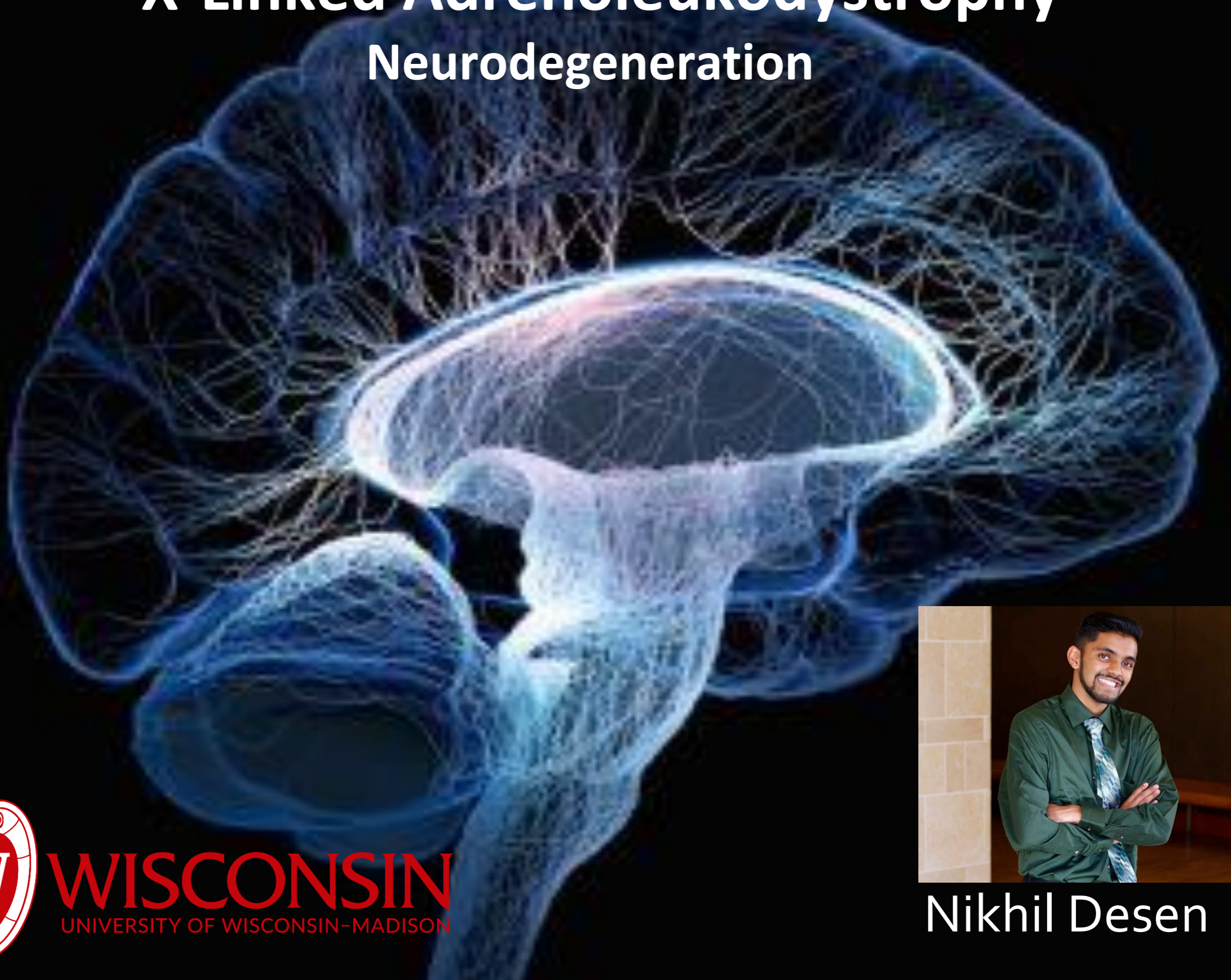


X-Linked Adrenoleukodystrophy

Neurodegeneration

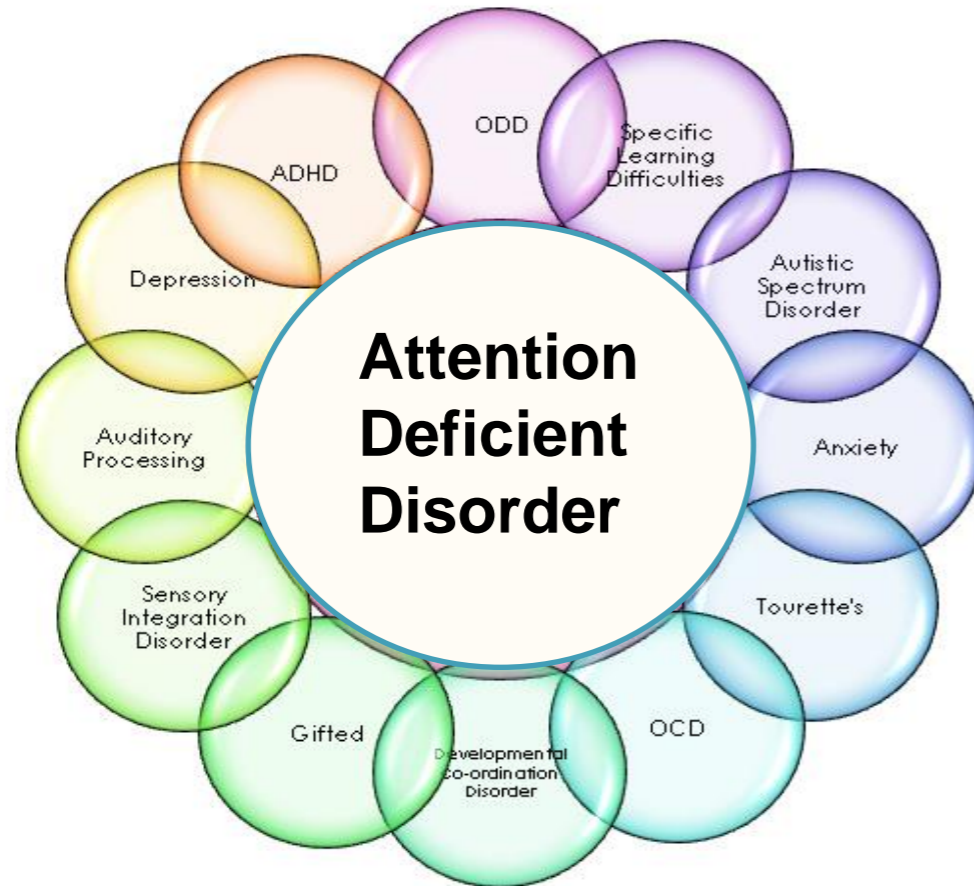


Nikhil Desen



WISCONSIN
UNIVERSITY OF WISCONSIN-MADISON

What are the symptoms X-linked ALD?



