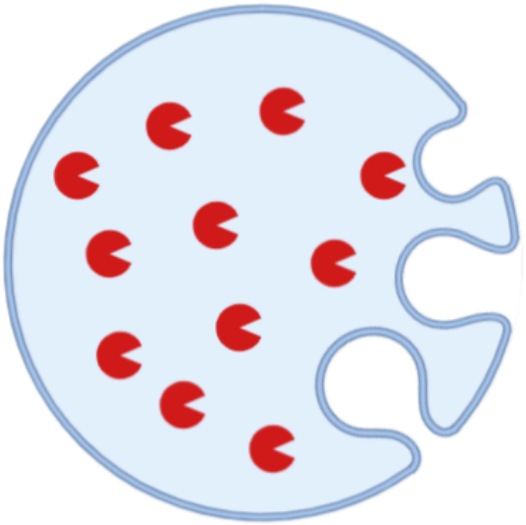
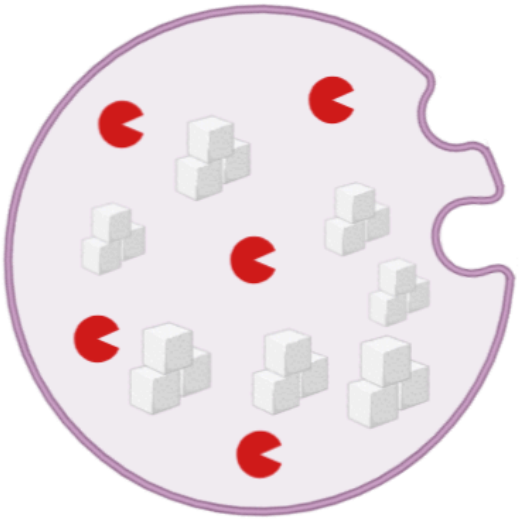
Sanfilippo Syndrome

Sheida Pourdashti

What is Sanfilippo Syndrome?



Healthy lysosome

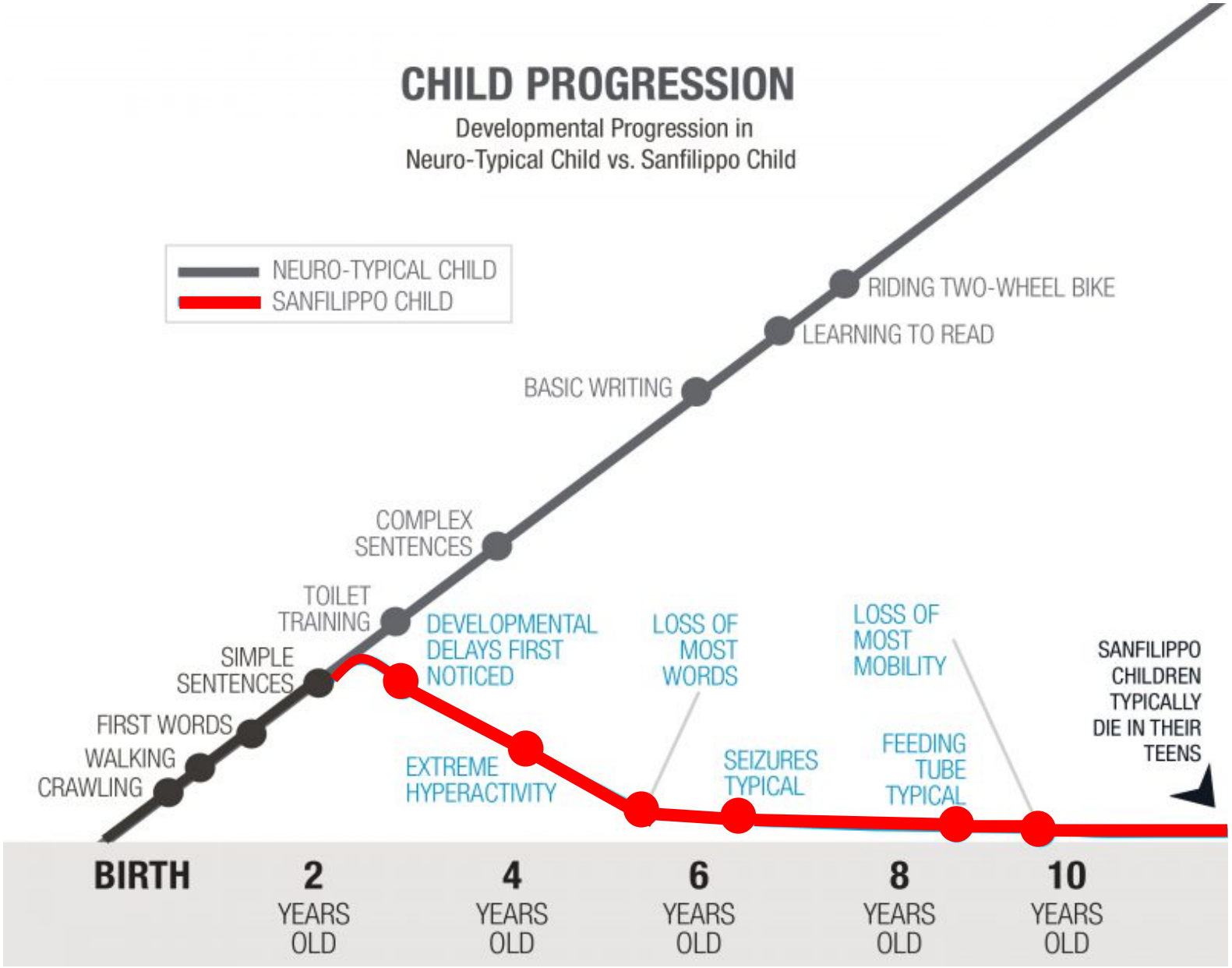


Diseased lysosome

Autosomal recessive lysosomal storage disorder

Muco**p**oly**s**accharidosis type III (MPSIII)

What are the symptoms?

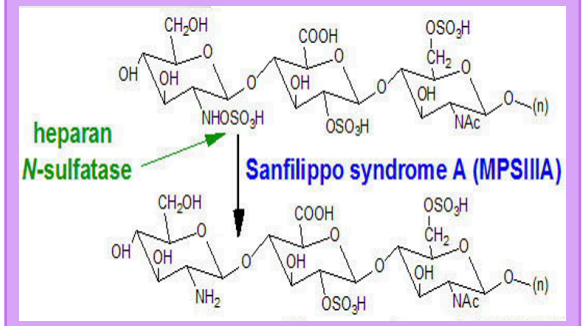


What causes Sanfilippo syndrome?

