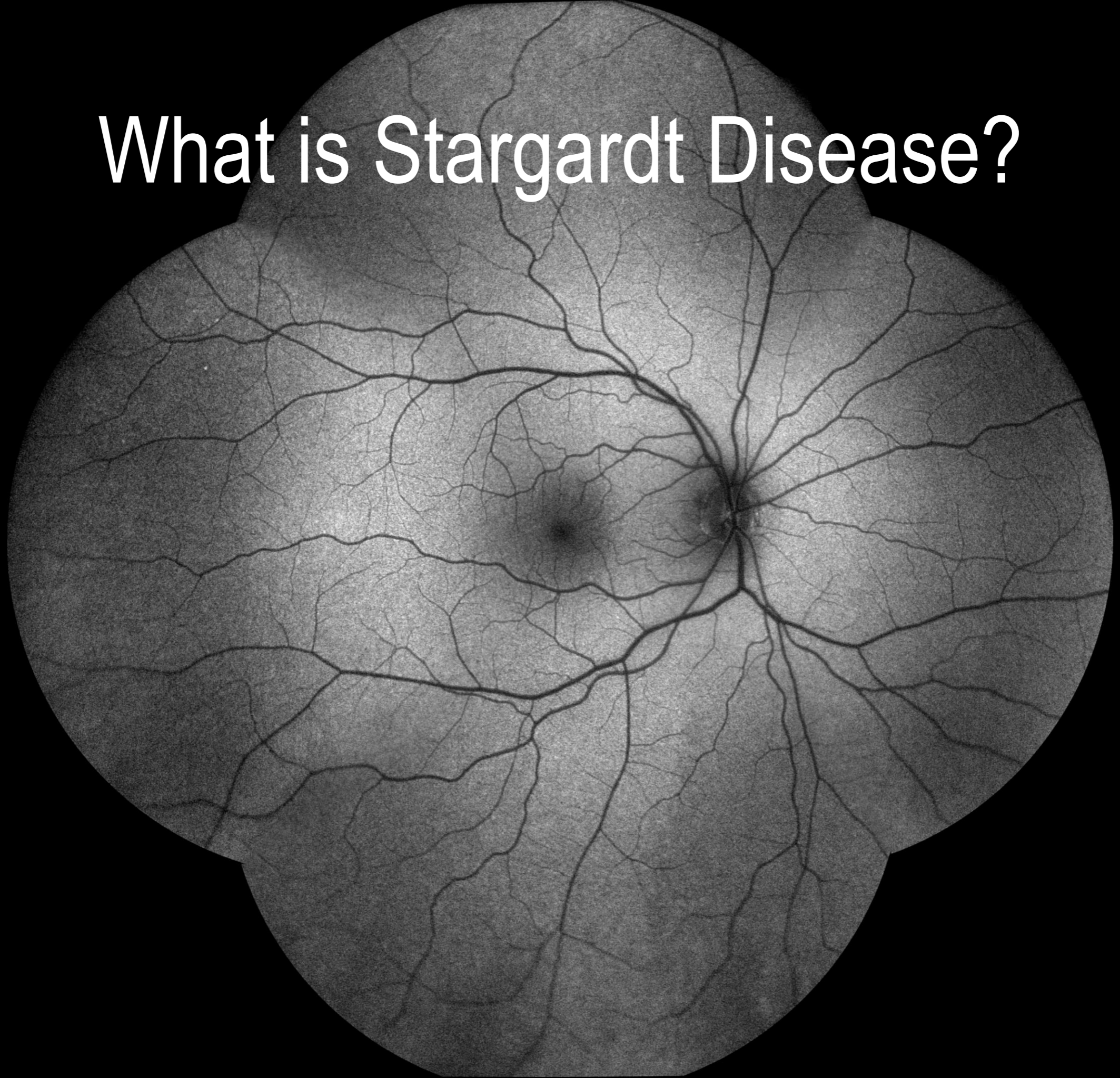




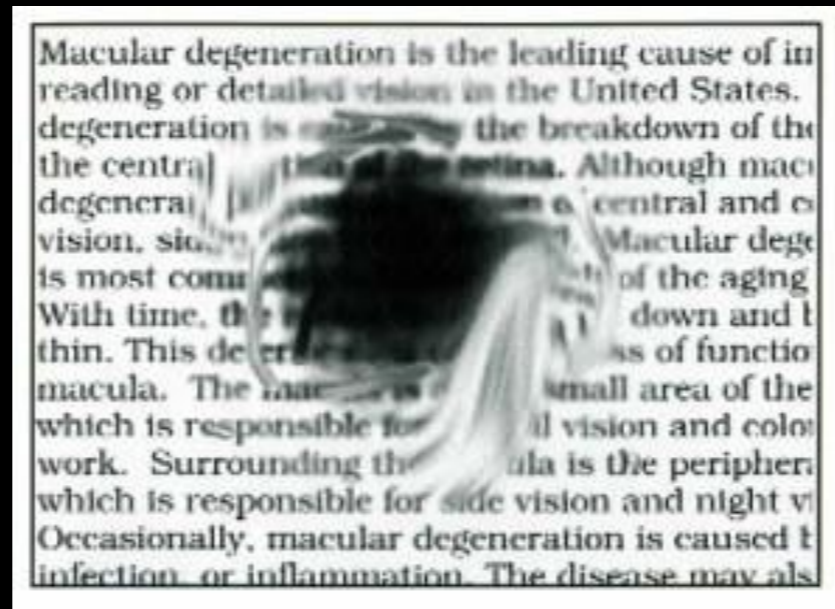
ABCA4 Responsible Stargardt Disease

Presented By: Timothy Biewer-Heisler

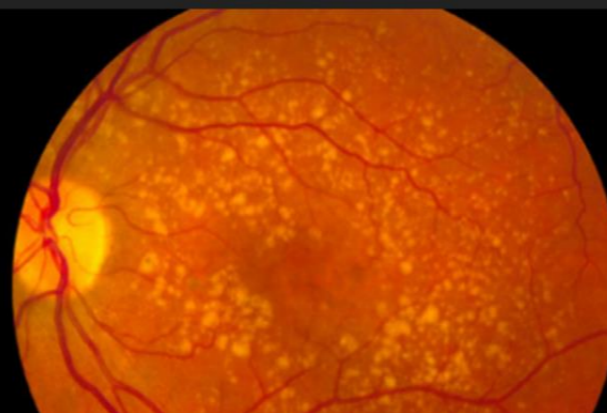
What is Stargardt Disease?



What are the Symptoms of Stargardt Disease?



Loss of central vision



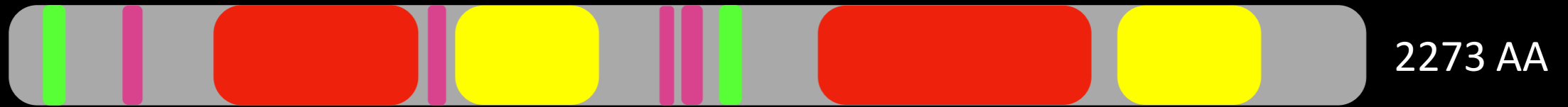
Yellow-white spots on retina



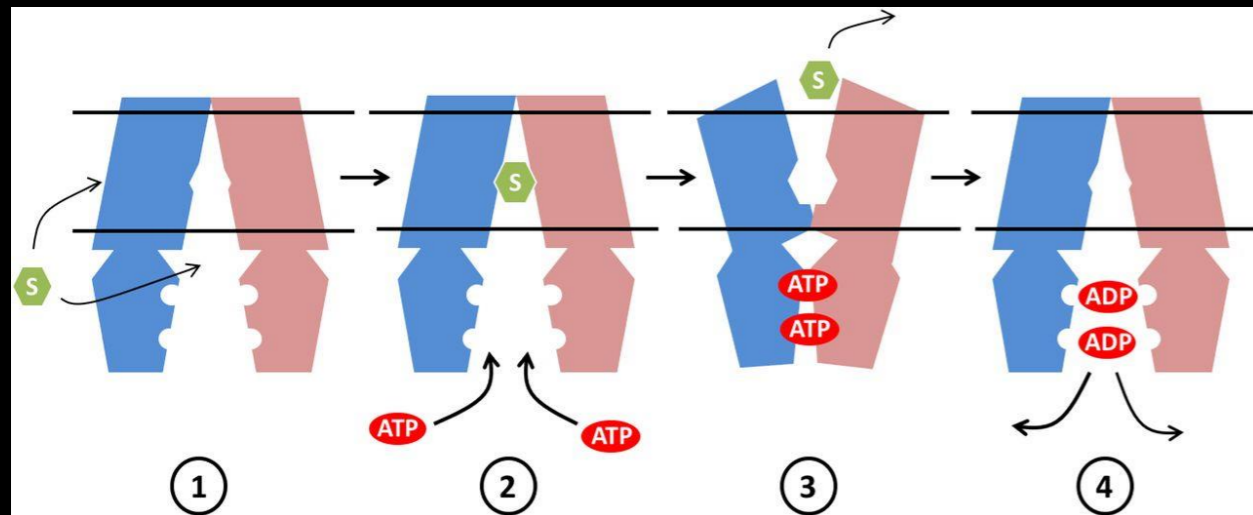
Colorblindness and eventual complete vision loss

How does the ABCA4 protein operate?

