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Forum

Hair Coloration by Gene Regulation: Fact or Fiction?

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The unravelling of hair pigmentation genetics and robust delivery systems to the hair follicle (HF) will allow the development of a new class of colouring products. The challenge will be changing hair colour from inside out by safely regulating the activity of target genes through the specific delivery of synthetic/natural compounds, proteins, genes, or small RNAs.

Genetics of HF Pigmentation and Greying

Pigmentation is one of the most striking phenotypic traits in humans. It has great social and psychological relevance and the possibility of controlling it has immense resonance for any individual or ethnic group. The colour of human hair, skin, and eyes is determined by the amount, type, and tissue distribution of melanin. Melanin is a complex mixture of pigmented indole-rich biopolymers that are synthesised by specialised cells called melanocytes. The main types of melanin polymer are the black-to-brown eumelanin (highly polymerised) and the yellow-to-reddish-brown pheomelanin (lighter, less polymerised, and containing sulfur) [1]. Black hair has the highest eumelanin-to-pheomelanin ratio while red-to-yellow hairs have the lowest ratio; grey or white hairs have insignificant or no melanin at all. For more information on melanin production by melanocytes, see Box 1.

Pigment synthesis, storage, and transport occur in lysosome-related organelles known as melanosomes. Although the biochemical synthesis of melanin is common to all pigmented tissues, melanogenesis is regulated differently among them. In hair, melanogenesis occurs only during the anagen (active growth) phase of the hair growth cycle in melanocytes located exclusively in the hair bulb, while in skin, for instance, melanin is constitutively produced. An interesting study [2] demonstrated that a SNP previously associated with blond hair in northern Europeans is responsible for a 20% reduction in the activity of a tissue-specific regulatory enhancer affecting KITLG gene transcription in the HF only. Different regulatory mechanisms underlie the discrepancy between the pigmentation phenotypes of hair, skin, and eyes commonly seen in an individual. Knowing how to interfere with melanogenesis in a tissue-specific manner will thus be an invaluable cosmetic tool.

Several approaches have contributed to identifying genes involved in melanin synthesis and in the biogenesis, transport, and distribution of melanosomes, as well as genes regulating those processes (Box 1) [3,4]. These approaches include comparative genomics of candidate genes such as those identified in animal models. By October 2011, the International Federation of Pigment Cell Societies database had described 378 putative pigmentation loci for mice and their human and zebrafish homologues (http://www.espcr.org/micemut/). Despite the many genes already implicated in melanogenesis, those

Box 1. HF Pigmentation

Among the various cells that comprise the HF, the relevant differences seen in gene expression between pigmented and grey HFs can be related to melanocyte biology (Table I and Figure I). Microarray analysis is a powerful technique that allows a global perspective on what is occurring in a cell, tissue, or organism at a particular moment through the comparison of the levels of all mRNAs corresponding to the genes being expressed: the transcriptome. Such analysis was conducted by a research group on pigmented and white human HFs [12].

Table I. Mean Fold Changes in the Expression of a Selected Group of Genes that were Upregulated in Pigmented HFs Compared with White HFs [8]

Gene Symbol	Gene Name	Mean Fold Change
TYRP1	Tyrosinase-related protein 1	116.58
SILV	Silver homologue (mouse)	36.21
TYR	Tyrosinase (oculocutaneous albinism IA)	26.36
MLANA	Melan-A	25.02
TRPM1	Transient receptor potential cation channel, subfamily M, member 1	8.58
SLC45A2	Solute carrier family 45, member 2	5.21
GPR143	G protein-coupled receptor 143	3.88
CAPN3	Calpain 3 (p94)	3.68
PLXNC1	Plexin C1	3.64
KIT	v-kit Hardy–Zuckerman 4 feline sarcoma viral oncogene homologue	2.81
PAX3	Paired box 3	2.23
OLFM1	Olfactomedin 1	2.06
MET	Met proto-oncogene (hepatocyte growth factor receptor)	2.04
HPS1	Hermansky–Pudlak syndrome 1	1.86
OSTM1	Osteopetrosis-associated transmembrane protein 1	1.66
EDNRB	Endothelin receptor type B	1.65

