

Eureka Journal of Physical and Chemical Research (EJPCR)

ISSN 2760-490X (Online)

Volume 2, Issue 8, August 2026



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MOLECULAR CROSSTALK BETWEEN IRON DEFICIENCY AND HAIR FOLLICLE INTEGRITY: A COMPREHENSIVE MECHANISTIC REVIEW

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Abstract

Despite investigating the role of iron in non-scarring alopecia, a number of molecular and cellular mechanisms are still unclear. Iron deficiency and iron overload affect cellular processes, including mitochondrial respiration, cellular redox homeostasis, oxidative stress, and hormone synthesis. To regulate iron homeostasis, body tightly shifts iron import/export via the

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ISSN 2760-490X (Online)

Volume 2, Issue 8, August 2026



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hepcidin-ferroprotein axis. Detection of DNA and RNA with iron-responsive element/iron-regulatory protein system is another known mechanism. Connective tissue growth factor (CTGF) expression was downregulated in iron-depleted human fibroblasts. In hyperplastic Fxn^{-/-} mice, iron deficiency was reported to exacerbate CTGF and TGF- β , leading to excessive fibroblast production and reduced vessel maturation. Also, Jansen et al. reported that iron depletion reduced the proliferation of normal cultured human fibroblasts. Decreased hematopoietic iron noticed in the absence of iron overload led to decreased hemoglobin synthesis in iron-deficient zebrafish, resulting in vasculogenesis failure. Regeneration of hypertrophic cartilage maturation was achieved by manipulating iron metabolism through ascorbate treatment. According to other studies, iron overload might also lead to iron-induced oxidative stress, causing endothelial damage in the vasculature. Iron homeostasis regulates the balance of multiple growth factors known to regulate skin and hair follicle development and function. Iron-mediated changes in activity of hair cycle regulation, including Wnt/ β -catenin BMP TGF- β networks, in dermal papilla cells and other hair matrix cells, might also play a role in iron-related alopecia. Moreover, several human diseases have altered hair cycle control. Regardless, studies utilizing other hair cycle regulation markers should be incorporated for informative iron deficiency and oxidative stress studies. For malignant and neurodegenerative diseases, metabolomics—metabolic profiling of altered metabolites—has been employed for systemic trace iron processing. In order to enhance iron diagnostics, mitochondrial profiling and iron regulations in primary human skin have been investigated, utilizing systems biology approaches. Iron deficiency and hair loss can be revealed in iron-deficient mice and studies on systems biology approaches and iron depletion show hair loss correlation.

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ISSN 2760-490X (Online)

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Overall, the biological mechanisms of iron deficits in hair growth and the interaction between proteins and molecular processes should be further analyzed.

Keywords: Iron deficiency; hair follicle; oxidative stress; mitochondrial dysfunction; telogen effluvium.

1. Introduction

Iron deficiency is a systemic metabolic issue, resulting in a range of chronic clinical conditions due to its effects on cellular energy production and oxidative stress, as well as the inability to effectively heal injured tissues [22], [29], [35]. This systemic nature of iron metabolism is exemplified during the growth of hair follicles (HFs), which when compared with other epidermal-derived tissues, have increased sensitivity to iron metabolism due to their dependence on mitochondrial-dependent ATP production [22], [24], [27], [36]. Iron is also essential for the function of ribonucleotide reductase, a key enzyme involved in nucleic acid synthesis and thus, cell proliferation [18], [19]. In addition, iron is at the center of a range of biological processes, such as oxidative stress-mediated signaling and reactive oxygen species production, which are crucial to the normal cycling of HFs [29], [35], [52], [53]. In iron-deficient conditions, the regulation of HO-1, a key enzyme involved in the metabolic conversion of heme degradation, is misregulated leading to disrupted metabolic homeostasis and cell survival [30], [52]. Given the complex effects of iron deficiency on HF function and the systemic nature of this disorder, the need for better diagnostic biomarkers is paramount in order to provide a more robust diagnosis of systemic iron status and its tissue-specific impacts on HFs [71], [72], [73]. Current serum biomarkers for iron

