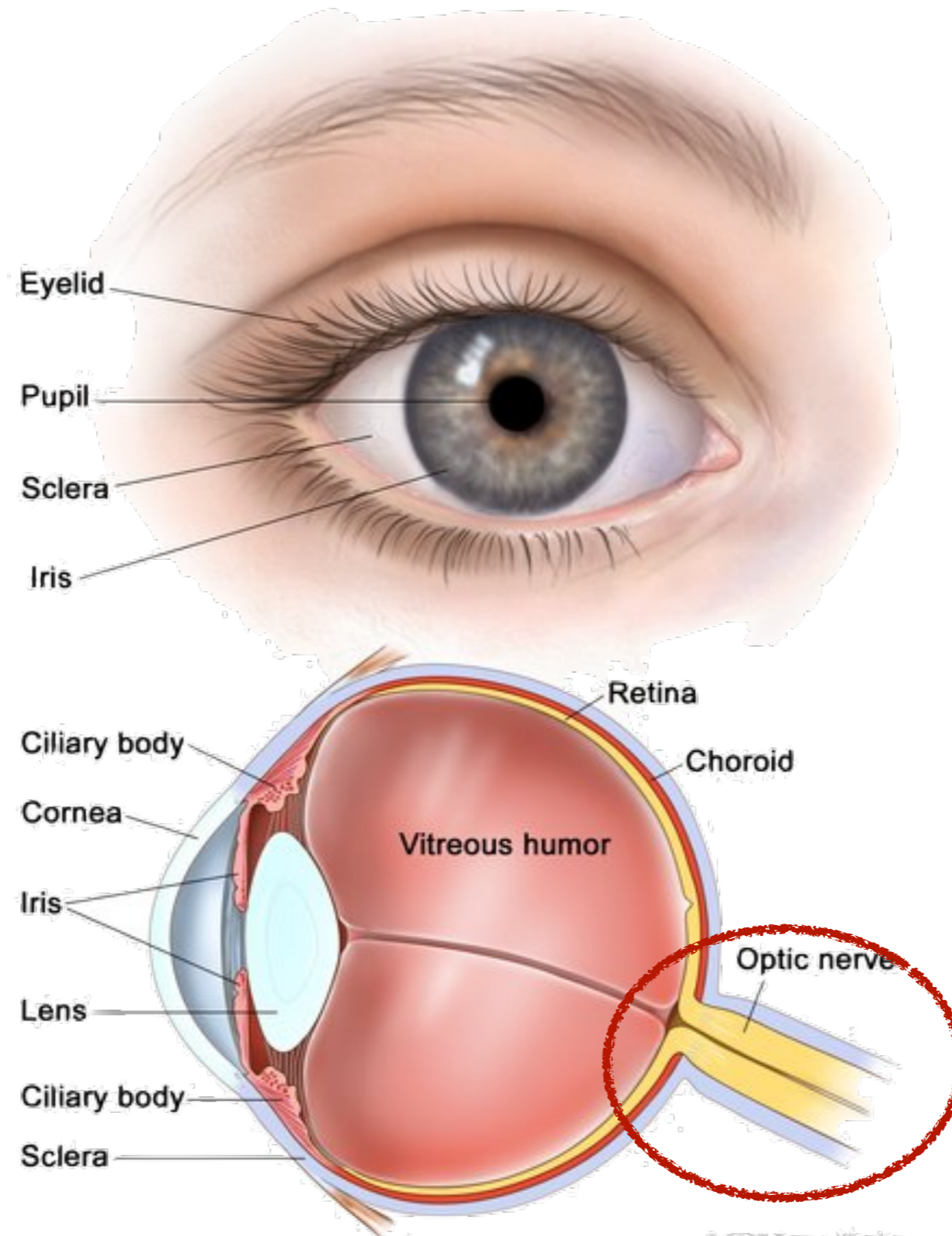


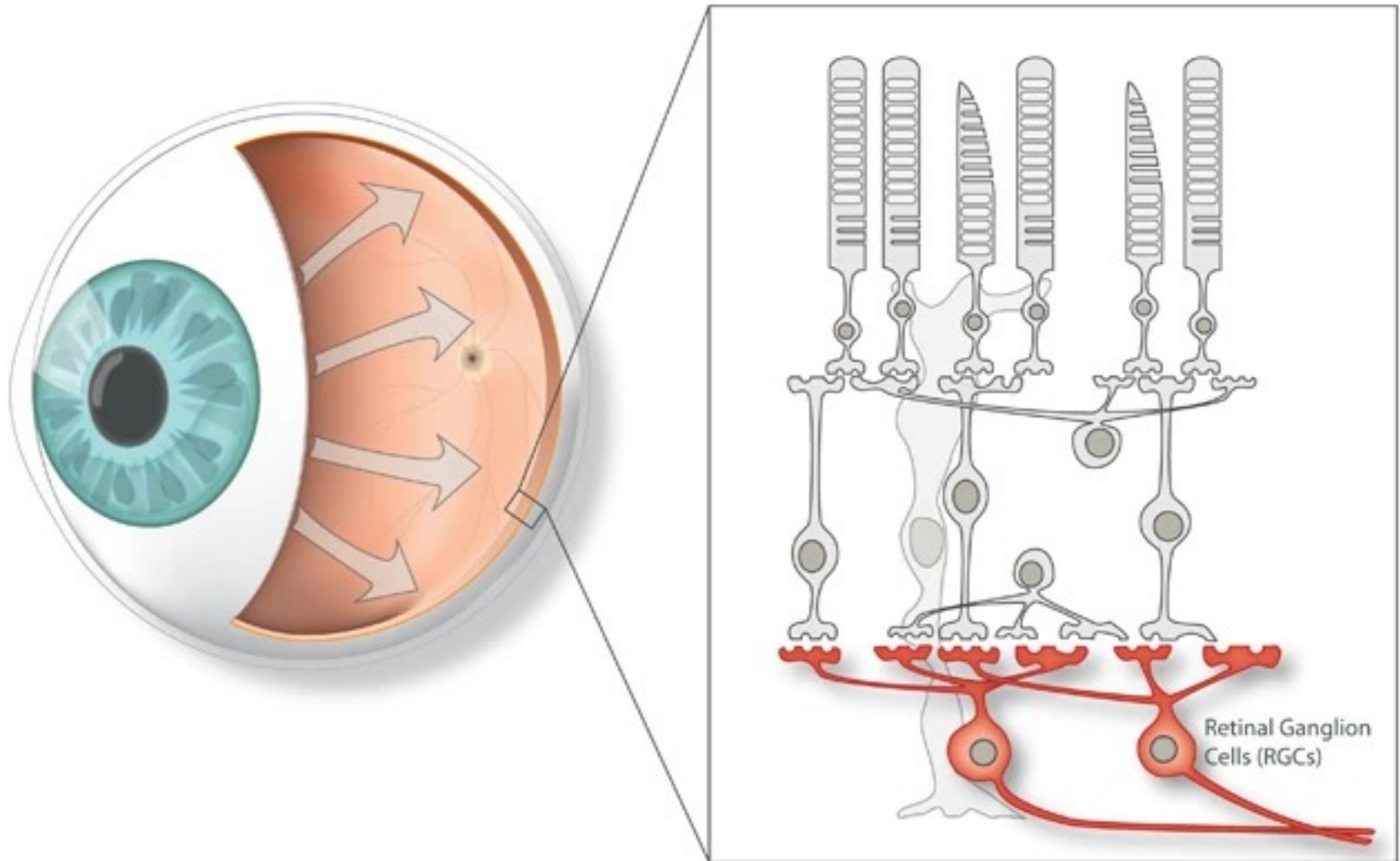


**OPA 1
&
OPTIC ATROPHY TYPE 1**

What is Optic Atrophy Type 1?