Back pain



Hearing loss



Vision Impairment

The Gene ABCD1 Causes ALD

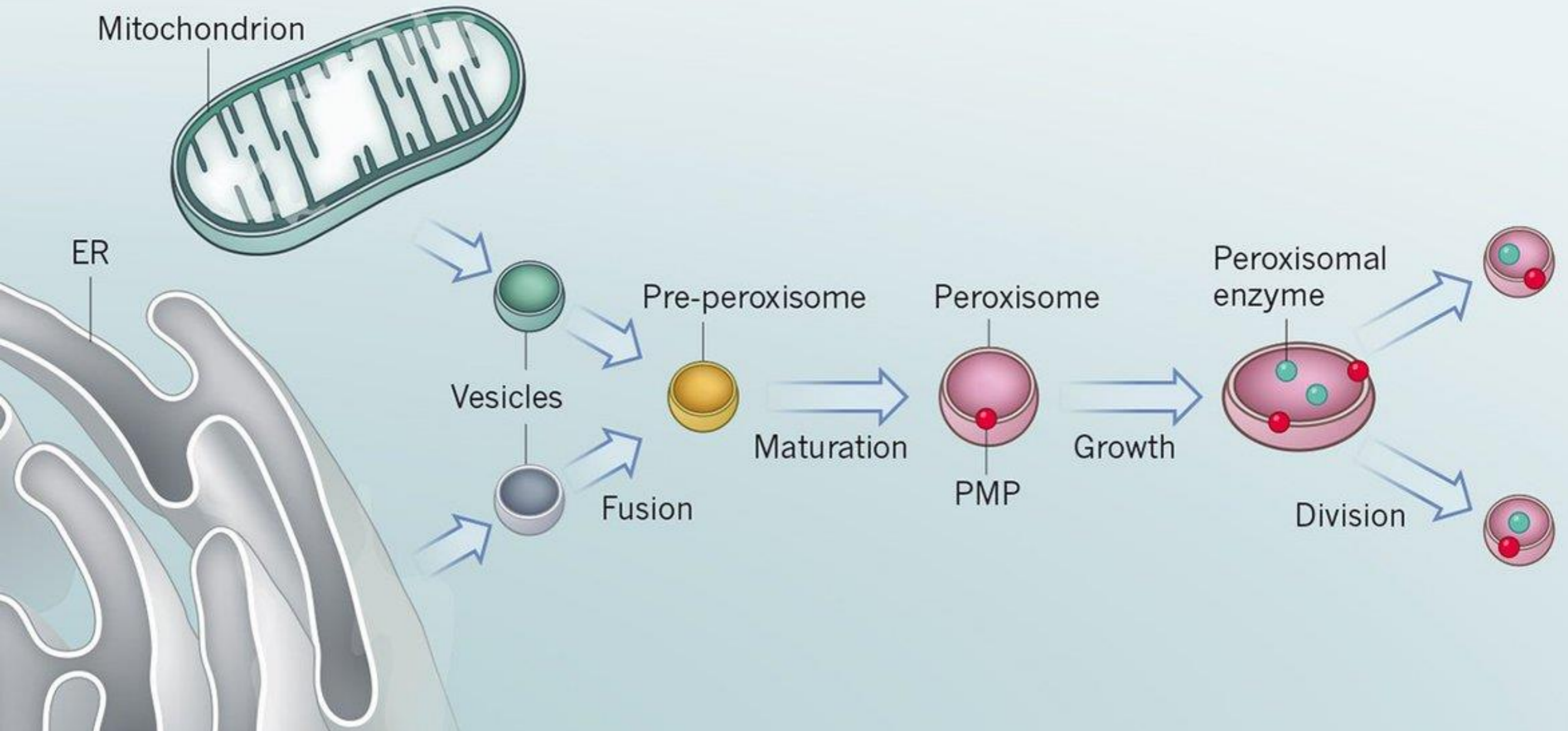


Molecular Function

Biological Process

**Cellular
Component**

What is a peroxisome?



What is X-linked ALD?

