Zebrafish and Skin Color Reference Data

Melanophores in zebrafish skin: The possible role of *SLC24A5* in human skin color was first suggested by a group of researchers analyzing the genomes of zebrafish. They were looking for genes with mutations that might lead to cancer. One of the varieties they were analyzing is known as the "golden" mutant.

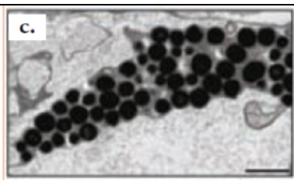
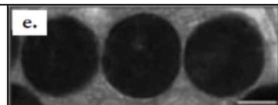
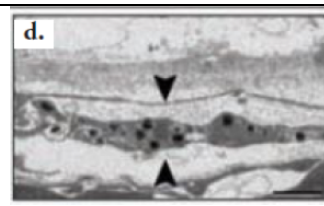
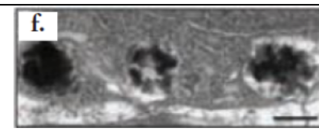
Wild-Type Zebrafish		***golden* Mutant**	
			
			

Figure 1. a. A typical (wild-type) zebrafish and **b.** *golden* zebrafish mutant, each with inset showing the melanophores present in the fish's skin (scale bars = 5 mm; 0.5 mm in insets). **Melanophores** are the melanin-containing cells within amphibians and fish**. c.–f.** Transmission electron micrographs (TEMs) of the melanophores (c, d) and **melanosomes** (organelles found in animal cells that are the site for synthesis, storage, and transport of melanin) (e, f) in the skin of wild-type (c, e) and *golden* mutant (d, f) zebrafish. (Image adapted from Lamason *et al*. 2005. *Science.* 310:1782–1786.)

Melanocytes in human skin: The figure below shows the melanin-containing melanosomes associated with three different natural skin colors.

Figure 2. Images showing the amount of melanin and the size and number of melanosomes in people with different skin colors. (Image adapted from *The Biology of Skin Color* film.)

***SLC24A5* alleles and allele frequencies:** Within the gene at a particular location, there is either an adenine (A allele) or a guanine (G allele). This single-nucleotide difference in DNA results in amino acid 111 of the protein being an alanine for the G allele and a threonine for the A allele. Alanine is nonpolar, and threonine is polar. This change likely significantly alters the function of the SLC24A5 protein.

The G allele is far more common among people of African descent than among people of European descent. This difference in allele frequency is unusual. For many other genes, West Africans and Europeans have similar allele frequencies. People with ancestors from even very distant geographic regions have far more genetic similarities than differences.

Table 1. *SLC24A5* Allele Frequency

Population	Frequency of the *SLC24A5* A allele at STR locus rs1426654
Europeans	0.96 (96%)
West Africans	0.09 (9%)

***SLC24A5* genotypes and phenotype distribution:** Scientists measured the relative amount of melanin in a group of people of both African and European ancestries with a range of skin colors. The melanin data were then sorted by the individuals' genotype for *SLC24A5* and represented in the graphs below.

