



Do You See What Eye See?

Eye Evolution and Development

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Part I – Fly Eyes

Madison sat down with her pumpkin-spiced coffee and her laptop. She thought to herself, “Why did I do this to myself again? Seems like I would have learned by now not to wait until the day before a paper is due to start my research.” As she was downloading another pdf from the library database, her friend Aiden plopped down next to her.

“Hey, Madison. Whatcha’ working on?”

“I have a paper due in my Poli Sci class tomorrow. Something about syncratic politics in Pakistan.”

“Syncratic politics? What the heck is that?”

Madison laughed ironically, “As soon as I figure that out, I’ll let you know. What’s up with you?”

“That’s ok. You can keep the politics. My bio prof was talking about something really weird today. Since you’re a major, I thought maybe you could fill me in. She said something about hedgehogs and six packs in cavefish, and I got totally lost.”

Madison laughed, “*Hedgehog* and *Pax6*! Lucky for you, we just covered that in my developmental bio class. Those are two genes that interact during eye formation in cavefish, or rather the lack of eye formation in cavefish. *Pax6* is usually involved in eye formation, but an overexpression of *hedgehog* suppresses *Pax6* during development.”

“Hold up, Madison. You’re telling me that only two genes are involved in eye formation? ...or not formation? ... Whatever! You know what I mean! Eyes are really complex, like really complex—I mean look at those bug eyes and, like, our eyes. I mean, didn’t Darwin even say that eyes are too complex to have evolved?”

“Nope. Not at all, Aiden. That’s a common misconception. Darwin did say that evolution of the eye by natural selection did not seem likely, but people forget that he went on to suggest how it could have happened. Here, let me look it up...”

Madison Googled Darwin’s quote on her laptop and found what she was looking for. She turned the screen toward Aiden for him to read:

“To suppose that the eye, with all its inimitable contrivances for adjusting the focus to different distances, for admitting different amounts of light, and for the correction of spherical and chromatic aberration, could have been formed by natural selection, seems, I freely confess, absurd in the highest possible degree. When it was first said that the sun stood still and the world turned round, the common sense of mankind declared the doctrine false; but the old saying of *Vox populi, vox Dei*, as every philosopher knows, cannot be trusted in science. Yet reason tells me, that if numerous gradations from a perfect and complex eye to one very imperfect and simple, each grade being useful to its possessor, can be shown to exist; if further, the eye does vary ever

so slightly, and the variations be inherited, which is certainly the case; and if any variation or modification in the organ be ever useful to an animal under changing conditions of life, then the difficulty of believing that a perfect and complex eye could be formed by natural selection, though insuperable by our imagination, can hardly be considered real.”

—Charles Darwin, *Origin of Species*, Chapter 6

“Um...yeah... so what? Madison, this really doesn't help me at all.”

“I'll admit Darwin is a little wordy, Aiden. When people say that Darwin didn't think eyes could evolve, they usually think of only the first sentence of that paragraph, which sounds like he did think eyes were too complex. Most of the rest of the paragraph, however, talks about what he really thought. Basically, what he is saying is that if intermediate steps could be demonstrated, then even complex eyes could have evolved. He then went on to offer examples over several pages. Since then we have even started to figure out how all of those intermediate forms could develop.”

“Like what?”

“I'm sorry, Aiden. I really need to work on this paper. I'll be here tomorrow after my 11 o'clock if you want to talk some more.”

Questions

1. Darwin's comments about eyes are often used as evidence against evolution by natural selection, but only because his quotes are taken out of context. Darwin did not think that the possibility that eyes evolved through natural selection was actually “absurd in the highest degree.” What was the basis of his logical argument and what evidence do we have to support it?
2. We see an enormous diversity of eyes in Kingdom Animalia. Until recently it was postulated that eyes must have evolved at least 40 times independently. Explain how the discovery of *Pax6* (and its homologs such as *eyeless*) has overturned this idea in favor of genes for eye development being present in an ancestor to all bilateral organisms.

Part II – Homology and Development

Aiden found Madison with her requisite pumpkin-spiced coffee, a grande this time. It had been a long night of syncratic politics in Pakistan.

“So, how’d that paper go?”

“Yeah, don’t wanna talk about it. I’m still not sure if I know what syncratic politics is. I did, however, look up some more stuff on *Pax6* before you got here.”

“Before we start that again, I still don’t get what Darwin said. I looked up some of those intermediate eyes. Looks like clams and squid and stuff have the intermediate forms just in that one group.”

Madison smiled, “That’s right! Eyes in molluscs vary from simple light sensitive spots in some slugs all the way up to complex eyes in squid. Did you know the eyes in squid are really close to ours? We have the same parts, the only big difference is that the layers at the back of the eye are in different orders. And the colossal squid has eyes the size of a basketball!”

