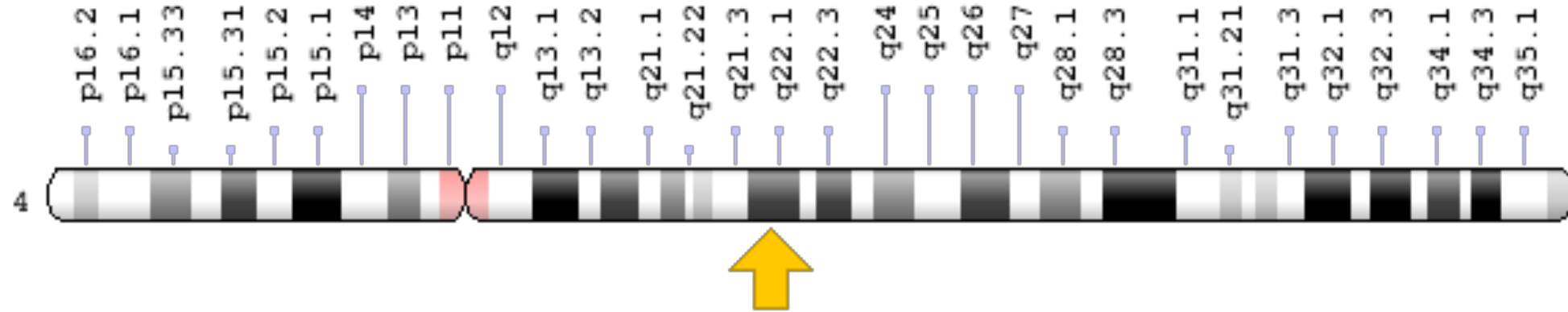


A microscopic image of brain tissue stained with hematoxylin and eosin (H&E). The image shows a dense population of cells with dark purple nuclei and pink cytoplasm/extracellular matrix. Several large, pale, eosinophilic (pink) structures are visible, which are characteristic of neurofibrillary tangles or neuroinflammatory cells. The overall appearance is consistent with the pathology of neurodegenerative diseases like SNCA and Lewy body dementia.

