

## Questioning colour

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**I**n the early days of the last century, scientists believed that the colour of our eyes was a straightforward inherited trait. Mendel's laws of inheritance had become fashionable and eugenicists saw in them an elegant and practical way to define our species. However, as the years passed and research in genetics progressed, ascribing the pigmentation of our eyes to the powers of a sole gene soon showed its weaknesses. Pigmentation proved to be a complex biological process. Nevertheless, as the 20<sup>th</sup> century bows out and the 21<sup>st</sup> bows in, it appears that – though pigmentation as a whole is part of an intricate biochemical network – the colour of our eyes does indeed seem to be in the hands of one gene which codes for a protein known as the P protein.



The albino Lucas family from the Netherlands became one of Phineas Barnum's most popular exhibits in the second half of the 19<sup>th</sup> century.

Research on the genetics underlying human pigmentation – i.e. the colour of our eyes, hair and skin – started in the very beginning of the 20<sup>th</sup> century thanks to two biologists who were also husband and wife: Charles and Gertrude Davenport. Their idea was to demonstrate the existence of simple Mendelian principles underlying human pigmentation. But things turned out to be a little more complicated than expected. How, for instance, can you define the colour of an eye? Would a hazel eye for me be a hazel eye for you? Furthermore, Sewell Wright (1889-1988), the American evolutionary theorist, demonstrated that eye, hair and skin

pigmentation could not be taken as separate entities. All types of pigmentation were the result of a same biochemical process, which is itself inherited.

What is pigmentation? What provides humans with ginger hair, green eyes or black skin? The pigment involved in natural body hues is melanin. Melanin is synthesized from the amino acid tyrosine and is a light-absorbing biopolymer. It does not have a defined chemical structure, binds quite happily to other chemical entities and is resistant to biochemical degradation. Melanin is produced and stored in cytoplasmic organelles known as melanosomes, which float around melanin-producing cells: the melanocytes. Within human populations, the number of melanocytes per tissue does not really vary. What does vary however is the number of melanosomes – and hence melanin – per melanocyte. Typically, a dark-haired, dark-skinned, dark-eyed woman would have many more melanosomes in her melanocytes than her fair-haired, fair-skinned, light-eyed counterpart.

So why are our eyes brown? Or hazel? Or greenish-brown? Or black? Or bluish-green? Or chestnut? Or dark brown? Or blue? Or greyish-blue? The answer is twofold: melanin and light. The lighter our eyes, the less melanin in our melanocytes. And when white light hits our irises, various wavelengths are either absorbed or reflected and give rise to the three most common colours of the eye: brown, greenish-hazel and blue. Such a classification is merely for practical purposes however, since eye

pigmentation – like skin pigmentation – ranges from dark to light in a continuous manner.

The P protein is a medium-sized protein lodged in the melanosome membrane. It has twelve membrane-spanning regions and seems to be involved in as many hypothetical activities. It could be involved in the transport of small molecules such as tyrosine for example. Or it may act as a stabiliser of the melanosomal protein complex, which includes a number of tyrosinases needed to synthesize melanin. P protein has also been proposed to function as a melanosome-specific ATP-driven proton pump thus regulating melanosomal pH. It may also play a part in the processing, sorting and regulation of the levels of tyrosinases, without which no melanin would be synthesized at all. Currently, there is not much of a consensus as to its function but what has been discovered is that modifications in its activity modify directly the colour of an iris – so it must be a major orchestrator in the pathway which ultimately leads to the colour of our eyes.

Albinism is a direct consequence of pigmentation abnormalities, of which many forms exist. The most current form – known as oculocutaneous albinism II or OCA2 – is caused by a mutation in the P protein gene. It is an autosomal recessive disorder characterised by an absence, or reduced amount, of pigmentation

in an individual's skin, hair and eyes and is unfortunately associated with relatively severe visual and auditory problems. The occurrence of OCA2 is 1/40000 in most populations worldwide. Historically, in the 19<sup>th</sup> century, albinos were thought to have all sorts of supernatural powers such as mind-reading or witchcraft and the infamous American businessman, circus man, impresario, politician, journalist and museum owner, Phineus Barnum, invited numerous albinos to be exhibited in his travelling show and museum.

Besides prenatal diagnosis of OCA2 and a greater understanding of melanogenesis itself, what is the point of studying human pigmentation? For one, it helps to demolish prejudices such as 'racism' since biologists are incapable of establishing barriers between populations with regards to skin colour. Genes involved in pigmentation, such as OCA2, also provide valuable information in the matter of population migrations and evolution, and one particularly interesting development is to be found in the field of forensics. If a specific eye colour can be objectively attributed to one gene, then a DNA sample on an unidentified body could lead forensic investigators to an enhanced physical profile of a victim and perhaps even its identification. The only drawback here though is agreeing on the definition of a given colour...

## Cross-references to Swiss-Prot

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