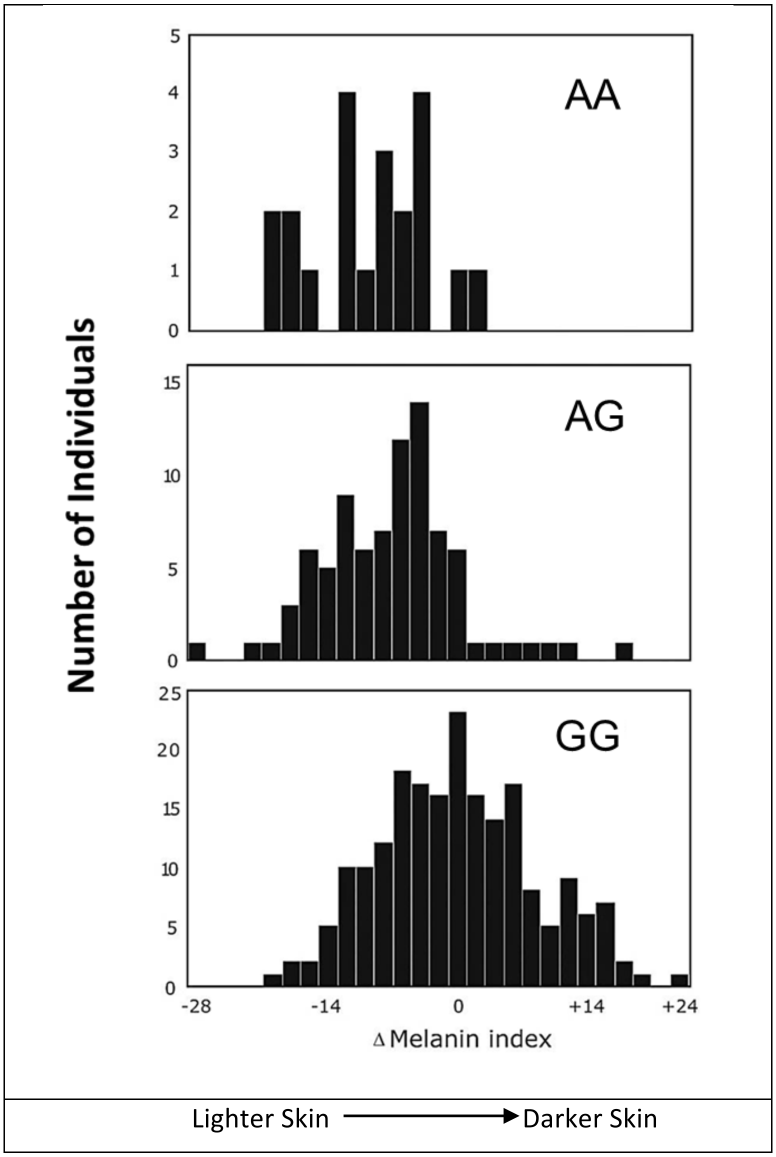


Figure 3. Amount of melanin versus genotype for the *SLC24A5* gene. A higher "Δ melanin index" value means that the individual had darker skin. (Image adapted from Lamason *et al*. 2005. *Science.* 310:1782–1786.)

Amino acids coded for by *SLC24A5* in different species: Researchers determined the DNA sequence of the mutated gene that results in golden zebrafish. They then sequenced the same gene in a large number of other vertebrates, including humans. The researchers quickly recognized that the zebrafish *SLC24A5* gene was very similar to the one in humans. Some of the amino acids coded for by the *SLC24A5* gene are shown below for a variety of species.

Z-fish	C	DE	YFLPSLE	V	I	SER	LGLSQVAGT	A	FMA	A	GSSAPE	L	VT	A	FLG
Medaka	C	DD	YFLPSLE	V	I	SER	LGLSQVAGT	A	FMA	A	GSSAPE	L	VT	A	FLG
Fugu	C	DD	YFLPSLE	V	I	SER	LGLSQVAGT	A	FMA	A	GSSAPE	L	VT	A	FLG
Stickleback	C	DD	YFLPSLE	V	I	SDR	LGLSQVAGT	A	FMA	A	GSSAPE	L	VT	V	FLG
Xenopus	C	ES	YFLPSLE	V	I	SER	LGLSQVAGT	A	FMA	I	GSSAPE	F	VT	A	FLG
Chicken	C	DD	YFLPSLE	I	I	TEC	LGLSQVAGT	A	FMA	A	GSSAPE	L	VT	A	FLG
Dog	C	DE	YFLPSLE	I	I	SET	LGLSQVAGT	A	FMA	A	GSSAPE	L	VT	A	FLG
Cow	C	DE	YFLPSLE	I	I	SES	LGLSQVAGT	A	FMA	A	GSSAPE	L	VT	A	FLG
Mouse	C	DK	YFLPSLE	I	I	SDS	LGLSQVAGT	A	FMA	A	GSSAPE	L	VT	A	FLG
Rat	C	DK	YFLPSLE	I	I	SDS	LGLSQVAGT	A	FMA	A	GSSAPE	L	VT	A	FLG
Rabbit	C	DE	YFLPSLE	I	I	SES	LGLSQVAGT	A	FMA	A	GSSAPE	L	VT	A	FLG
Chimp	C	DE	YFLPSLE	I	I	SES	LGLSQVAGT	A	FMA	A	GSSAPE	L	VT	A	FLG
Human (G)	C	DE	YFLPSLE	I	I	SES	LGLSQVAGT	A	FMA	A	GSSAPE	L	VT	A	FLG
Human (A)	C	DE	YFLPSLE	I	I	SES	LGLSQVAGT	T	FMA	A	GSSAPE	L	VT	A	FLG