# **SNCA and Lewy Body Dementia**

**Caroline Say**

# What is SNCA?

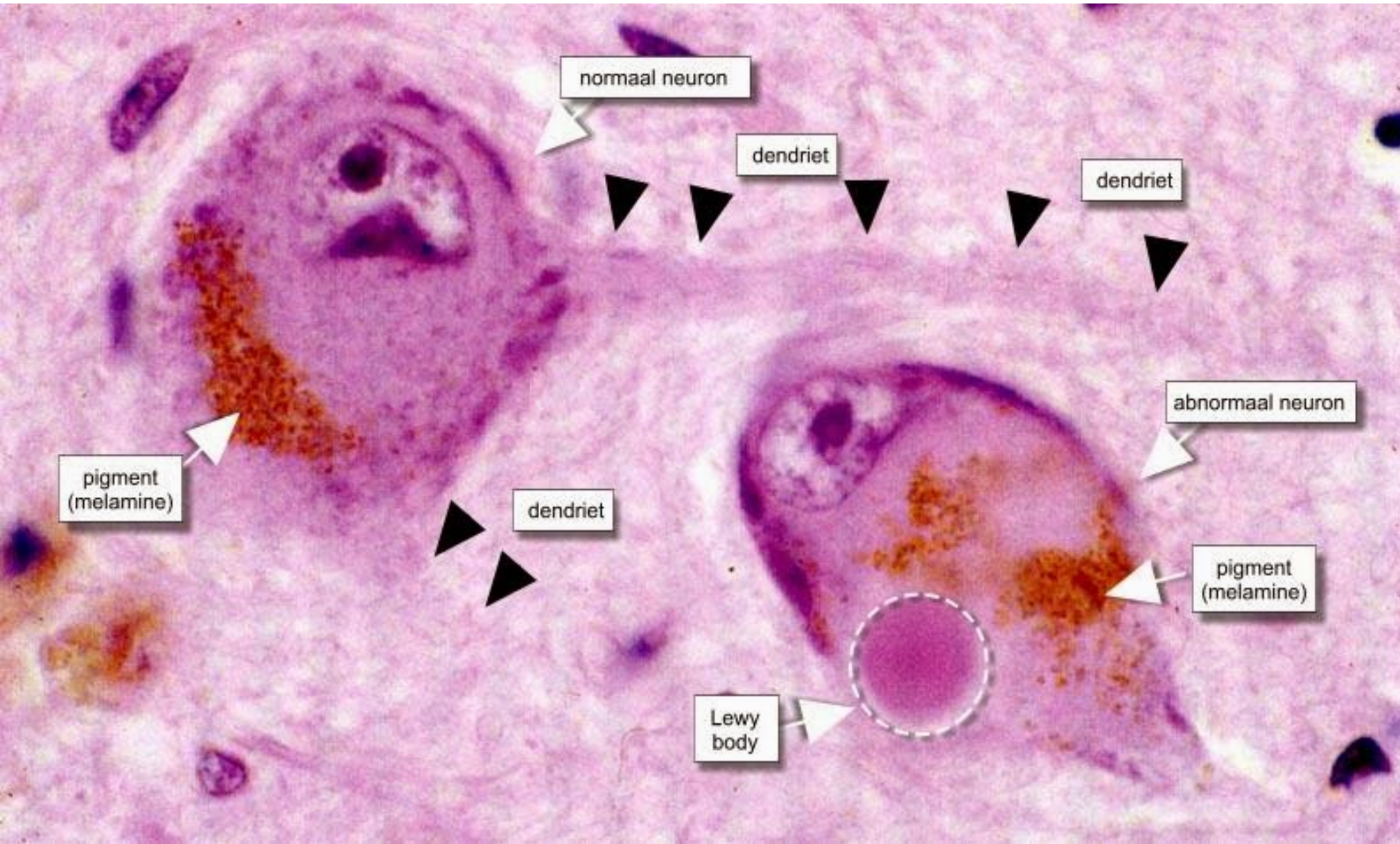


**Encodes the alpha synuclein protein, found in the brain and throughout the body.**

**Often located in presynaptic terminals in the cytosol.**



# What is Lewy body dementia?



**A neurodegenerative disorder caused by protein accumulation in the neurons.**

# What are the symptoms of LBD?

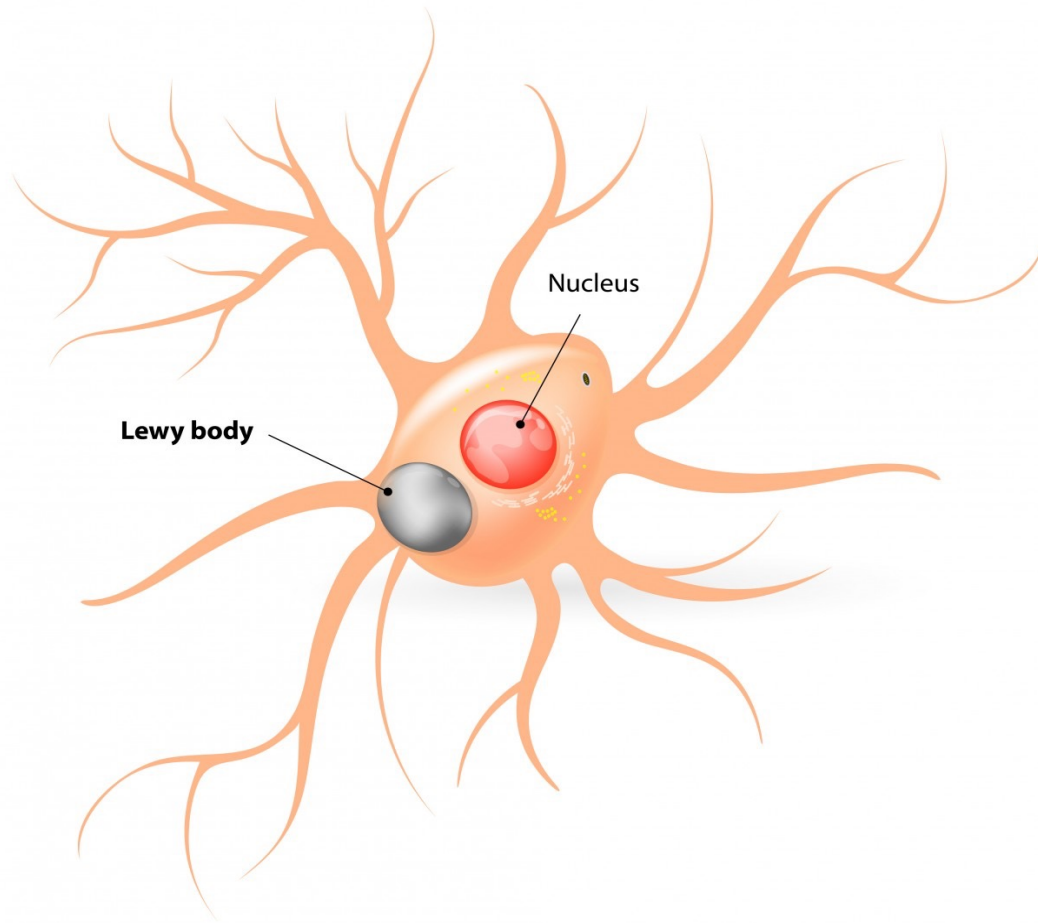
*Early Symptom Comparison*

	Lewy Body Dementia (LBD)	Parkinson's Disease (PD)	Alzheimer's Disease (AD)
Decline in thinking abilities that interfere with everyday life	Always	Possible Years After Diagnosis	Always
Significant Memory Loss	Possible	Possible Years After Diagnosis	Always
Planning or Problem Solving Abilities	Likely	Possible	Possible
Difficulty with sense of direction or spatial relationships between objects	Likely	Possible	Possible
Language Problems	Possible	Possible	Possible
Fluctuating Cognitive Abilities	Likely	Possible	Possible