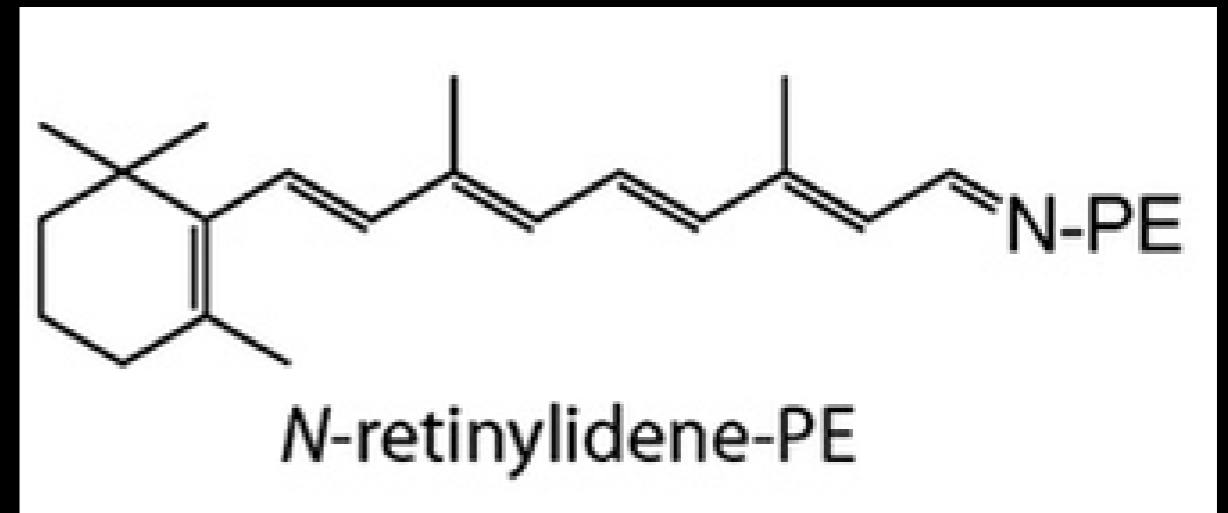
Human



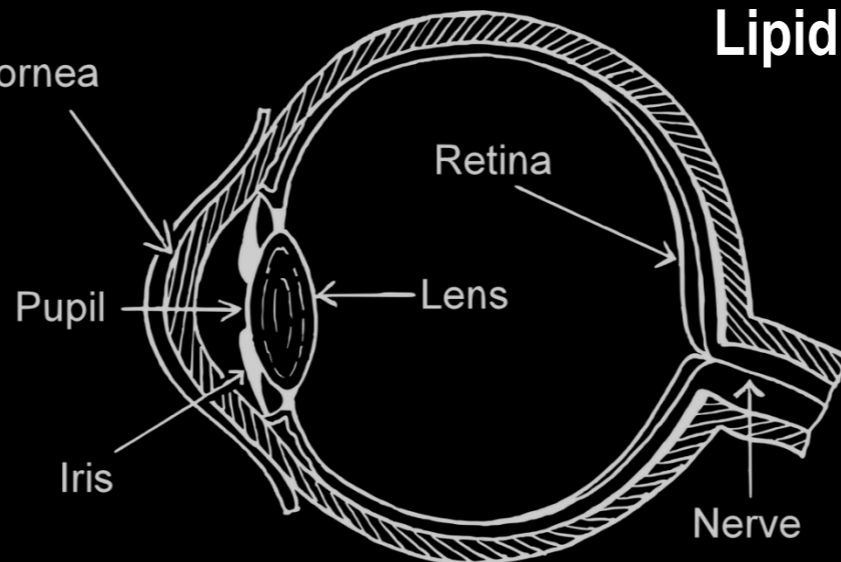
ABC2 Membrane 3: █ Unknown region: █ Transmembrane region: █ AAA ATPase: █