Figure 4. Much of this small section of the protein encoded by the *SLC24A5* gene is the same across several species (shown in black). Each of the 20 amino acids found in humans is assigned its own one-letter code. For example, A stands for alanine. In humans, a single-nucleotide change (from G to A) at a particular locus in the gene changes the resultant amino acid from alanine (A) to threonine (T). The *SLC24A5* gene is larger than the region shown above. Recall that the *golden* phenotype in zebrafish is also caused by a change in the *SLC24A5* gene, but it is the result of a different mutation. The mutation that causes the *golden* phenotype in zebrafish is located farther upstream of the amino acids shown. (Image adapted from Lamason *et al*. 2005. *Science.* 310:1782–1786.)

Transplanted mRNA: Researchers made a messenger RNA (mRNA) fragment from the human DNA sequence for the *SLC24A5* G allele. This human mRNA was injected into *golden* zebrafish embryos where it was translated into a protein. The researchers then compared the embryo to wild-type zebrafish and *golden* zebrafish. The results are shown below.

"Golden" zebrafish larvae injected with human mRNA from *SLC24A5* | Wild-type zebrafish larvae | "Golden" zebrafish larvae

Figure 5. Zebrafish embryos showing differing amounts of melanin. Note that pigmented melanophores in larvae appear as dark patches on the head, back, and throughout their large eyes. The messenger RNA (mRNA) transcribed from the human *SLC24A5* gene was injected into the fish on the left. (Image adapted from Lamason *et al*. 2005. *Science.* 310:1782–1786.)

Partial vertebrate phylogeny: The zebrafish is a ray-finned fish. All ray-finned fish as well as all reptiles (and birds), amphibians, and mammals have the *SLC24A5* gene. The figure below shows a phylogeny of these groups based on fossils and sequences from other regions of DNA.

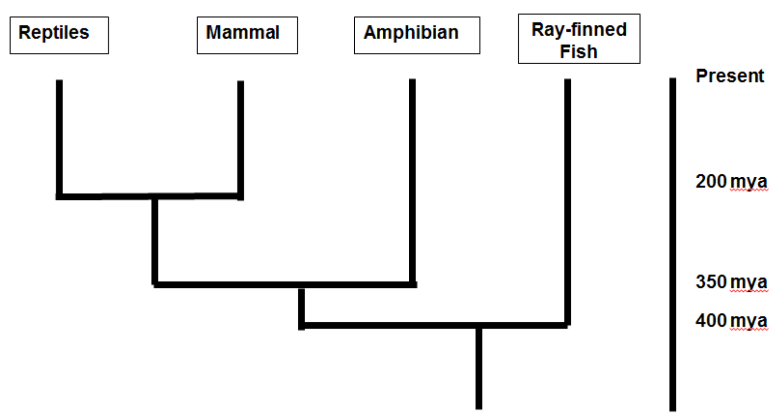


Figure 6. A phylogeny for some of the major groups of vertebrates. Branch lengths are proportional to time. Note: "mya" means "millions of years ago."

Indigenous skin color throughout the world: Nina Jablonski and George Chaplin collaborated on a map that shows how natural (untanned), indigenous (native) skin color varies throughout the world.