Defects in Mitochondria lead to Optic Atrophy Type 1



Phenotypes of Optic Atrophy Type 1



Blurred



Blocked

Normal Vision

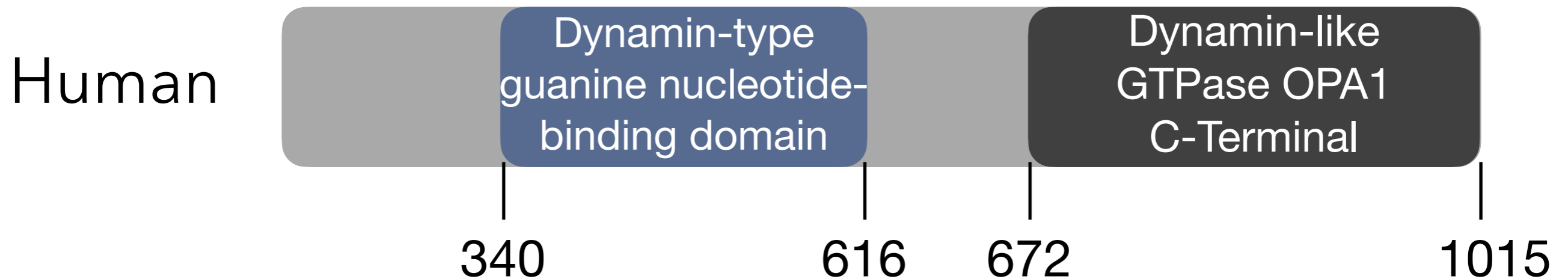


Color Vision Deficiency

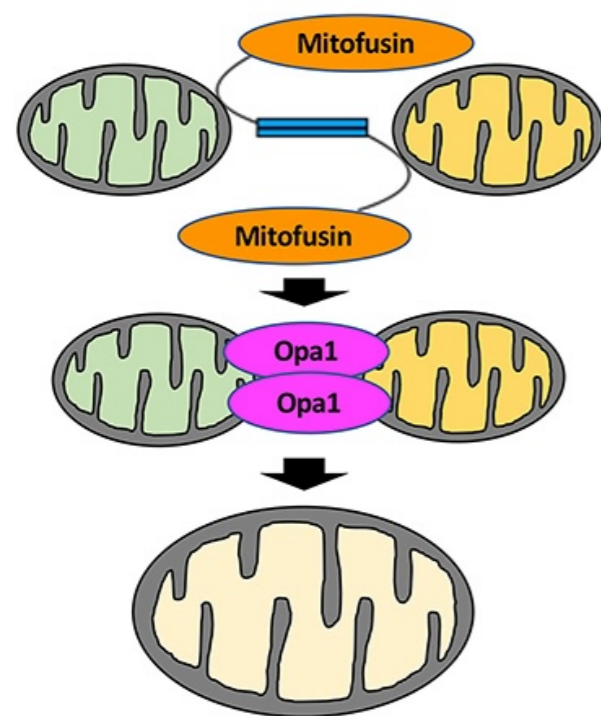


Color vision deficiency

Optic Atrophy Type 1 is associated with OPA1

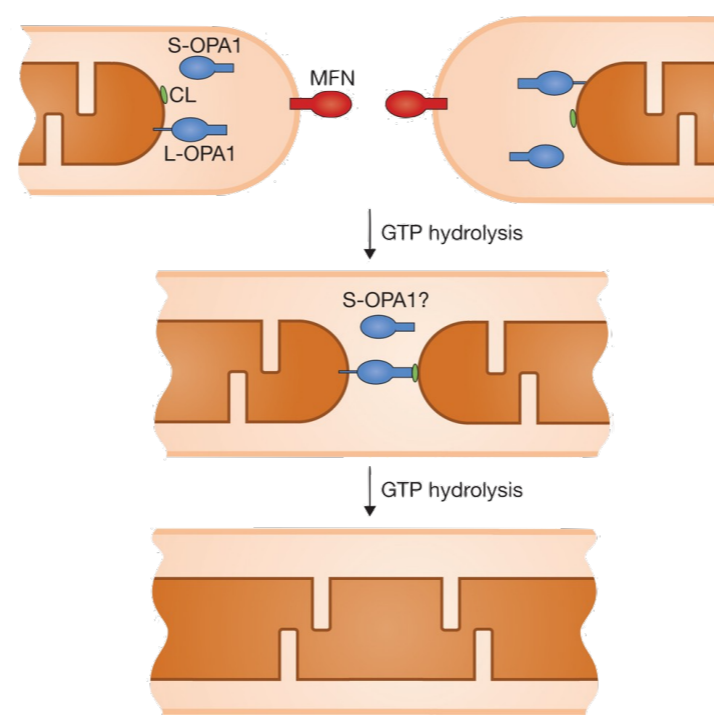


Biological process



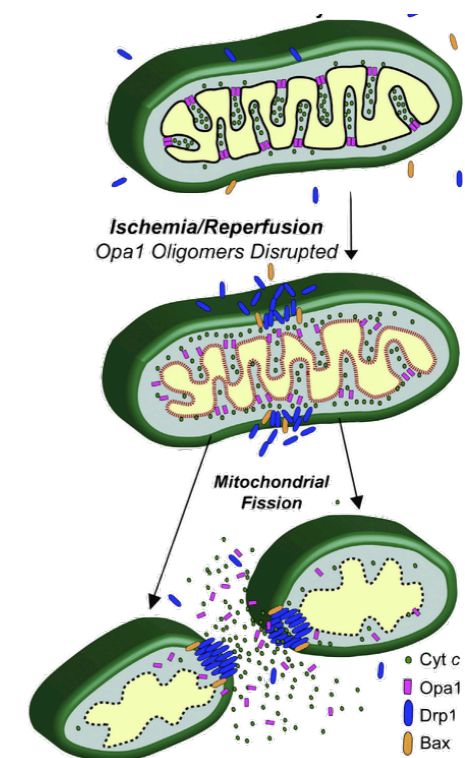
