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Commentary
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Role of α-MSH-MC1R-cAMP Signaling Pathway in Regulating the Melanin Synthesis in Silky Fowl

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Commentary

Silky fowl (*Gallus gallus domesticus Brisson*), which is also named Chinese Taihe chicken, black-bone chicken, is originated in Taihe county of Jiangxi province, China. This bird is a special rare chicken in the poultry gene pool of China. Silky fowl has special nutritive and medicinal values, and is also an ornamental breed due to its special conformation and appearance.

Silky fowl are both consumed as a healthy food and used particularly as a kind of traditional Chinese medicine. Silky fowl is typically distinct from the other chicken breeds in that silky fowl is hyperpigmented with melanin in its various internal tissues and organs.

Melanin is the key component in silky fowl by which silky fowl exerts its medicinal tonic effect. The melanin from silky fowl has anti-mutagenic, antioxidant, and anti-aging effects that can boost immunity and regulate the endocrine system [1,2]. However, the regulation of melanin synthesis in silky fowl has been rarely reported and merits further study.

α-Melanocyte stimulating hormone (α-MSH) is a neuroendocrine regulatory peptide containing 13 amino acids derived from proopiomelanocortin (POMC), with an amino acid sequence of Ser-Tyr-Ser-Met-Glu-Glu-Phe-Arg-Trp-Gly-Lys-Pro-Val [3]. The melanocortin 1 receptor (MC1R) gene is encoded by an extension locus in mammals, and the corresponding encoded protein with seven transmembrane domains is a melanocytic Gs protein-coupled receptor crucial for the regulation of melanocyte proliferation and function [4,5].

α-MSH is known to play an important and evolutionarily conserved role in stimulating melanogenesis in mammalian species [6]. Cyclic adenosine monophosphate (cAMP) is the main intracellular messenger responsible for the melanogenic actions of α-MSH [7].

Binding of melanocortin ligand α-MSH to MC1R activates cAMP-dependent signaling pathway, leading to an increase in tyrosinase activity, increased expressions of tyrosinase-related protein (TRP) including tyrosinase (TYR), TRP-1 and -2, and, ultimately, upregulation of eumelanin production and deposition in melanocytes (Figure 1) [4,8-10]. The importance of the α-MSH-MC1R-cAMP signaling pathway in melanin synthesis has been extensively demonstrated in mammals and humans.

However, the regulatory effects of α-MSH and MC1R on melanin synthesis in avian species, and the mechanisms involved, are still poorly understood.

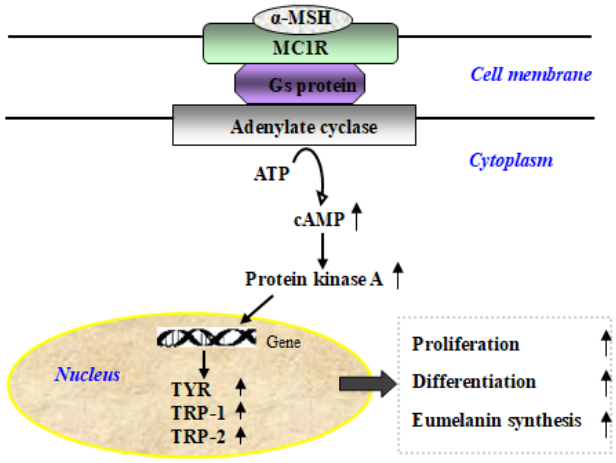

Figure 1: Role of α-MSH-MC1R-cAMP signaling pathway in melanin biosythesis in mammalian. Binding of melanocortin ligand α-MSH to MC1R activates cAMP-dependent signaling pathway, leading to an increase in tyrosinase activity, increased expressions of tyrosinase-related protein (TRP) including tyrosinase (TYR), TRP-1 and -2, and, ultimately, upregulation of eumelanin production and deposition in melanocytes. α-MSH: α-Melanocyte Stimulating Hormone; MC1R: Melanocortin 1 Receptor (MC1R); ATP: Adenosine Triphophate; cAMP: cyclic Adenosine Monophosphate; TYR: Tyrosinase; TRP-1: Tyrosinase-Related Protein-1; TRP-2: Tyrosinase-Related Protein-2.

