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Editorial

Agouti-Signaling Protein: Structure and Function

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EDITORIAL NOTE

Agouti-Signaling Protein (ASIP) is a protein that is encoded by the ASIP gene in humans. In mammals, it regulates the distribution of melanin pigment. Agouti interacts with the melanocortin 1 receptor to determine whether phaeomelanin or eumelanin is produced by the melanocyte. This interaction is what causes unique light and dark bands in the hairs of animals like the agouti, after which the gene is called. Agouti signalling is crucial for selecting which sections of the body will be red or black in other species, such as horses. Mice with wildtype agouti will be grey, with yellow and black hairs on each strand. Loss of function mutations in mice and other animals result in black fur, whereas mutations that cause expression throughout the body result in yellow fur and fat in mice. When it comes to binding with melanocortin 1 receptor proteins, the agouti-signaling protein competes with alpha-Melanocyte-stimulating hormone. When activated by -MSH, the darker eumelanin is produced, whereas when activated by ASIP, the redder phaeomelanin is produced.

Structure

An inhibitor cystine knot motif is used in the Agouti signalling peptide. These are the only known mammalian proteins to adopt this fold, together with the homologous Agouti-related peptide. There are 131 amino acids in the peptide. Because homozygous lethal yellow mice (Ay/ Ay) die early in development due to a trophectoderm differentiation defect, the lethal yellow mutation (Ay) was the first embryonic mutation to be identified in mice. Today, lethal yellow homozygotes are uncommon, whereas lethal yellow and viable yellow heterozygotes (Ay/a and Avy/a) are more prevalent. Agouti is only expressed in the skin of wild-type mice during hair growth, but these dominant yellow mutations cause it to be expressed in other tissues. The yellow obese syndrome, which is characterised by early onset obesity, hyperinsulinemia, and cancer, is linked to ectopic production of the agouti gene. An upstream loss at the start point of agouti transcription causes the deadly yellow (Ay) mutation. Except for the promoter and the first non-encoding exon of Raly, a ubiquitously expressed gene in mammals, the genomic sequence of agouti is lost as a result of this loss. The Raly promoter is used to control the expression of agouti's coding exons, resulting in ubiquitous expression of agouti, increased production of pheomelanin over eumelanin, and the development of a yellow phenotype.

Function

The agouti gene in mice produces a paracrine signalling protein that causes hair follicle melanocytes to produce pheomelanin instead of eumelanin, a black or brown pigment. Adult-onset obesity, increased tumour susceptibility, and premature infertility are all pleiotropic effects of constitutive expression of the mouse gene. This gene, which is very similar to the mouse gene, produces a secreted protein that may impact hair pigmentation quality, operate as an inverse agonist of alpha-melanocyte-stimulating hormone, have a role in neuroendocrine aspects of melanocortin action, and regulate lipid metabolism in adipocytes. The wild type agouti allele (A) in mice results in a grey coat, but genetic investigations has revealed multiple allele variations that result in a wide range of phenotypes other than the conventional grey coat. The lethal yellow mutation (Ay) and the viable yellow mutation (Avy), both generated by ectopic production of agouti, are the most well-studied allele variations. Yellow obese syndrome, which is characterised by early onset obesity, hyperinsulinemia, and cancer, is also linked to these mutations. On chromosome 2, the mouse agouti gene locus encodes a 131-amino-acid protein. This protein regulates melanin pigment dispersion in epithelial melanocytes at the base of hair follicles, with ventral hair expression being more sensitive than dorsal hair. Agouti is a paracrine factor that inhibits the release of melanocortin by dermal papillae cells. It is not directly released by melanocytes. Melanocortin stimulates the formation of eumelanin, the melanin pigment responsible for brown and black hair, by acting on follicular melanocytes. When agouti is expressed, the formation of pheomelanin, a melanin pigment that gives hair its yellow or red hue, takes precedence.

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