Mitochondria function

Molecular Function



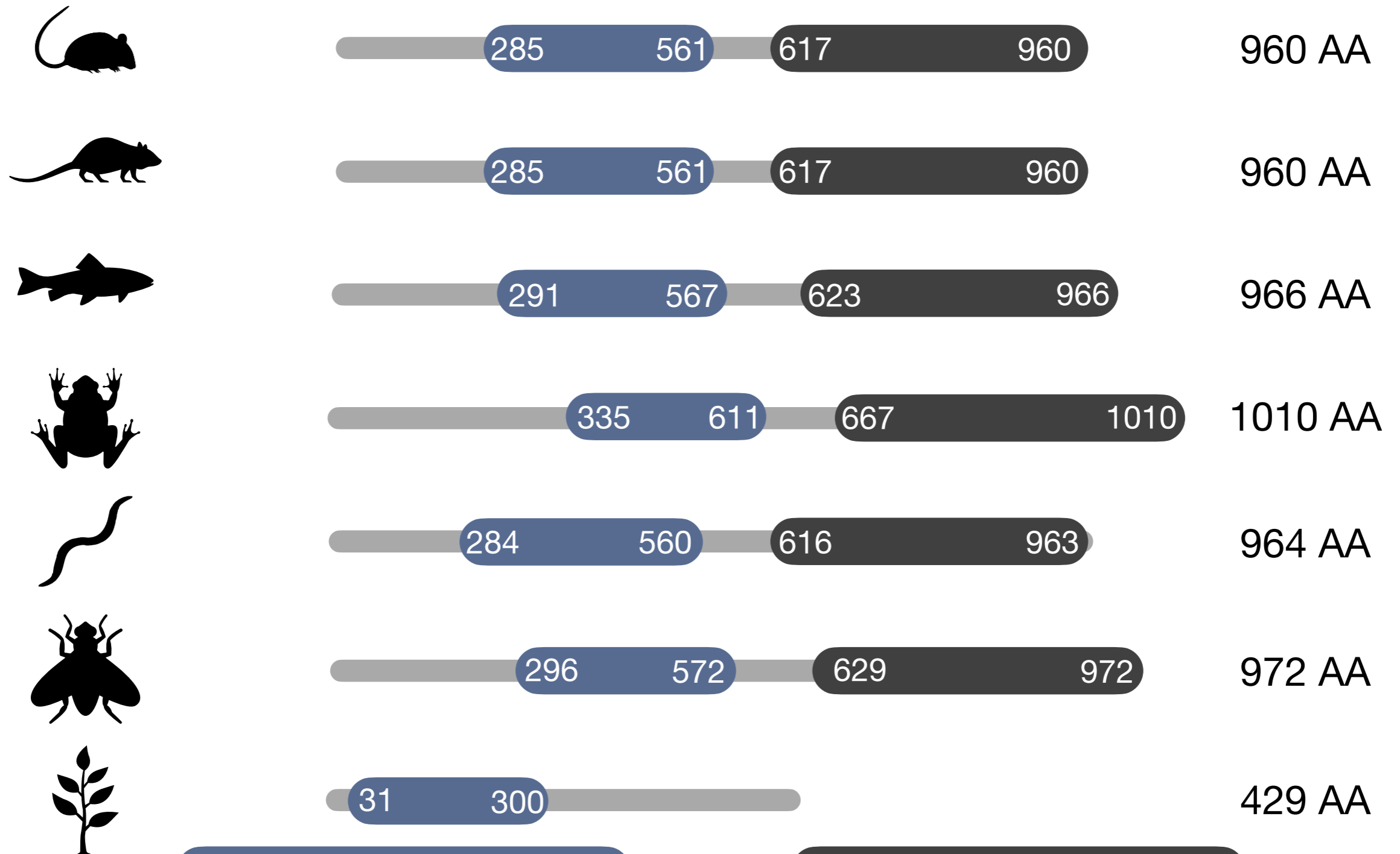
GTP binding

Cellular Component



Mitochondrial membrane

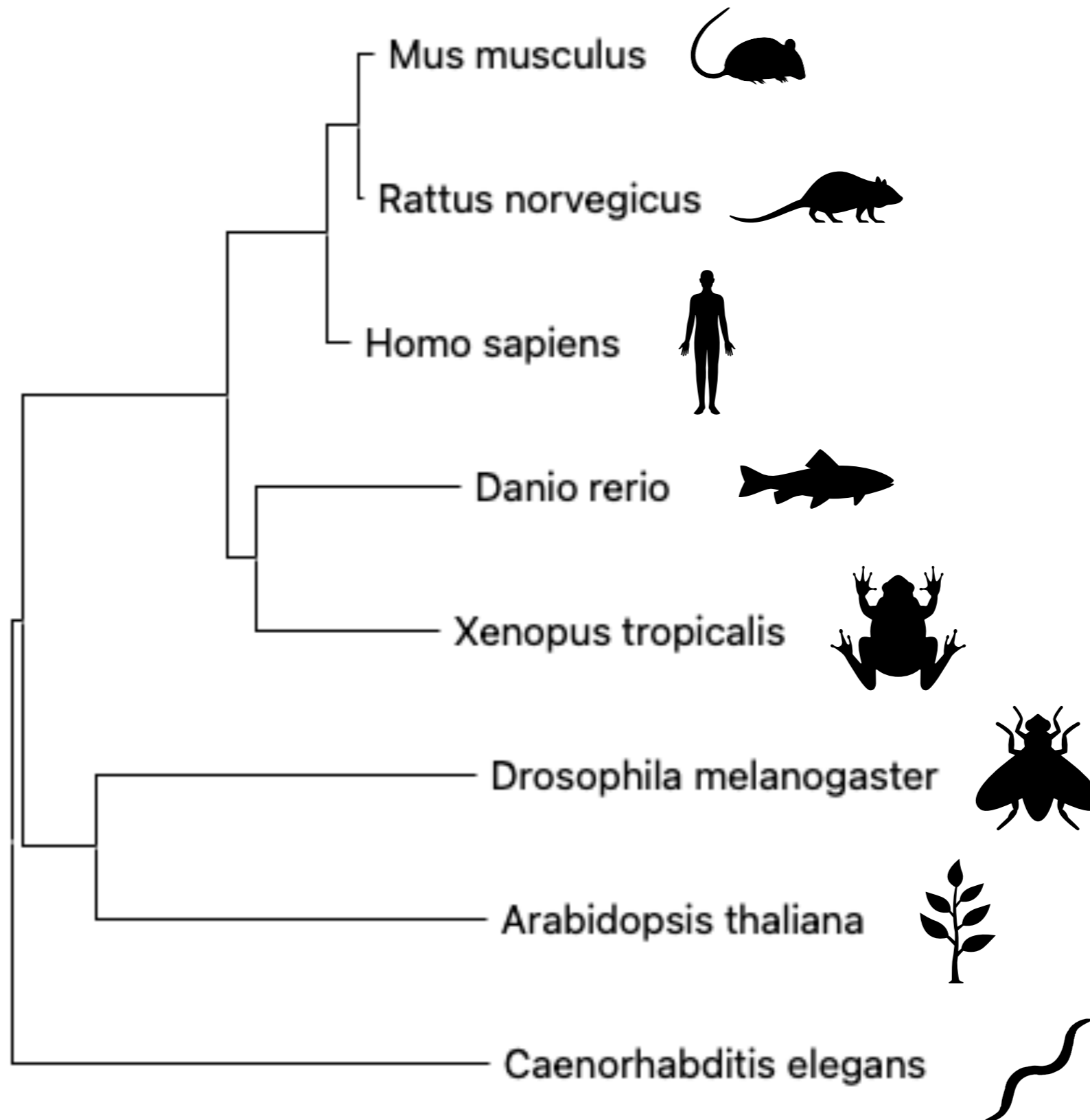
OPA1 is well conserved across the animal and plant kingdoms



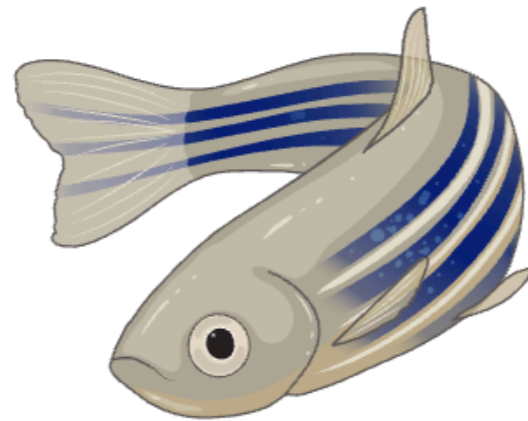
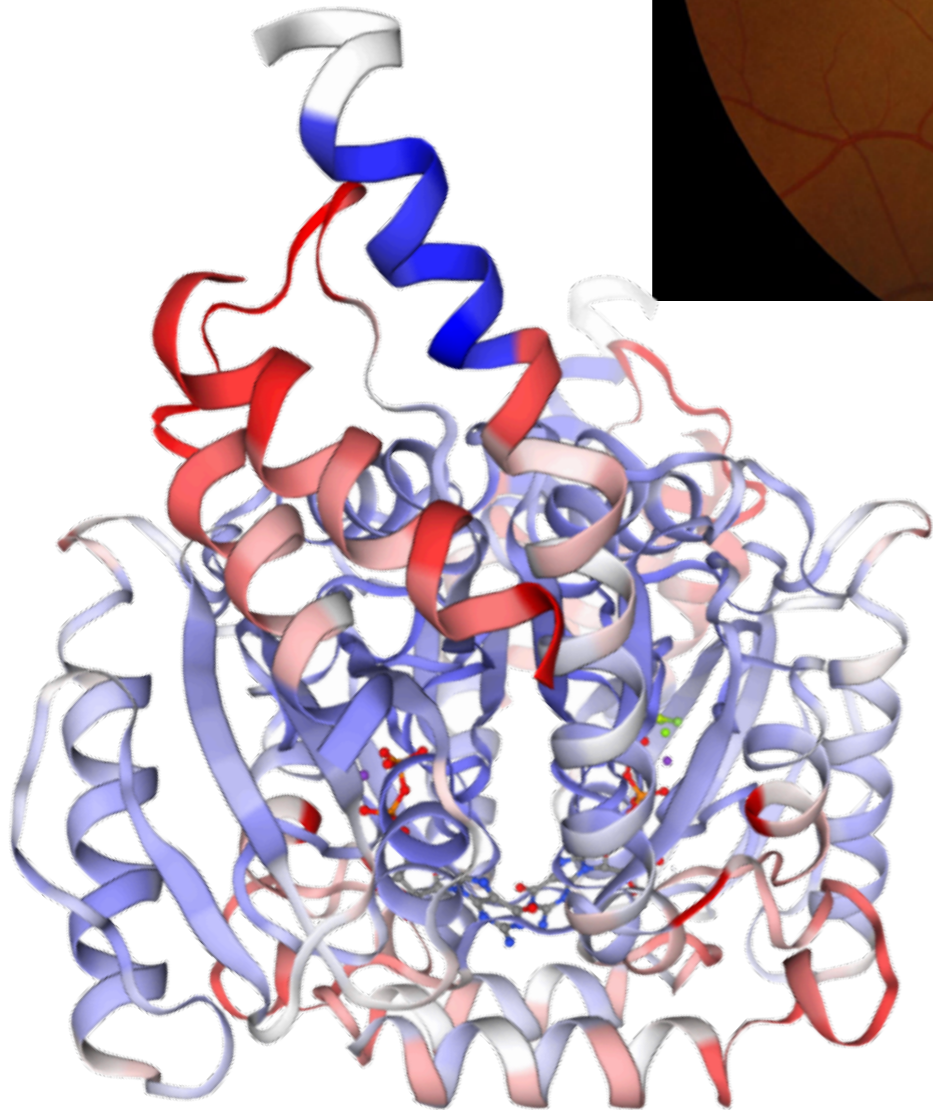
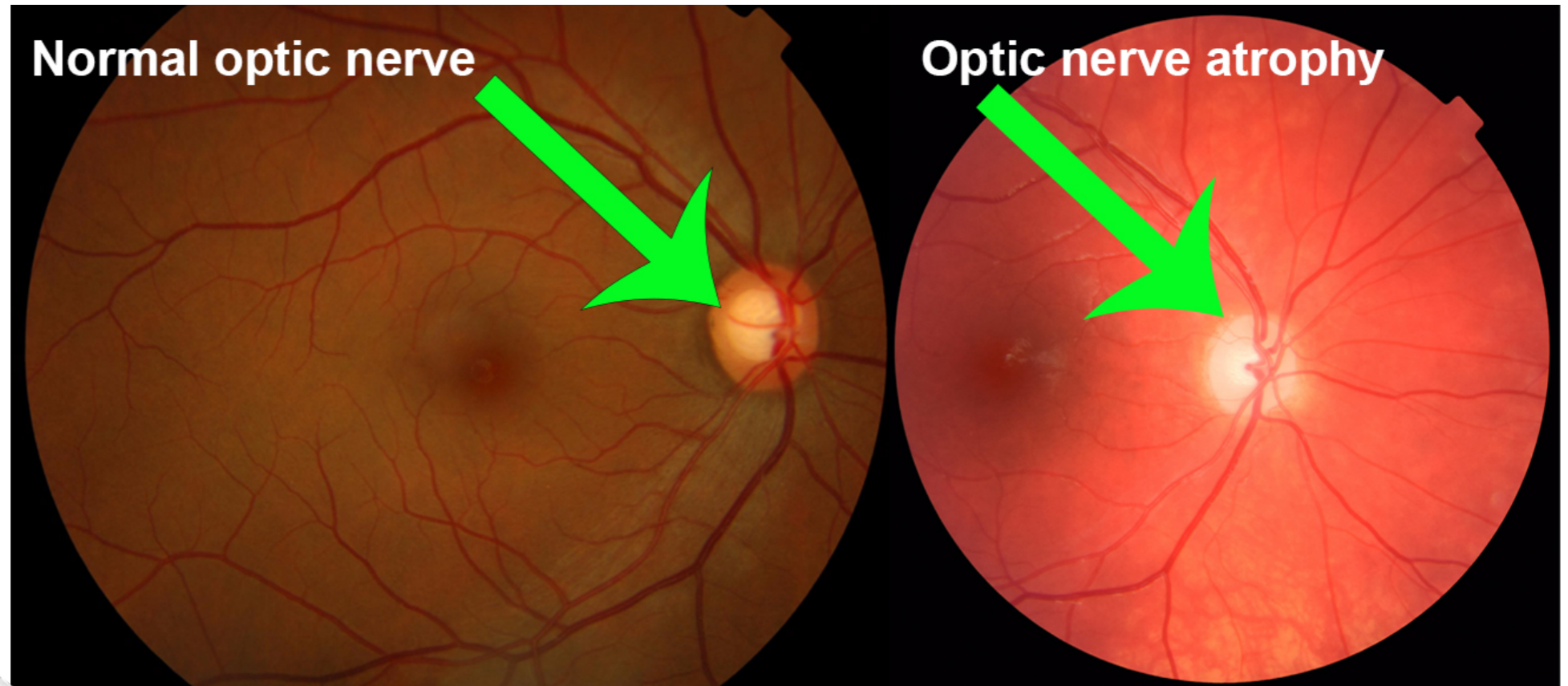
Dynamamin-type
guanine nucleotide-
binding domain

