East Asian genes may solve the skin cancer puzzle

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Skin colour doesn't just affect your tanning ability. Credit: PA

Europeans fall prey to skin cancer because of their lighter skin, while Africans' dark skin protects them. But East Asians, whose skin colour resembles that of Europeans, are similar to Africans in their low susceptibility to melanoma – the deadliest skin cancer. No one yet knows why, but our research might hold the answer and perhaps help find treatment for the cancer.

In 2005, Keith Cheng at Pennsylvania State University stumbled upon the genetic mutation responsible for light skin colour in Europeans. This was an accidental discovery made using a zebrafish mutant known as "golden". Zebrafish is an ideal model organism because it has considerable genetic similarities to humans, enabling testing that would

otherwise be impossible.

Cheng was initially looking for a gene that was causing a peculiar instability in the fish. The process of finding genes that have a particular function is called genome editing. It involves selectively knocking out genes from a species (which is done while it is still at the egg-stage) and then observing what difference it makes as the species is born and grows up. Repeating the process enough times narrows down the genes acting in the function of interest.

Their last knock out test was on the gene SLC24A5, which led to change in zebrafish's skin colour. This gene is found in humans, too, and it must have the same role. When Cheng compared the international human genome databases, such as HapMap and 1,000 Genomes, he spotted that SLC24A5 was found in all those with European ancestry.

While the discovery that a gene controls skin colour was huge, applications were not immediately apparent. That is until Cheng came across reports from the Surveillance, Epidemiology and End Results (SEER) program. The data indicated that people with European ancestry are approximately 20 times more susceptible to melanoma than those of African or East Asian descent.

Cheng reasoned the genes responsible for skin colour could also play a role in determining melanoma susceptibility. To investigate this, with Cheng leading the research, we collected more than 500 DNA samples from the Orang Asli, an indigenous Malaysian tribe. Our analysis helped narrow down the number of genes that determine skin colour in East Asians. But here we hit a roadblock: using just one population left us with more possibilities than we can test experimentally. In order to reduce the number of candidate genes to a manageable size, we needed to find another population with a similarly preserved, ancient gene pool.

This is trickier than it might seem. Globalisation means there are less isolated, indigenous populations with a similar genetic ancestry to the Orang Asli. There is one such population that still exists on the Caribbean island that Christopher Columbus spotted over 500 years ago and locals have now dubbed it "Nature Island". The island is the Commonwealth of Dominica, home to the indigenous Kalinago people, and it remains undeveloped.

Kalinago people have lived in reserve territory, which means we know very little about them. We don't share a foundation of friendship or culture with them. Our team visited the Kalinago territory twice this year in order to begin building relationships, hoping to familiarise them with us and our project. Our goal is to collect 500 samples from them voluntarily that will allow meaningful data comparison with the Malaysian tribe and help narrow down our list of candidate genes considerably.

With our narrower list of candidate genes, we can begin testing their function using zebrafish mutants, as Cheng did in the 2005 research. Finding the genes responsible for East Asian's skin colour will kick off a new phase in melanoma research. We can compare the mechanisms and pathways of pigmentation in East Asians and Europeans, which can help find how melanoma occurs and drive the development of new treatments like gene therapy.

Treating cancer via gene therapy has already proven successful. The most recent examples are the treatment of chronic lymphocytic leukemia and multiple myeloma. Is gene therapy an option for melanoma patients? Perhaps, but most importantly, we are getting closer to finding out.

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