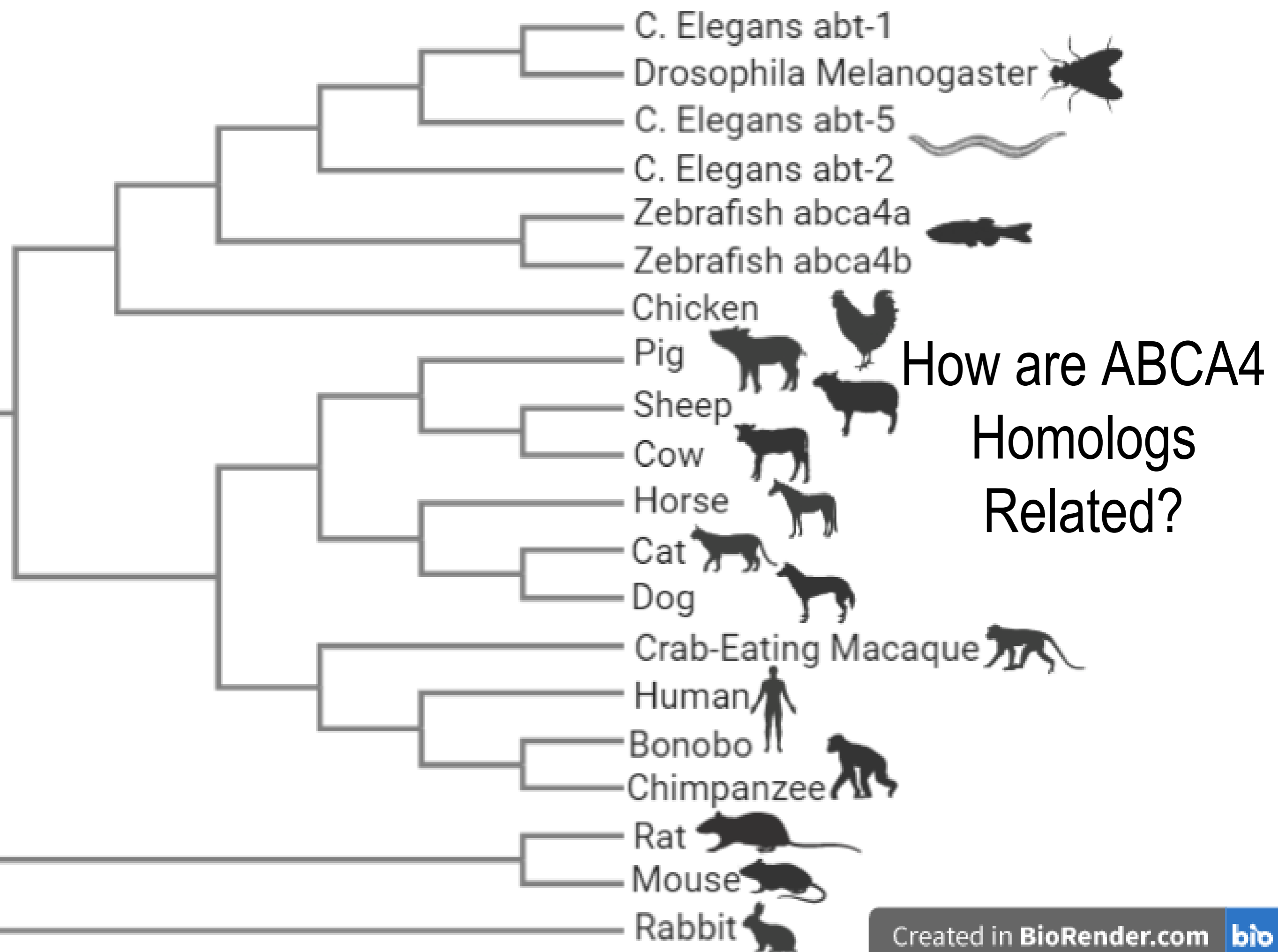
ATP-Binding Cassette
Molecular function



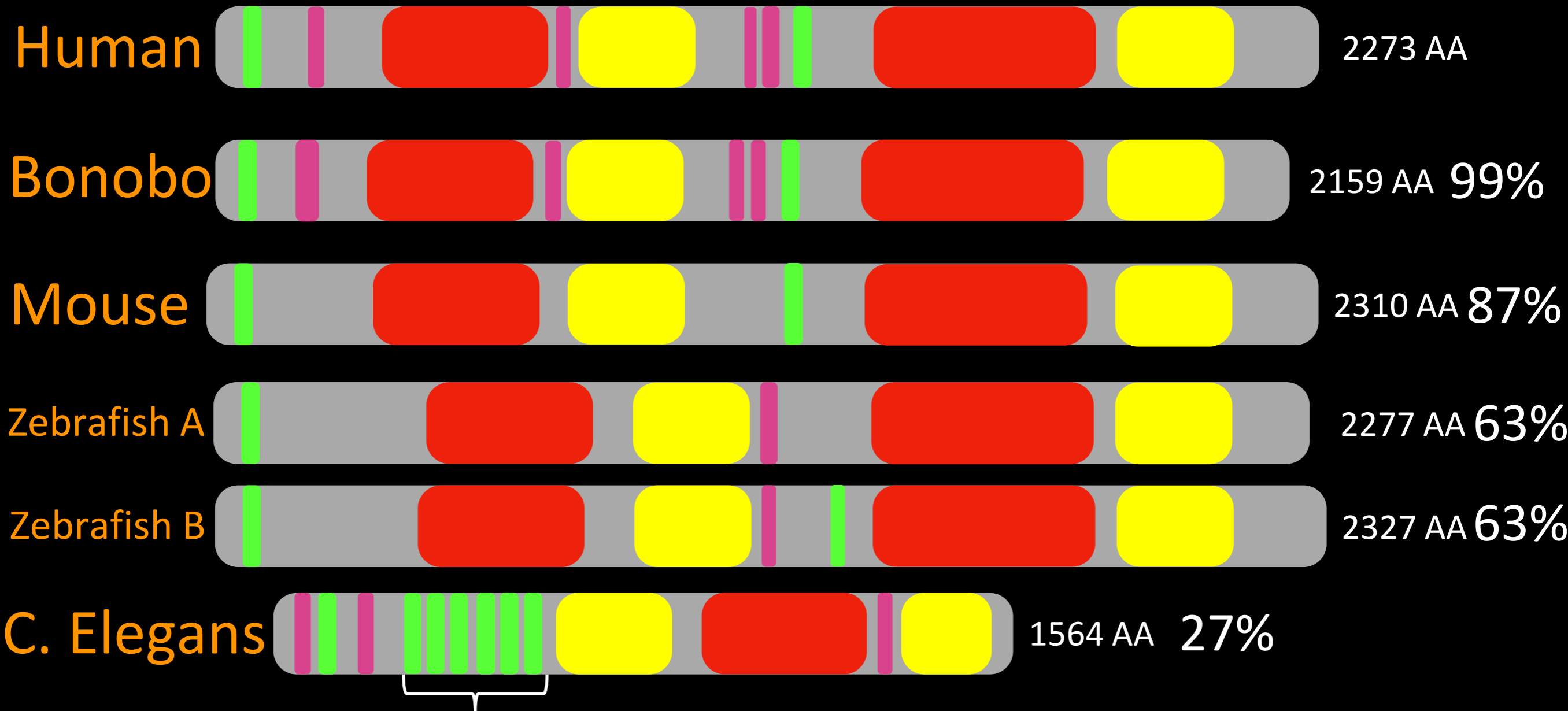
Lipid Transport on membrane
Cellular component



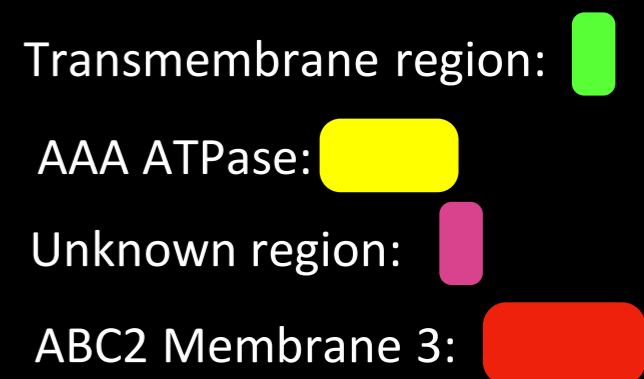
Visual Perception
Biological process



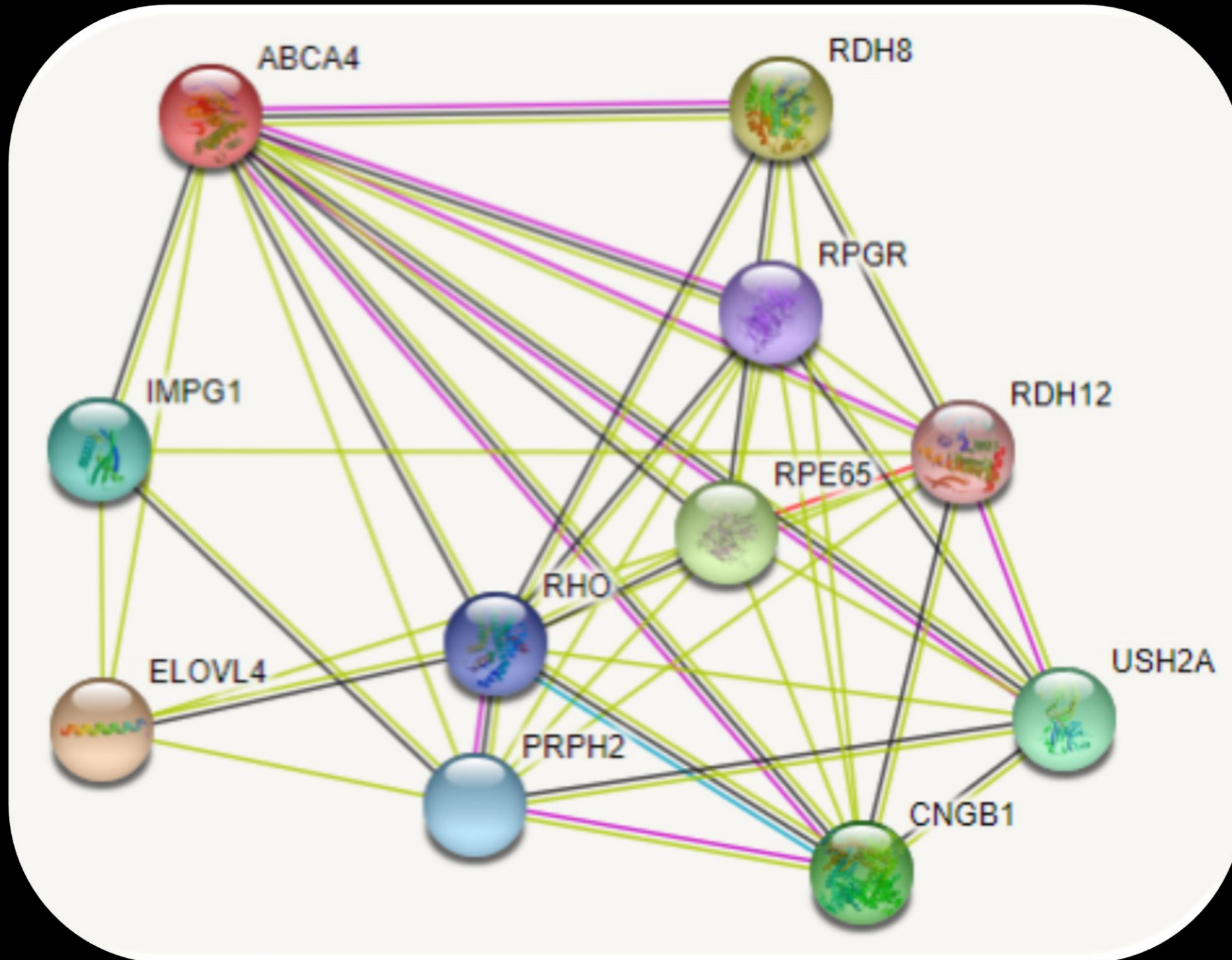
How well is ABCA4 conserved?