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deficiency such as ferritin are inadequate tests of systemic iron status and, moreover, are not tissue-specific, excessively variable and confounded by a wide range of biological parameters [71], [72]. This wide range of factors that can influence the efficacy of iron biomarkers complicates the accurate determination and diagnosis of iron deficiency [71], [72]. Remarkably, this systemic nature of iron metabolism and its tissue-specific impact on HFs is poorly understood, and this gap in our understanding is likely due to the absence of an integrated systems biology approach combining high-throughput sequencing of tissue specimens obtained from adult and neonatal HFs as well as precociously and abnormally cycling HFs [73]. Given the complex nature of hair cycling and the systemic metabolism of iron, a systems biology approach is likely to provide insight into the molecular processes driving aberrant iron and metabolic homeostasis in HFs, potentially leading to tissue-specific biomarkers of iron deficiency [73]. Furthermore, a detailed understanding of the metabolic pathways dependent on iron metabolism would provide novel insights into how HFs respond to and efficiently utilize the iron they require for normal cycling, creating the potential to develop new therapies for the treatment of iron deficiency-associated hair loss through precision diagnostics and personalized treatments [73], [76], [81].

2. Systemic and Cellular Iron Homeostasis

The peptide hormone hepcidin, which is derived from the liver, is thought to play a key role in systemic iron homeostasis by causing the transmembrane iron exporter ferroprotein to internalize and degrade. In mammals, hepcidin is a regulatory peptide that, when necessary, can reduce iron accessibility for the body. [9]. Under physiological conditions, dietary iron absorption by duodenal enterocytes and macrophage iron recycling are dynamically

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ISSN 2760-490X (Online)

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regulated by systemic cues including inflammatory cytokines (e.g., IL-6) and erythroid regulators like erythroferrone [12, 15] (Fig. 1).

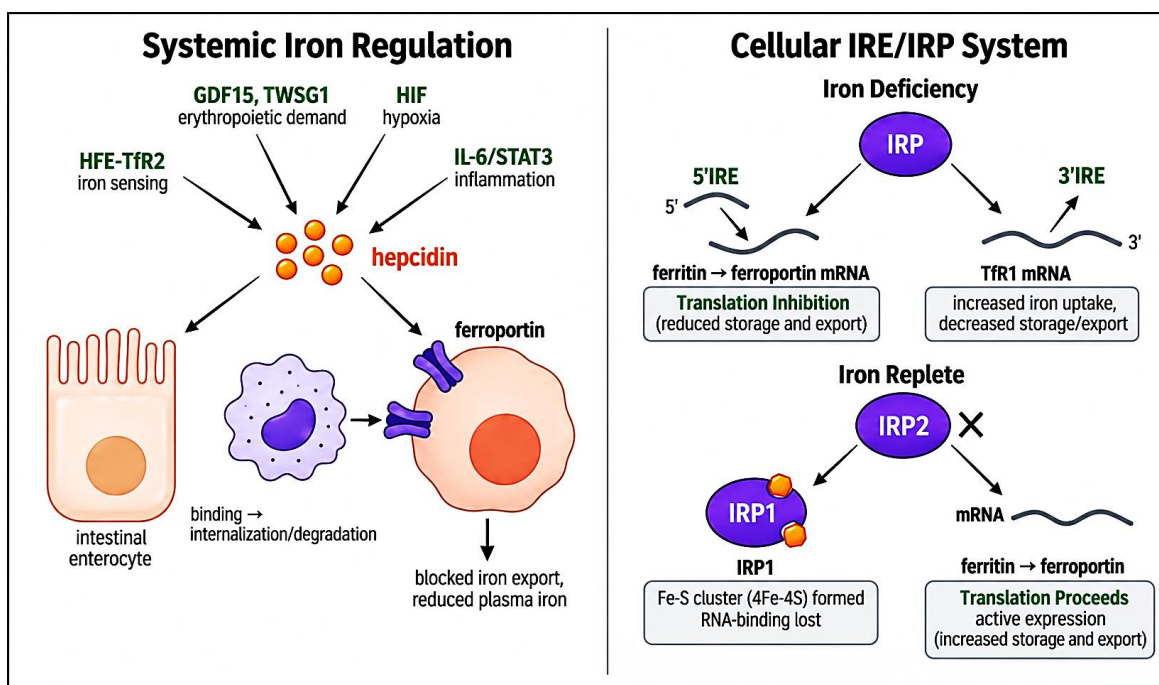


Figure 1. Systemic and cellular regulation of iron homeostasis through hepcidin-ferroportin signaling and the IRE/IRP system.