ABCD1 is widely conserved



78 to 352

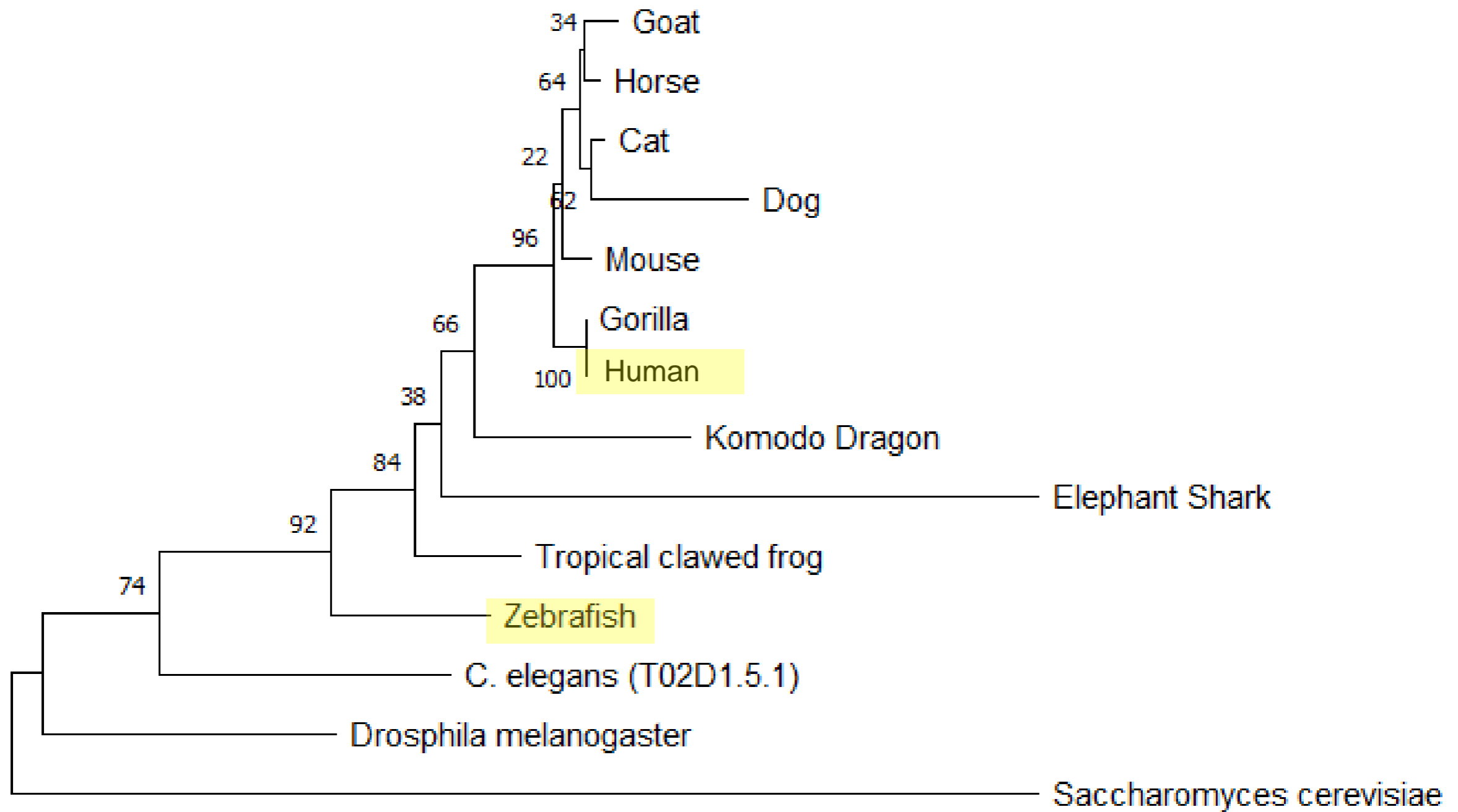
490 to 633

ABC_membrane_2

ABC_tran



ABCD1 is an Ancient Gene



0.20

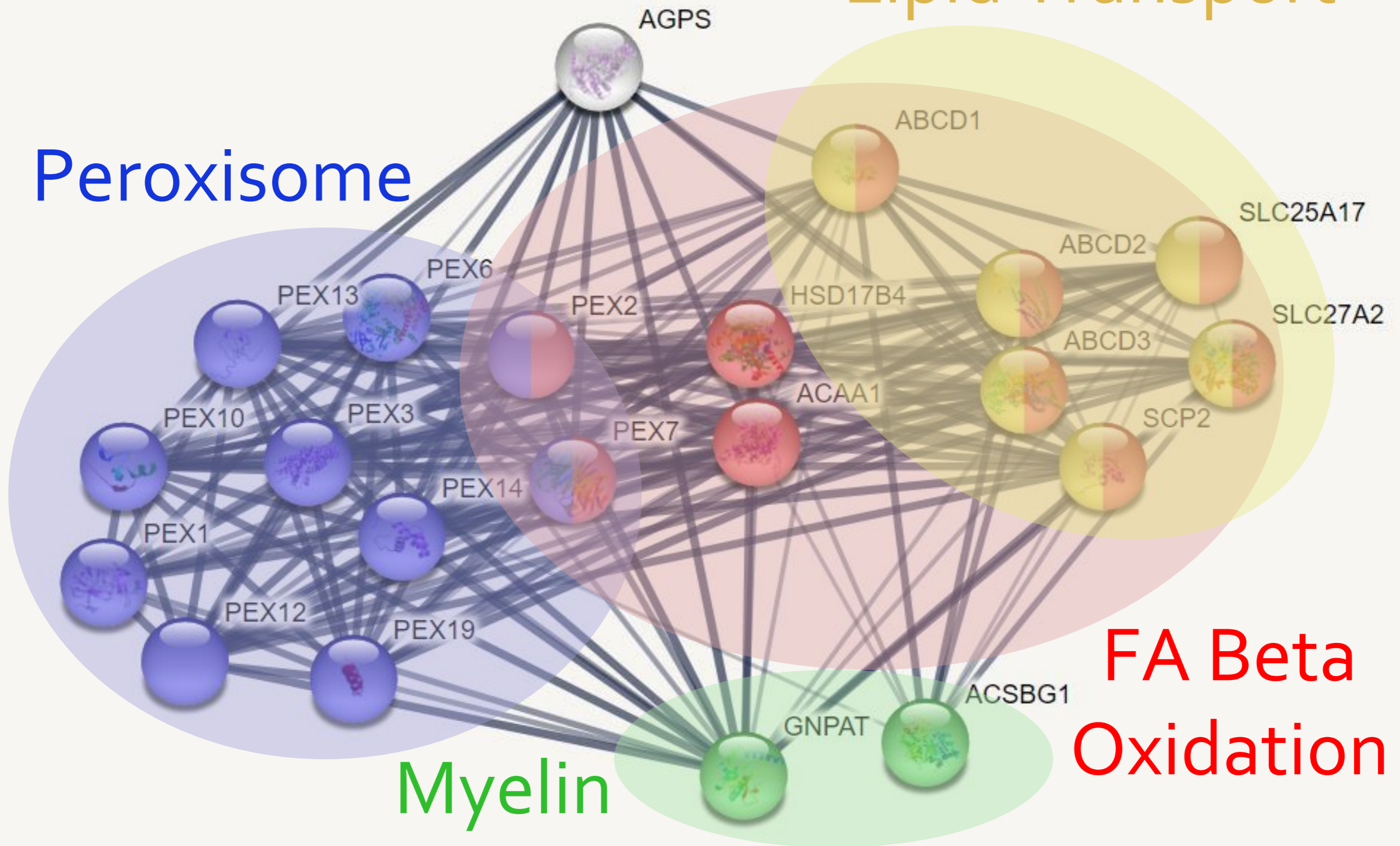
