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Physical traits

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There is widespread variation in human hair, eye and skin colour, and this results from alterations in the amount and ratio of the two types of melanin pigment, brown-black eumelanin and red-yellow phaeomelanin, in these tissues. Furthermore, in addition to differences in constitutive (untanned) skin pigmentation, there is also variation between individuals in facultative pigmentation (the degree of cutaneous tanning following exposure to single or multiple doses of ultraviolet radiation). In the mouse, over 50 genetic loci are known to be involved in the control of pigmentation, and many patterns of altered coat colour have been demonstrated to result from monogenic abnormalities. In man, however, most inter-individual differences in pigmentation are estimated to result from polymorphisms at approximately four or five genetic loci. Pigmentary disorders resulting from pathological alterations in single genes, including oculocutaneous albinism type I (*tyrosinase*), oculocutaneous albinism type II (*p-gene*), piebaldism (*c-kit*), etc., account for only a minority of the overall variation in human pigmentation.

Research during the last decade on the melanocortin 1 receptor (*MC1R*) gene has provided evidence for variants in this gene being an important determinant in a substantial amount of the phenotypic variation in normal human pigmentation. *MC1R* variants are associated with red hair and fair skin, and investigations employing cell transfections and transgenic mice have confirmed that certain variants are compromised in their ability to signal intracellularly via cAMP, and to promote the synthesis of eumelanin. The complete absence of non-synonymous variants in African negroes, and their prevalence in white Caucasians suggests that most non-synonymous *MC1R* variants may result in lighter skin colour. Case control studies support a role for *MC1R* variants, when present in the heterozygous state, in causing fair skin type, and kindred studies suggest that the majority of red-haired individuals have two variant *MC1R* alleles. However, over 30 *MC1R* variants have been identified to date, and further research is necessary to characterise the effects of the majority of the less frequently encountered variants, as well as to identify the other genes which determine variation in normal human pigmentation.

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