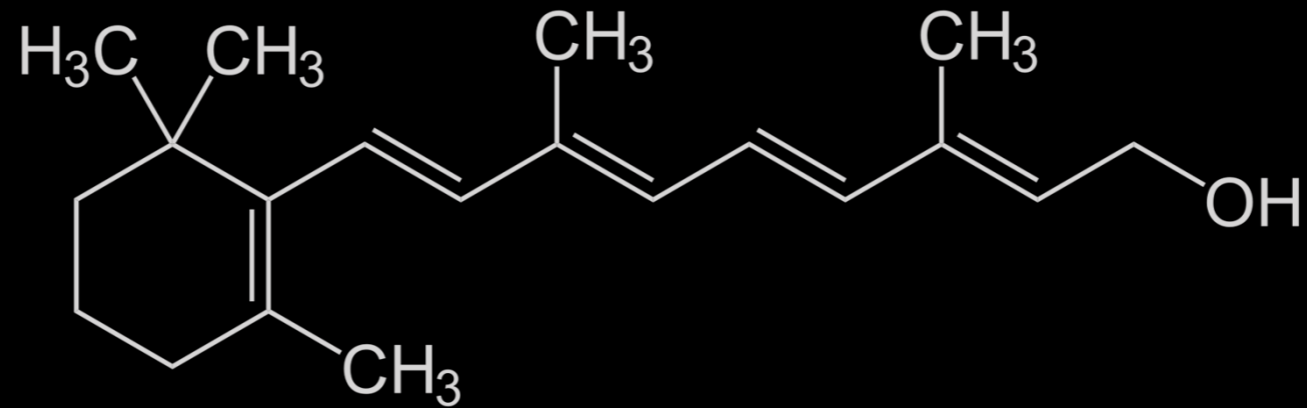
Similar to ABC2 Membrane 3



What protein interactions does ABCA4 perform?

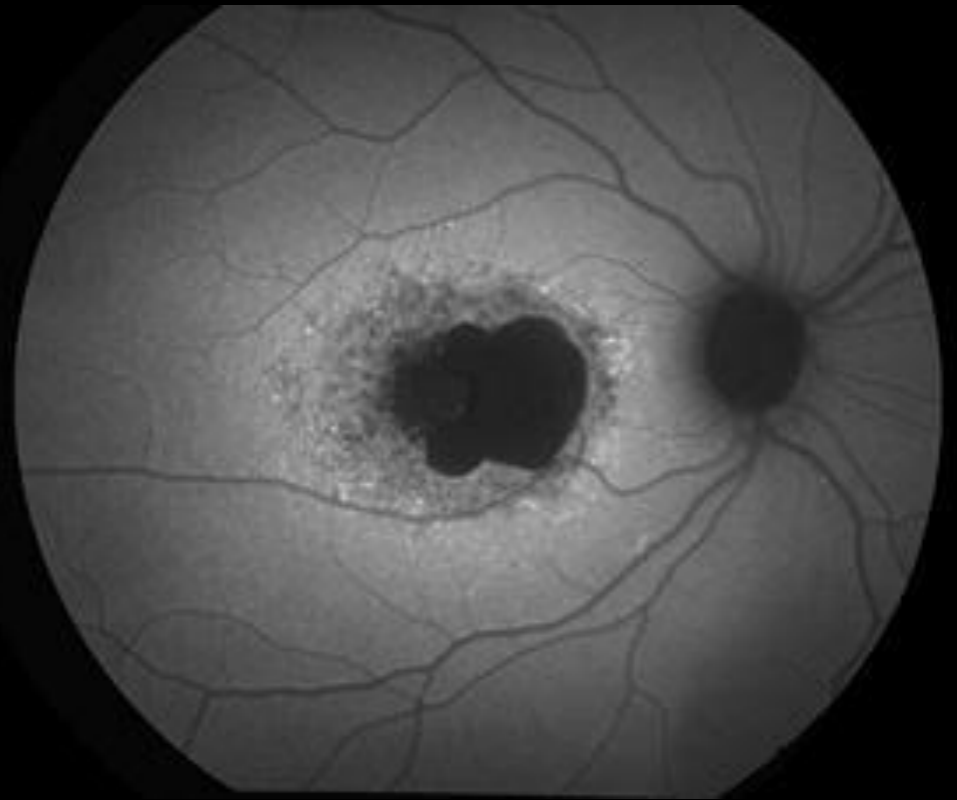
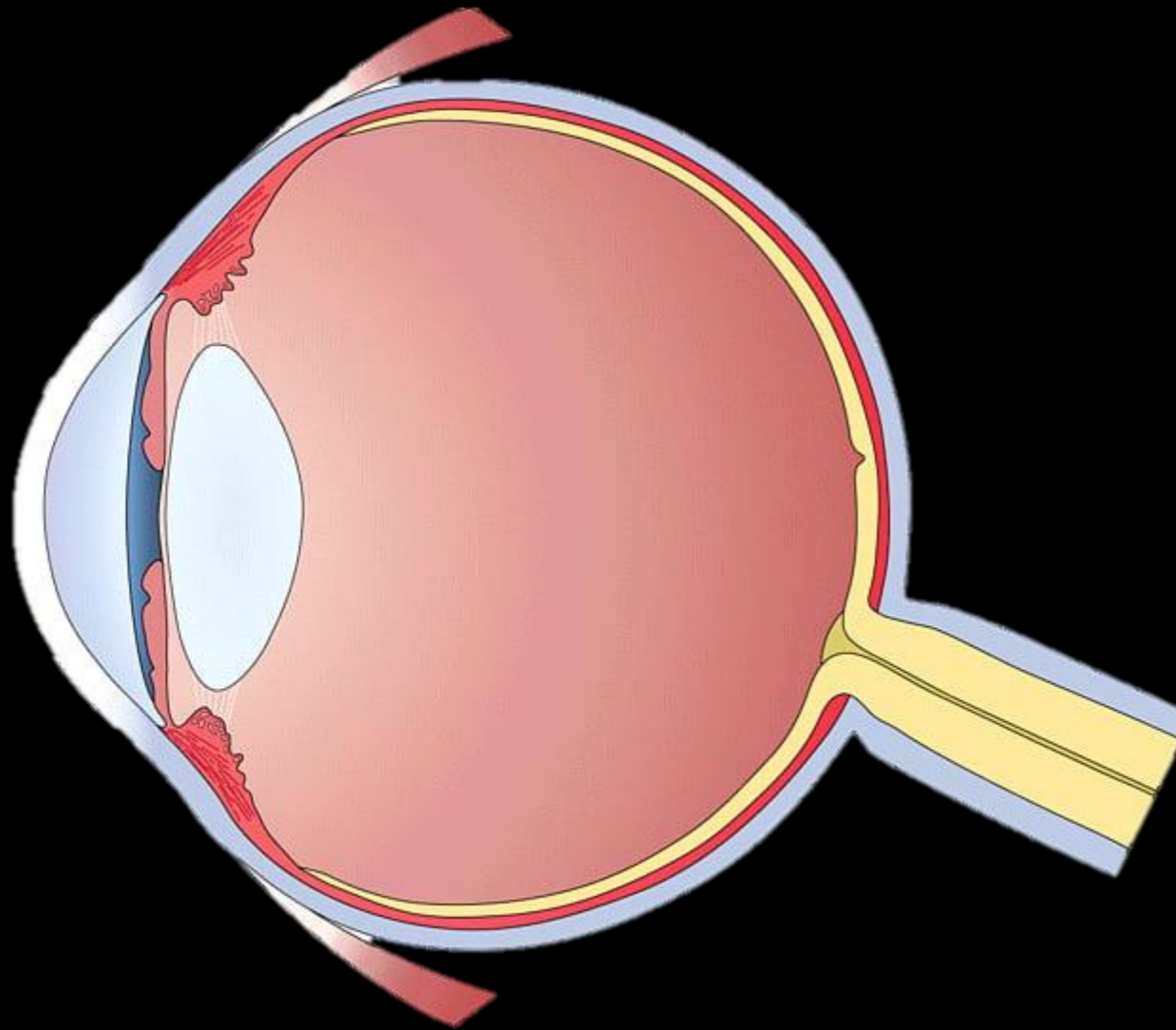