2.1 Systemic Iron Regulation: The Hepcidin-Ferroportin Axis

Systemic iron homeostasis is chiefly regulated by the hepatic peptide hormone hepcidin and its target, the cellular iron exporter, ferroportin (SLC40A1) [9,10]. Hepcidin is a 25-amino acid defensin family peptide that is mostly secreted by hepatocytes. It serves as the master regulator of systemic iron flux because it binds to ferroportin on the surface of cells that release iron—namely, duodenal enterocytes, macrophages, and hepatocytes. These binding

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ISSN 2760-490X (Online)

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initiates receptor internalization, ubiquitination, and lysosomal degradation [9]. Thus, this mechanism prevents cellular iron export and lowers plasma iron concentrations.

Hepcidin transcription integrates several physiological signals: (i) systemic iron availability, sensed through diferric transferrin (Tf-Fe₂) and mediated by the HFE-TfR2 complex; (ii) erythropoietic demand suppressed by erythroblast-derived factors such as growth differentiation factor 15 (GDF15) and twisted gastrulation 1 (TWSG1); (iii) hypoxia stabilizing hypoxia-inducible factors (HIF-1 α and HIF-2 α) suppresses hepcidin while enhancing iron absorption; and inflammatory signals, especially interleukin-6 (IL-6), activate the JAK/STAT3 pathway to induce hepcidin expression [11-14].

In a state of iron deficiency, hepcidin should be low to allow for increased intestinal absorption of iron at levels between 1–2 mg/day, coupled with enhanced macrophage release recycling of approximately 20–25 mg/day from old red cells [15]. The paradox is that inappropriate high levels of hepcidin found in anemia of chronic disease (ACD) and iron-refractory iron deficiency anemia (IRIDA), resulting from TMPRSS6 mutations block egress despite a systemic deficiency creating what can be termed functional iron deficiency [16,17].

2.2 Cellular Iron Metabolism and the IRE/IRP System

At the cellular level, the regulation of iron homeostasis is carried out by iron regulatory proteins 1 and 2 (IRP1 and IRP2), which attach themselves to iron-responsive elements (IREs) located within the untranslated regions of target mRNAs [18, 19]. This post-transcriptional regulatory system allows cells to quickly respond to changes in the availability of intracellular iron [18].

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Under conditions in which cellular iron is limited, active IRPs bind to 5' IREs present in the mRNAs for ferritin (FTH1, FTL) and ferroportin. This binding inhibits their translation, thereby preventing sequestration and export of iron; simultaneously, IRPs bind to 3' IREs in transferrin receptor 1 (TfR1) and divalent metal transporter 1 (DMT1) mRNAs, thereby stabilizing these transcripts and enhancing iron uptake under such conditions [18, 19]. Under conditions replete with iron, IRP1 assembles a 4Fe-4S cluster and loses RNA-binding activity, whereas IRP2 undergoes an iron dependent ubiquitination pathway, resulting in proteasomal degradation; this allows for translation to proceed during storage as well as protein export. The body precisely controls iron homeostasis through two layers of regulation: the systemic level and cellular level. At the systemic level, hepcidin inhibits ferroportin to reduce iron absorption and transportation. At the cellular level, cellular iron status is tightly controlled through the binding of iron-to-iron response elements (IRE) and iron response proteins (IRP). While this mechanism is efficient, it is not perfect, as it has its weaknesses. For example, when the body is in iron-deficiency states for a long time, high levels of iron absorption can occur with the inadequate amounts of iron storage, leading to the development of iron toxicity in the body. Moreover, the cellular level mechanism can also fail, especially in the case of oxidative stress. Oxidative stress leads to the modification of cysteine at position 399 of IRP1, and the loss of the ability of the protein to bind to IRE, thereby initiating the dysfunctionality of the protein.