Sanfilippo Types	Missing Enzyme	Gene
A	**Heparan N-sulfatase**	**SGSH**
B	N-acetyl-alpha-D-glucosaminidase	NAGLU
C	Acetyl-CoA:alpha-glucosaminide acetyltransferase	HGSNAT
D	N-acetylglucosamine-G-sulfate sulfatase	GNS

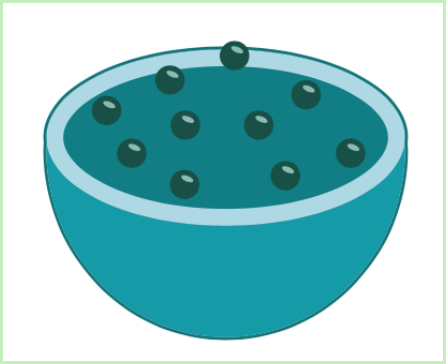
Sanfilippo syndrome and SGSH gene

Molecular function



Enzyme regulation
Catalytic activity

Cellular component

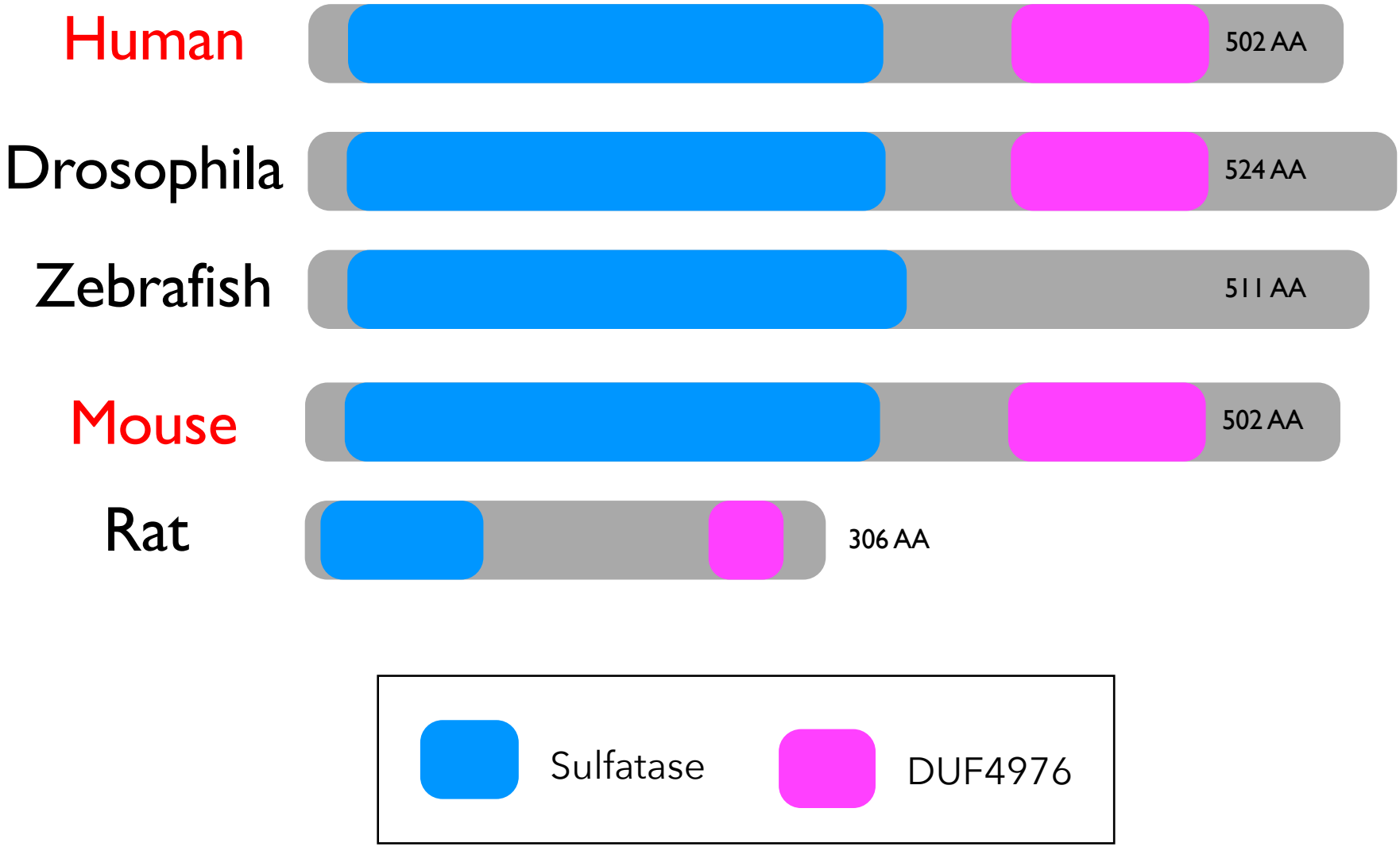


Lysosome
Extracellular exosome

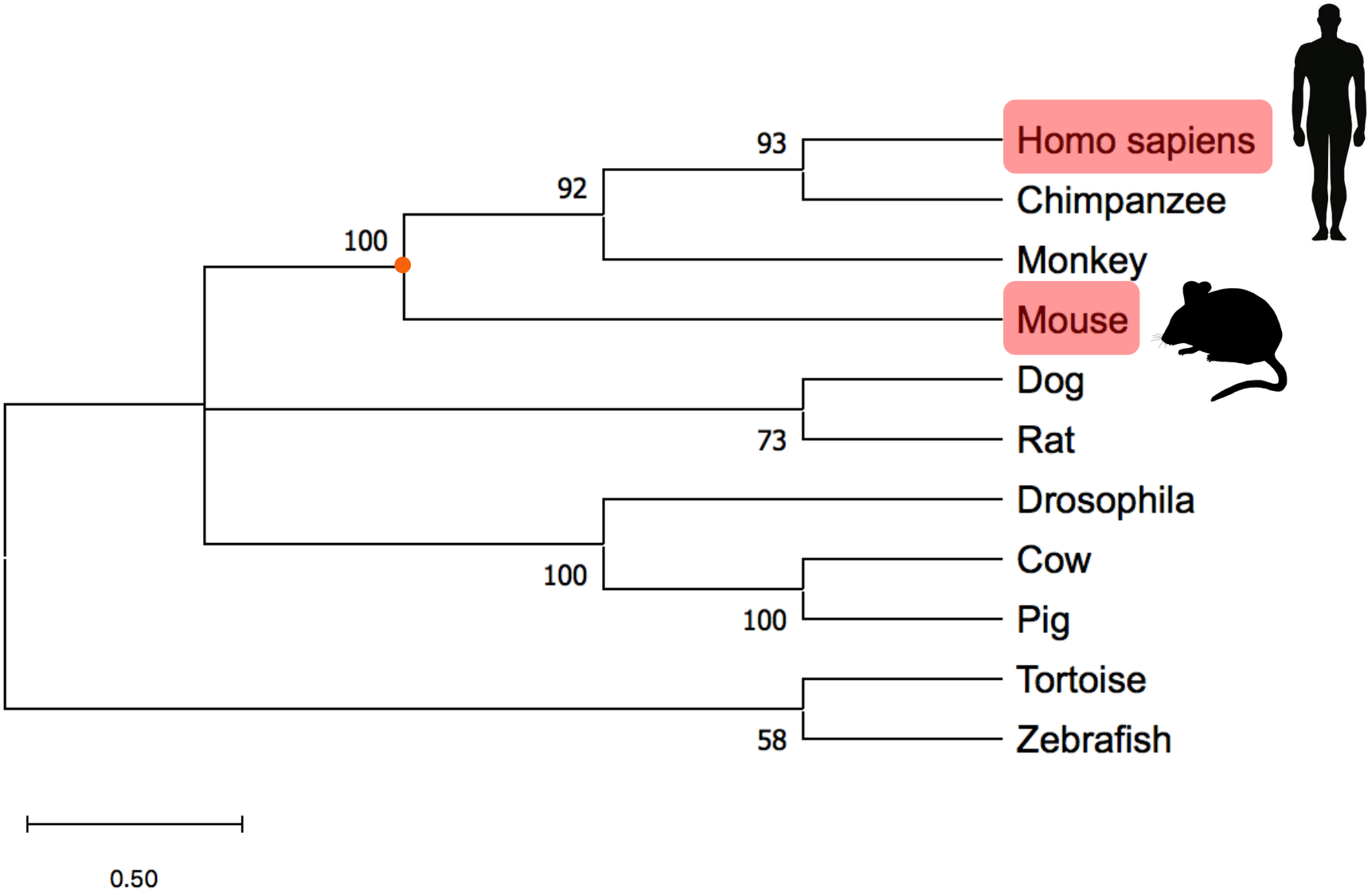
Biological process

Catabolic process
Brain development

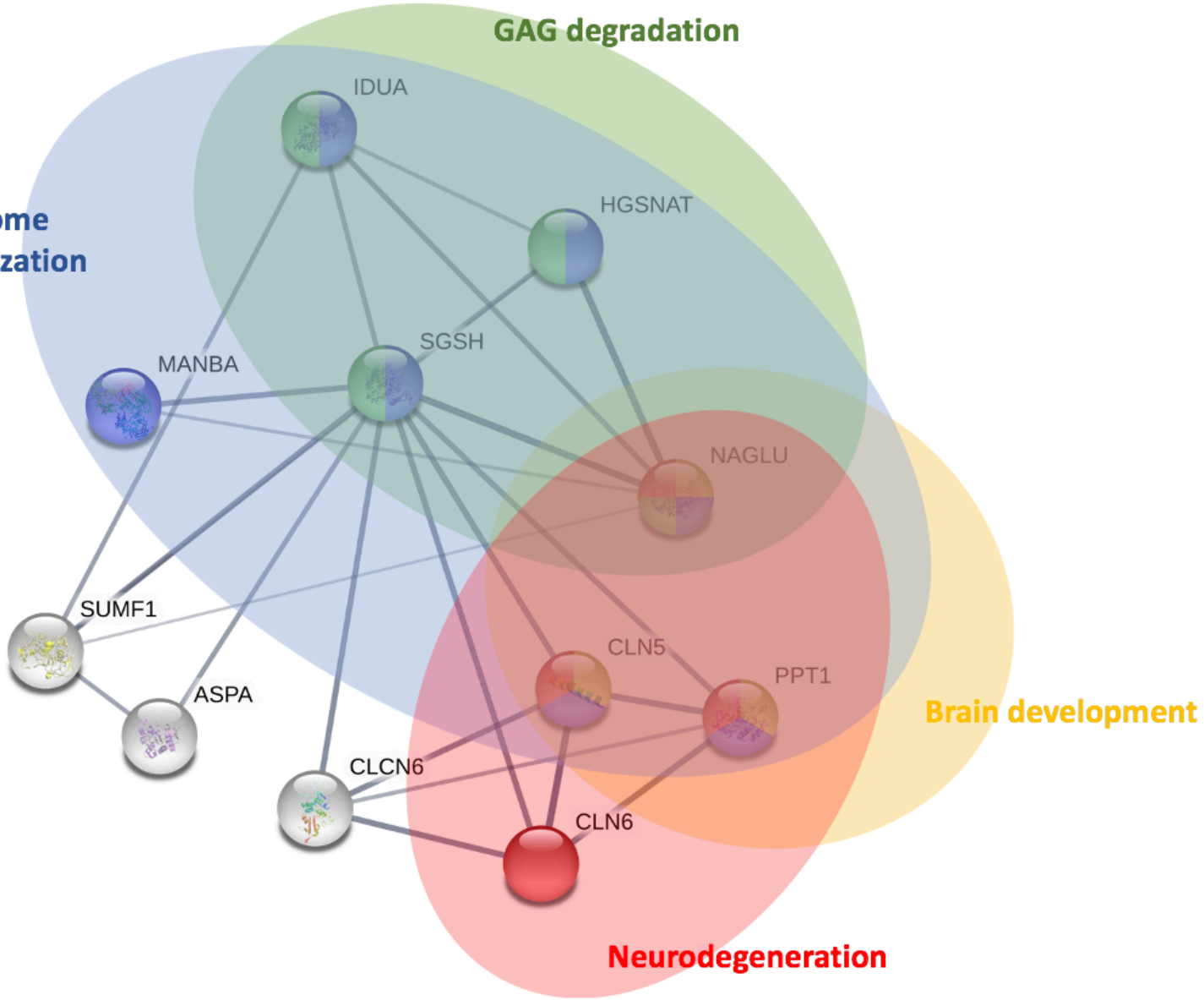
What domains are conserved in SGSH?



How are SGSH homologs related?



What genes does SGSH interact with?