Gap in knowledge

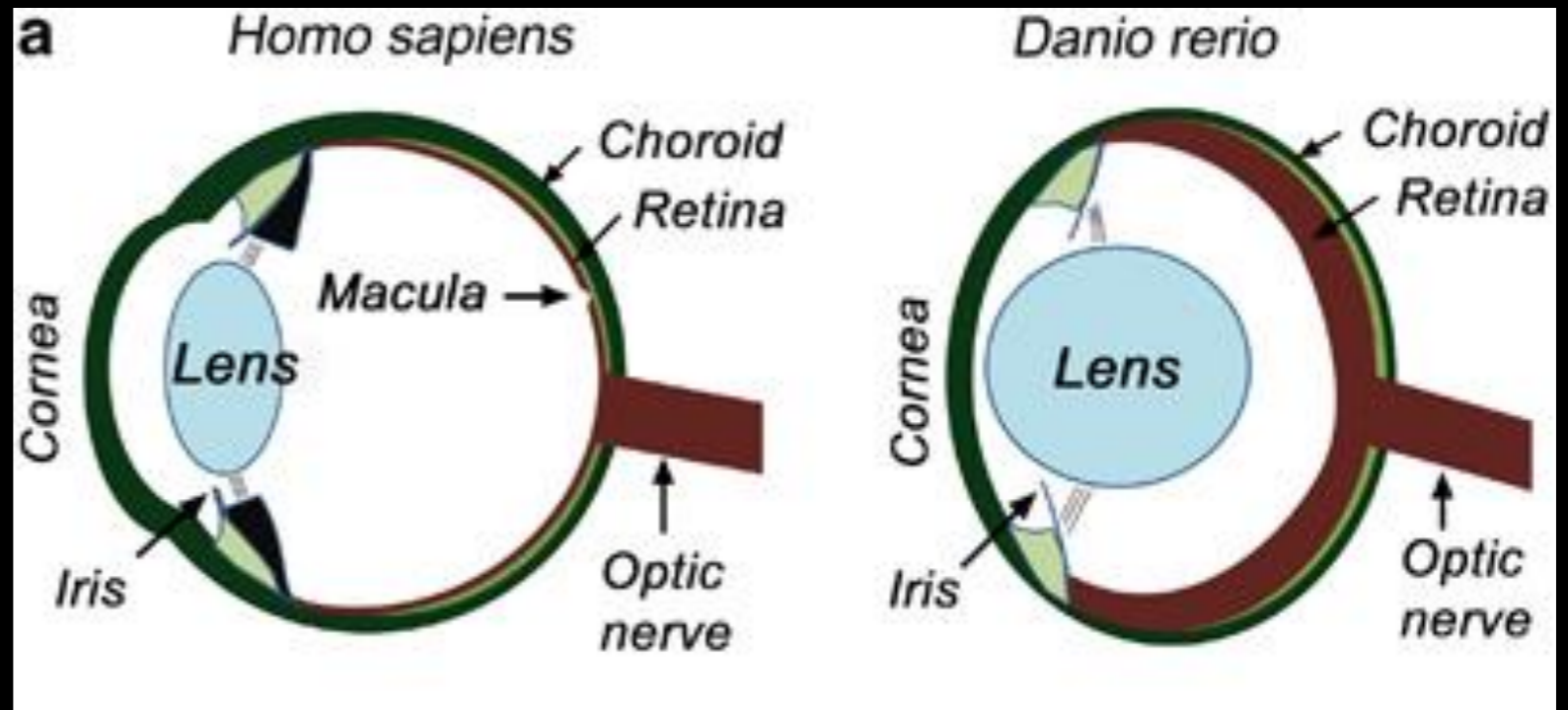
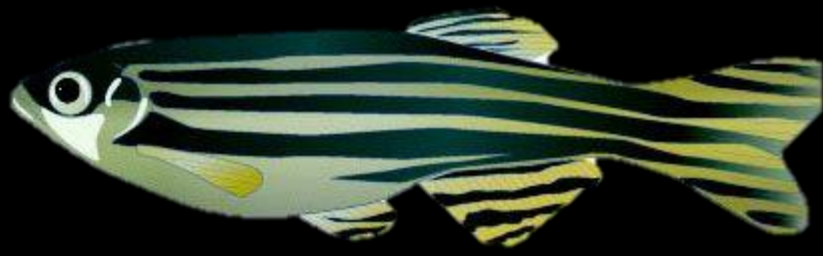


Lipofuscin buildup

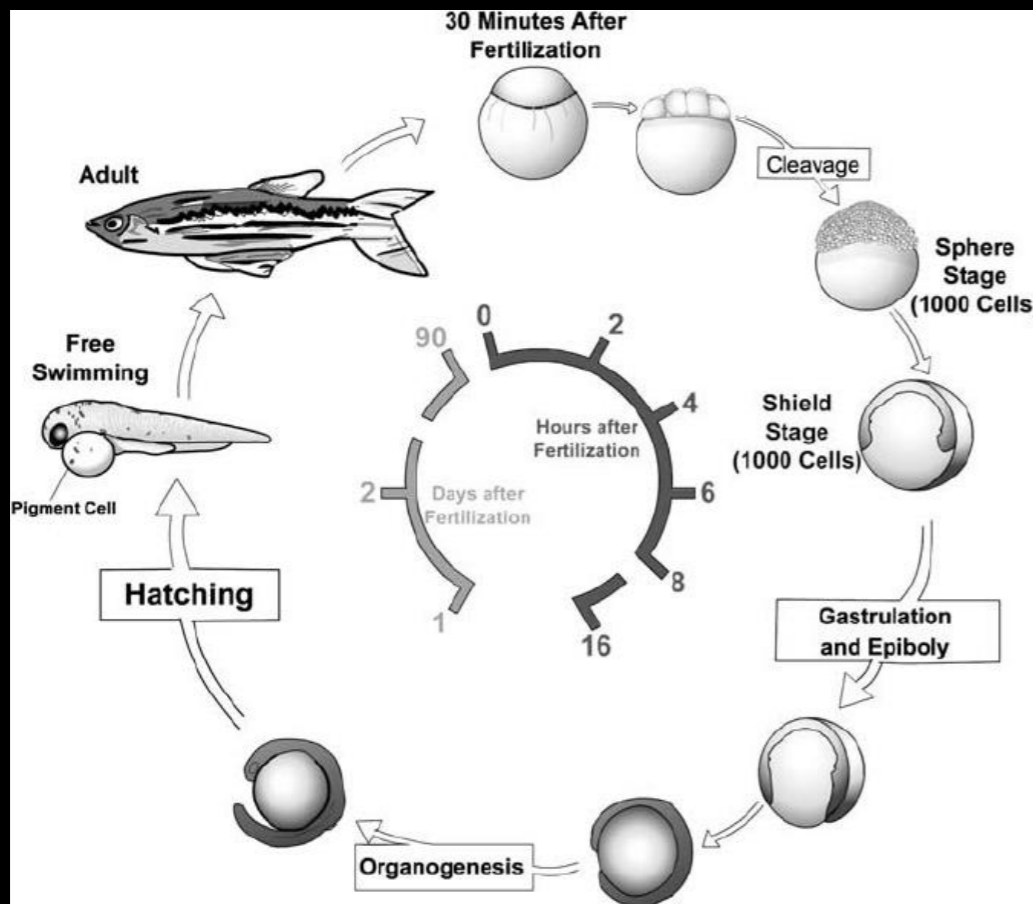
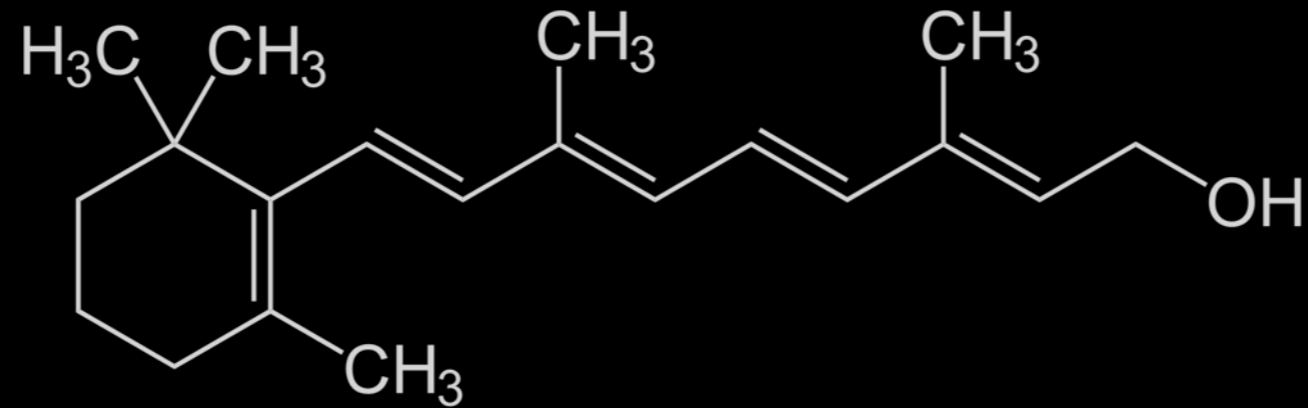
What model organism is best to study ABCA4 and Stargardt disease?



