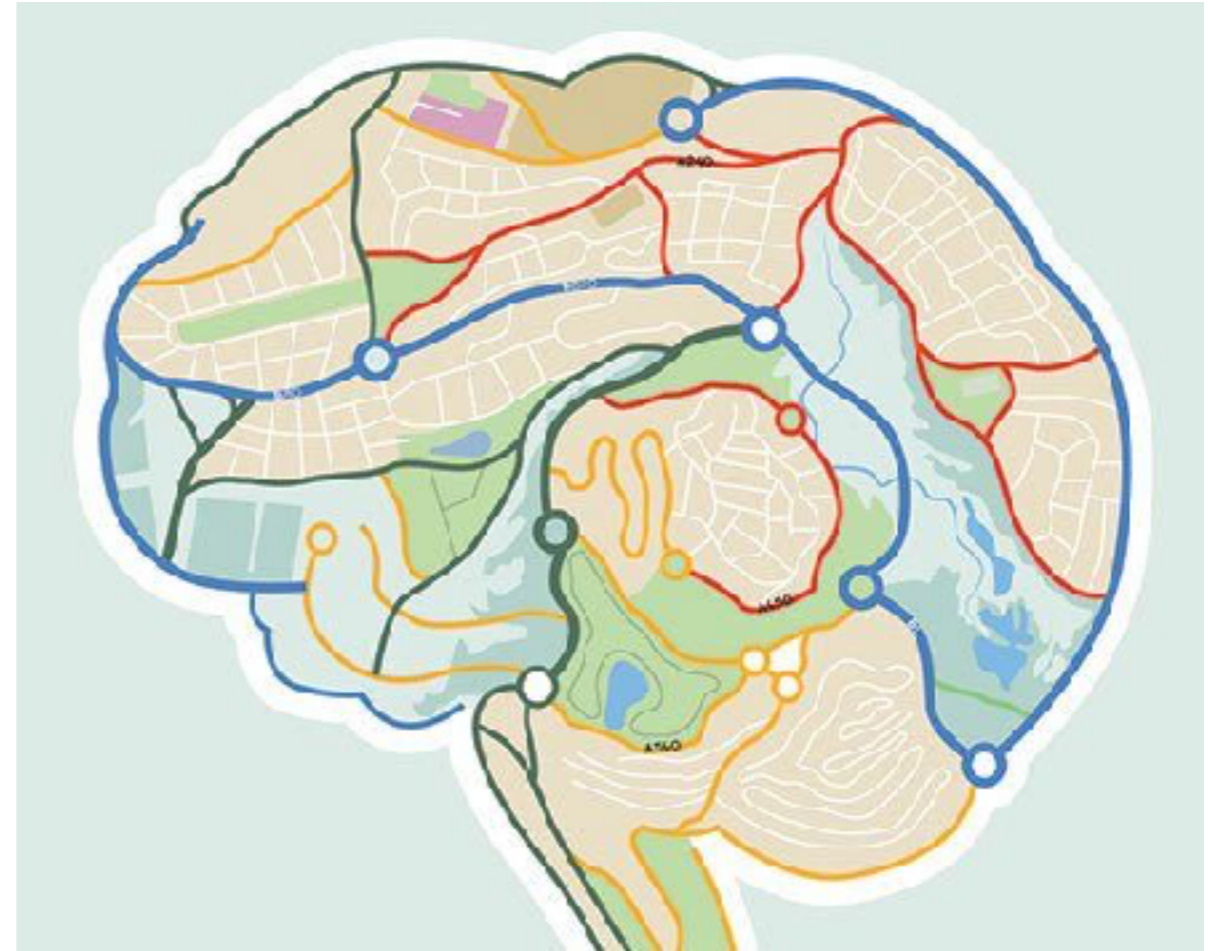


SYNGAP1 interacts with many other proteins that play a role in social behavior and there are gender differences.

Future Directions



**Repetitive
Behaviors**





References

Images:

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