



PUBLIC UNDERSTANDING OF  
BIOTECHNOLOGY

# Genetics of Skin Colour

## Background

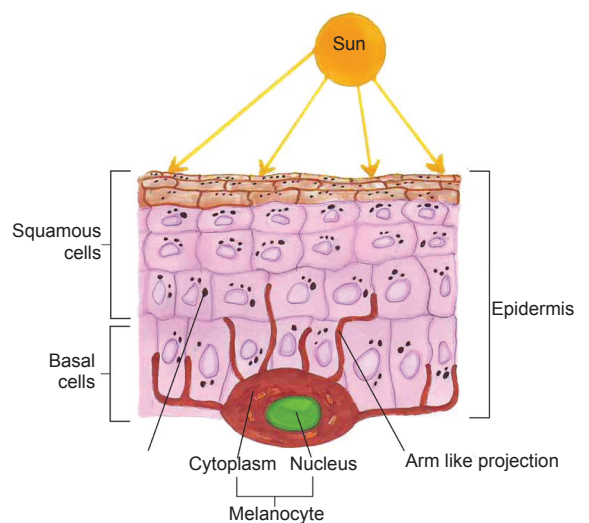
Skin colour is the most visible of all human traits. In fact, it is so obvious, and the variation between people so striking, that it is not surprising that it has caused much interest and controversy. The colour of human skin is influenced by both internal and external factors but is primarily due to pigments, the most important of which is melanin, produced in the body. Like all characteristics of humans, the colour of our skins is controlled by genes and inheritance.

## What causes differences in skin colour?

The skin, like all human organs such as the liver and kidney, is made up of cells which all have the basic structure of a nucleus, which contains the genes, surrounded by cytoplasm, which has a different composition depending on the cell type. The top layer of the skin is called the epidermis and has cells that are arranged like a tiny brick wall of less than 1mm high (Fig 1). These cells grow from the base or bottom layer and flatten as they move to the surface where they are continuously shed. On this journey, which takes an individual cell about 28 days, it loses its nucleus which stores its genetic material or DNA. The skin pigment melanin is made in specialised cells called melanocytes that remain at the base of the epidermis. Melanin is packaged into tiny bundles called melanosomes, which are transferred to adjacent skin cells, via the melanocyte's arm-like projections. These melanosome particles become arranged like an umbrella over the nucleus giving

Fig 1

The brick wall-like structure of epidermal cells and their relationship to a melanocyte which has arm like projections that transfer melanosomes (containing melanin) to adjacent cells. More melanin is deposited on the side of the cell closest to the rays of the sun (thus, protect the nucleus like an umbrella). Note that as cells move toward the surface they flatten eventually losing their nucleus before being shed.



protection to the DNA against ultraviolet rays from the sun. When epidermal cells travel towards the skin's surface, they carry their melanin with them, and it remains even after the nucleus is lost. It is this melanin which is mainly responsible for the colour of an individual's skin.

Amazingly, the palette of human skin colour, famously described in South Africa as the Rainbow Nation, is the result of small variations in the packaging and type of melanin produced. People generally have the same number of melanocytes irrespective of their skin colour; but



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those with black/brown skin have melanosomes that are large, arranged individually, and contain more concentrated melanin compared to paler skinned people who have smaller melanosomes with less melanin and where the melanosomes are grouped together in a membrane structure.

Melanocytes are factories for melanin production, which is a complex process involving many different stages. Two types of melanin are produced, namely eumelanin which is a dark brown/black pigment and pheomelanin which is a lighter reddish/yellow pigment. Changes in the amount of each pigment produced is also under genetic control and the ratio of eu- to pheo-melanin is responsible for variations in both skin and hair colour. Thus the melanocytes of pale-skinned redheads produce lots of pheomelanin, whilst those of people with a range of skin colours from "beige" to "black" and with hair from blonde to brown to black produce more eumelanin than pheomelanin. Subtle changes in this ratio account for the yellower or redder hue of Asians and Native American Indians, respectively.

A striking variation in skin colour is seen in people with albinism; here small genetic changes

that cause an interruption in any one of the many steps that control melanin production result in failure to produce the pigment and the person has extremely pale skin.

### What does melanin do?

Melanin protects the skin from the harmful rays of sunlight, which is made up of visible and invisible light. Invisible light, also called ultraviolet or UV light, can be divided into UVA, B and C. It is UVA and UVB that cause damage to the skin, but melanin protects the skin from damage by reflecting and absorbing some of the UV energy. In the absence of melanin, UV energy penetrates deep into the skin where it can cause small amounts of damage to the DNA in the nucleus of the still living epidermal cells. Although small amounts of such damage can be spontaneously fixed by the cell's repair machinery, unrepaired, accumulated damage can cause cells to multiply uncontrollably, resulting in skin cancers. The amount of UV exposure over a life time, as well the shade of skin colour, influence the chance of developing skin cancers. People with skins in which there is little or no eumelanin, or which predominantly contain pheomelanin, are all at increased risk of developing skin cancers. Thus people with albinism or very pale skin generally suffer sun-burn easily without tanning when exposed to the sun and are at greatest risk. It is not only the sun's rays that damage the skin, sun beds used for salon and home tanning are just as dangerous.