Human ABCD1 Interaction Network

Lipid Transport

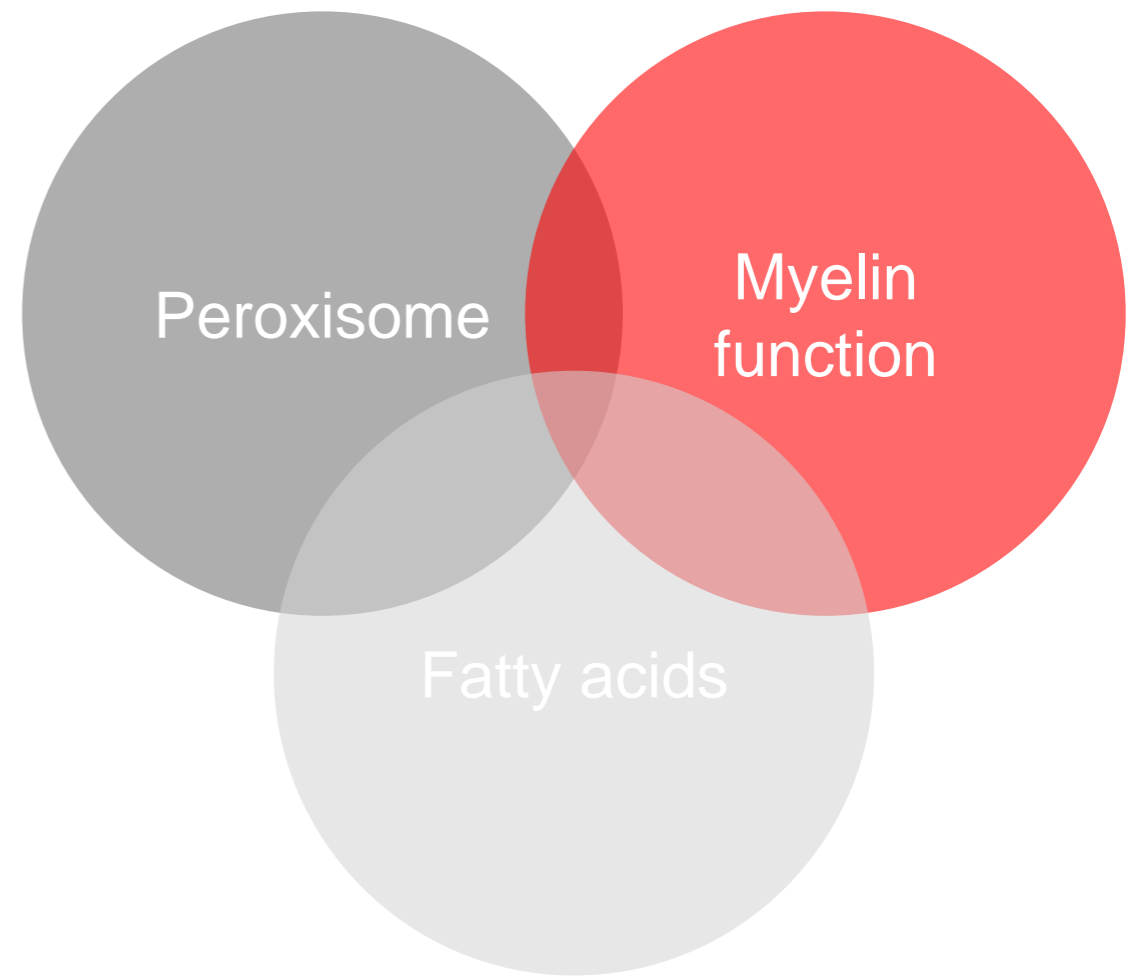
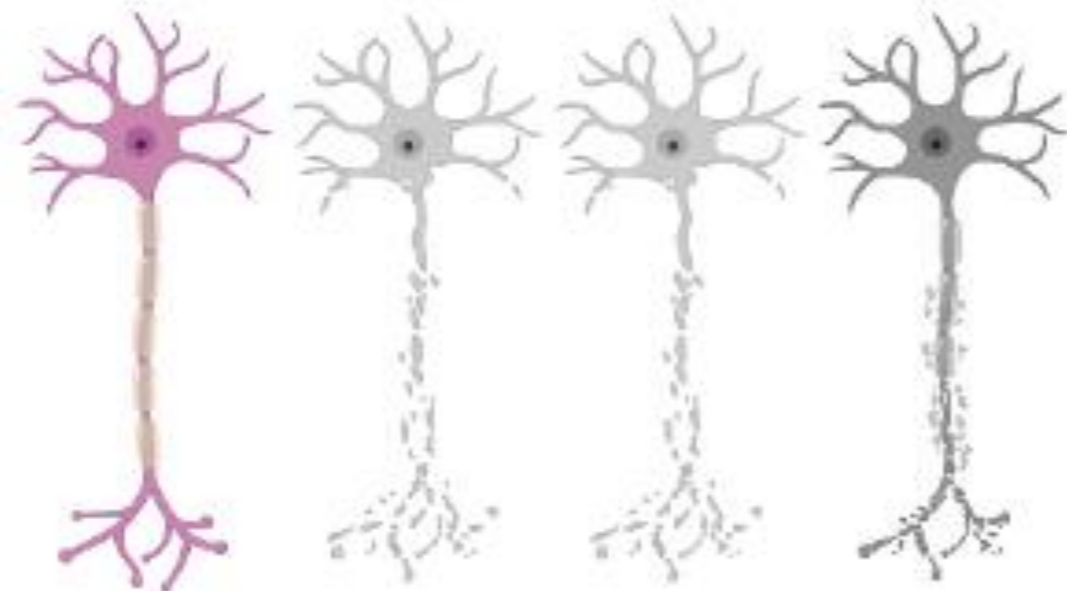
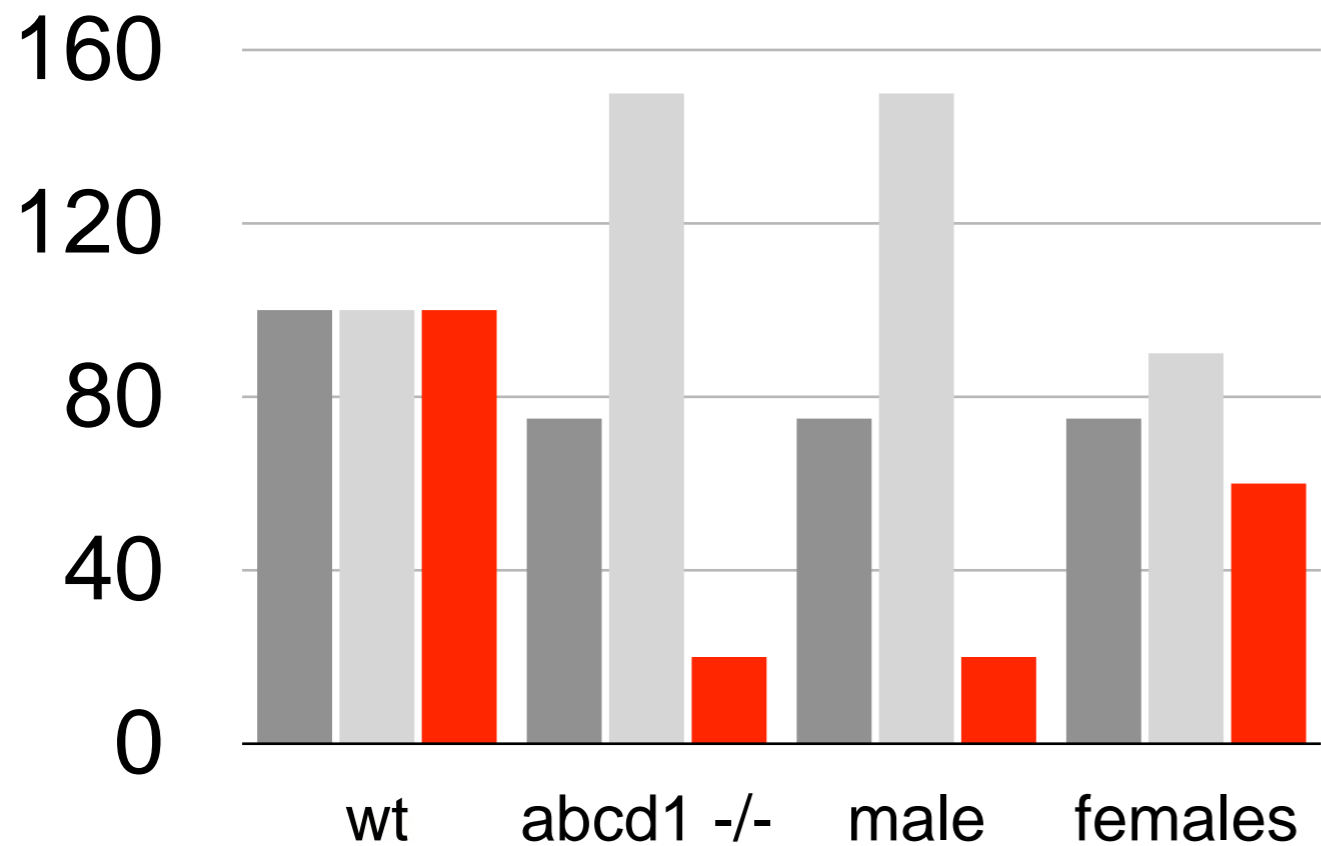
Peroxisome