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ISSN 2760-490X (Online)

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3. Iron in Mitochondrial Bioenergetics and Redox Regulation

3.1 Mitochondrial Iron Utilization and Fe-S Cluster Biogenesis

Mitochondria are the principal sites of cellular iron utilization, which is essential for heme and Fe-S cluster production [22, 24, 27]. Because mitochondria account for the majority of cellular iron use, they also play a central role in iron homeostasis, containing roughly 80% of cellular iron [22, 24]. Mitochondria import iron to synthesize heme and Fe-S clusters that are critical for metabolic functions, including cellular respiration and as cofactors in many mitochondrial enzymatic reactions [22, 24, 27]. Heme is synthesized in an eight-step pathway, with the initial step being the formation of porphobilinogen from succinyl-CoA and glycine. This step is catalyzed by the enzyme ALA synthase (ALAS) and requires iron [22]. The putative second step, the formation of uroporphobilinogen from uroporphobilinogen decarboxylase (PBGD), is also inhibited under conditions of iron deficiency [22]. For the remainder of the pathway, heme is synthesized from the addition of several moieties, each requiring iron [22]. Iron is also important for mitochondrial usage in synthesizing Fe-S clusters. The first step requires the formation of a sulfurated backbone (cysteine desulfurase NFS1) that contains sulfur, along with a scaffold protein (ISCU) and several additional factors to obtain a fully functional cluster [24, 27]. Mitochondria are able to import certain mitochondrial iron transporters. Recent evidence suggests several mechanisms for iron entry via mitochondrial proteins, such as mitoferrin-1 and mitoferrin-2. These two transporters belong to the SLC25 family of solute carriers, specifically those involved in the transport of various metals [24, 27]. Iron overload associated with dysregulation may also arise as a consequence of genetic issues in SLC25A38 [24, 27]. Increased levels of iron-containing heme and Fe-S clusters in the mitochondria specifically may contribute to

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ISSN 2760-490X (Online)

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mitochondrial oxidative stress via a Fenton reaction, which degrades both iron and reactive oxygen species (ROS) [27, 49]. In addition, intermediates in the TCA cycle may be recycled to supply critical amino acids for other cellular processes as a cellular response to iron loading [27].

Many of the iron-regulatory processes in mitochondria are interrelated with mitochondrial redox reactions associated with oxidative phosphorylation [22, 27]. Iron is essential for the proper accumulation of iron in mitochondrial electron transport chain complexes I–IV [22, 27]. As a result, iron deficiency limits electron entry in the TCA cycle and reduces iron in the electron transport chain. This subsequently impairs oxidative phosphorylation and increases the levels of reactive oxygen species [22, 27, 49]. Thus, iron is essential in maintaining close ties in cellular iron regulation and oxidative phosphorylation [22, 27]

3.2 The Labile Iron Pool and Oxidative Stress

Labile iron pool (LIP) is a key source of free iron for a myriad of cellular metabolic processes. Too much free iron can, however, react in degenerative chemical processes that cause oxidative stress, such as the Fenton reaction and the Haber-Weiss cycle [29, 30]. A main mechanism that safely buffers excess free iron is via conversion to less soluble forms through ferritin. Decreased ferritin expression precipitates an increase in LIP, culminating in elevated levels of generation of reactive oxygen species (ROS) [29, 35]. The heavy chain (FtH1) of ferritin possesses iron-oxidizing (ferroxidase) activity, while the light chain (FtL) is responsible for iron nucleation and assembly of the ferritin cage. Interestingly, targeting of FtH1 in the mouse causes embryonic lethality, indicating a crucial dependence of both early development and adult life on iron ferrooxidation by ferritin [35].

