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Fish help unlock mystery of our skin color

One gene may play big role in making some fish golden, some people white

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Zebrafish zipping around an aquarium have led researchers to a gene that may play an important role in human skin color, an attribute that has served as a basis for social discrimination through the ages.

Researchers searching for cancer genes in zebrafish noticed that pigment cells in a peculiar golden variety of zebrafish look like pigment cells from light-skinned humans. This human-fish similarity motivated the researchers to track down the zebrafish gene responsible for the golden hue and lighter-than-usual stripes.

Then the scientists identified the human version of the gene, which has two main types — a version shared by Africans and East Asians, and a slightly different variant carried by nearly all Europeans. The researchers went on to show that this gene is partly responsible for light human skin in Europeans. This study appears in Friday's issue of the journal Science, published by AAAS, the nonprofit science society.

Most of the color in human skin comes from the pigment melanin, which protects against ultraviolet rays from the sun. Melanin is packaged in special cellular containers called melanosomes. Differences in the number, size and nature of these tiny pigment-filled packages are responsible for the many shades of human skin color. Scientists have long wondered about the genetic factors underlying this vast color palette.

Zebrafish out of water

Zebrafish stripes provided a surprising opportunity to learn about the nature of human skin color, said one of the Science authors, Keith Cheng of the Pennsylvania State University College of Medicine in Hershey, Pa.

In both golden-toned zebrafish and lighter-skinned humans, the melanosomes are less abundant, less dense and smaller than the pigment-holding compartments of dark-striped zebrafish and darker-skinned humans.

With these similarities in mind, Cheng and his colleagues applied a variety of genetic tools to identify the zebrafish gene, or genes, responsible for the golden color. They pinpointed a gene called SLC24A5.

There is a human version of this gene as well — apparently thanks to some ancient creature that both zebrafish and humans claim as an ancestor. The human and fish versions of the gene share nearly 70 percent of the same protein sequence.

When the researchers injected the human gene's protein-making instructions into golden zebrafish embryos, the pigment cells from these golden embryos returned to normal pigment levels. This finding strengthens the idea that the SLC24A5 gene may work in a similar way in humans and zebrafish. This gene is thought to play an important role in the formation of pigment-holding melanosomes.

Diving into the human factor
Next, the researchers checked to see what was already known about the human version of the SLC24A5 gene. Nearly all the people sampled from African and East Asian populations carry a version of the gene that is thought to be the "original" or "ancestral" version, the scientists found. In contrast, nearly all people with European ancestry have a slightly different variation of the gene — one that has the amino acid threonine where the African and East Asian version has the amino acid alanine.

This information came from an online database of human genetic variation and diversity called the "HapMap."

The researchers then looked at two different human populations in which people with European and African ancestors had mixed relatively recently — African-Americans and African-Caribbeans. They found that, on average, people with two copies of the European version of the gene had the lightest skin. People with two copies of the non-European version of the gene had darker skin, and people with one copy of each version of the gene had skin color somewhere in between.

In addition to skin color, the European version of the SLC24A5 gene may also be necessary for light hair color and light eye colors, such as blues and greens, the researchers suggest.

Origins of light skin?
Why so many Europeans have one particular version of this gene is not yet clear. It is possible that the SLC24A5 version now seen in nearly all Europeans may have been useful for some specific reason and swept through a human population that gave rise to Europeans.

This new research does not conclusively explain why light skin might have been favored among Europeans, but the work is consistent with the longstanding but unproven hypothesis suggesting that light skin allows more absorption of the ultraviolet rays in sunshine that are necessary for making the essential vitamin D. Such a trait could have been favored at European latitudes.

The SLC24A5 gene, however, cannot explain all the differences in skin color in humanity. For example, Asians and Africans have the same version of the gene but quite different skin tones. More research will likely uncover other pieces of the genetic puzzle of human skin color.

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