Dynamamin-like
GTPase OPA1
C-Terminal

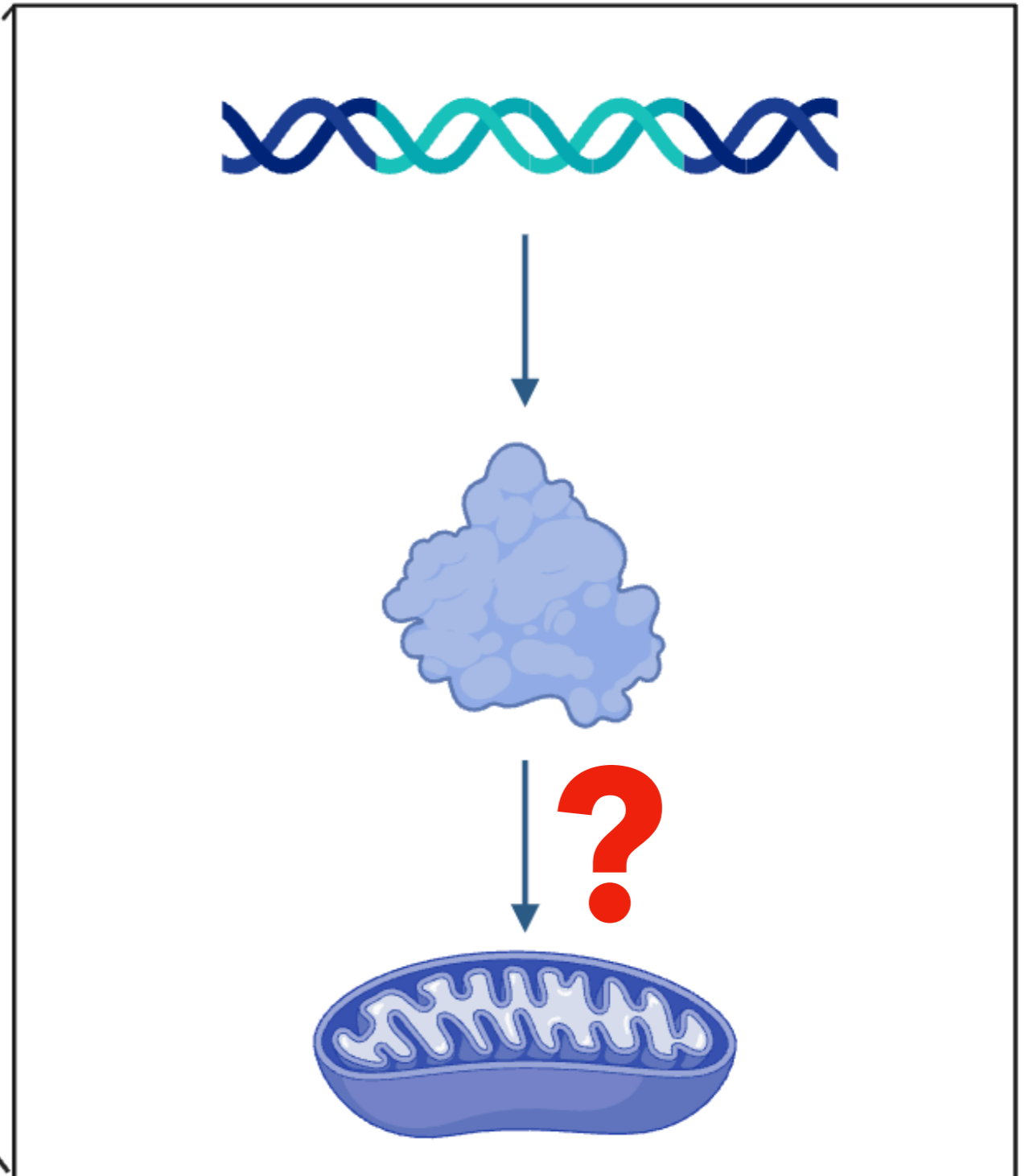
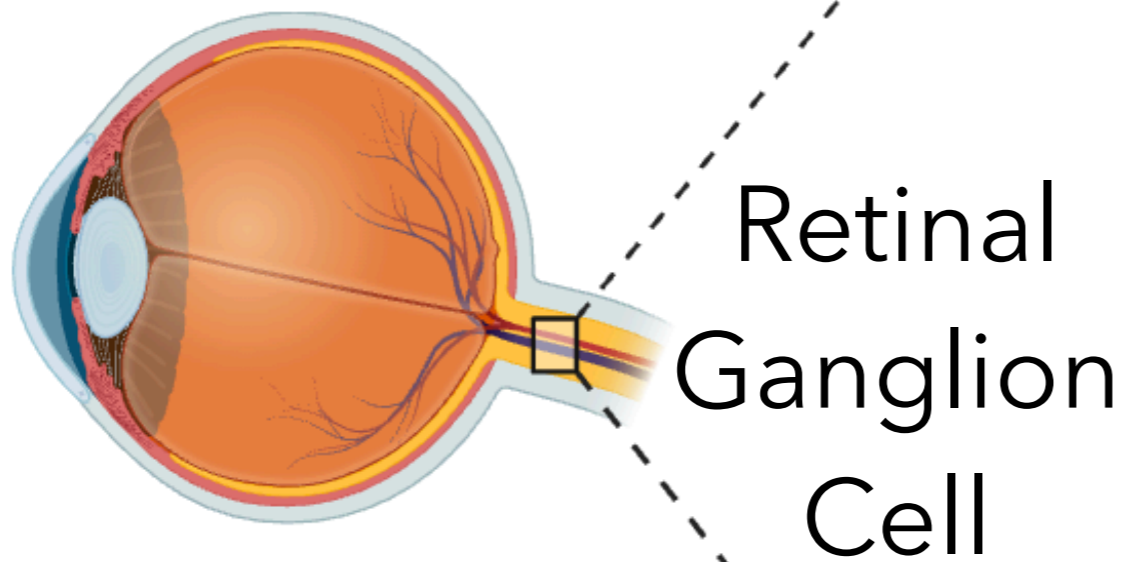
How are OPA1 Homologs Related?