### Why different skin colours in different parts of the world?

The prevailing scientific view of the origin of modern man is the "Out of Africa" theory, which proposes that the rest of the world has been populated by the descendents of a small clan of humans who migrated from Africa within the last 100 000 years. It is therefore likely that the skin colour of these early humans was dark brown. Thus changes in skin colour occurred following the migration out of Africa of early populations into different global regions, giving rise to the many shades of skin colour present today. It is known that in pale skinned people, UV light can damage the genetic material in the deeper skin cells and induce skin cancer. However, because most sun induced skin cancers develop well past the reproductive age in people older than 50 years, skin cancer is unlikely to have been a significant evolutionary factor for skin colour.



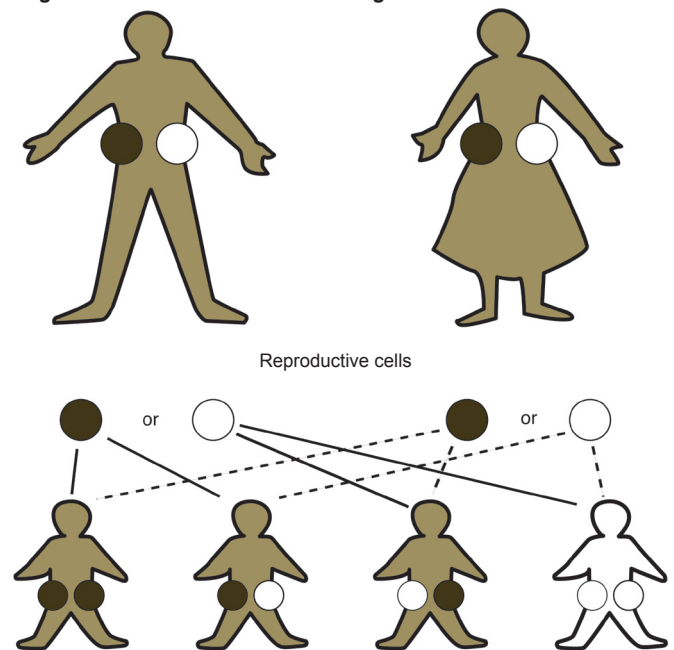
*Portrait of an African albino man with heavily freckled lips and skin.*



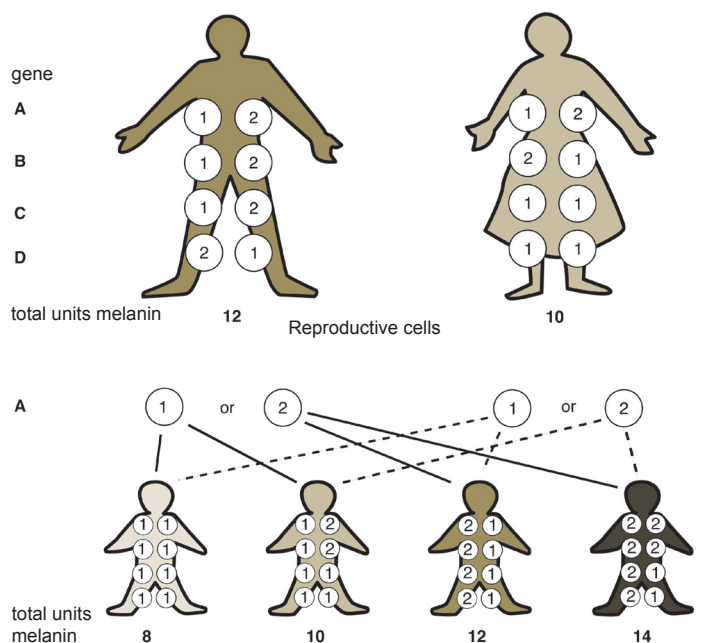
Nina Jablonski and George Chaplin noted that in areas where UV radiation was highest, people's skins were darkest and vice versa. They and others have suggested that UV exposure does not only induce skin cancer but has other consequences which may have contributed to the development of skin colour variation over long periods of time. Two plausible hypotheses have been explored. Firstly, UV rays are also known to break down folate (vitamin B6) in the blood vessels just beneath the skin. Folate is essential for dividing cells and therefore the developing foetus is most vulnerable to the effects of low folate levels, which is why pregnant women are advised to take folate supplements. A shortage of folate can result in abnormalities of the spine and brain of the baby. It is thought that melanin offers protection from folate damage in the same way that it lessens DNA damage. Thus individuals with a paler skin living in areas of high UV radiation, for example within the tropics, would be less likely to reproduce successfully and would have fewer descendants over a long period of time. Secondly, sunlight is needed to form vitamin D in the skin. This vitamin is essential for processing calcium, needed for making strong bones and for healthy pregnancies. Shortage of calcium, especially early in life, causes children to develop weak bones (a disease called rickets); and can reduce survival and hence the number of descendants who will contribute to future generation. So dark eumelanin-enriched skin reduces UV penetration and thus limits the ability of the skin to make vitamin D. In countries at higher latitudes with already reduced amounts of UV light, vitamin D production is likely to be less efficient in individuals with dark skin.