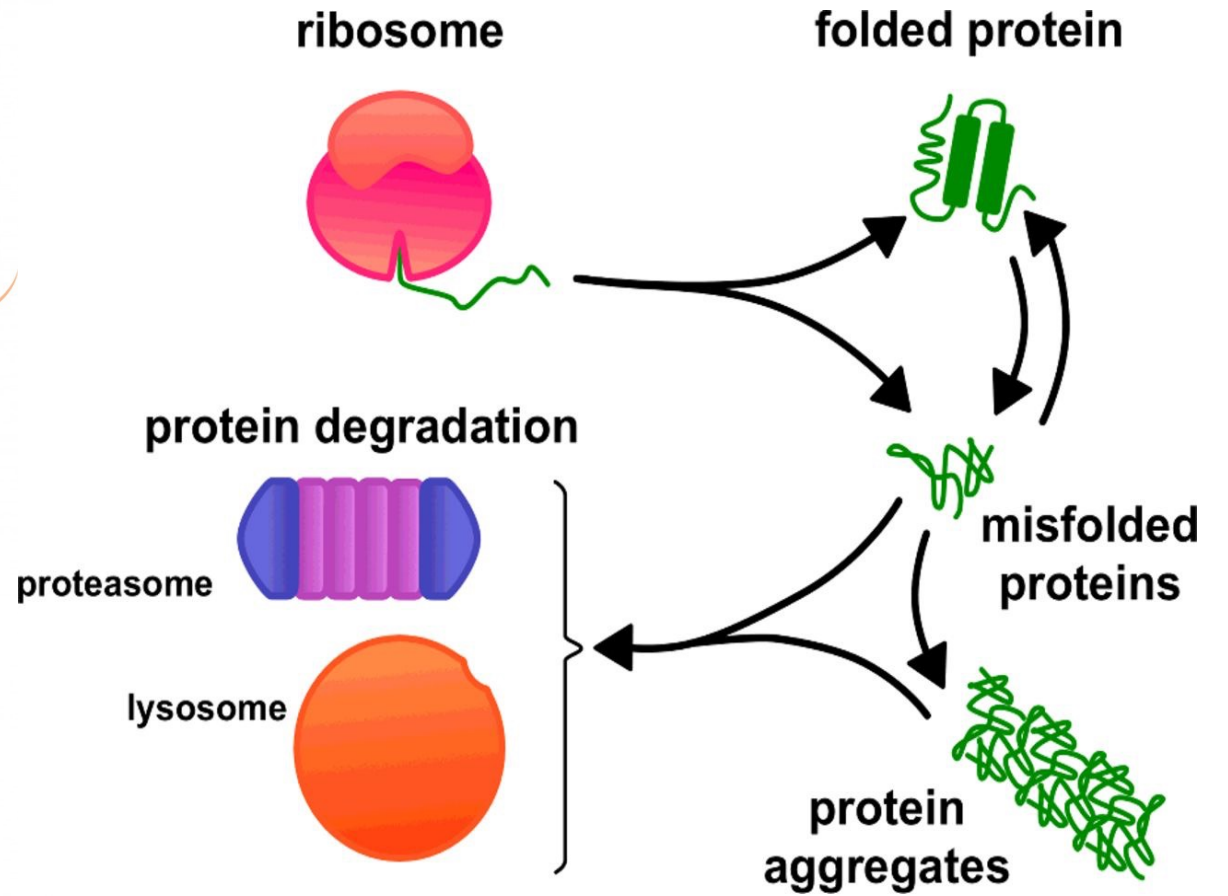
**Memory loss, hallucinations, declining cognitive abilities, motor impairment.**



# What is a Lewy body?



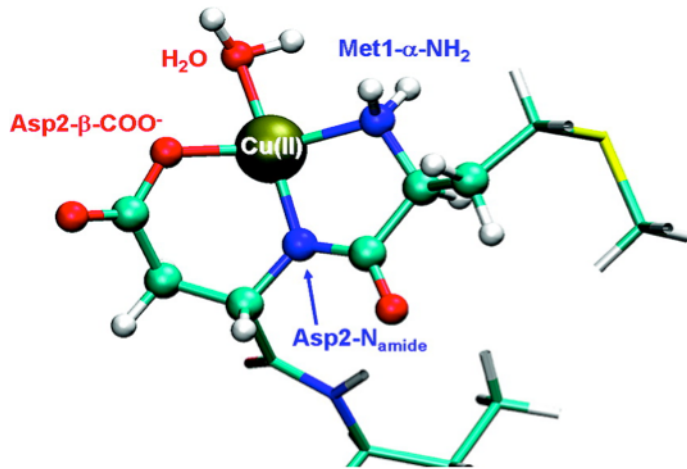
**Alpha-synuclein proteins form Lewy bodies**