Why is Zebrafish a great model species for ABCA4?



Primary goal: Determine function of ABCA4 retinol regulation



Aim 1: Determine domains important for retinol metabolism throughout development

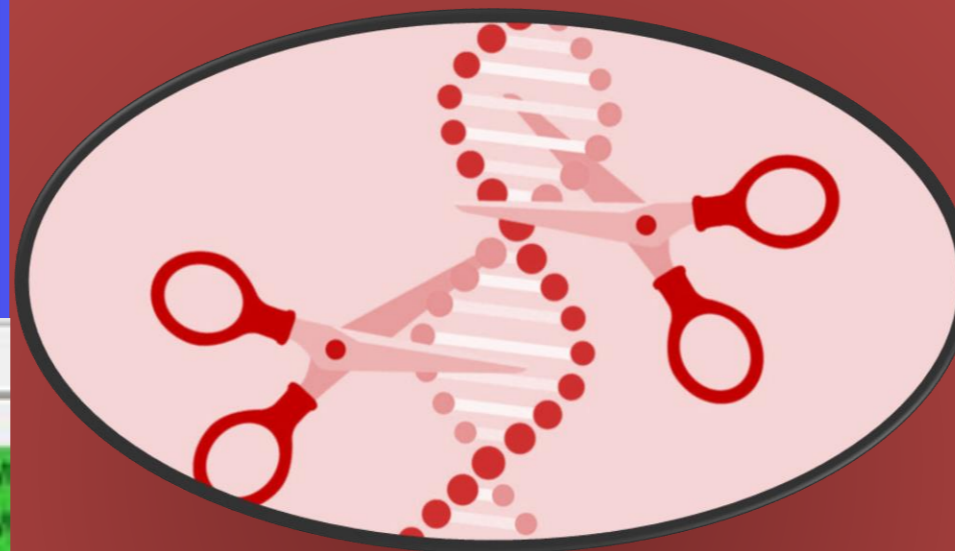
Align sequences



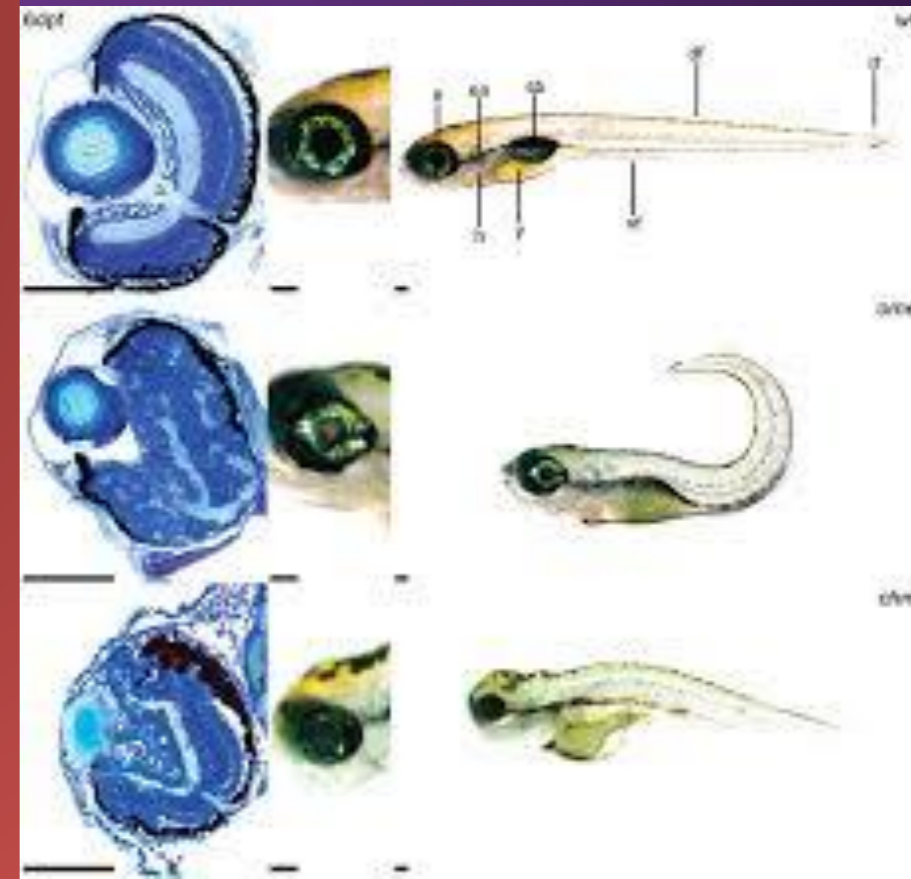
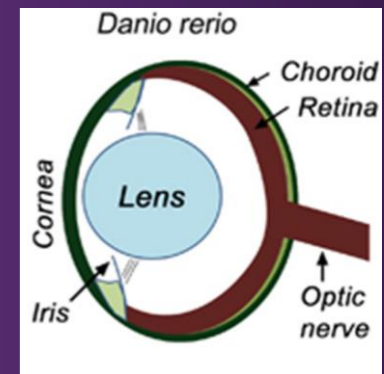
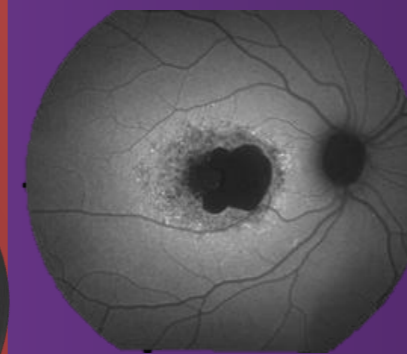
Protein Sequences