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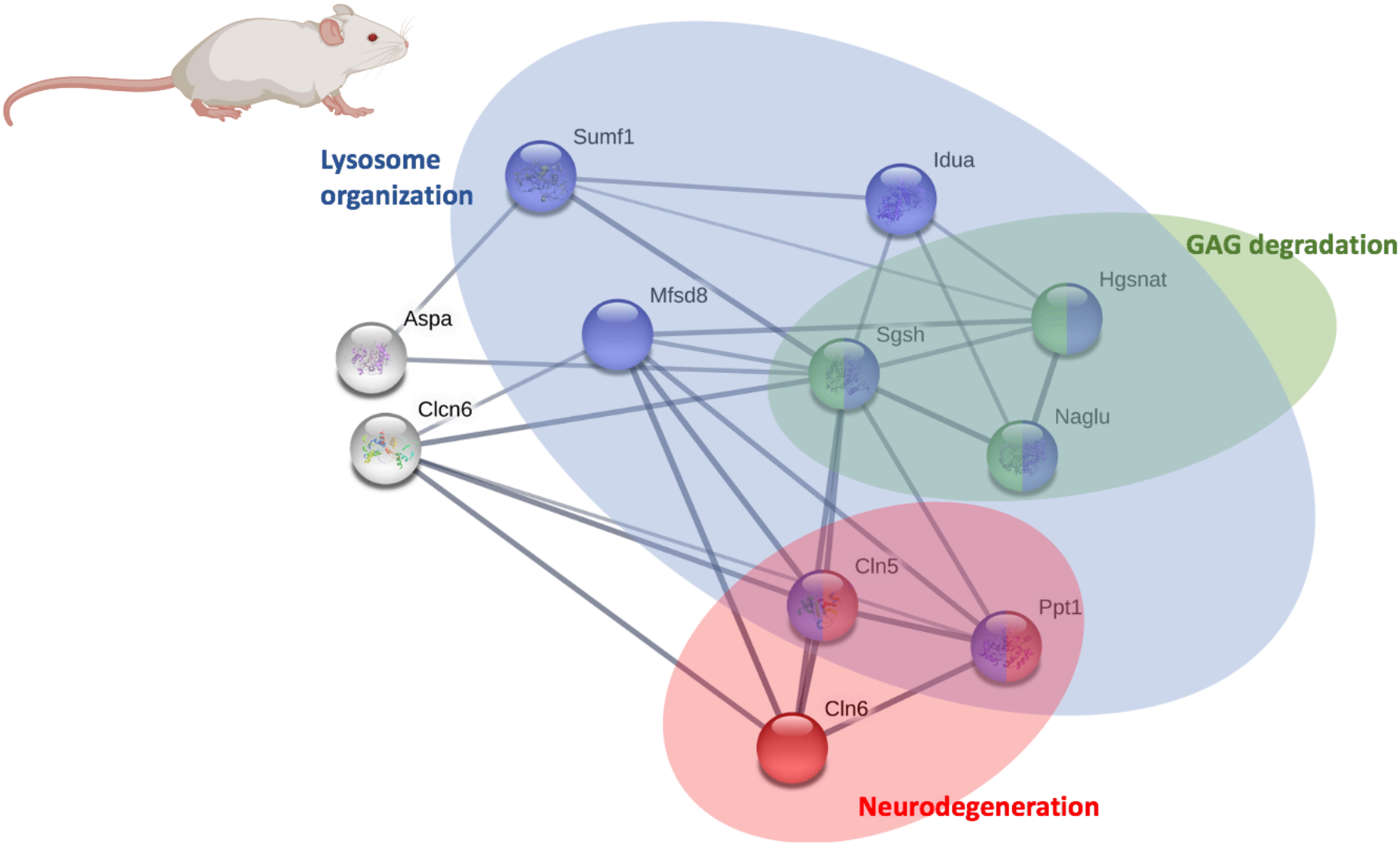
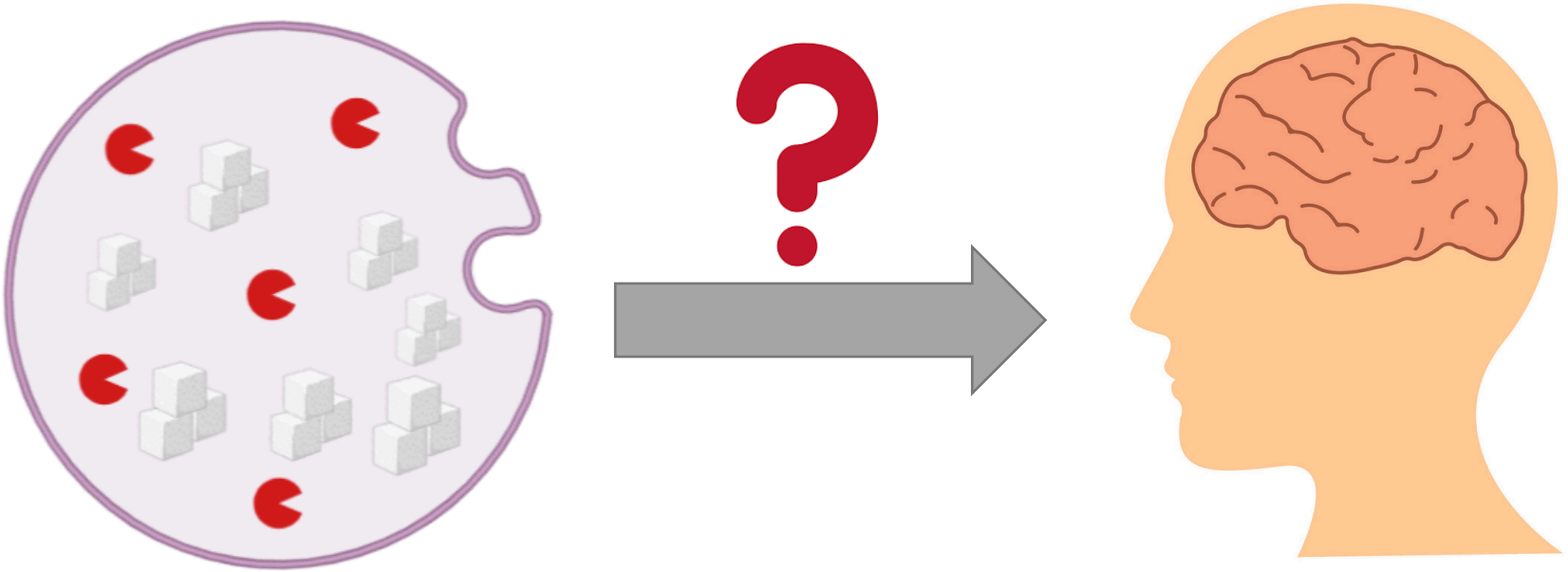