**Formed through improper protein degradation.**

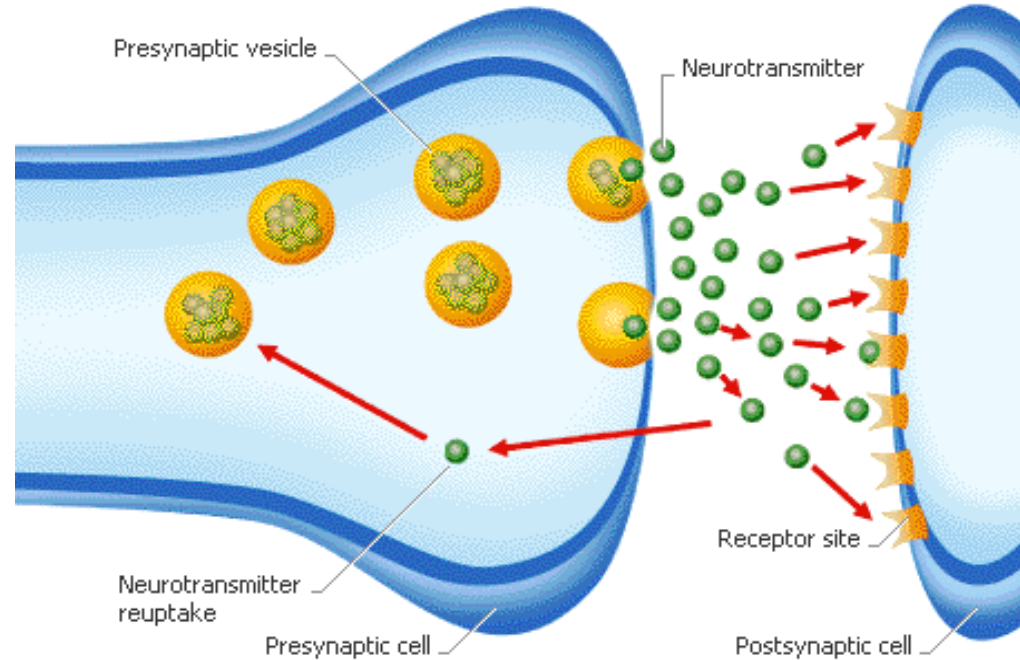
# What are the gene ontology terms?