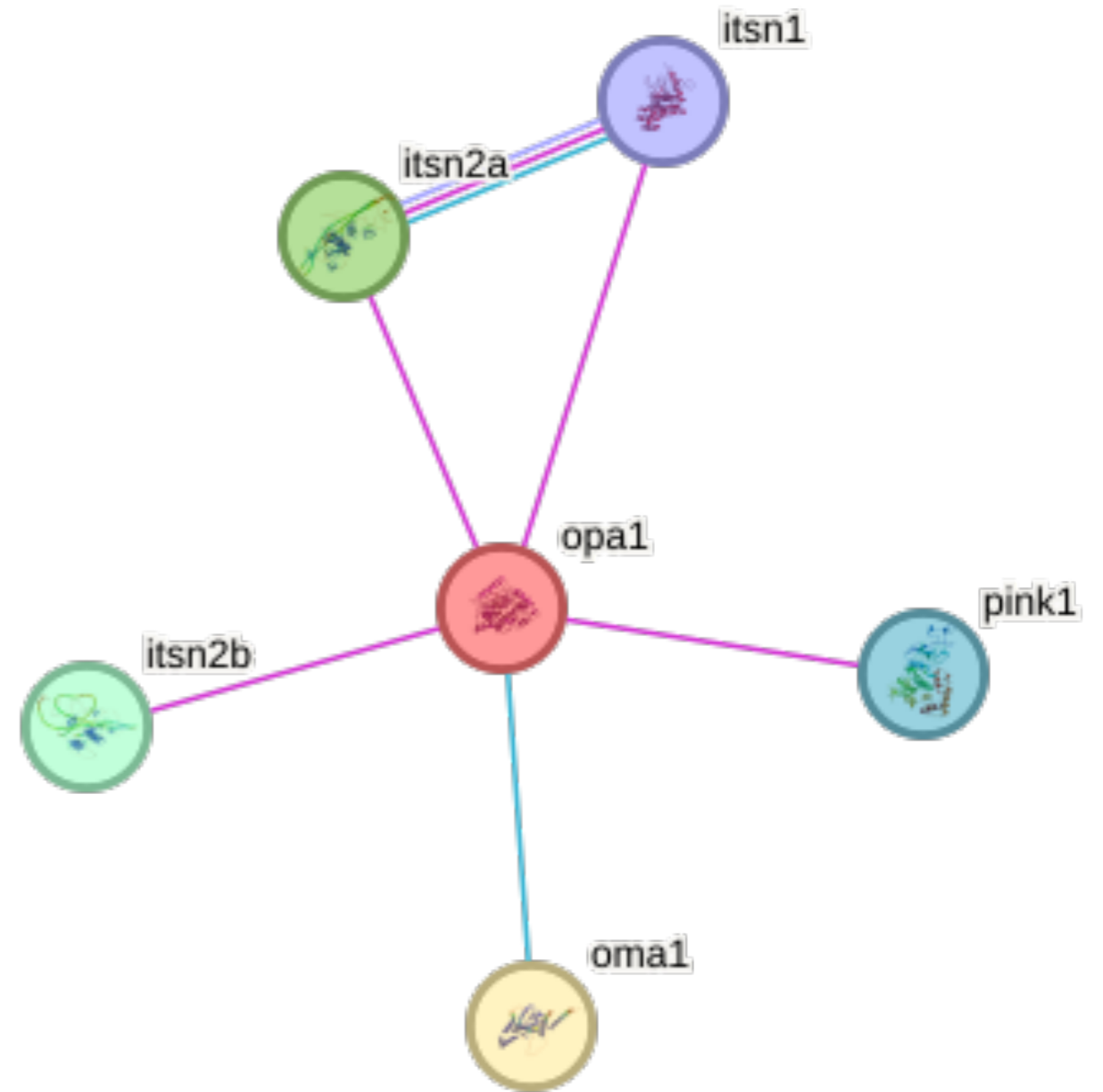
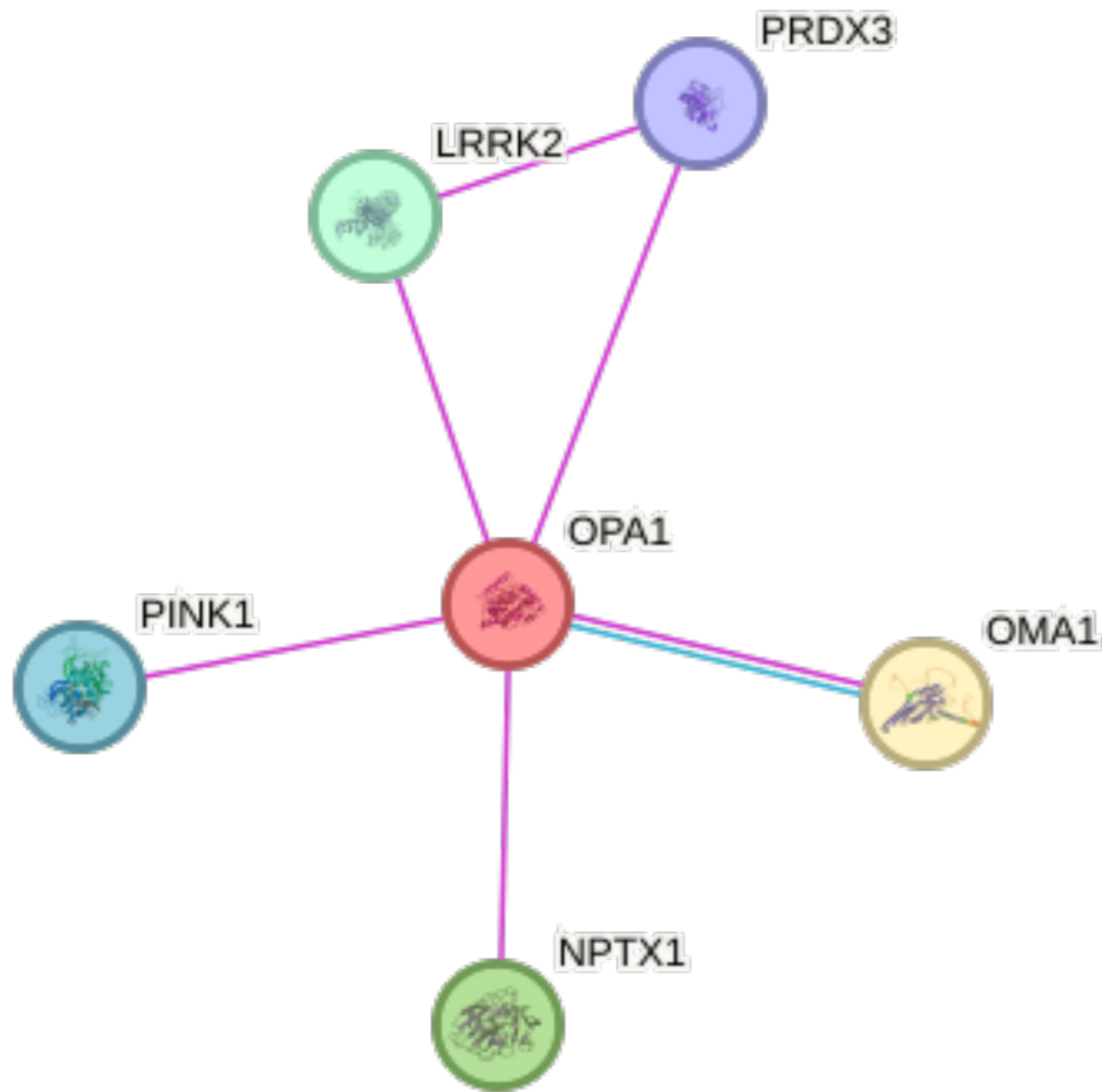
Which Model Organisms to Use?



Knowledge Gap



Interaction Networks Comparison

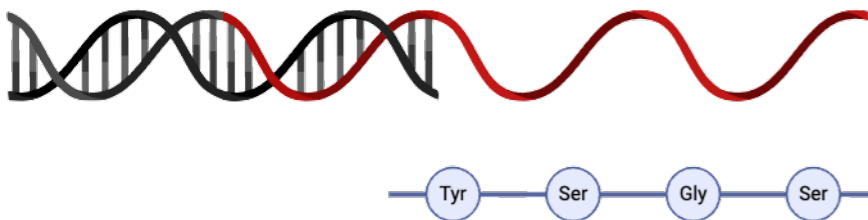


Primary Goal

Investigate the role of OPA1 in mitochondria during retinal development

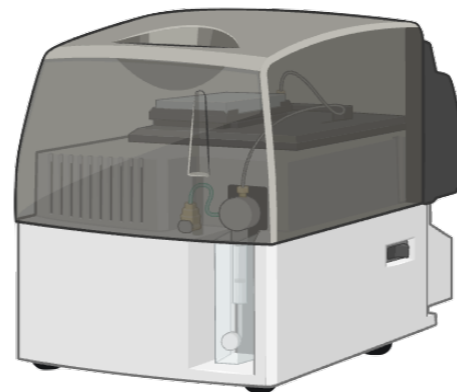
Aim 1

Identify amino acids of OPA1 that are crucial for retinal development using domain analysis



Aim 2

Find chemical compounds that reuse the phenotype using chemical screening



Aim 3

Primary Goal

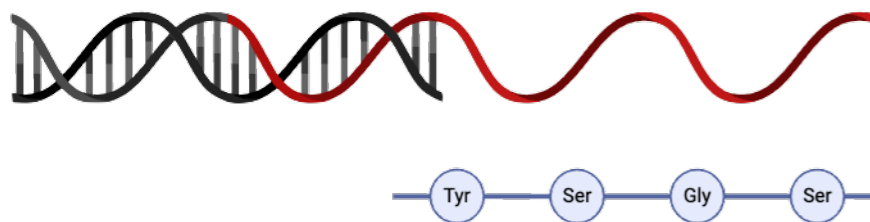
Investigate the role of OPA1 in mitochondria during retinal development

Aim 1

Identify amino acids of OPA1 that are crucial for retinal development using domain analysis

Hypothesis: Zebrafish with mutations in OPA1 amino acids will inhibit disease-like phenotype

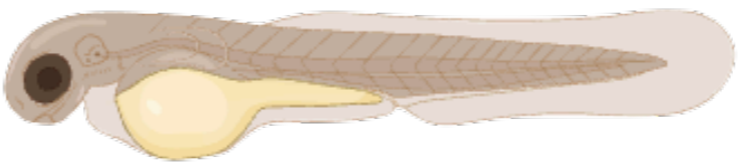
Rationale: Capable to determine which amino acids affect protein function and further affect mitochondria function



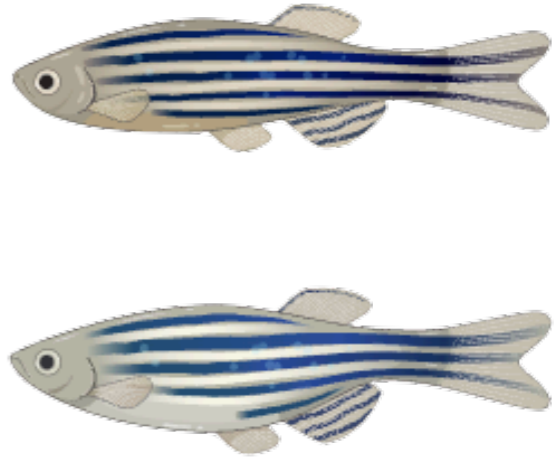
Aim 1: Identify amino acids of OPA1 that are crucial for retinal development using domain analysis