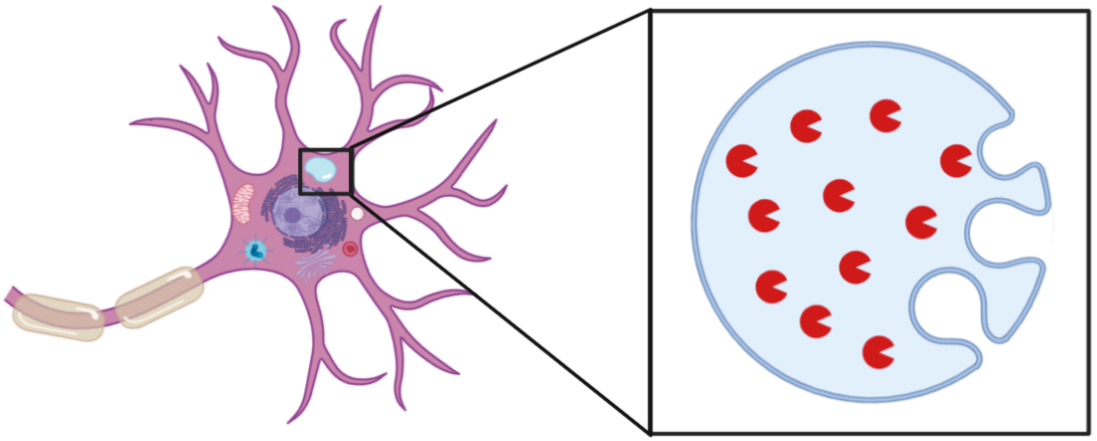
What is the gap in knowledge?



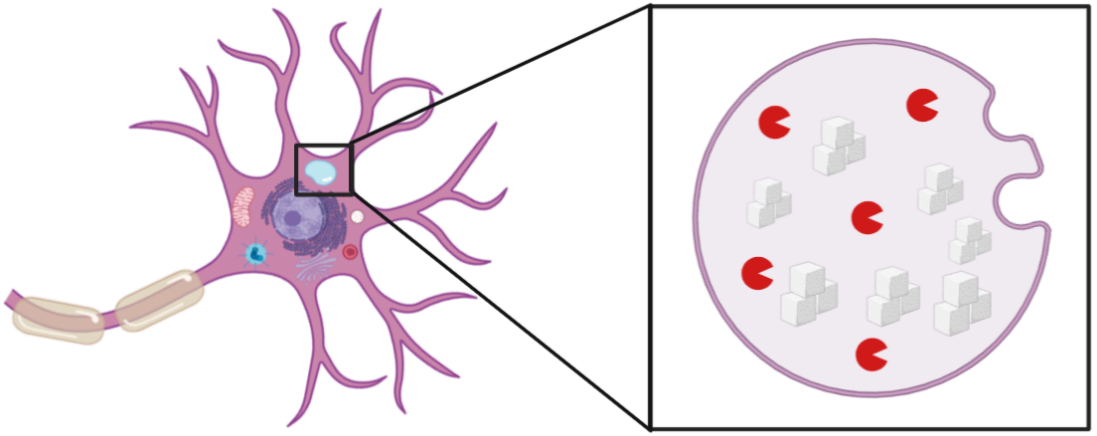
It is unknown why GAGs accumulation in the lysosomes mostly affects the nervous system in Sanfilippo syndrome patients.

What model organism to use?

Wildtype mouse



SGSH mutant mouse

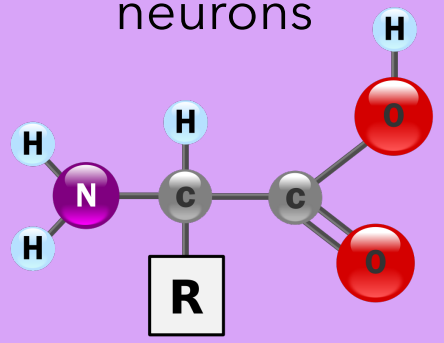


What is the primary goal?

Provide insights into the neuropathology of Sanfilippo syndrome

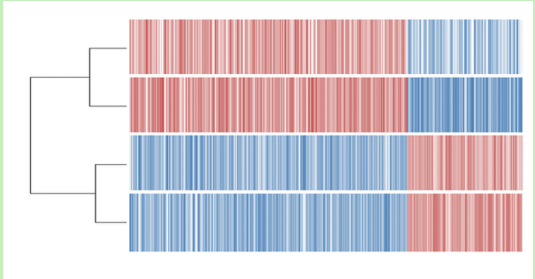
Aim 1

Identify amino acids important for GAGs accumulation in neurons



Aim 2

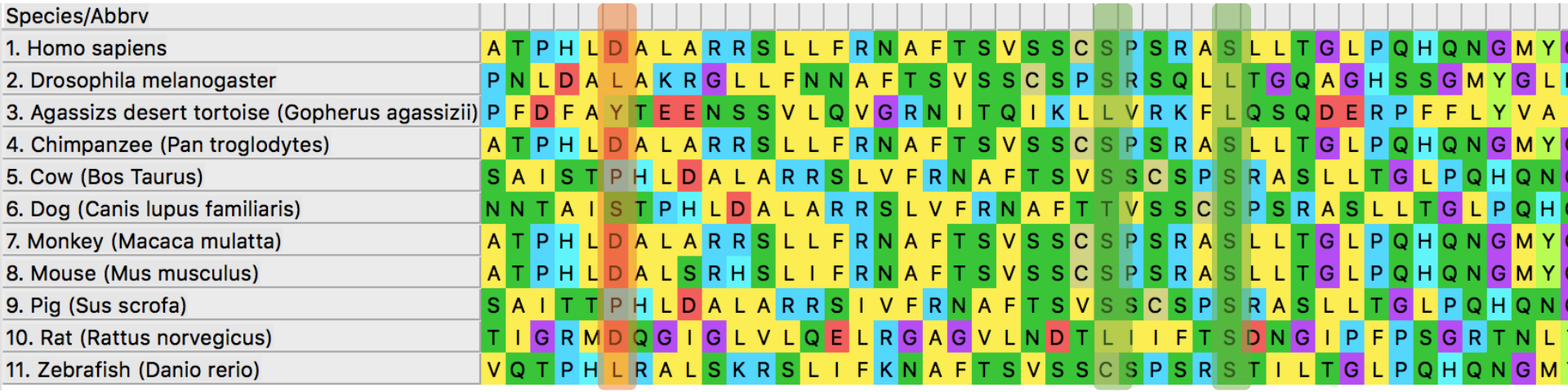
Identify differentially expressed genes associated with GAGs accumulation