## Molecular function

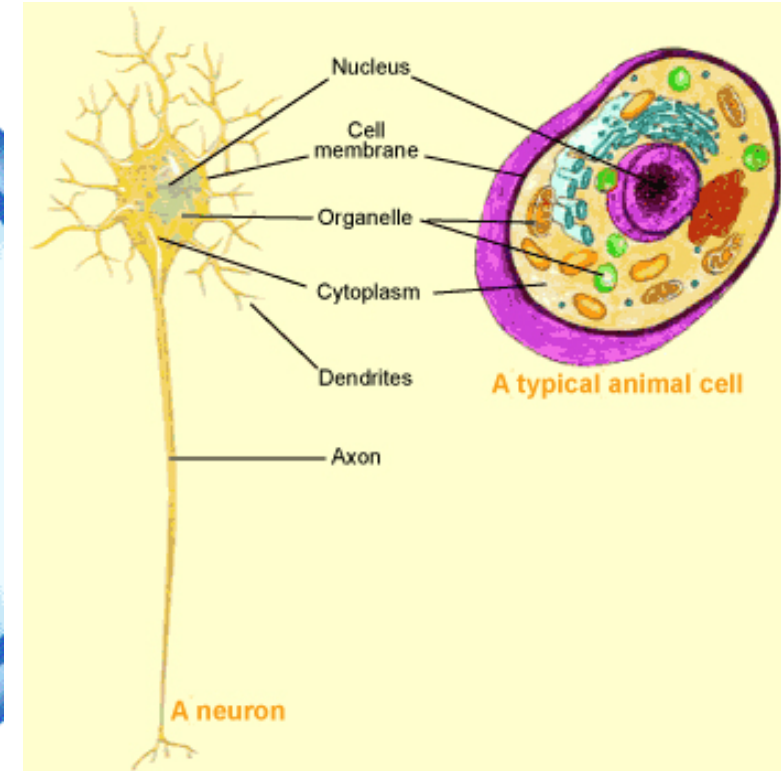


Copper binding

## Biological process



## Cellular component



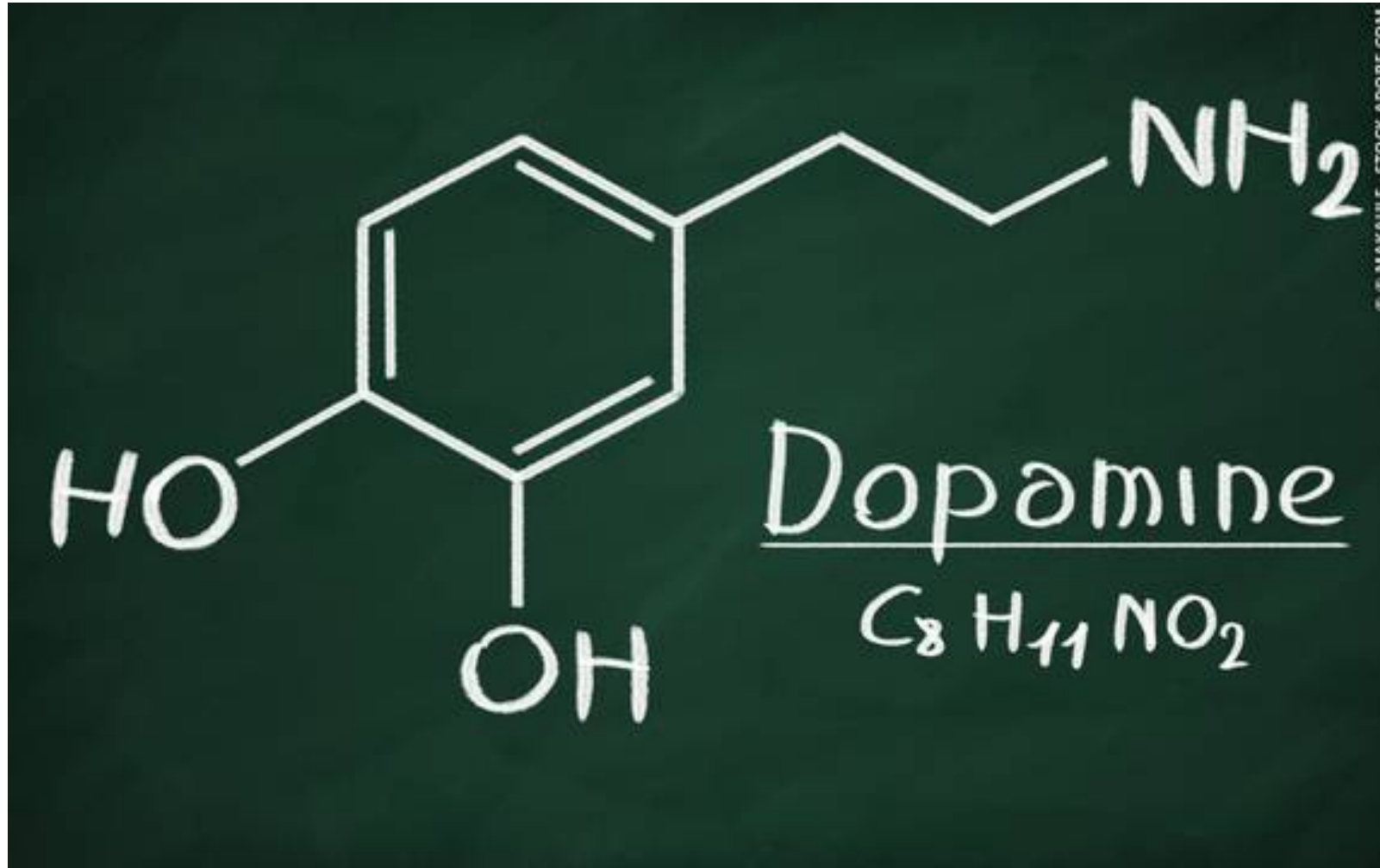
Localizes in the cytoplasm

# What is the gap in knowledge?



**How does over expression of SNCA affect dopamine regulation machinery in the brain?**

# Why is dopamine important?