FA Beta
Oxidation

Myelin

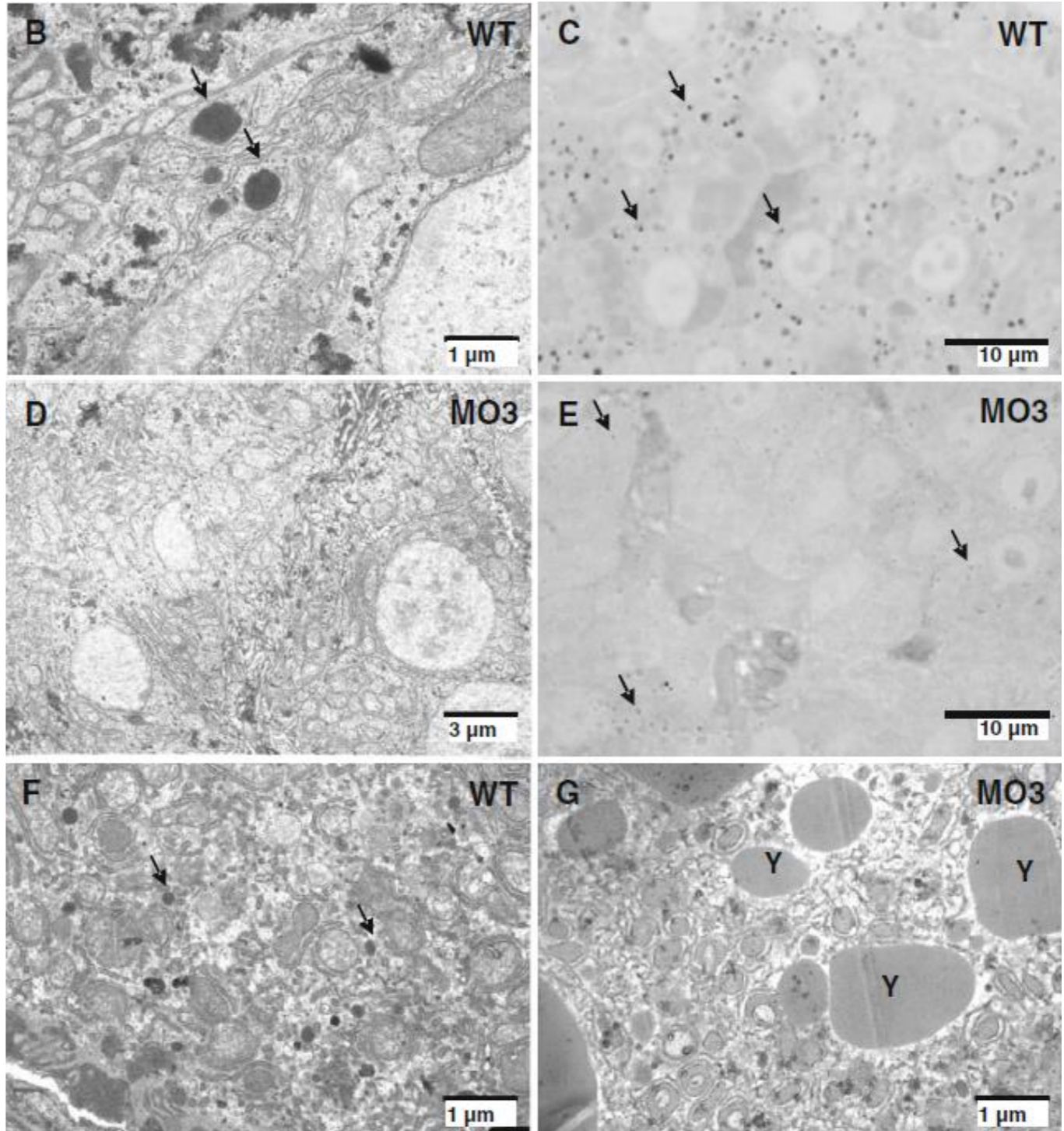


GAP: It is unclear why they are sex-specific defects on myelin.



Why are zebrafish the best model to study ALD?

Peroxisome



GOAL: To determine how **myelin and peroxisome genes** are affected in males.

Hypothesis: The loss of ABCD1 affects males more because of hormonal differences involved in the maintenance of myelin.

Aim 1

Determine conserved sequences in ABCD1 that are important for Myelin maintenance between males and females.

Aim 2

Identify myelin maintenance in males and females with RNA-SEQ

Aim 3

Identify male specific proteins that mediate peroxisome function of ABCD1 that are important for myelin preservation

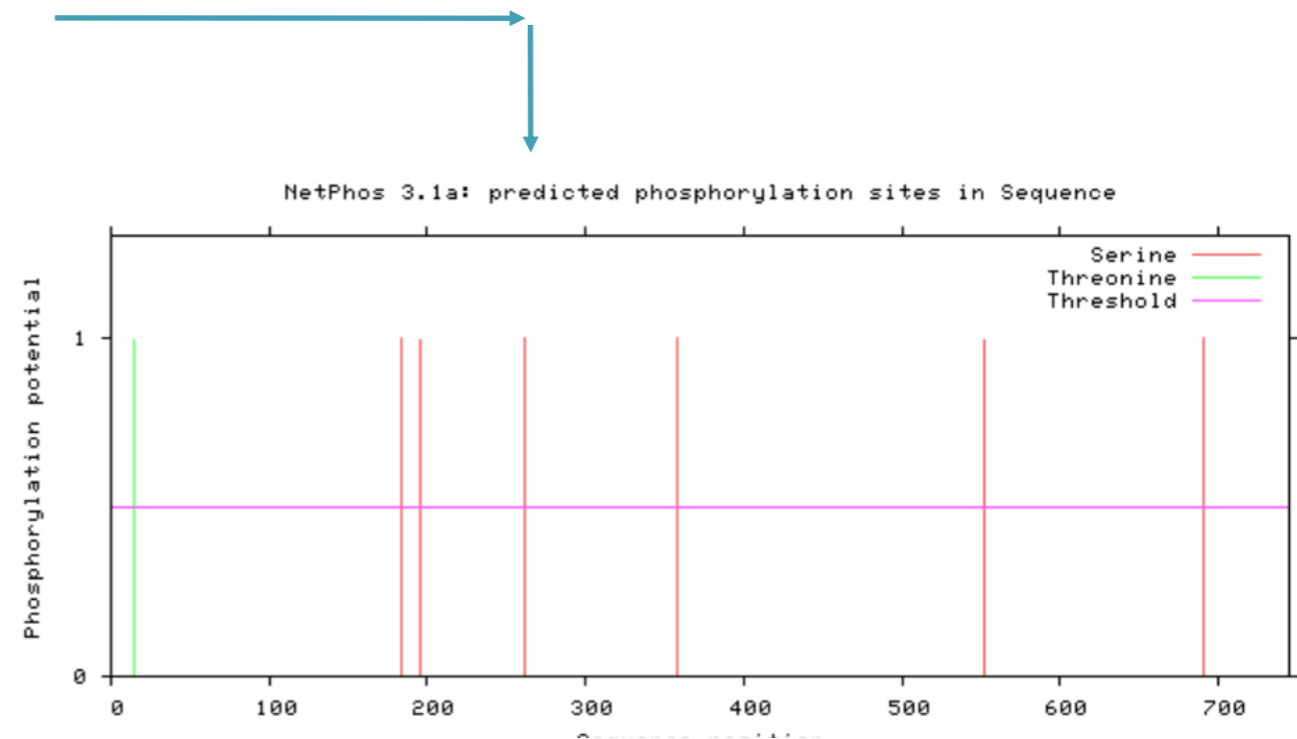
Aim 1a: Determine conserved sequences in ABCD1 that are necessary for Myelin maintenance.

Hypothesis: A mutation to S269A in the abc transport membrane domain of ABCD1 is important for sex-specific defects.