Aim 3

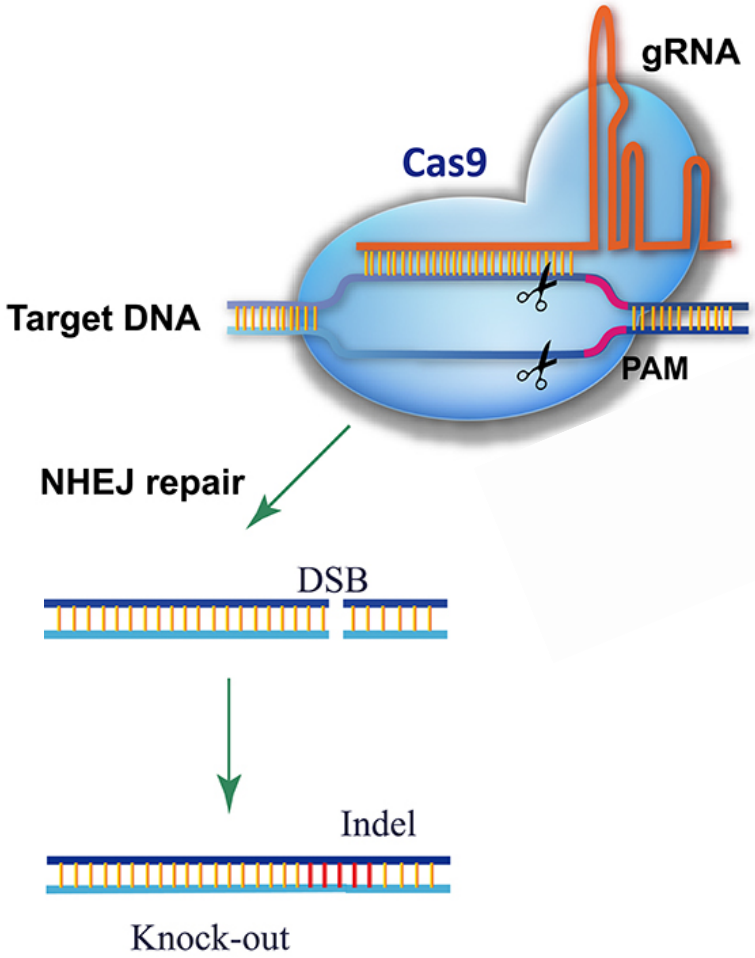
Hypothesis: SGSH mutants will result in GAGs accumulation in the lysosomes of neurons, leading to decreasing levels of lysosomal degradation and brain development as models age.

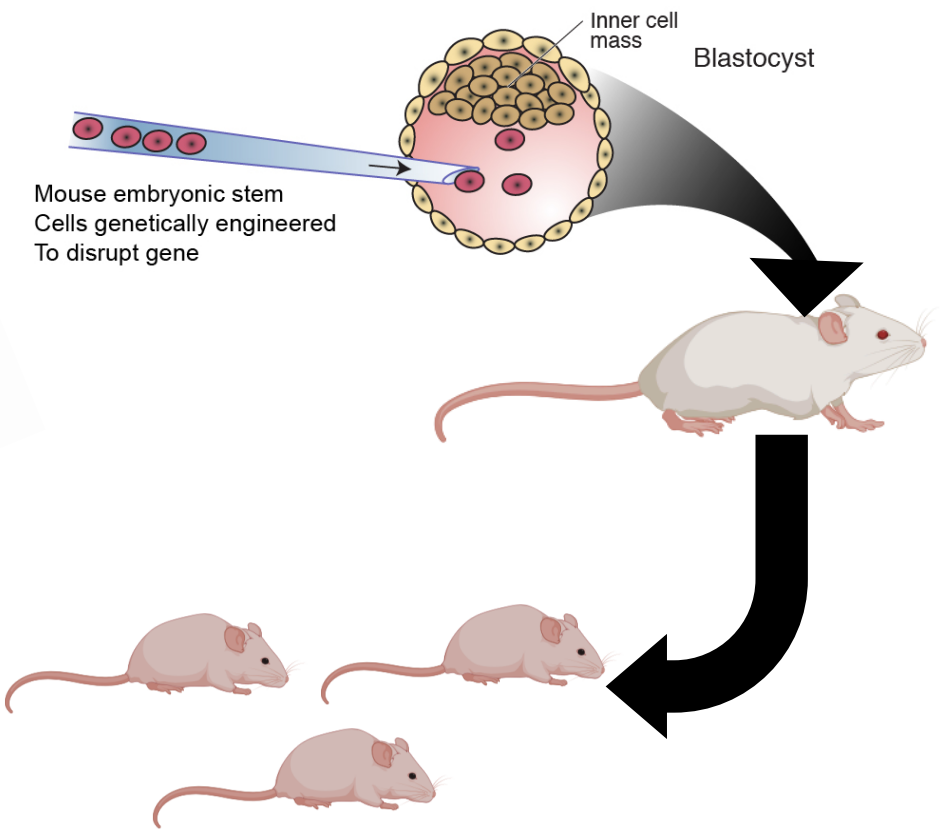
Aim 1:Identify conserved amino acids of SGSH that are important for GAGs accumulation in neurons



BLAST and ClustalOMEGA → CRISPR/Cas9 → GAGs Assay

Aim 1:Identify conserved amino acids of SGSH that are important for GAGs accumulation in neurons



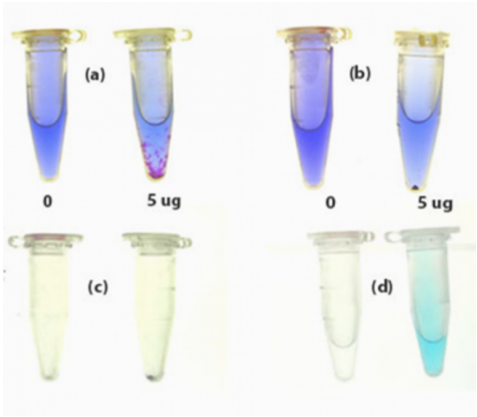


BLAST and ClustalOMEGA → CRISPR/Cas9 → GAGs Assay

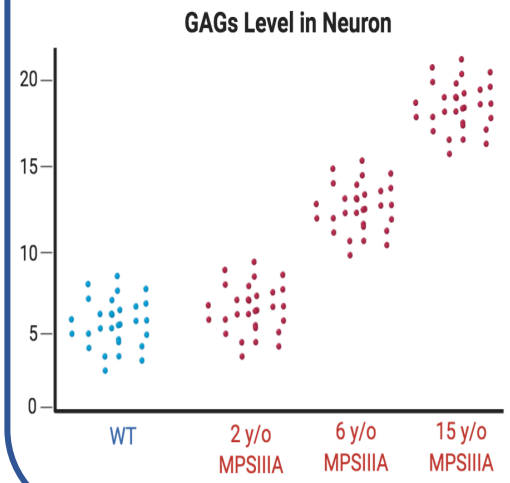
Aim 1:Identify conserved amino acids of SGSH that are important for GAGs accumulation in neurons