Species/Abbrv	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
1. ENSDARP00000018379	M	G	F	A	R	Q	I	K	L	L	L	W	K	N	V	
2. ENSRNOP00000017878	M	G	F	L	R	Q	I	Q	L	L	L	W	K	N	V	
3. ENSMFAP00000018204	M	G	F	V	R	Q	I	Q	L	L	L	W	K	N	V	
4. ENSPPAP00000024958	M	G	F	V	R	Q	I	Q	L	L	L	W	K	N	V	
5. ENSPTRP00000062840	M	G	F	V	R	Q	I	Q	L	L	L	W	K	N	V	
6. ENSDARP000000113256	M	S	T	G	R	Q	I	R	L	L	L	W	K	N	V	
7. ENSDARP000000123162	M	G	T	N	S	Q	V	R	L	L	L	W	K	N	V	
8. ENSGALP00000009224	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
9. ENSBTAP000000023982	M	G	F	A	R	Q	I	K	L	L	L	W	K	N	V	
10. ENSFCAP00000001439	M	G	F	V	R	Q	I	Q	L	L	L	W	K	N	V	
11. ENSECAP00000001236	M	G	F	A	R	Q	I	Q	L	L	L	W	K	N	V	
12. ENSCAFP00000000497	M	G	F	A	R	Q	I	Q	L	L	L	W	K	N	V	
13. ENSOCUP00000000845	M	G	F	A	R	Q	I	Q	L	L	L	W	K	N	V	
14. ENSSSCP00000000734	M	G	F	A	R	Q	I	R	L	L	L	W	K	N	V	
15. ENSMUSP00000001399	M	G	F	L	R	Q	I	Q	L	L	L	W	K	N	V	
16. ENSP0000000359245	M	G	F	V	R	Q	I	Q	L	L	L	W	K	N	V	