Thus, it is reasoned that, originally, it was advantageous for people living in regions with high UV radiation to have dark skins, which protected them from folate damage, while still allowing formation of enough vitamin D. Scientists call this "selection pressure", a phenomenon that occurs over many generations and in this case refers to the preferential survival of dark skinned descendants resulting in a predominantly dark skinned population. But, as these people moved north into regions with lower UV radiation, the high melanin content in their skin reduced UV-mediated vitamin D synthesis and strong bone formation. A situation therefore arose where the selection pressure was in favour of reducing the amount of melanin, resulting in the preferential survival of pale skinned descendants. The outcome of these selective pressures is that as people moved and settled in regions of the world with different amount of UV radiation, the colour of their skin would have to adapt and strike a balance between being dark enough to limit sun destruction of folate and light enough to allow vitamin D production and calcium absorption.

**Fig 2**  
**Monogenic Inheritance - Albinism one gene**



**Fig 3**  
**Polygenic Inheritance - Normal skin colour variation - many genes**



**Monogenic and polygenic inheritance**

Albinism is a monogenic trait, it follows a Mendelian pattern of recessive inheritance under the control of a single primary gene. The parents (albinism carriers) both carry a gene variant that prevents melanin production; as they each also have a melanin-producing variant, they have pigmented skin. Depending on which variant their children inherit from each parent, they will be non-carriers, carriers or have no skin pigment (albino).

Normal skin colour is a polygenic trait, following a multi-factorial pattern of inheritance under the control of an interacting set of genes and environmental influences, eg, skin darkening (tanning) induced by sunlight. In this representation, variant 2 of each gene results in more pigment, so the more 2s a person has, the darker their skin shade (represented by total melanin units under each person). Consequently, children may have a lighter or darker skin shade than either of their parents (as was the case with Sandra Laing). Note: only four sets of genes, with apportioning and recombining of gene variants at only one of these, are shown. It is believed that more than 20 genes affect skin colour in humans.



## What about skin colour genes?

Melanin is made in a complex multistep “assembly line”, which is under the control of many different genes. Genes are the units of inheritance that carry the code that determines the body’s components and are responsible for giving us our recognisable characteristics. Genes are made of DNA and are carried on paired chromosomes in the cell’s nucleus, one member of each pair from our mother’s egg and the other from our father’s sperm. One couple can therefore have children who have many different potential combinations of genes, depending on how these are apportioned in the reproductive cells and paired at conception. Small differences, called variants, in individual genes of each pair can give rise to different outcomes, for example, skin colour.

The inheritance of genetic variation is easier to follow when only one pair of genes affects a characteristic, for example in albinism (monogenic inheritance), and one can predict the likely outcome (*Fig 2*). However, when scores of genes are involved in producing the final products, for example eu- and pheo-melanin, which account for shades of skin colour (polygenic inheritance), it is much harder to predict what the outcome will be (*Fig 3*). Thus, depending on the combinations following conception, a spectrum of skin colours may be seen between parents and their individual children; very much depending on the underlying genetic variation in the melanin-associated gene pairs.

Currently, research suggests that variants in more than twenty known genes, determine human skin colour. Their products are nearly all involved in stages of melanin production, some variants specified by a particular gene encourage the production of more melanin, others switch the ratio of eu- to pheo-melanin or alter packaging of melanin into melanosomes. Overall, the effects of these genes are additive; for example, a variant of the human equivalent of the zebra fish gene accounts for up to 30% of the difference in melanin-determined skin colour between Europeans and Africans.

Particular variants in the many genes determining skin colour are found more commonly in particular populations, reflecting past selection pressures; for example, almost 100% of pale skinned Europeans have the same variant of the SLC24A5 gene, thought to have become prevalent in this population group about 6 000 years ago, while this variant is virtually absent in African and Asian populations. Such underlying genetic homogeneity explains why children generally have a similar skin tone as their parents. In contrast, if there is underlying genetic heterogeneity, for example, resulting from recent admixture of population groups, children may inherit different combinations of particular variants from their two parents. Thus explaining why skin colour in children of one set of parents, each with visibly different amounts of melanin (“black” or “white”), can range from very pale to very dark.

Thus, masked variants of genes in very pale skinned parents can be rearranged and combined to produce a much darker skinned child, as was the case in the tragic story of Sandra Laing who was born to “white” parents in apartheid South Africa. She inherited a set of skin colour-determining gene variants that additively conferred more melanin units to her skin than her parents’ own combinations and she was classified as “coloured”. These gene variants were passed down by her parents even though they were not apparent in them.

In conclusion, human skin colour is controlled by the complex interplay of many different genetic variants, most of which control production and cellular arrangement of melanin; and has also been molded by the environment in different regions of the world over thousands of years. Thus skin colour does indeed have a biologic or genetic basis. However, the notion of race cannot be rationally assigned based on skin colour and the Sarah Laing story should serve as a tragic reminder of the futility of racial classification.