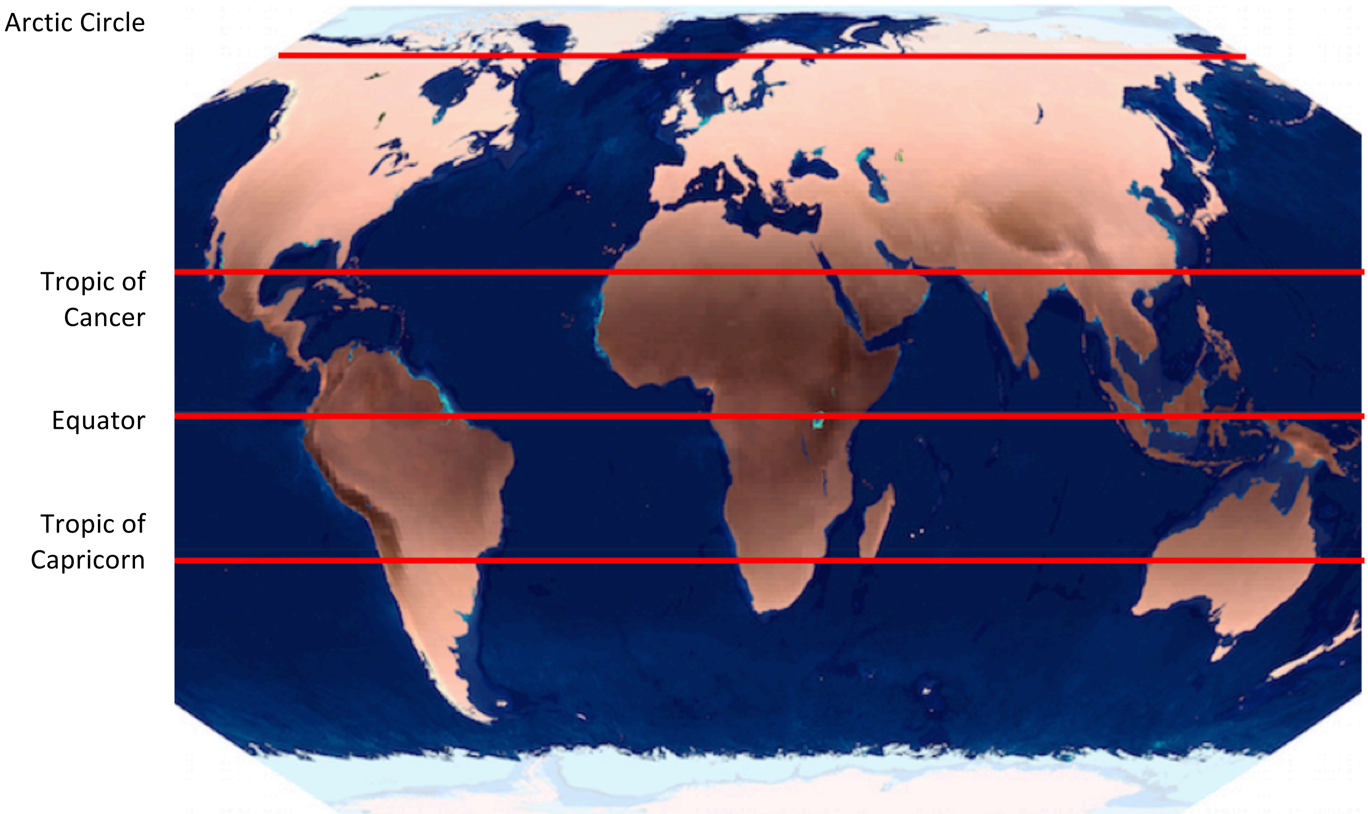


Figure 7. Map of the world colored to show natural, indigenous skin color. (Image adapted from *The Biology of Skin Color* film.)

***SLC24A5* allele frequencies in populations around the world:** The map below shows the relative frequencies of the G and A alleles for the *SLC24A5* gene. Each circle represents a distinct group of people. The location of the circle corresponds to the ancestral origin of the population. High frequencies of the G allele are shown with increasing amounts of black. (No data is available for Australia and much of North and South America.)