S269Q

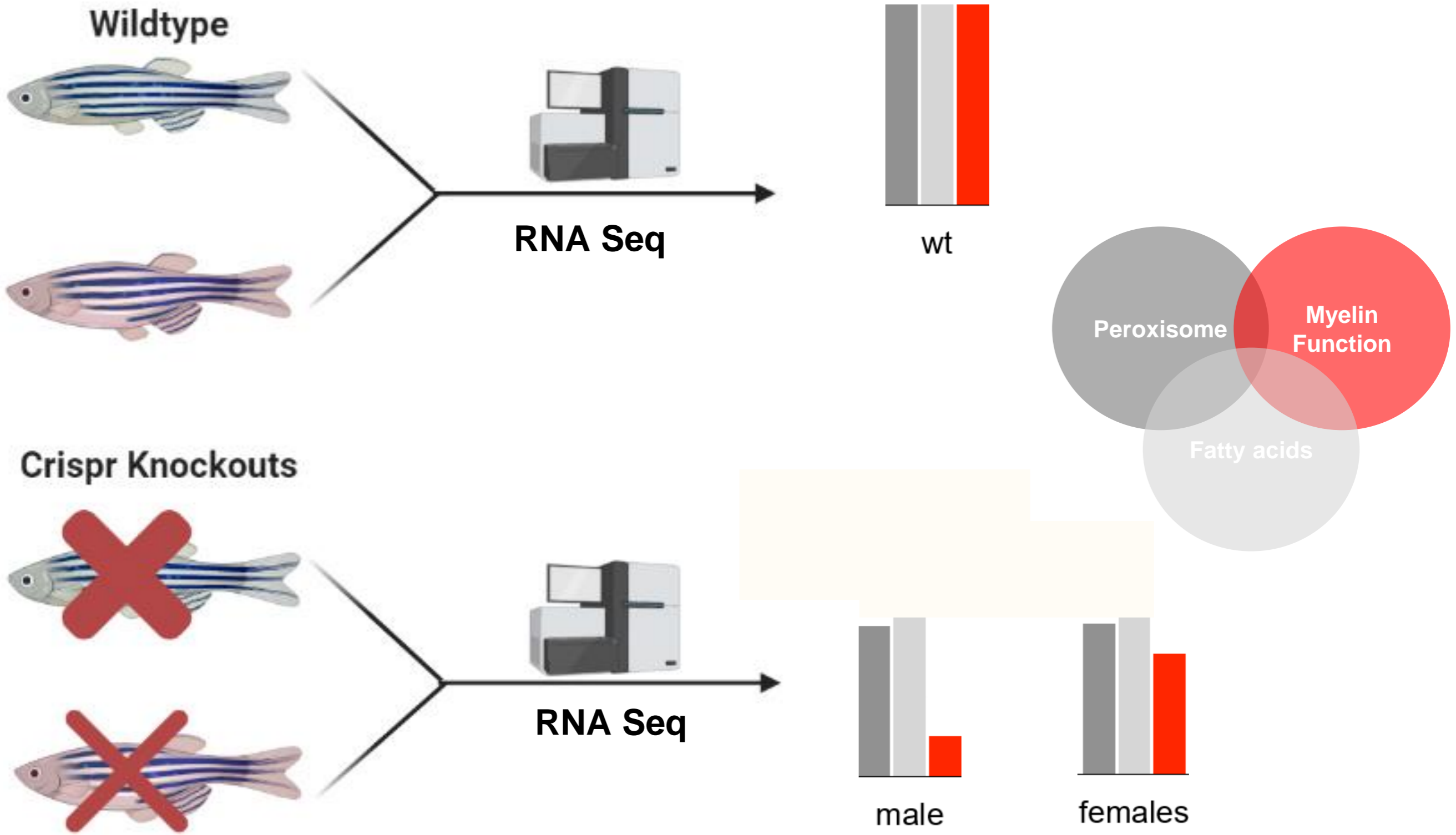
Species/Abbrv	L	R	A	F	S	P	K	F	G
1. Human	L	R	A	F	S	P	K	F	G
2. Zebrafish	L	R	A	F	S	P	R	F	G
3. Gorilla	L	R	A	F	S	P	K	F	G
4. Mouse	L	R	A	F	S	P	K	F	G
5. Dog	L	R	A	F	S	P	K	F	G
6. Cat	L	R	A	F	S	P	K	F	G
7. Goat	L	R	A	F	S	P	K	F	G
8. Horse	L	G	V	C	S	P	D	F	G
9. Tropical_clawed_frog	L	R	A	V	S	P	R	F	G
10. Elephant_Shark	L	R	S	C	S	P	K	F	G
11. C._elegans_(T02D1.5.1)	L	R	A	F	S	P	K	F	G
12. Komodo_Dragon	L	R	S	C	S	P	K	F	G
13. Drosophila_melanogaster	L	R	I	V	S	P	K	F	G
14. Saccharomyces_cerevisia	L	R	K	Y	T	P	P	L	G



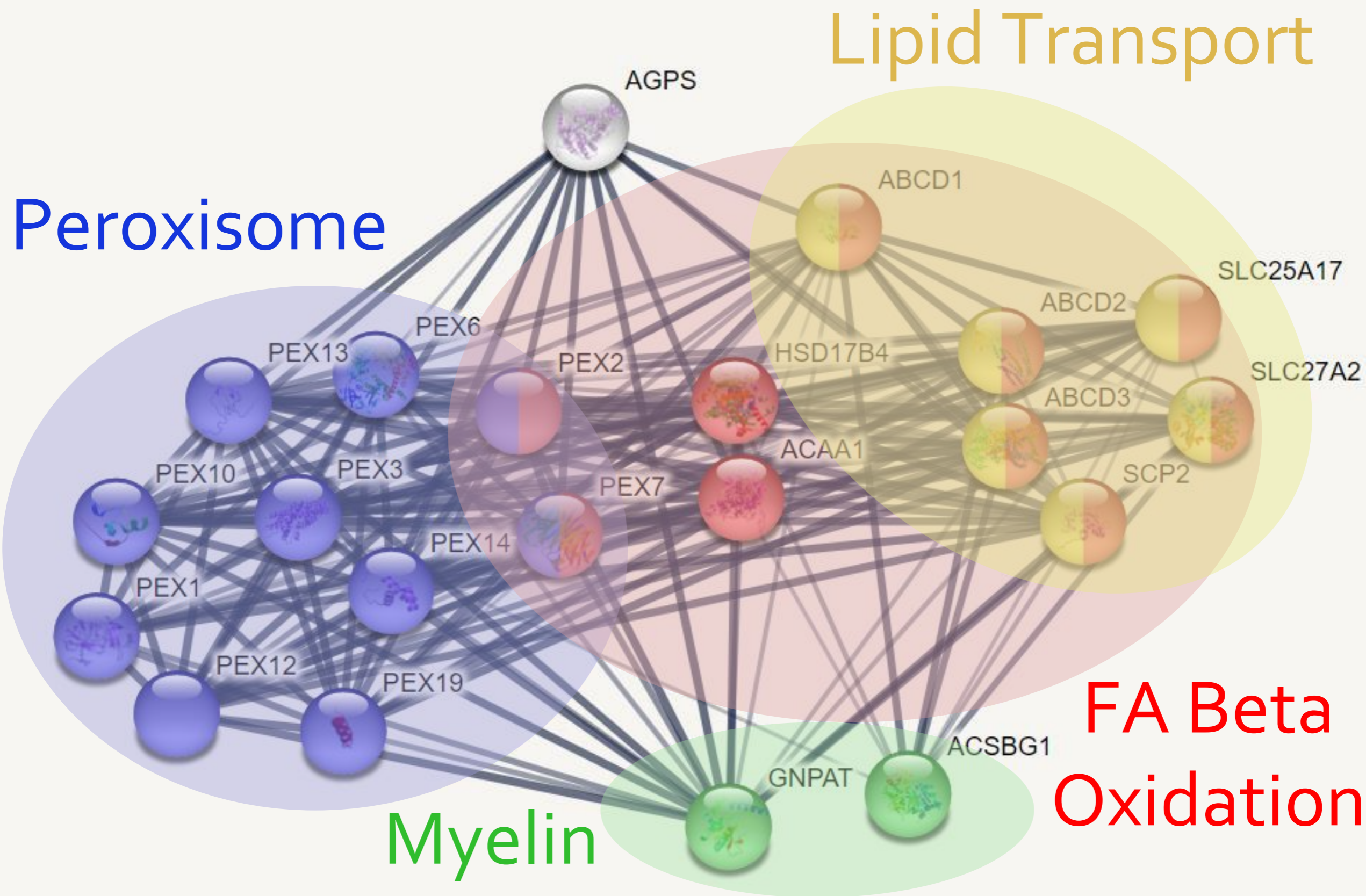
Aim 1b: Confirm whether a S269 mutation causes sex-specific myelin defects.

