A clear, molecular view of how human color vision evolved

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Many genetic mutations in visual pigments, spread over millions of years, were required for humans to evolve from a primitive mammal with a dim, shadowy view of the world into a greater ape able to see all the colors in a rainbow.

Now, after more than two decades of painstaking research, scientists have finished a detailed and complete picture of the evolution of human color vision. *PLOS Genetics* is publishing the final pieces of this picture: The process for how humans switched from ultraviolet (UV) vision to violet vision, or the ability to see blue light.

"We have now traced all of the evolutionary pathways, going back 90 million years, that led to human color vision," says lead author Shozo Yokoyama, a biologist at Emory University. "We've clarified these molecular pathways at the chemical level, the genetic level and the functional level."

Co-authors of the *PLOS Genetics* paper include Emory biologists Jinyi Xing, Yang Liu and Davide Faggionato; Syracuse University biologist William Starmer; and Ahmet Altun, a chemist and former post-doc at Emory who is now at Fatih University in Istanbul, Turkey.

Yokoyama and various collaborators over the years have teased out secrets of the adaptive evolution of vision in humans and other vertebrates by studying ancestral molecules. The lengthy process involves first estimating and synthesizing ancestral proteins and pigments of a species, then conducting experiments on them. The technique combines microbiology with theoretical computation, biophysics, quantum chemistry and genetic engineering.

Five classes of opsin genes encode visual pigments for dim-light and color vision.

Bits and pieces of the opsin genes change and vision adapts as the environment of a species changes.

Around 90 million years ago, our primitive mammalian ancestors were nocturnal and had UV-sensitive and red-sensitive color, giving them a bi-chromatic view of the world. By around 30 million years ago, our ancestors had evolved four classes of opsin genes, giving them the ability to see the full-color spectrum of visible light, except for UV.

"Gorillas and chimpanzees have human color vision," Yokoyama says. "Or perhaps we should say that humans have gorilla and chimpanzee vision."

For the *PLOS Genetics* paper, the researchers focused on the seven genetic mutations involved in losing UV vision and achieving the current function of a blue-sensitive pigment. They traced this progression from 90-to-30 million years ago.

The researchers identified 5,040 possible pathways for the amino acid changes required to bring about the genetic changes. "We did experiments for every one of these 5,040 possibilities," Yokoyama says. "We found that of the seven genetic changes required, each of them individually has no effect. It is only when several of the changes combine in a particular order that the evolutionary pathway can be completed."

In other words, just as an animal's external environment drives natural selection, so do changes in the animal's molecular environment.

In previous research, Yokoyama showed how the scabbardfish, which today spends much of its life at depths of 25 to 100 meters, needed just one genetic mutation to switch from UV to blue-light vision. Human ancestors, however, needed seven changes and these changes were spread over millions of years. "The evolution for our ancestors' vision was very slow, compared to this fish, probably because their environment changed much more slowly," Yokoyama says.

About 80 percent of the 5,040 pathways the researchers traced stopped in the middle, because a protein became non-functional. Chemist Ahmet Altun solved the mystery of why the protein got knocked out. It needs water to function, and if one mutation occurs before the other, it blocks the two water channels extending through the vision pigment's membrane.

"The remaining 20 percent of the pathways remained possible pathways, but our ancestors used only one," Yokoyama says. "We identified that path."

In 1990, Yokoyama identified the three specific amino acid changes that led to human ancestors developing a green-sensitive pigment. In 2008, he led an effort to construct the most extensive evolutionary tree for dim-light vision, including animals from eels to humans. At key branches of the tree, Yokoyama's lab engineered ancestral gene functions, in order to connect changes in the living environment to the molecular changes.

The *PLOS Genetics* paper completes the project for the evolution of human color vision. "We have no more ambiguities, down to the level of the expression of amino acids, for the mechanisms involved in this evolutionary pathway," Yokoyama says.

Provided by Emory University