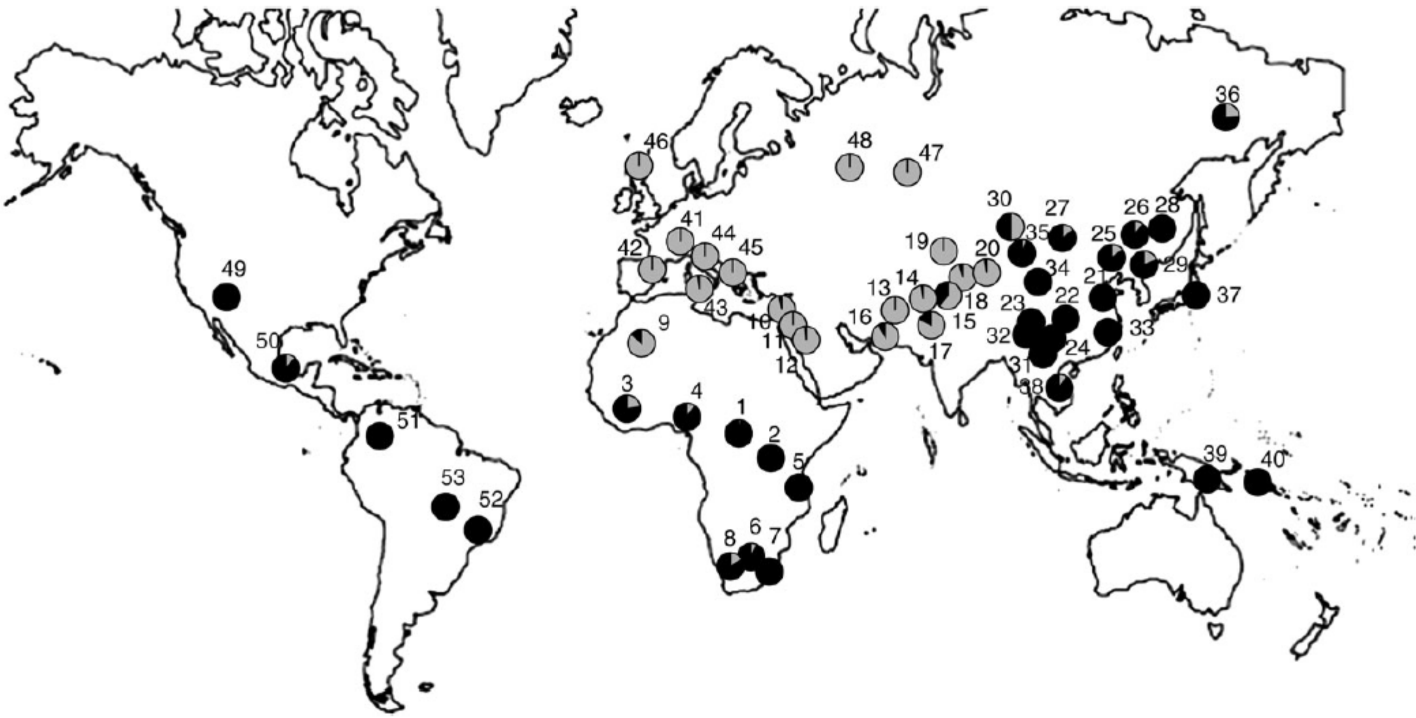


Figure 8. Map showing frequencies of the two alleles for *SLC24A5* among ancestral populations around the world. Each population is represented by a circle filled in proportionally according to allele frequency. The G allele is coded black and the A allele gray. The numbered populations correspond to the following: 1) Biaka pygmies, 2) Mbuti pygmies, 3) Mandenka, 4) Yoruba, 5) Bantu N.E., 6) San, 7) Bantu S.E., 8) Bantu S.W., 9) Mozabite, 10) Bedouin, 11) Druze, 12) Palestinian, 13) Brahui, 14) Balochi, 15) Hazara, 16) Makrani, 17) Sindhi, 18) Pathan, 19) Kalesh, 20) Burusho, 21) Han, 22) Tujia, 23) Yizu, 24) Miaozu, 25) Orogen, 26) Daur, 27) Mongola, 28) Hezhen, 29) Xibo, 30) Uygur, 31) Dai, 32) Lahu, 33) She, 34) Naxi, 35) Tu, 36) Yakut, 37) Japanese, 38) Cambodian, 39) Papuan, 40) NAN Melanesian, 41) French, 42) French Basque, 43) Sardinian, 44) Northern Italian, 45) Tuscan, 46) Orcadian, 47) Adygei, 48) Russian, 49) Pima, 50) Maya, 51) Columbian, 52) Karitiana, 53) Surui. (Image adapted from Norton et al. 2007. *Mol. Biol. Evol.* 24:710–722.)