Develop mutants

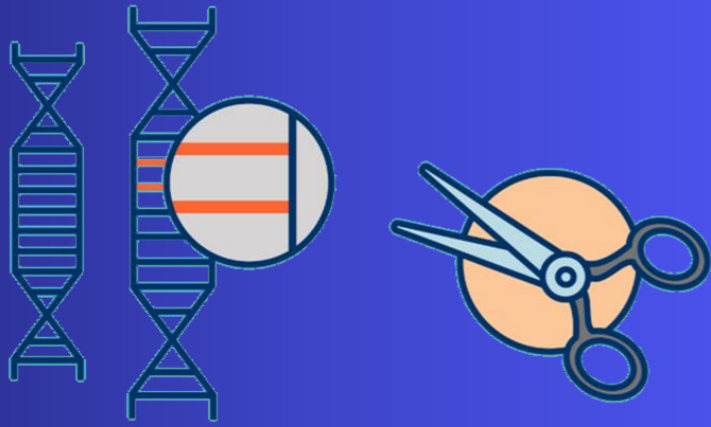


Screen phenotypes

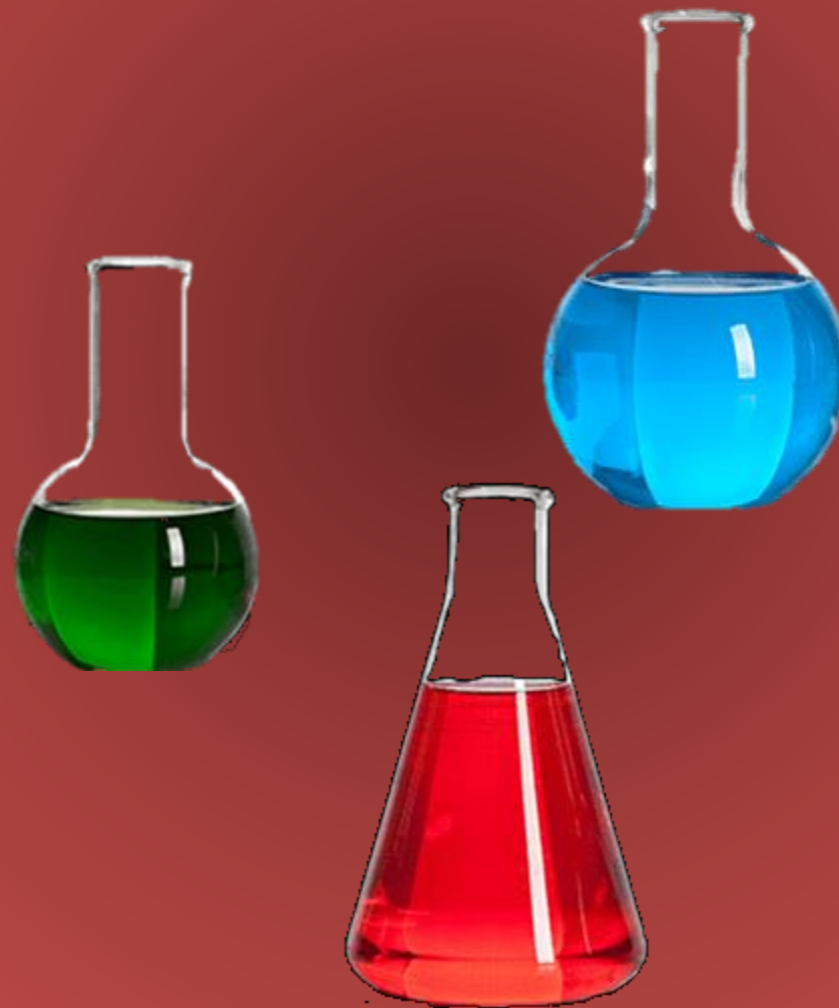


Aim 2: Determine modulation of retinol metabolism

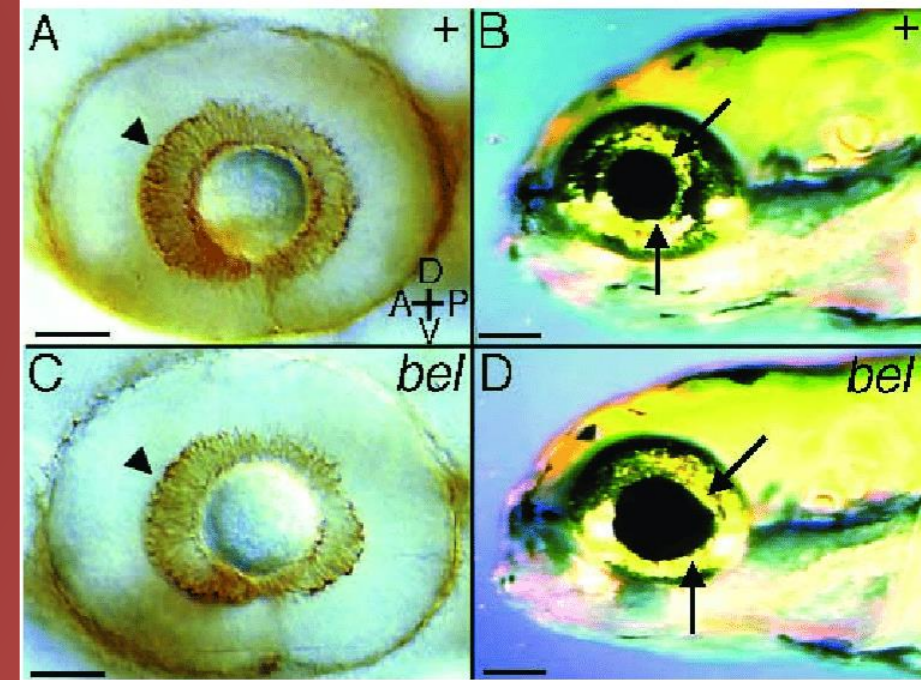
Develop mutant and WT ABCA4 populations



Perform chemical screen

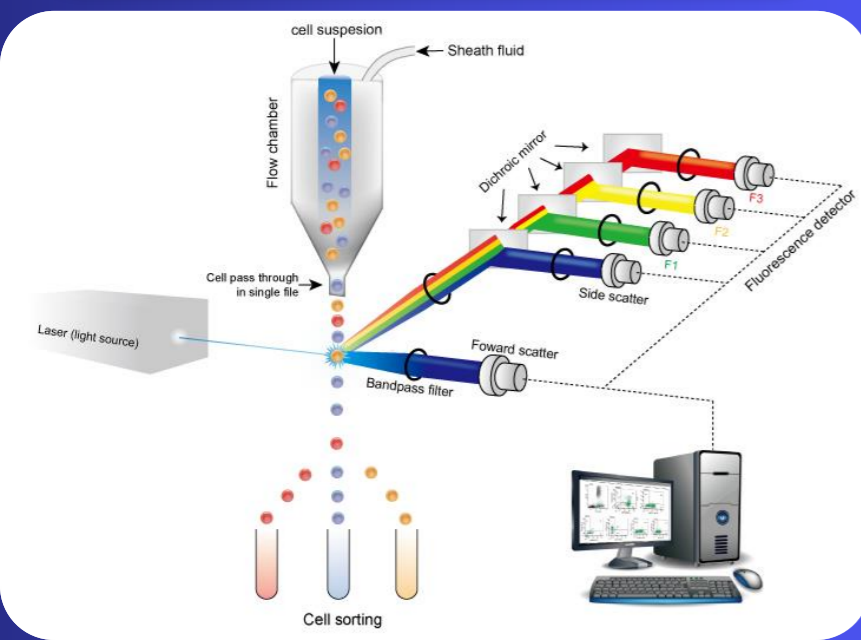
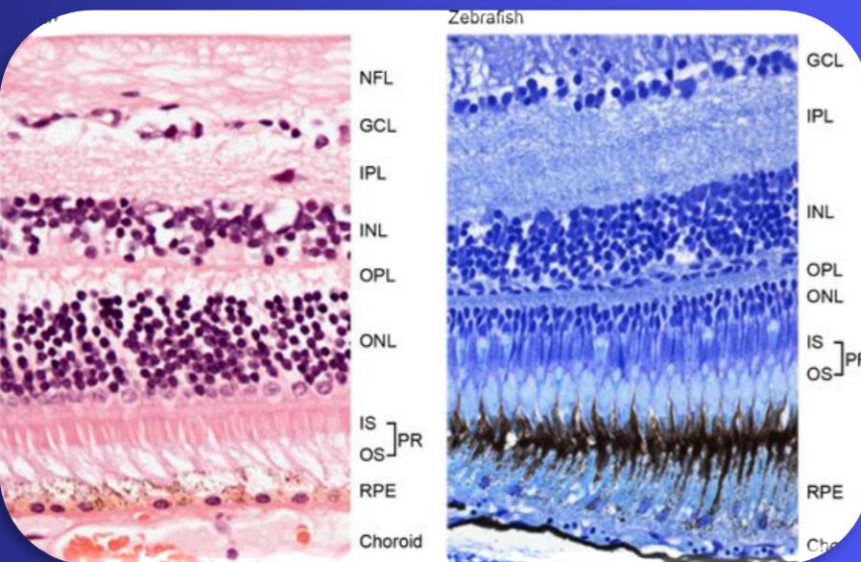


Analyze resulting phenotypes



Aim 3: Determine the expression of retinol metabolism genes through time

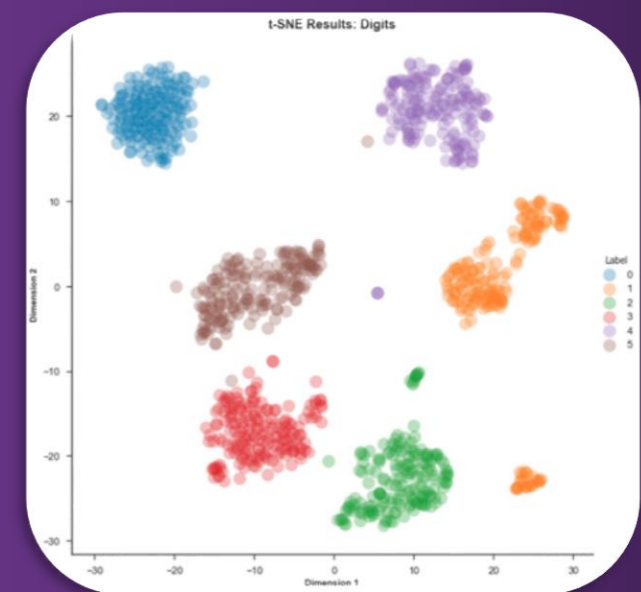
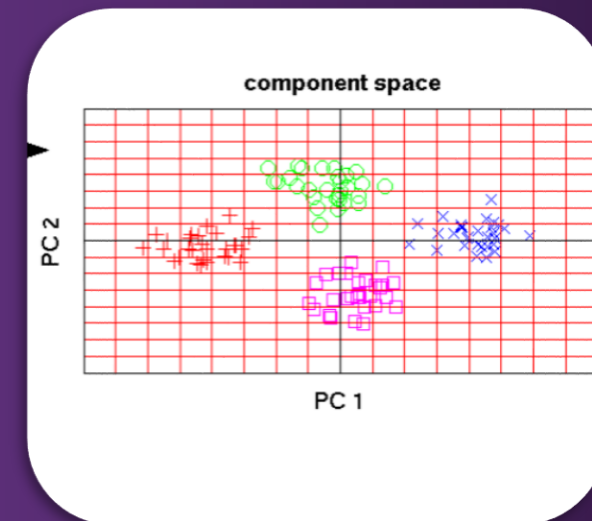
Isolate cells



Single-Cell RNA Sequencing



Dimensional reduction and analysis

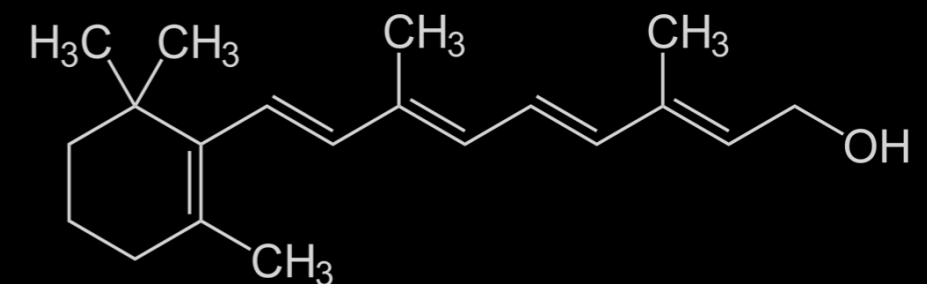


Conclusion

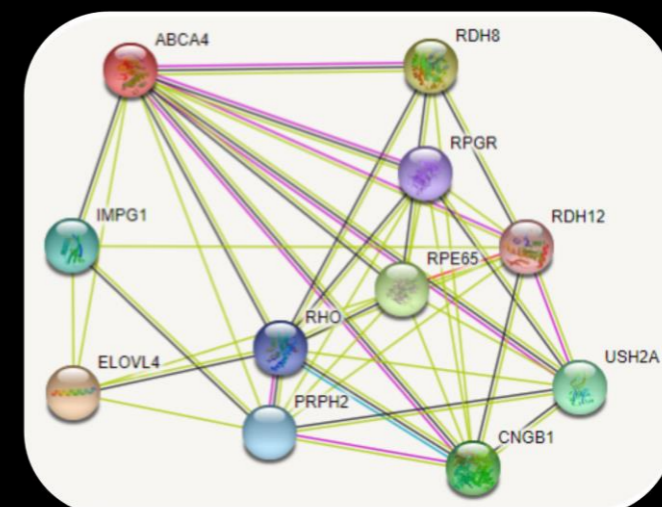
Alignment of sequences and determination of mutant Zebrafish phenotypes may assist with understanding of similar disease phenotypes in humans.

Protein Sequences	
Species/Abbrv	
1. ENSOARP00000018379	M G F A R Q I K L L L W K N V
2. ENSRNOF00000017878	M G F L R Q I Q L L L W K N V
3. ENSMFAP00000018204	M G F V R Q I Q L L L W K N V
4. ENSPPAP00000024958	M G F V R Q I Q L L L W K N V
5. ENSPTRP000000062840	M G F V R Q I Q L L L W K N V
6. ENSDARP000000113256	M S T G R Q I R L L L W K N V
7. ENSDIAR000000123162	M G T N S Q V R L L L W K N V
8. ENSGALP00000009224
9. ENSBTAP00000023982	M G F A R Q I K L L L W K N V
10. ENSFCAP0000001439	M G F V R Q I Q L L L W K N V
11. ENSECAP0000001236	M G F A R Q I Q L L L W K N V
12. ENSCAFP0000000497	M G F A R Q I Q L L L W K N V
13. ENSOCUP00000000845	M G F A R Q I Q L L L W K N V
14. ENSSSCP00000007345	M G F A R Q I R L L L W K N V
15. ENSMUSP0000001399	M G F L R Q I Q L L L W K N V
16. ENSP000000359245	M G F V R Q I Q L L L W K N V

Performing chemical screens on wildtype and mutant Zebrafish can elucidate chemical modulation of retinol metabolism.



Understanding RNA expression of single-cell types in the retina can further the understanding of ABCA4 expression and retinol metabolism



Future Directions



Questions?

Image References

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