Aiden’s eyes got big, although not as large as those of a colossal squid. “I’ll bring DeAndre along if I ever run into one of those! He’d smack that eye right back where it came from.”

“Uh, is that a basketball reference? I have no clue what you’re talking about.” Madison continued, “Did you look into *Pax6*?”

“No, I couldn’t remember what that gene was called. I’m still not sure I believe you that one gene is involved in eye formation.”

“It’s not just the one gene, but *Pax6* is sort of a control gene that influences other genes that eventually cause the formation of the eye. In fact, it is so important that we see homologous forms in multiple animals all the way from flatworms to humans. *Pax6* helps activate other genes in the formation of eyes. Different varieties of the *Pax6* gene are involved in the compound eyes of fruit flies and the complex eyes in mammals. In fact, the genes are so similar that we can use the gene from a mouse and cause compound eyes to form in fruit flies.”

“Wait, wait, wait, Madison. Slow down! Homologous? Mouse genes in fruit flies? Are you off your rocker? You’re completely losing me.”

“Sorry, Aiden, I just got really excited. This is pretty cool stuff that is helping us understand how even complex structures like the eye could evolve through relatively simple mechanisms. Let me back up...”

Questions

1. How should Madison explain to Aiden the meaning of “homologous” in evolutionary theory? Textbooks typically introduce the term with anatomical structures, but the term is more broadly applicable. How might the term apply to DNA sequences?
2. If *Pax6* is so important, predict how similar homologous sequences would be in humans, mice, squid, fruit flies, and sharks. Would you expect the amino acid sequences in the proteins expressed from the *Pax6* genes to follow a similar pattern? Explain.

Part III – Activity: Matching Homologous *Pax6* Genes and Phylogeny

K Mouse *Pax6* gene:

GTATCCAACGGTTGTGTGAGTAAATCTGGGCAGGTATTACGAGACTGGCTCCATCAGA

Unknown species 1:

GTGTCCAACGGTTCTGTGAGTAAATCCTGGGCAGATACTATGAAACAGGATCCATCAGA

Unknown species 2:

GTATCAAATGGATGTGTGAGCAAAATCTCGGGAGGTATTATGAAACAGGAAGCATAACGA

Unknown species 3:

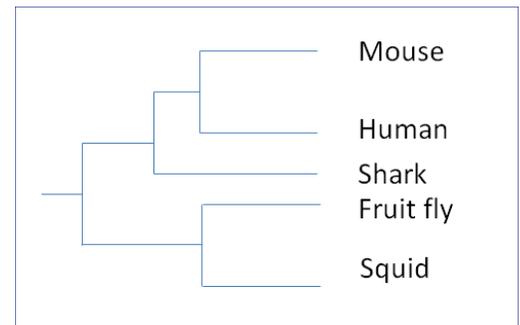
GTGTCCAACGGATGTGTGAGTAAATCTGGGCAGGTATTACGAGACTGGCTCCATCAGA

Unknown species 4:

GTCTCCAACGGCTGCGTTAGCAAGATTCTCGGACGGTACTATGAGACGGGCTCCATAAGA

Instructions

- Using the mouse *Pax6* gene as a baseline, determine the similarity of the homologous genes from the unknown species.
 - For each unknown species, determine the number of nucleotides that are different from the nucleotides found in the mouse sequence.
 - There are 60 nucleotides in each sequence. To determine the percent similarity, subtract the number of different nucleotides from 60, divide the result by 60, and multiply by 100.
- One of Darwin's main ideas was that evolution involves descent with modification from common ancestry. We know today that the modification can be simply divergence in gene sequences. The diagram to the right shows a phylogeny for the organisms represented in the sequences above. The degree of similarity in gene sequences is representative of how long ago two organisms have diverged from each other. In other words, organisms with a more recent common ancestor will have a greater similarity in gene sequences than organisms that have a much more ancient common ancestor. Make a hypothesis for which gene sequences listed above represent each branch of the phylogeny.



Questions

- Explain the pattern in nucleotide variation you observe in this exercise. Is there a relationship between divergence and *Pax6* sequences?
- There is variation in nucleotide sequences, but the amino acid sequences for the partial sequence presented in this case are identical between the five species. Explain why natural selection might have favored conservation of the amino acid sequence.
- If covered earlier in your course, how could different nucleotide sequences result in the same amino acid sequences?
- In the mouse/fly experiment that Madison referred to, the mouse *Pax6* gene is used in place of the fly *eyeless* gene (a copy of the homolog to *Pax6*; fruit flies have two homologs). The gene codes for a transcription factor, a protein that controls expression of other genes. Explain how a mammalian gene can successfully induce development of a compound eye in fruit flies.