Protruding mouth stage



Long pec stage



Adult stage

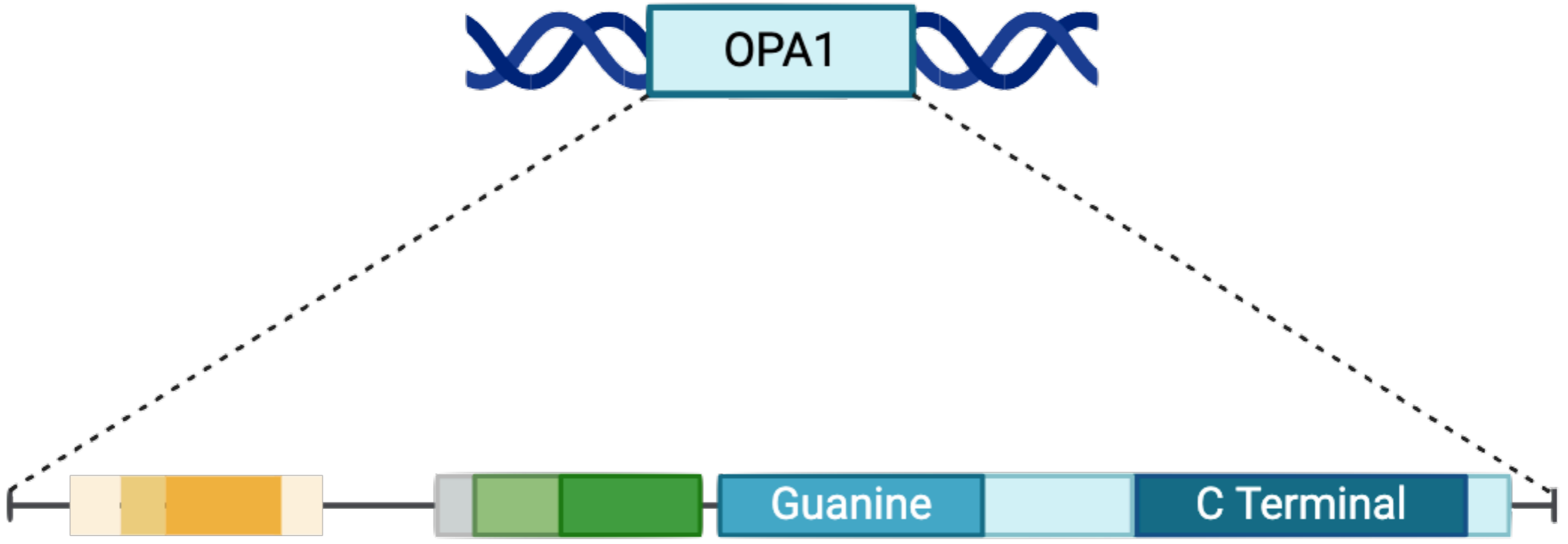
Zebrafish breeding

Domain analysis

CRISPR-Cas9

Chemical screening

Aim 1: Identify amino acids of OPA1 that are crucial for retinal development using domain analysis



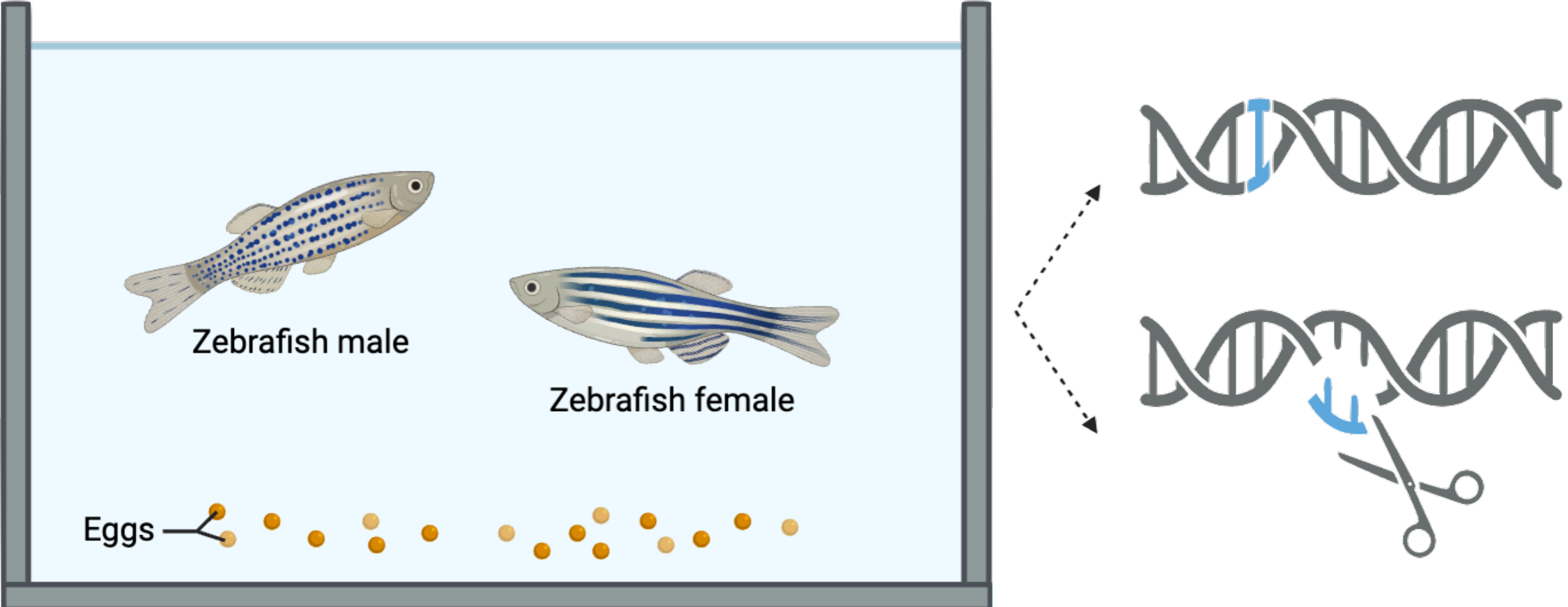
Zebrafish breeding

Domain analysis

CRISPR-Cas9

Chemical screening

Aim 1: Identify amino acids of OPA1 that are crucial for retinal development using domain analysis