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ISSN 2760-490X (Online)

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Additionally, cellular inactivity of an iron chaperone, PCBP1, leads to an increase in LIP. Conversely, PCBP1-dependent temporary retention of iron in a soluble form leads to a decreased pool of excess metabolic iron [35]. Mitochondrial iron deficiency leads to imbalance in the electron transport chain (ETC) and apoptosis [22, 29]. Hence, in addition to essential physiological processes, the capacity to temporarily buffer excess iron is a key requirement for oxidative repair, cellular persistence in the face of iron starvation, and metabolic homeostasis. Reactive iron, mitochondrial integrity, and persistent iron homeostasis are all cellular requirements that must be coordinated through the action of intracellular iron chaperones, buffering molecules, and a network of iron transport channels that ensure iron remains safely and accurately metabolized [29, 35]

4. Hair Follicle Biology and Cyclic Regeneration

Mitochondria serve as critical hubs for cellular iron utilization, utilizing mitoferrin transporters (MFRN1/2) to import iron into the matrix [24]. Once imported, iron is utilized for iron-sulfur (Fe-S) cluster biogenesis and heme biosynthesis, essential processes for maintaining electron transport chain activity and cellular bioenergetics [22, 27]. Disruption of mitochondrial iron trafficking leads to bioenergetic failure and oxidative stress [49] (**Fig. 2**).

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ISSN 2760-490X (Online)

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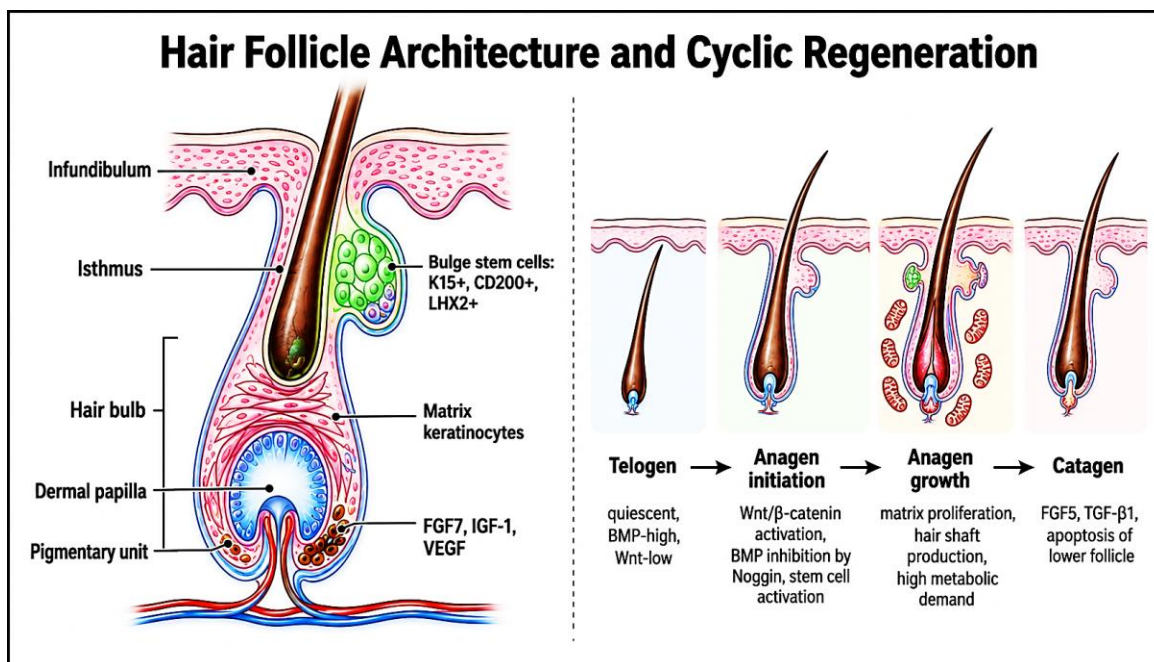


Figure 2. Hair follicle architecture and cyclic regeneration from telogen through anagen and catagen.

4.1 Hair Follicle Architecture and Stem Cell Compartments

The hair follicle is a complex mini-organ that has already reached maturity [36]. It consists of epithelial, mesenchymal, melanocytic, and neural components [36, 40]. In terms of structure, it can be divided into a permanent upper region (infundibulum and isthmus) and a cycling lower region (suprabulbar epithelium and hair bulb) [36, 39]. The isthmus contains the bulge area where human epithelial hair follicle stem cells are found; these are marked by expressions of keratins 15 and 19, CD200, and LHX2 [37, 38]. These quiescent cells are activated during the transition from telogen to

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ISSN 2760-490X (Online)

Volume 2, Issue 8, August 2026



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anagen to create transient amplifying matrix cells that form hair shafts [36, 38, 39].