Aim 2: Determine myelin and peroxisome gene expression by using RNA Seq.

Hypothesis: Genes involved in myelin maintenance and peroxisome function will be downregulated to a greater extent in males.



Aim 3a: Identify male-specific proteins that mediate peroxisome function of ABCD1 that are important for myelin preservation.

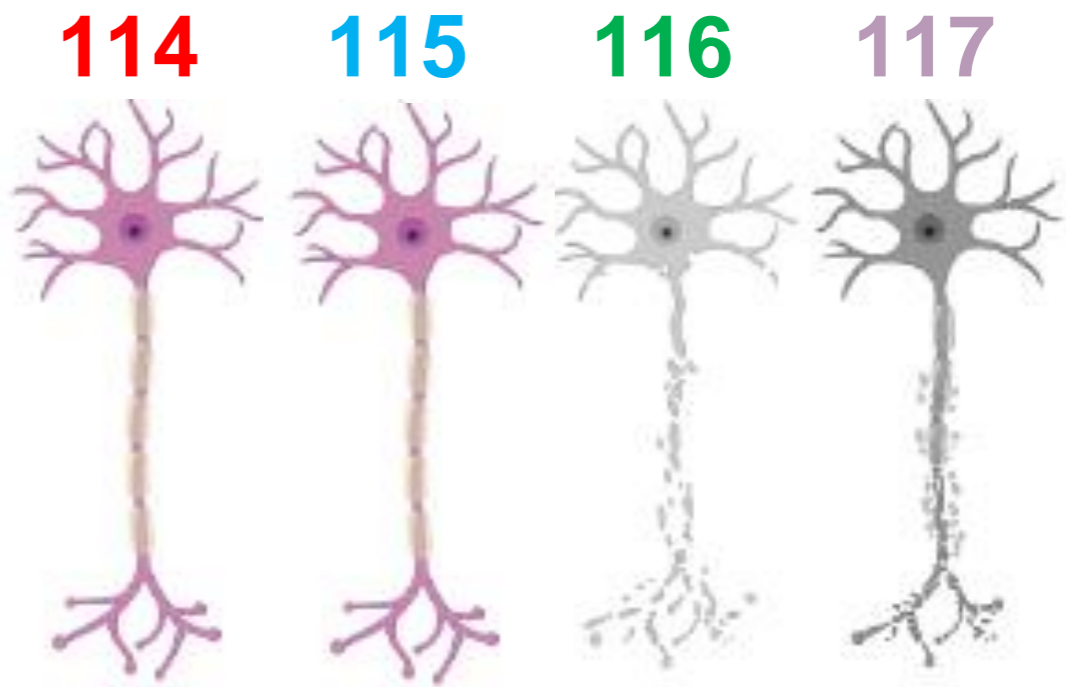
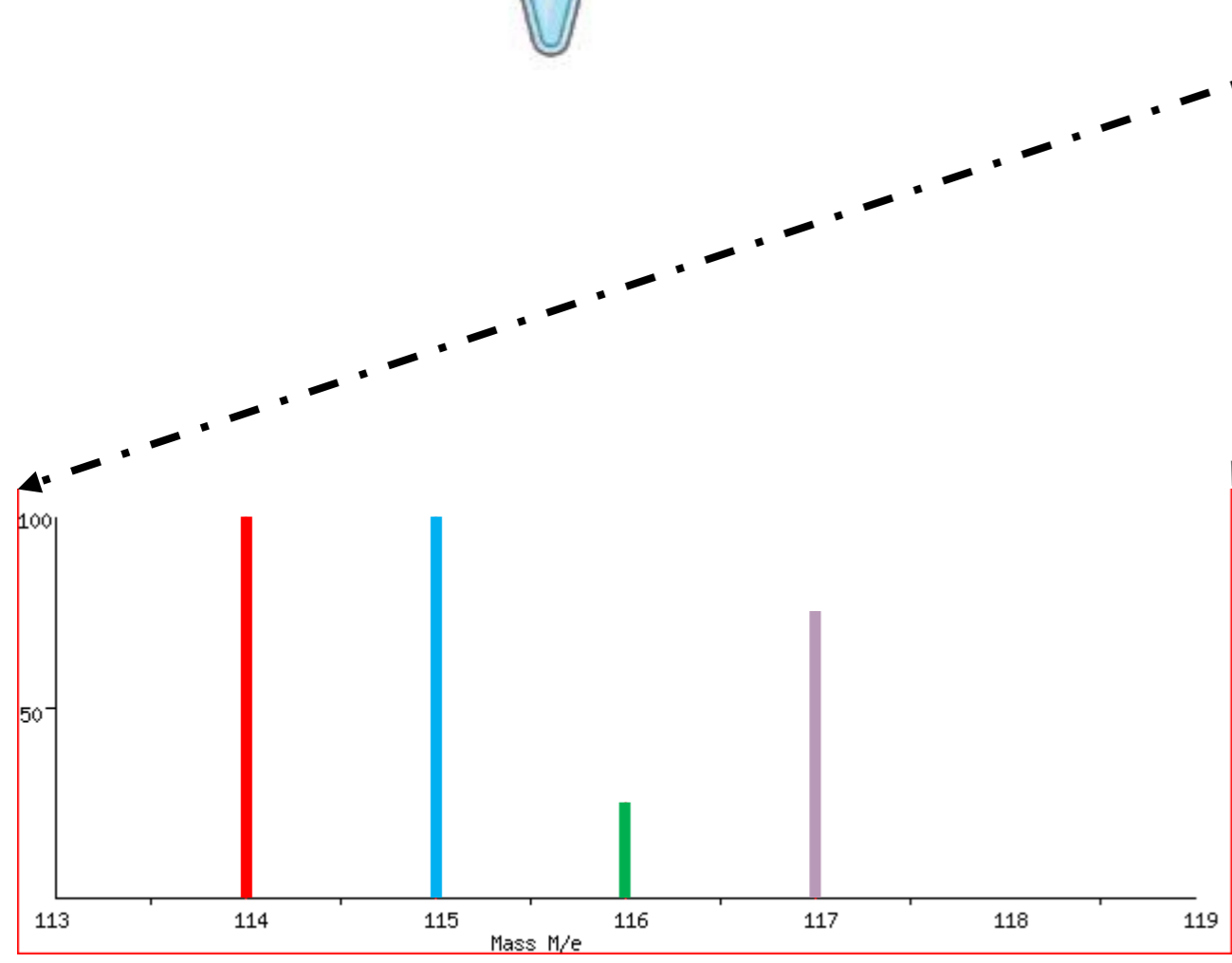
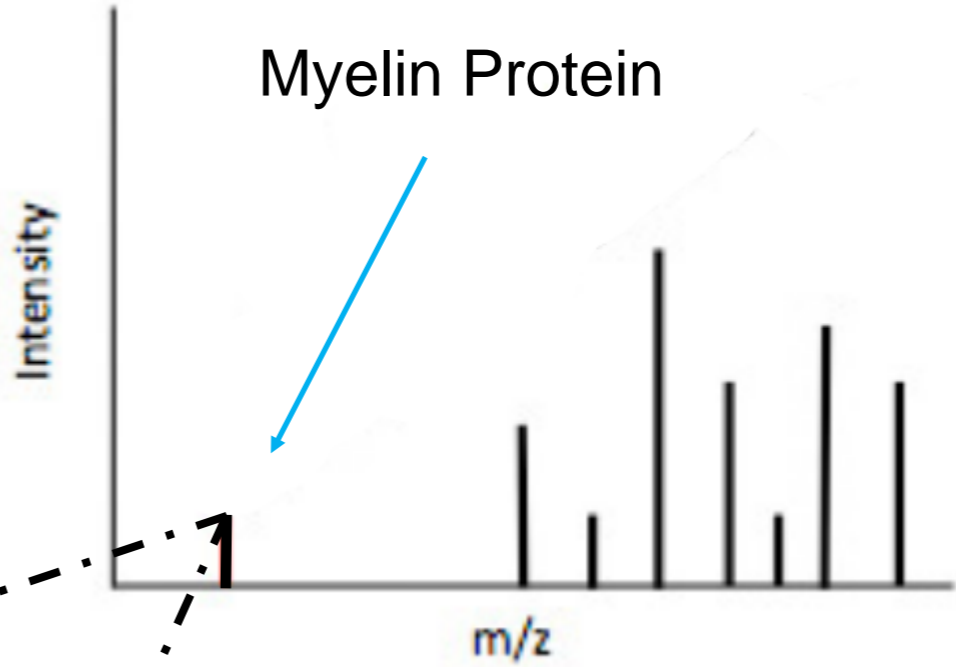
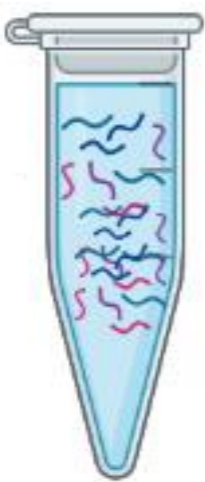