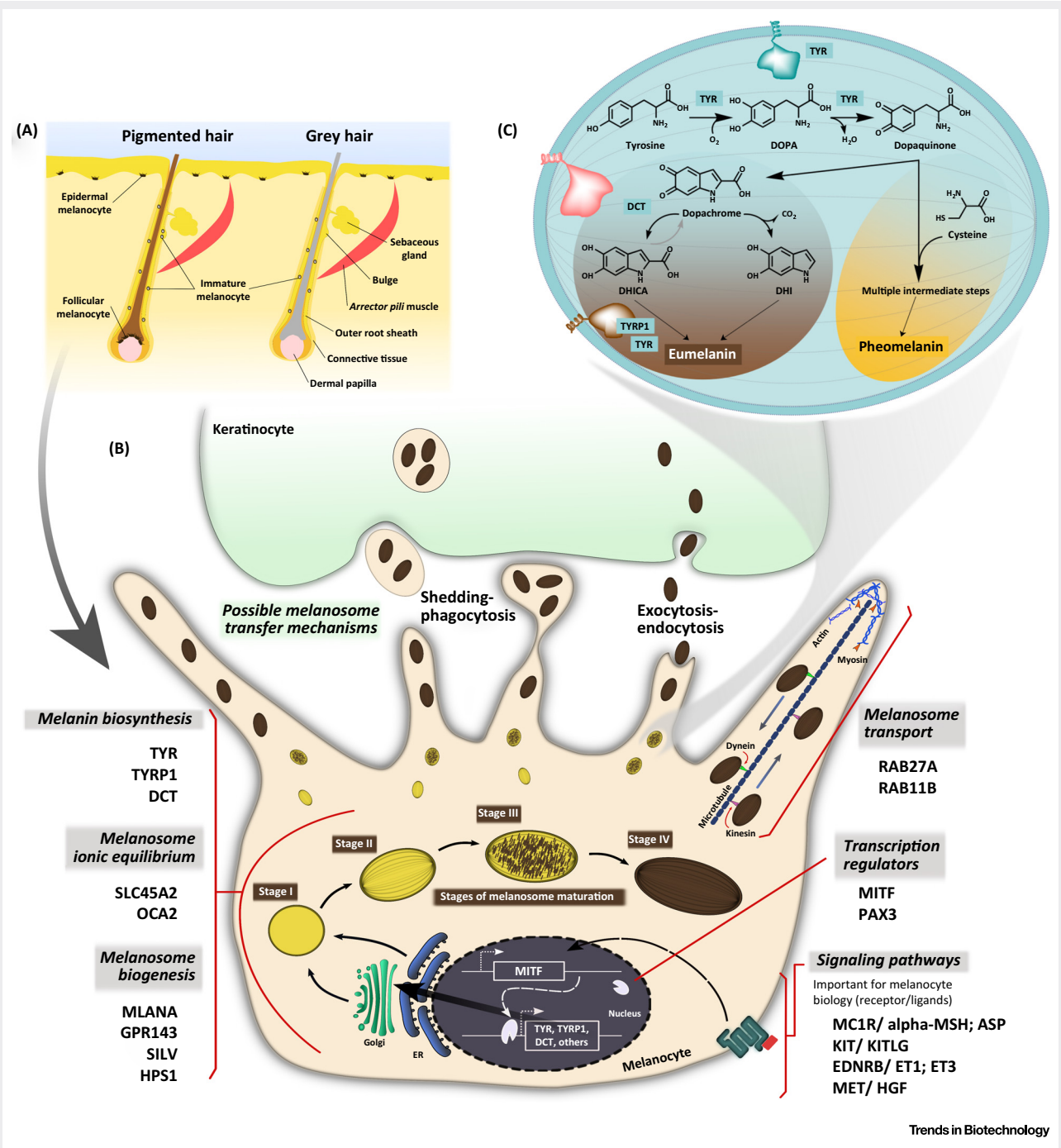

Figure I. Melanocyte Function in HF Pigmentation. (A) Schematic drawing of a pigmented and a grey HF, where some structures and cells are highlighted. (B) Differentiated melanocyte showing its typical cellular processes and some of the most frequently associated genes. (C) Biochemical synthesis of both types of melanin, which occurs inside specialised organelles called melanosomes. Abbreviation: HF, hair folicle.

associated with natural human hair colour variation are rather few [4]. A research group has created a model with very good predictive accuracy for hair-colour categories based on no more than 45 SNPs related to only 12 different genes [5]. We think that the already reported genes, included those in the hair-colour prediction model, are an excellent starting point to develop cosmetic strategies to modulate gene activities, changing hair colour from the follicle (Box 2). However, any