Nishimura et al. found that the number of α-MSH secreting cells in the anterior pituitary of silky fowl was significantly higher than common chickens with either low, or no melanin deposition, suggesting that α-MSH was closely related to deposition of melanin in the tissues [11]. Takeuchi et al. cloned the MC1R gene, located on chromosome 11, for α-MSH (melanocyte-stimulating hormone) receptor from chickens for the first time in 1996 [12]. They observed that the MC1R gene exhibited highly conserved synteny in the chromosomal location in chickens, humans, and other vertebrates, and different MC1R genotypes corresponded to different plumage colors. Additionally, since the same MC1R mutations in chickens and mice corresponded to the same pigment variation, it was hypothesized that the regulatory mechanisms of MC1R functions in chickens and mammals might be consistent [13]. A comparative study on MC1R genes in silky fowl and broiler confirmed the key regulatory role of MC1R in melanin synthesis in silky fowl [14]. Our previous study observed that α-MSH (melanocyte-stimulating hormone) promoted

the proliferation of melanocytes in the skin of silky fowl, enhance the expression of MC1R, cAMP content and TYR activity, and promote melanin synthesis, whereas pre-treatment with α-MSH antagonist D-A-D-MSH (melanocyte-stimulating hormone) significantly inhibited the stimulatory effects of α-MSH on MC1R mRNA expression, cAMP formation, tyrosinase activity and melanin synthesis in skin melanocytes of silky fowls [15]. More recently, we reported that cAMP increased TYR activity, stimulated pigmentation in silky fowl skin melanocytes [16]. We also observed in this study that pre-treatment with Rp-cyclic AMPS significantly inhibited the stimulatory effects of cAMP TYR activity and melanin synthesis in skin melanocytes of silky fowl. Moreover, both pre-treatments with Rp-cyclic AMPS or Adenylate Cyclase (AC) inhibitor NKY80 significantly inhibited the stimulatory effects of α-MSH on TYR activity, cAMP formation and melanin synthesis in skin melanocytes of Taihe silky fowls. These results confirm that, as a downstream signaling molecule of the α-MSH-MC1R signaling pathway, cAMP plays an important regulatory role in mediating melanin synthesis promoted by α-MSH in melanocytes of silky fowl.

Studies have indicated that maintaining cellular oxidative/anti-oxidative homeostasis is vital for melanin synthesis and oxidative stress can inhibit eumelanin synthesis by downregulating the expression of MC1R, TRP-1 and TYR genes [17-19]. It has been showed that heat stress induces oxidative stress in poultry, as reflected by tissue and lipid peroxidation, decreased antioxidant enzyme activity, and production of excessive free radicals, disturbing normal redox homeostasis, and leading to tissue and organ damage [20-23]. Dietary supplementation of antioxidants improves antioxidant capacity of cell and tissue, and effectively mitigates oxidative injury in heat stressed poultry [24]. Selenium (Se) is an essential trace element important for many physiological processes including the cellular response to oxidative stress, redox signaling, cellular differentiation, the immune response and reproduction [25]. Se is an integral component of selenoproteins with antioxidant function [26]. Dietary supplementation with Se improved total superoxide dismutase, catalase and glutathione peroxidase activities in serum, liver, kidney, pectoral muscle and skin of heat-stressed silky fowls [27]. Interestingly, our studies demonstrated that dietary supplementation of Se stimulates melanin biosynthesis in liver, kidney, pectoral muscle and skin of heat-stressed silky fowls and silky fowls reared under thermo-neutral temperature (21-24°C), and the stimulating effect of selenium on melanin synthesis is related to the increased antioxidant capacity of body exerted by Se [27,28]. Moreover, we found that heat stress reduced α-MSH secretion and MC1R gene expression and cAMP content in hypothalamus, liver, kidney, skin and pectoral muscle of silky fowl. Dietary Se supplementation alleviates negative effects on these parameters caused by heat stress. We also observed that heat stress also depressed melanin synthesis-related genes expression, and reduces TYR activity and melanin synthesis in tissues of silky fowls, whereas dietary supplementation with Se alleviates the negative effects caused by heat stress [27]. It is noteworthy that the expression level of MC1R was consistent with α-MSH secretion (hypothalamic and serum contents) under heat stress and Se regulation, and the variation trends of cAMP content in the pectoral muscles of heat-stressed silky fowls was similar to that of α-MSH content and MC1R expression in the same tissue. Based on the above results, it was hypothesized that heat stress affects the synthesis of melanin in silky fowl by affecting the secretion and expression of related factors α-MSH, MC1R and cAMP, while selenium could reverse these changes to maintain or promote the synthesis of melanin in the tissues of heat-stressed silky fowl, which further indicating that α-MSH-MC1R-cAMP signaling pathway also plays an important regulatory role in the synthesis of melanin in the tissues of silky fowl.

Collectively, the results indicated that α-MSH-MC1R-cAMP signaling pathway plays vital role in regulating the synthesis of melanin in melanocytes of silky fowl, and is a phylogenetically conserved pathway in the regulation of melanogenesis shared by both mammals and silky fowls.

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Conflict of Interest

There is no conflict of interest.

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