Aim 3a: Identify male-specific proteins important for myelin maintenance with ITRAQ.

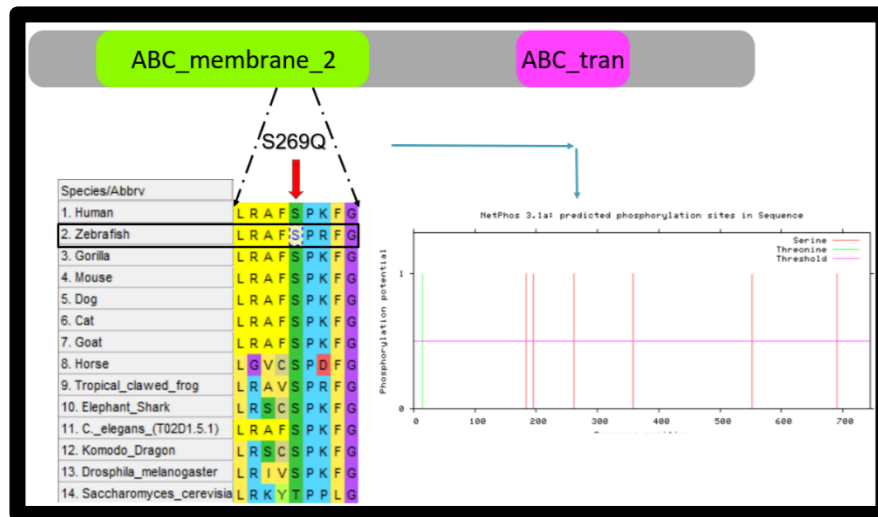
Hypothesis: Male-specific proteins important for myelin maintenance will be identified by comparing Wild type and ABCD1 mutant males and females.



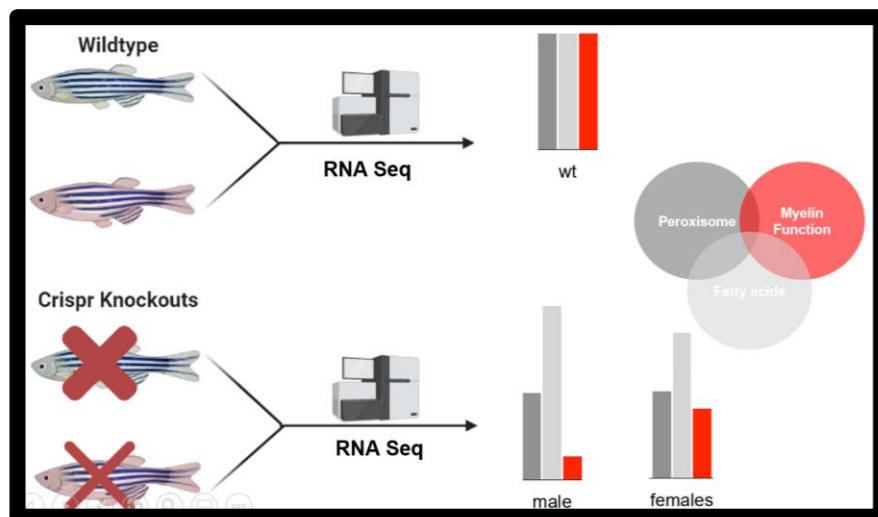
Aim 3b: Analyze mass spec graphs from iTRAQ.



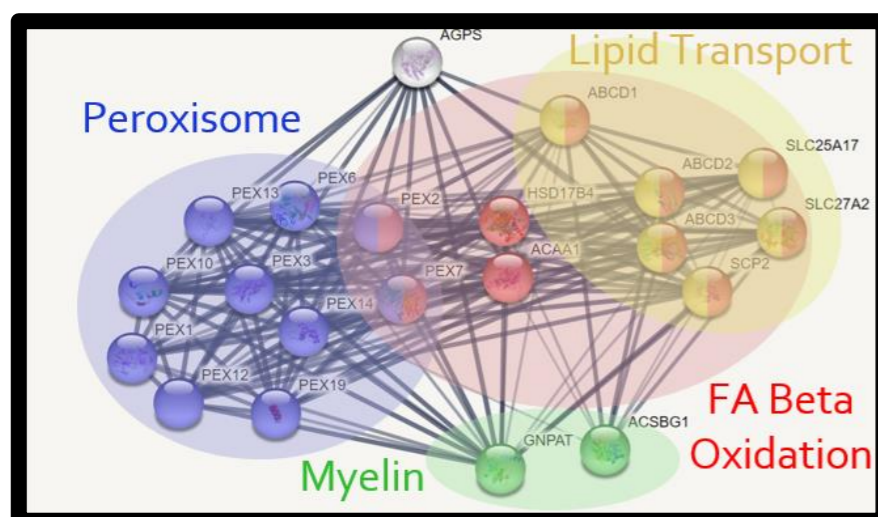
Conclusions



Conserved phosphorylation site Serine 269 in ABCD1 may play a part in sex specific defects.



ABCD1 and other myelin genes may be downregulated more in males than in females.



ABCD1 interacts with many proteins that influence myelin maintenance.

Future Directions



Image References

- <https://cdn.britannica.com/02/114902-050-0D7352BF/cells-organelles-mitochondria-chloroplasts-endoplasmic-reticulum-lysosomes.jpg>
- <https://www.creative-proteomics.com/images/iTRAQ-Workflow.jpg>
- <https://www.sisweb.com/mstools/spectrum.htm?id=507246695699227>
- <https://dmm.biologists.org/content/dmm/7/7/915/F1.large.jpg>
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- <https://g.foolcdn.com/editorial/images/569850/pills-and-bottle.jpg>

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Questions?