Matrix keratinocytes in the hair bulb are among the fastest dividing cells in mammals, dividing every 12–24 h at peak anagen times [36, 39]. The matrix keratinocytes surround the dermal papilla; this is an exceptionally small group of mesenchymal fibroblasts which controls how big a hair bulb gets, how wide its shaft will be, how long it stays in the anagen phase, and so on by means of signaling between cells [36, 40]. The dermal papilla contains growth factors, such as IGF-1, FGF7, and VEGF, which promote the proliferation of matrix cells and inhibit apoptosis [40].

The pigmentary unit of the hair follicle is situated at the very top of the bulb and consists of melanocyte stem cells and differentiated melanocytes that provide melanin to keratinocytes to determine color [41]. Melanocytes are very vulnerable to oxidative stress because melanin synthesis is pro-oxidant; this process requires tyrosinase to hydroxylate tyrosine [41].

4.2 The Hair Cycle: Molecular Orchestration

The hair cycle has three main phases: anagen (growth), catagen (regression), and telogen (resting). The start of anagen requires the coordinated activation of Wnt/ β -catenin signaling, which stabilizes β -catenin in the nucleus to activate TCF/LEF transcription factors and drive the expression of cell cycle regulators, including cyclin D1 [42]. BMP signaling keeps stem cells quiet in telogen; it must be inhibited by BMP antagonists, such as noggin, before stem cells can be activated [43].

Catagen is marked by a huge, coordinated killing off cells in the lower part of the follicle, led by signals that encourage apoptosis, such as FGF5, TGF- β 1, and neurotrophins through their receptors [44,45]. The induction of certain

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ISSN 2760-490X (Online)

Volume 2, Issue 8, August 2026



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phases of the hair cycle is mediated by the immune system. Macrophages at the base of the hair follicle are thought to be important mediators of the prolonged growth phase of anagen, and several barriers must be breached before tissue macrophages are able to migrate to the hair follicle. As a hair follicle becomes quiescent, these tertiary lymphoid structures must disband. Other immune cell types poised at the base of the follicle, such as mast cells, provide rapid immune responses that facilitate the transition to an actively cycling hair follicle. In addition, T cells play a role in hair cycling, likely aiding the transition from telogen to anagen [44, 45].

To maximize the intrafollicular metabolic demands required for the rapid proliferation of matrix keratinocytes, the hair follicle during the anagen phase requires high energy, and several metabolic pathways must be upregulated to meet these demands. Suprabasal matrix keratinocytes produce keratins, melanin pigment granules, and lipids that function as structural components and reservoirs for lipophilic vitamins. These biosynthetic processes rely on mitochondrial ATP production and, consequently, on efficient mitochondrial oxidative phosphorylation. Mitochondrial electron transport chain can be regulated by iron supply, which is essential for the reduction of coenzymes such as cytochrome c and the expression of mitochondrial ncRNA. Consequently, iron can regulate mitochondrial oxidative respiration and ATP synthesis directly and indirectly via other cellular signaling pathways that can potentially influence DNA synthesis and subsequent mitochondrial biogenesis. [22, 27, 36, 39, 40].

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ISSN 2760-490X (Online)

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5. Mechanisms of Iron Deficiency-Induced Follicular Dysfunction

5.1 Mitochondrial Bioenergetic Failure

The hair follicle undergoes cyclical transitions between resting (telogen phase) and active (anagen phase) states, during which large quantities of ATP are produced, required for the high proliferative and metabolic activity of hair follicle matrix keratinocytes. Such high turnover rate of matrix keratinocytes requires a continuous supply of nucleotides, which are crucial for DNA synthesis and cell cycle progression, while cytoskeleton components and ATP are required for hair shaft formation. ATP is extensively produced in mitochondria as a result of oxidative phosphorylation (OXPHOS), an energy-generating process in which molecular oxygen participates as a terminal electron acceptor in the oxidation of substrates in mitochondrial matrix and proton transport into intermembrane space. Due to requirement of iron for heme biosynthesis, deficiency in this mineral leads to impaired heme and cytochrome synthesis and ultimately reduced activity of the electron transport chain and diminished oxidative phosphorylation as well. [22], [27], [36], [39]. Iron deficiency adversely impacts cellular metabolism through various cellular and molecular mechanisms. Iron plays a pivotal role in modulating cellular metabolic pathways, thus iron deficiency can cause metabolic dysregulation within cells. One of the hallmarks of cellular iron deficiency is cytosolic and/or mitochondrial protoporphyrin IX accumulation, caused by dysregulated heme synthesis (due to lack of iron) which subsequently suppresses the expression of mitochondrial and cellular cytochromes that are vital for mitochondrial function and cellular respiration. Deleterious accumulations of protoporphyrin IX, compounded by suppression of cytochromes, contribute to disrupted TCA cycle metabolism and impaired iron-dependent enzymes involved in cellular respiration (for example,