Extract brain tissues from both WT and mutant mice

Assay GAGs level by following Blyscan protocol



Collect data and graph the results



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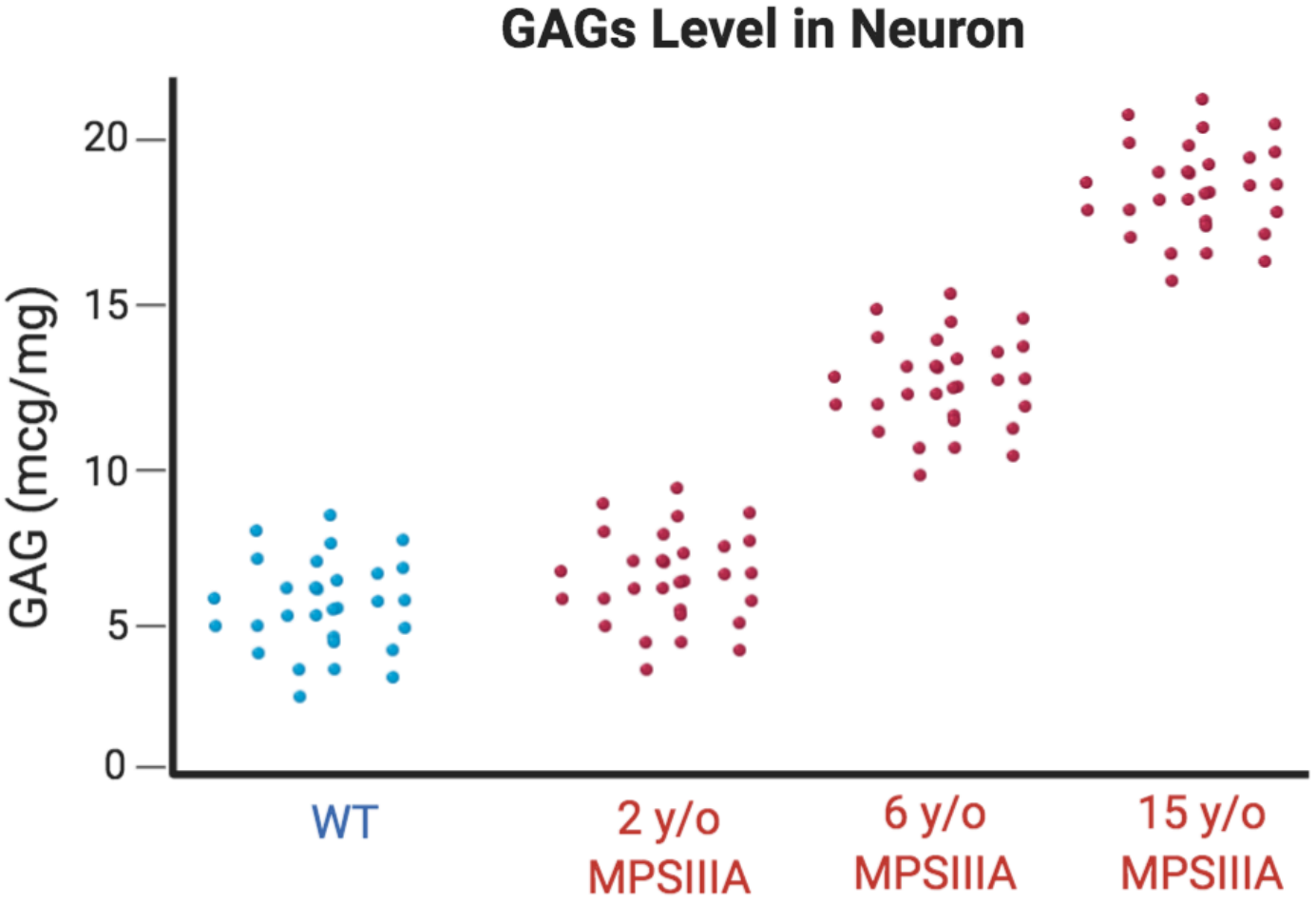
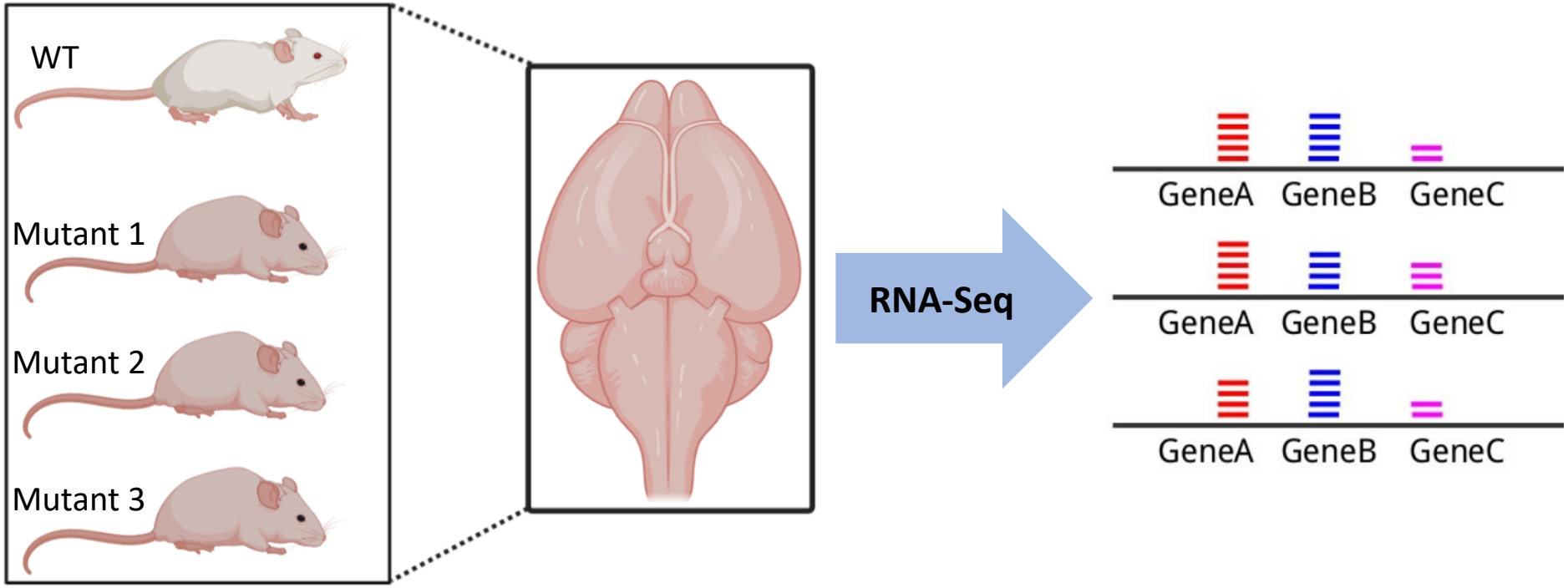


