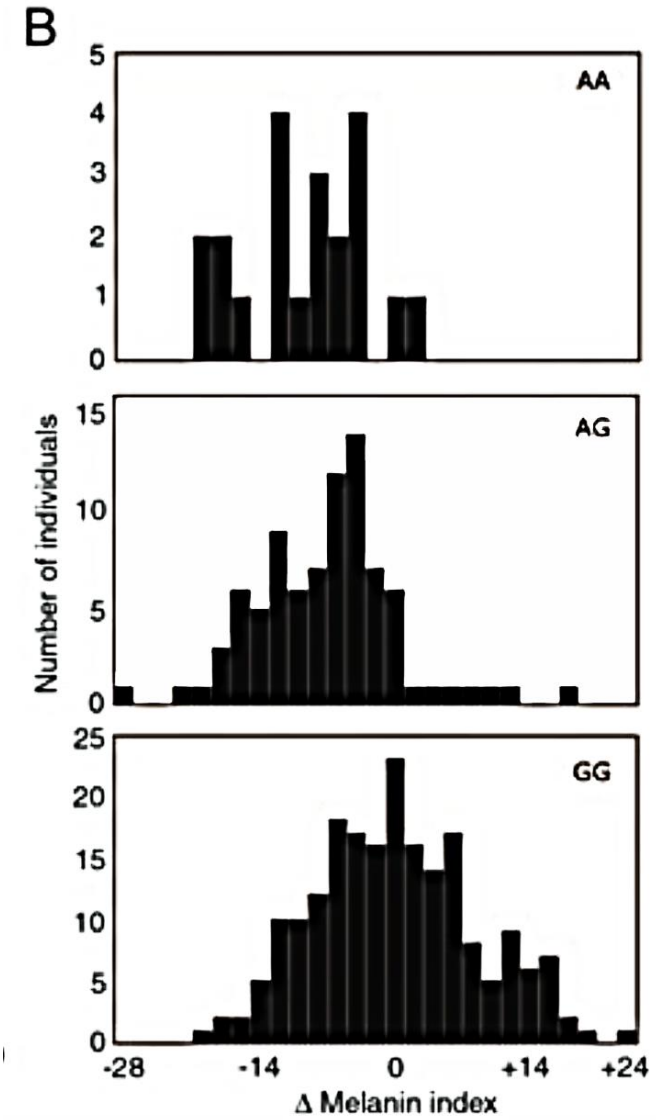


***Caption: Histograms showing the distributions of human skin pigmentation (melanin index) of three SLC24A5 genotypes (GG, AG, and AA) relative to the GG genotype. The plotted values are the difference between the melanin index measured for each individual and the regression line calculated for the GG genotype. The mean values for each genotype are 0 (GG), -7 (AG), and -9.6 (AA).***

**BACKGROUND INFORMATION**

Human skin color is a highly variable trait. Human skin cells contain the pigment melanin, which gives skin its color. In general, individuals with lighter skin tones have fewer, smaller, and less densely pigmented melanosomes, the melanin-producing organelles, in their skin cells than individuals with darker skin tones have. To better understand the genetic origin of variation in human skin color, Rebecca Lamason and colleagues turned to a model organism: the zebrafish (*Danio rerio*), which also displays variations in skin color. They identified a gene (called *golden*) that, when mutated, leads to more lightly pigmented, or golden, fish. Whereas wild-type zebrafish have numerous, dense, round-to-oval melanosomes in their skin cells, the melanosomes of

*golden* zebrafish are less numerous, smaller, and less densely pigmented. The scientists searched for an ortholog (a corresponding gene of similar sequence and function) of the *golden* gene in humans. The closest match was a gene called *SLC24A5*. Like the *golden* gene, the *SLC24A5* gene encodes a membrane protein that affects melanosome production.

To determine the gene's role in human skin pigmentation, the researchers searched for polymorphisms within the gene. They identified one single-nucleotide polymorphism with two alleles. The G allele, which encodes alanine, is found in most individuals in African, Indigenous American, and East Asian populations (with an allele frequency of 93% to 100%), while the A allele, which encodes threonine, is found in European-American populations (frequency of 98.7% to 100%). They then studied two populations of recently mixed ancestry, African-American and African-Caribbean, with a range of skin colors to determine whether allele frequencies correlate with skin pigmentation. Skin pigmentation was measured using reflectometry, which involves measuring the amount of light reflected back by an individual's skin to calculate the melanin index. Individuals with a higher melanin index have darker skin.