**Essential for proper movement and cognitive function.**



# What model organisms can be used to study SNCA?

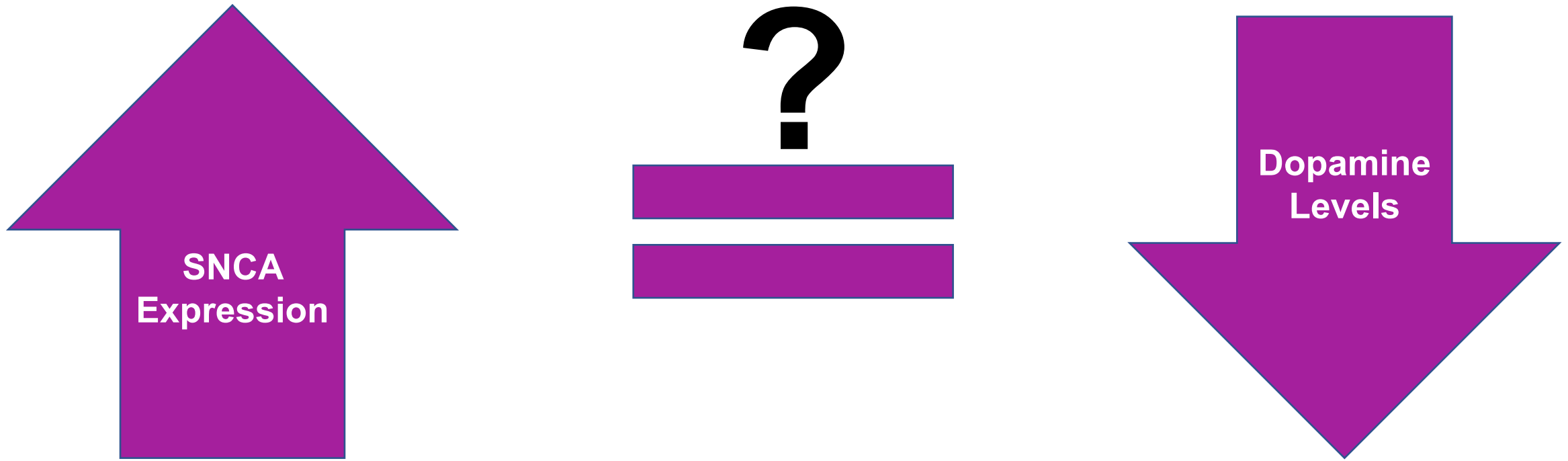


**Similar mutant SNCA phenotypes**



**Easily observed neurons**

# What is the primary goal?



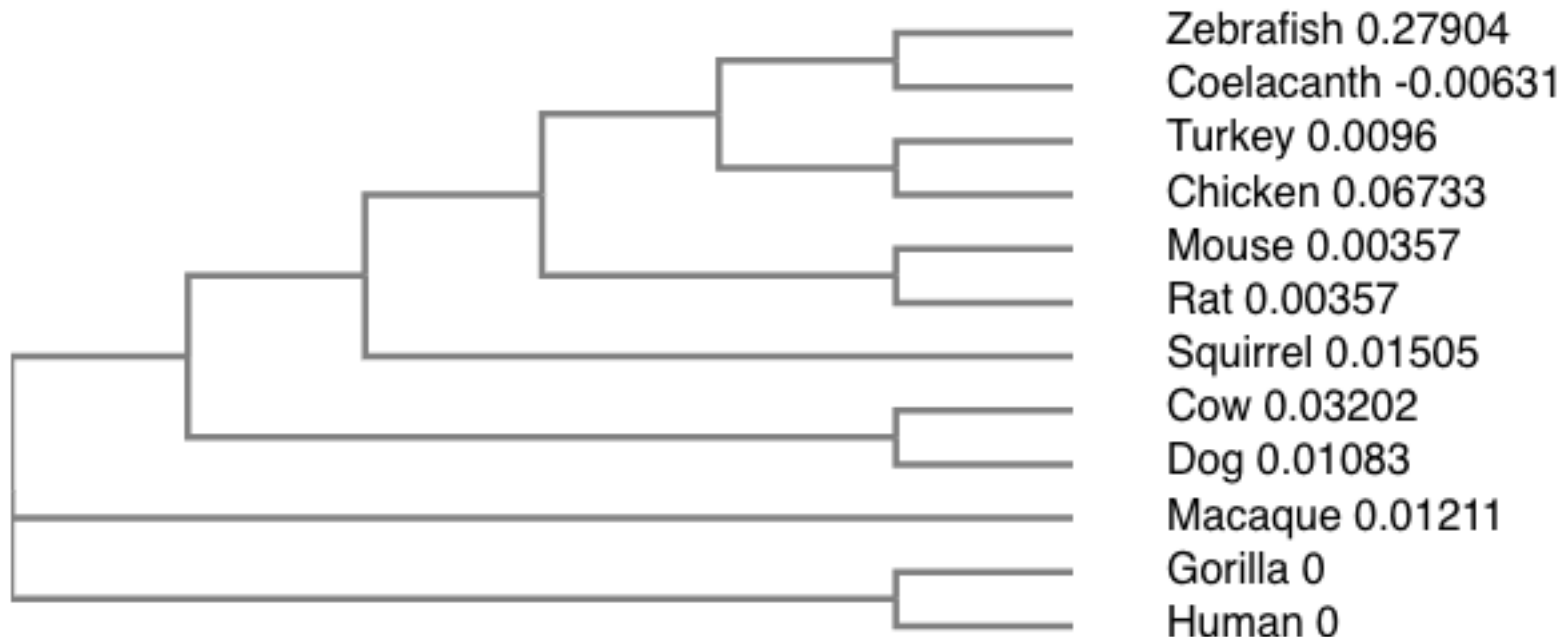
Determine how SNCA **overexpression** leads to a decrease in dopamine expression in neurons.