Hypothesis: Mutated mice show higher levels of GAGs in the lysosomes of neurons and the accumulation increases with age.

Aim 2: Identify differentially expressed genes associated with GAGs accumulation



RNA-Seq → Expression profiling → Gene ontology

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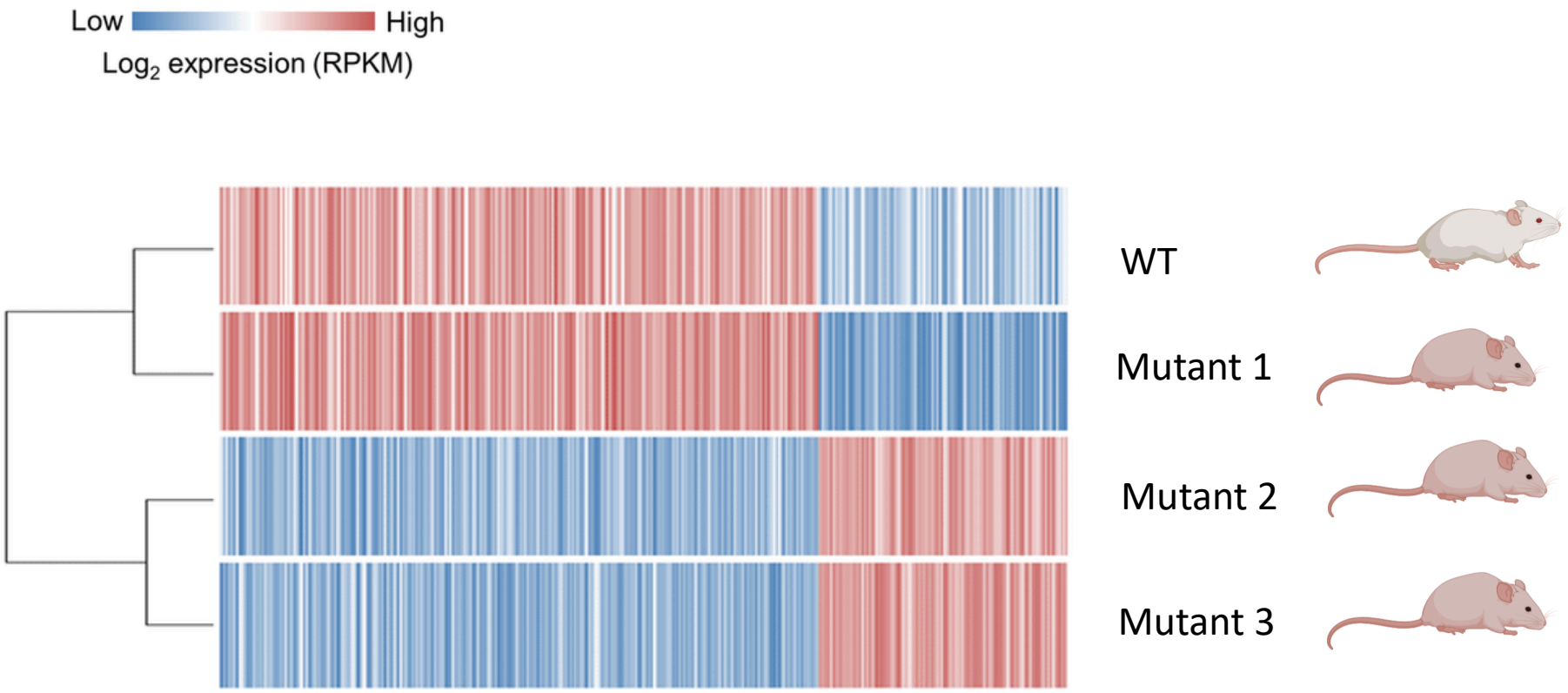

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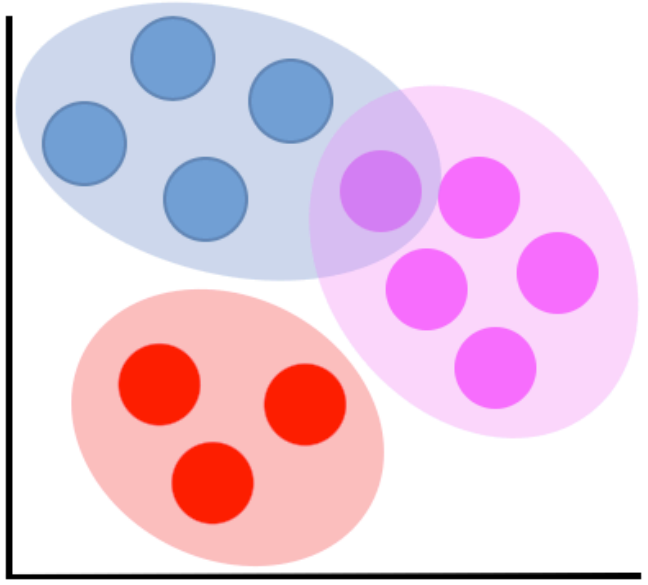

Hypothesis: Differentially expressed genes are involved in brain development and are downregulated in mutant mice.

RNA-Seq → Expression profiling → Gene ontology

References

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Images:
Title: https://i1.wp.com/researchaustralia.org/wp-content/uploads/2016/11/sanfilippo.jpg?w=2048&ssl=1

Lysosome: https://www.Biorender.com

Symptoms: https://curesanfilippofoundation.org

Cellular and biological: https://biorender.com

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Neuron: https://socratic.org/questions/as-every-cell-has-organelles-what-type-of-organelles-are-located-in-the-neuron