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ISSN 2760-490X (Online)

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aconitase and isocitrate dehydrogenase), ultimately compromising mitochondrial function and limiting the supply of energy to rapidly proliferating matrix keratinocytes. [22], [27].

Reduced ATP availability impairs DNA replication, chromatin remodeling, mitotic spindle formation, and cell cycle progression, ultimately triggering activation of the p53/p21 signaling pathway and cell cycle arrest. Persistent iron deficiency may therefore promote premature transition from anagen to catagen or telogen, contributing to the development of telogen effluvium through impaired follicular proliferation and mitochondrial dysfunction [22], [36], [39].

5.2 Oxidative Stress and Lipid Peroxidation

The effects of iron deficiency on redox environments of cells cannot be underestimated. Paradoxically at iron deficiency, cells even show a decreased total intracellular iron while at the same time elevated steady state levels of increased redox-active iron species. This is the result of iron responsive element (IRE)-mediated translational repression of ferritin expression which in turns leads to an increased labile iron pool. Here, we present the case of how an iron deficiency-associated objectification of redox ‘silencing’ at the level of gene expression contributes to total loss of iron-dependent regulation [52]. At the same time, ETC function impairment leads to more electron leakage and superoxide ($O_2^{\bullet-}$) generation. Superoxide dismutase converts $O_2^{\bullet-}$ into hydrogen peroxide (H_2O_2), which in turn can create hydroxyl radicals if there is low but catalytically active iron present through Fenton chemistry [30].

Hair follicles have an increased susceptibility to oxidative damage due to multiple reasons. First, they have a very high proliferation rate of matrix cells

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ISSN 2760-490X (Online)

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that produce large amounts of endogenous ROS as byproducts of mitochondrial respiration. Second, melanin synthesis in the pigmentary unit generates hydrogen peroxide due to tyrosinase activity. Third, this structure is exposed to exogenous oxidative insults, such as ultraviolet radiation and environmental pollutants [53].

Oxidative stress manifests in multiple pathways of damage within the follicle. Lipid peroxidation increases membrane permeability by affecting mitochondrial and plasma membranes, while compromising compartmentalization. DNA is oxidized when guanine is modified into 8-oxoguanine, which brings mutations and activates pathways for responding to DNA damage through p53 and PARP-1, potentially triggering cell cycle arrest or apoptosis [54]. Protein oxidation affects structural proteins (keratins) and enzymes (tyrosinase, ribonucleotide reductase) that would both the hair shaft integrity and melanogenesis. The "free radical theory of graying" places cumulative oxidative damage to melanocyte stem cells as well as differentiated melanocytes among primary drivers of hair graying [55].

Iron deficiency is among the most prevalent nutritional disorders worldwide and is closely associated with oxidative stress, a condition characterized by an imbalance between pro-oxidant and antioxidant systems that contributes to the development of chronic diseases. Although free heme-bound iron can promote oxidative damage, it is also indispensable for maintaining mitochondrial metabolism and antioxidant defense through its role as a cofactor for heme-containing enzymes, including catalase, glutathione peroxidase, and heme oxygenase-1 (HO-1). Consequently, disruption of iron homeostasis impairs mitochondrial function, disturbs redox balance, and promotes oxidative stress [29], [30], [35].