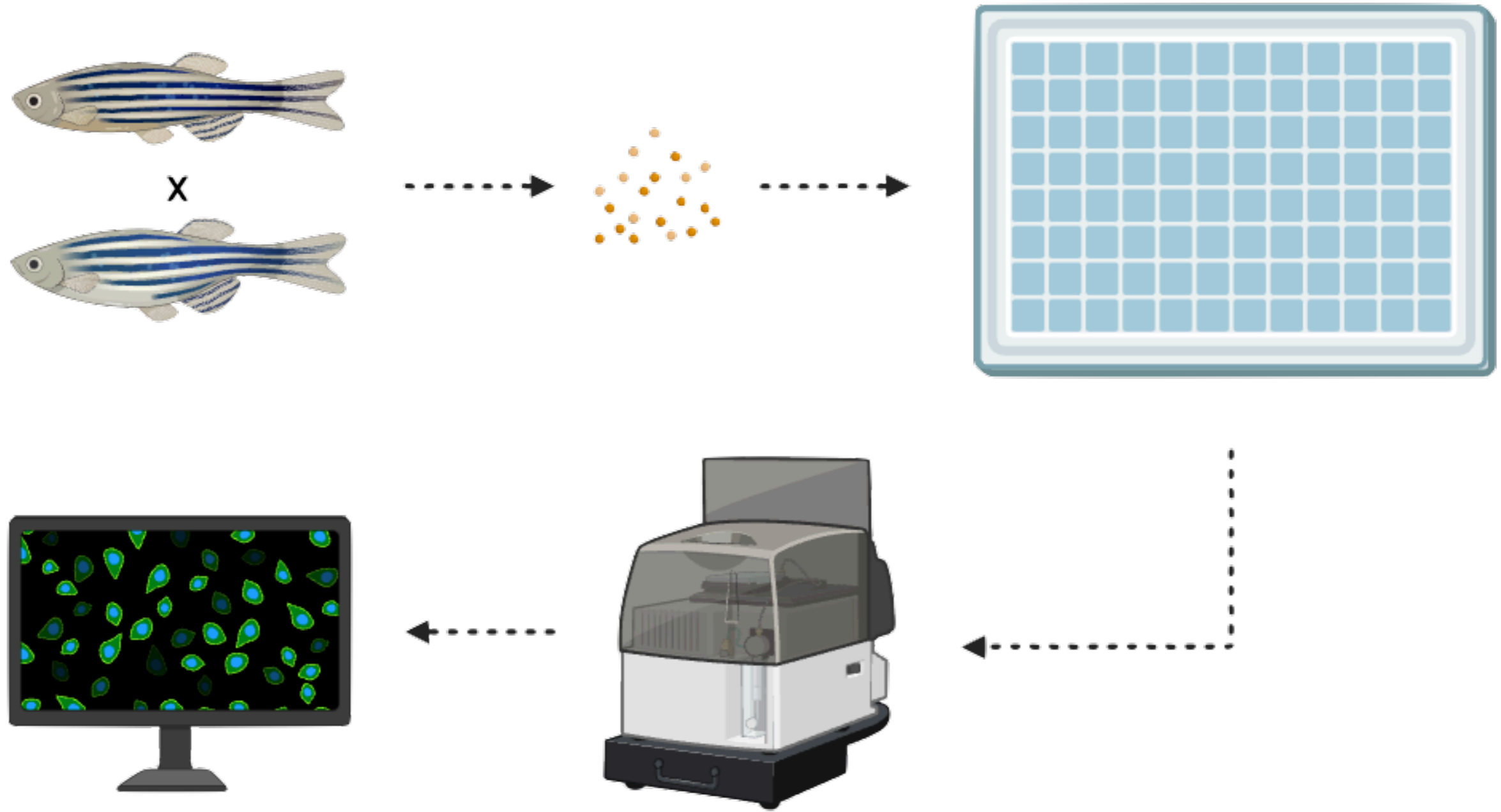
Zebrafish breeding

Domain analysis

CRISPR-Cas9

Chemical screening

Aim 1: Identify amino acids of OPA1 that are crucial for retinal development using domain analysis



Zebrafish breeding

Domain analysis

CRISPR-Cas9

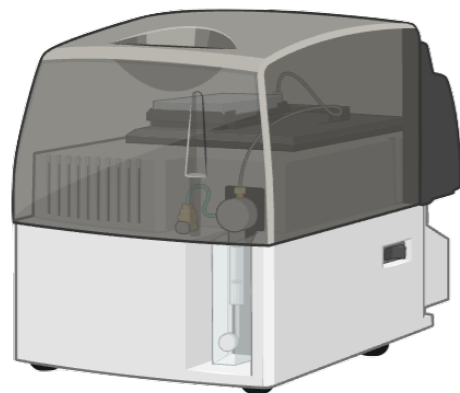
Chemical screening

Primary Goal

Investigate the role of OPA1 in mitochondria during retinal development

Aim 2

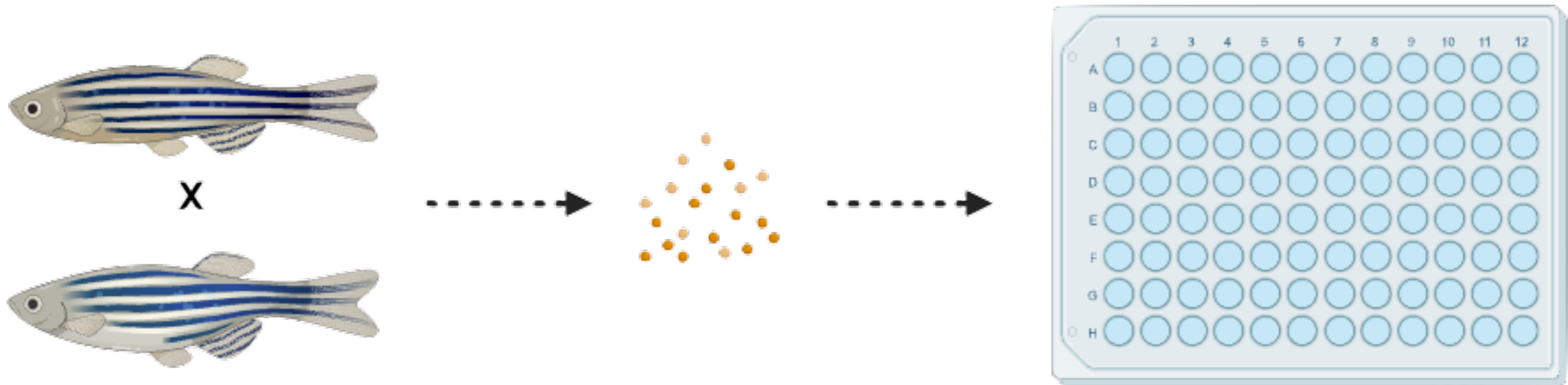
Find chemical compounds that reuse the phenotype using chemical screening



Hypothesis: Different compounds can rescue different disease-like phenotypes

Rationale: Chemical screens visualize the changes within the cell structure, can determine which compound is suitable for drug discovery