# **What are the aims?**

- 1. Identify conserved SNCA protein domains involved in neurotransmitter regulation.**
- 2. Identify small molecules that improve synaptic vesicle maintenance and dopamine release.**
- 3. Identify proteins that interact with SNCA and decrease dopamine expression.**



# Aim 1: Identify conserved SNCA protein domains involved in neurotransmitter regulation



# Aim 1: Identify conserved SNCA protein domains involved in neurotransmitter regulation

## Synuclein

**Humans**

1-131

Length: 140 AA % Identity: ---

**Mouse**

1-131

Length: 140 AA % Identity: 95%

**Gorilla**

1-131

Length: 140 AA % Identity: 100%

**Chimpanzee**

1-131

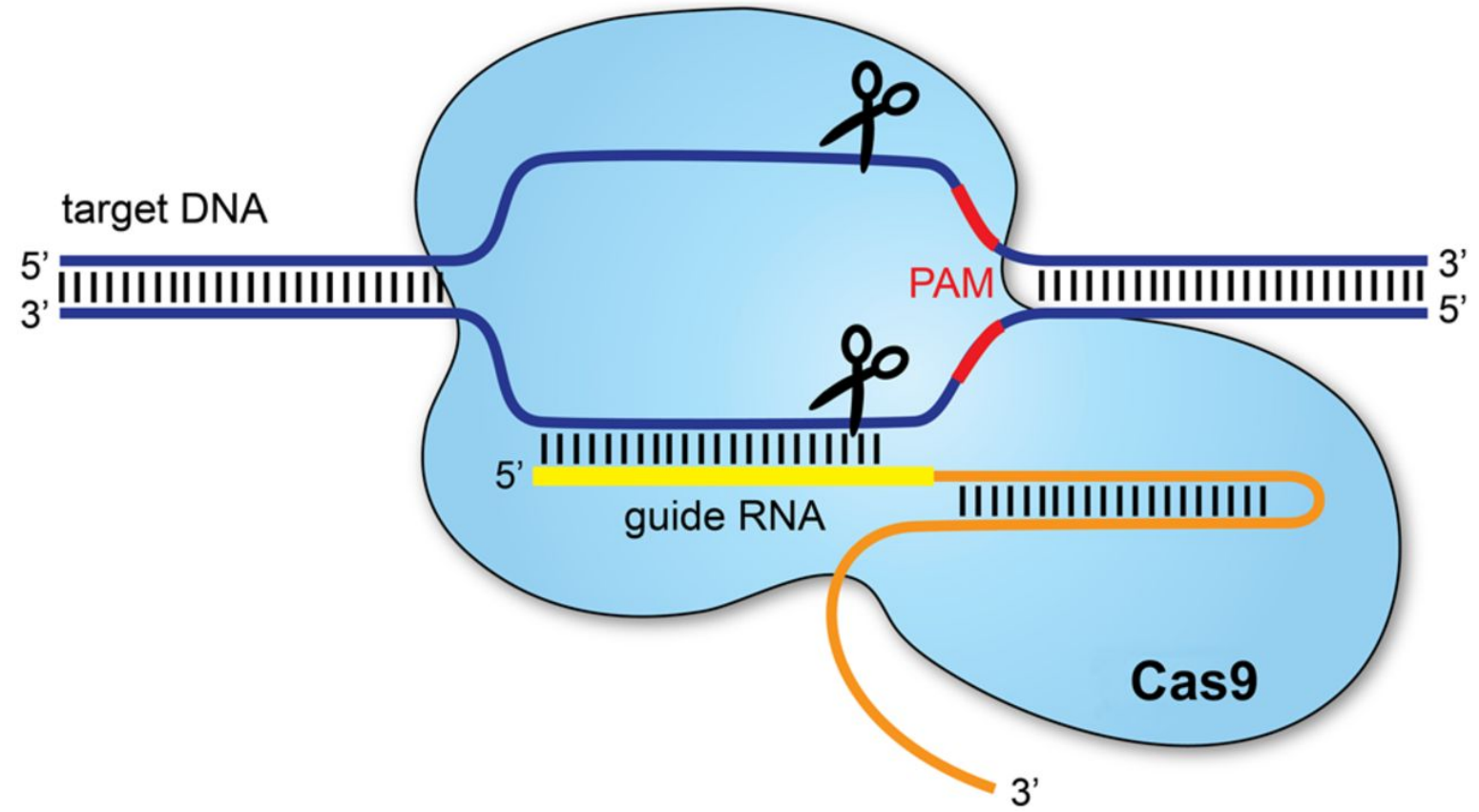
Length: 140 AA % Identity: 100%

**Zebrafish**

1-119

Length: 127 AA % Identity: 54%

# Aim 1: Identify conserved SNCA protein domains involved in neurotransmitter regulation

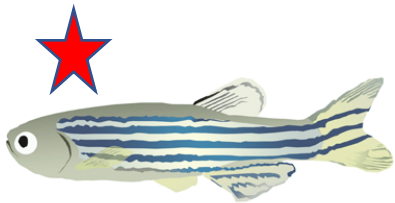




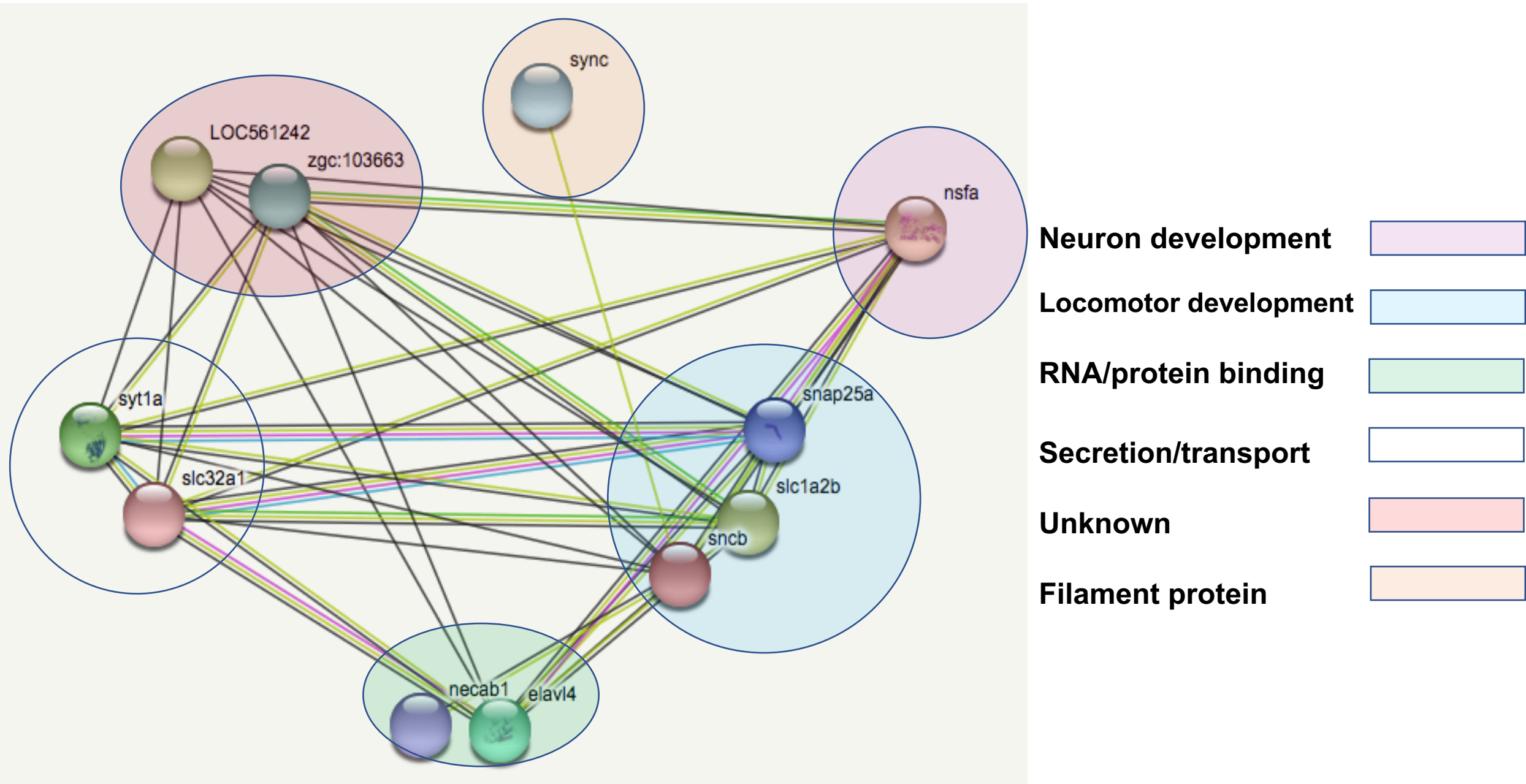
# **Aim 1: Identify conserved SNCA protein domains involved in neurotransmitter regulation**



# Identify small molecules that improve synaptic vesicle maintenance and dopamine release.



# SNCB Interaction networks in *Danio rerio*





# SNCA interaction networks in Mus Musculus