Aim 2: Find chemical compounds that reuse the phenotype using chemical screening



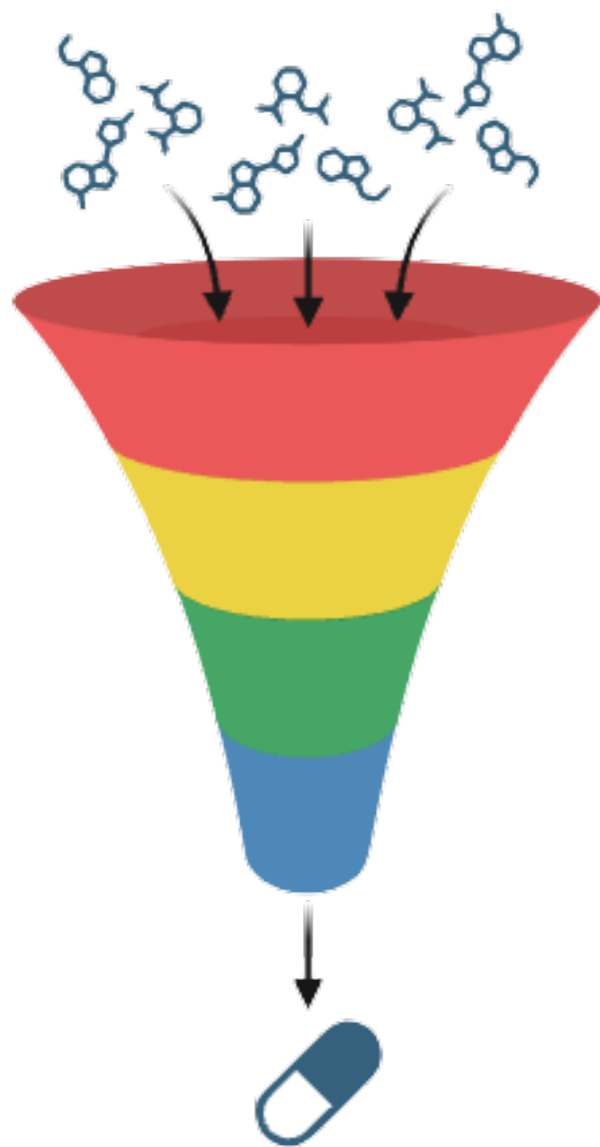
Zebrafish
breeding

Compound
selection

Staining &
assay

Chemical
screening

Aim 2: Find chemical compounds that reuse the phenotype using chemical screening



Stanford
MEDICINE

TargetMoi®
A DRUG SCREENING EXPERT

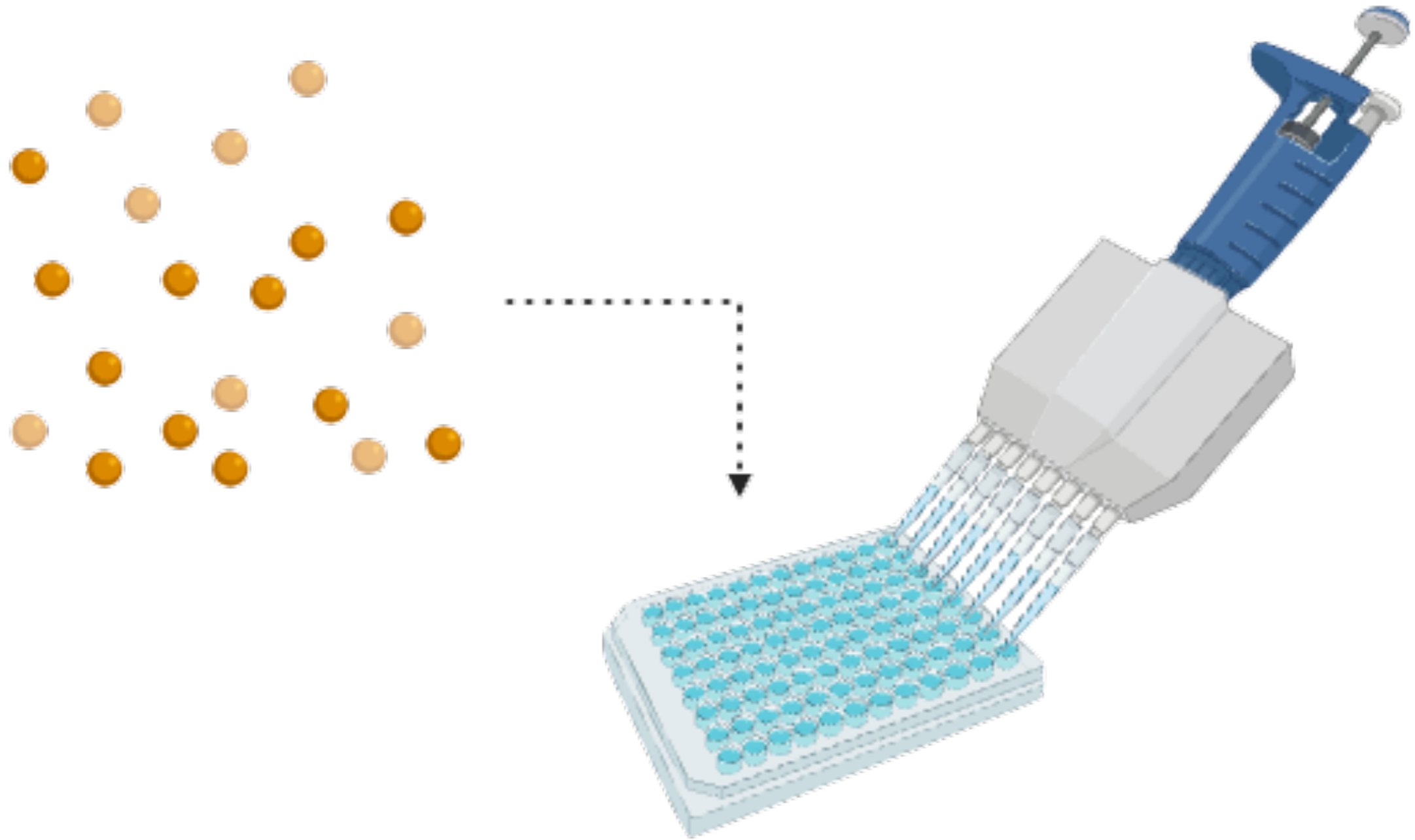
Zebrafish
breeding

Compound
selection

Staining &
assay

Chemical
screening

Aim 2: Find chemical compounds that reuse the phenotype using chemical screening



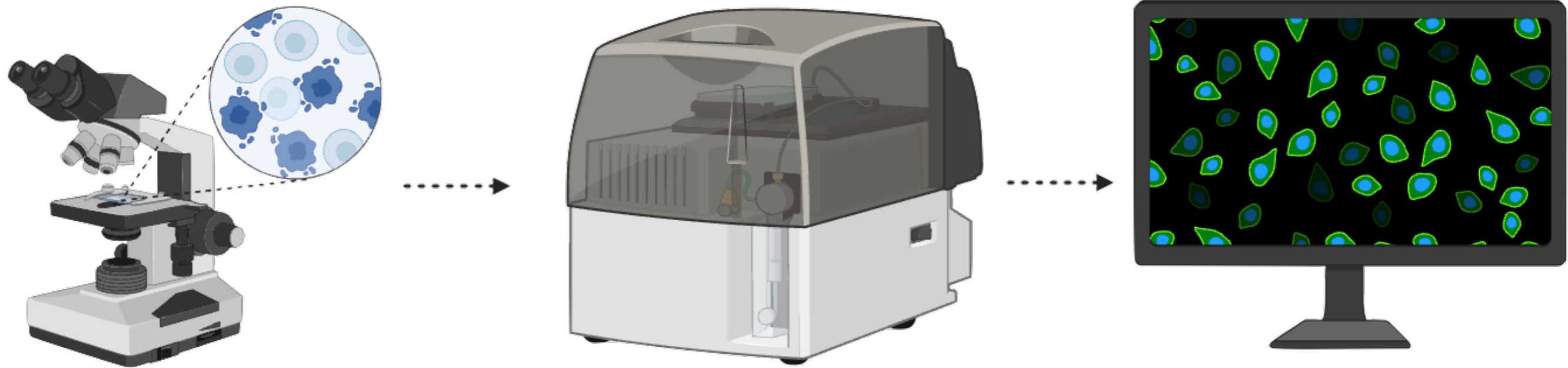
Zebrafish
breeding

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Chemical
screening

Aim 2: Find chemical compounds that reuse the phenotype using chemical screening



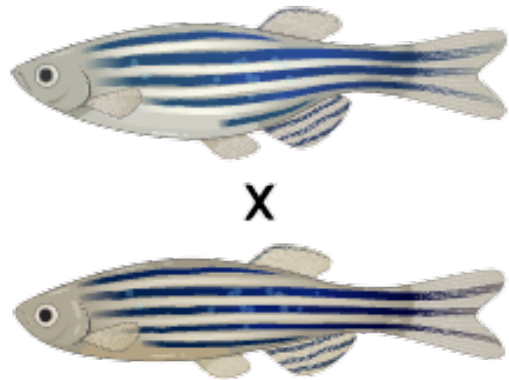
Zebrafish
breeding

Compound
selection

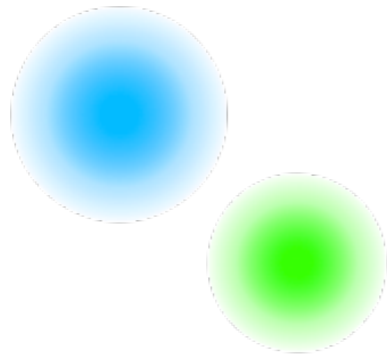
Staining &
assay

Chemical
screening

Conclusion

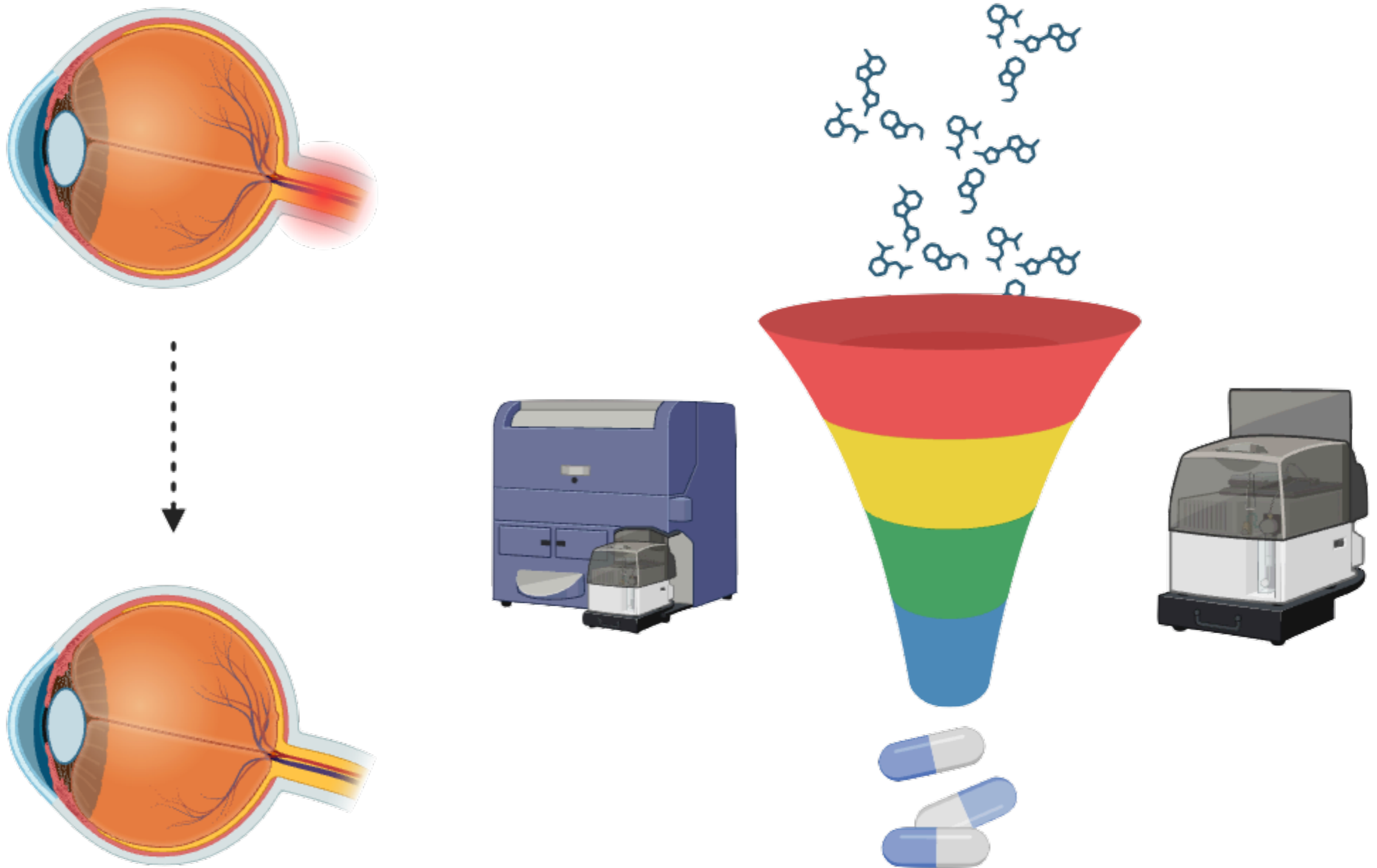


Mutations in OPA1 gene will lead to mitochondria dysfunction in zebrafish embryos



Few compounds were identified to treat the phenotype of optic atrophy type 1

Future Direction



References

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- [8] Zanna, C., Ghelli, A., Porcelli, A. M., et al. (2008). OPA1 mutations associated with dominant optic atrophy impair oxidative phosphorylation and mitochondrial fusion. *Brain : a journal of neurology*, 131(Pt 2), 352-367. <https://doi.org/10.1093/brain/awm335>

Image reference:

- [1] Biorender