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Increased reactive oxygen species (ROS) generation, resulting from nutrient deficiency, metabolic dysfunction, or activation of NADPH oxidase, further exacerbates oxidative damage and compromises cellular redox homeostasis. Collectively, these mechanisms contribute to persistent redox dysregulation and mitochondrial dysfunction associated with iron deficiency [29], [30], [35].

5.3 Ferritin Dysregulation and Intracellular Iron Maldistribution

Serum ferritin is commonly used as a biomarker for assessing body iron stores; concentrations below 15 ng/mL, for instance, indicate iron deficiency. However, serum ferritin is not as adequate in reflecting tissue iron availability and status despite normal or elevated levels. Its concentrations are influenced by a variety of physiological and pathological factors, and therefore may not indicate intracellular iron pool information related to those factors. In addition, ferritin is not only involved in storing iron, but it also has roles that are important for erythropoiesis and immune responses. Due to these additional roles, it is possible that the amount of iron stored in ferritin does not reflect tissue iron availability. Ferritin cannot be considered an ideal biomarker for monitoring body iron stores and making clinical decisions regarding iron therapy. [71], [72].

Mechanism mediating cellular iron homeostasis, To regulate cellular iron homeostasis, cells employ the iron-regulatory proteins (IRPs) that directly interact with the iron-responsive elements (IREs) located in the mRNAs of the targets (Fig. 1B). Under iron-deficient conditions, the IRP binds to IREs to stabilize and increase translation of the mRNA of iron transport proteins, such as the transferrin receptor (TfR) and divalent metal transporter 1, and inhibit translation of ferritin to reduce iron bioavailability. Conversely, upon

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increased intracellular iron bioavailability, mostly by uptake of transferrin-bound iron through endocytosis-mediated exocytosis, IRP releases from IREs thereby stimulating ferritin expression, and blocking the protein synthesis of iron transport proteins to prevent excessive iron uptake. By utilizing the expression of ferritin and iron transport proteins, cells effectively regulate cellular iron homeostasis. Besides the roles of IRPs and ferritin during the cellular iron homeostasis, there are also cellular mechanisms for systemic iron homeostasis. [18], [19], [71].

Ferritins are the biological substrates for iron biomineralization in a wide range of organisms. The ferritins consist of subunit proteins that self-assemble into an essentially spherical structure to form the mineralization core. Mitochondrial ferritin (FtMt) as a nuclear-encoded protein that is imported into the mitochondria, and for which there are indications that it is organelle-specific for iron storage. Different from the classical ferritin, FtMt iron storage is not regulated in a manner considered conventional with an iron-responsive element/iron regulatory protein (IRE/IRP) system, and FtMt appears to be predominantly expressed in the high oxidative metabolism tissues. [59]. Although its expression in hair follicles has not been fully characterized, FtMt may protect mitochondrial DNA and electron transport chain components from iron-mediated oxidative damage while maintaining iron availability for heme and Fe-S cluster biosynthesis. Dysregulation of FtMt under iron-deficient conditions may therefore enhance mitochondrial oxidative stress and further impair mitochondrial iron metabolism [59].

5.4 Disruption of Follicular Signaling Pathways

Iron metabolism is closely integrated with the signaling pathways that regulate hair follicle stem cell activation, proliferation, and survival. Iron

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deficiency disrupts these molecular networks, thereby impairing normal hair follicle cycling and contributing to the development of alopecia. Canonical Wnt/ β -catenin signaling is a key regulator of anagen initiation through stabilization of β -catenin and activation of target genes, including cyclin D1 and c-myc. Iron deficiency-associated oxidative stress destabilizes β -catenin through oxidation of critical cysteine residues and activation of glycogen synthase kinase-3 β (GSK-3 β), promoting β -catenin degradation. In addition, iron-dependent prolyl hydroxylases regulate hypoxia-inducible factors (HIFs), thereby modulating Wnt signaling. Consequently, impaired Wnt signaling suppresses stem cell activation and prolongs the telogen phase [42], [60].

Bone morphogenetic protein (BMP) signaling maintains quiescent bulge stem cells through Smad-mediated transcription of cell-cycle inhibitors, whereas suppression of BMP activity is required for anagen initiation. Aberrant BMP activation results in stem cell depletion, impaired follicular cycling, and scarring alopecia. Iron deficiency may disrupt BMP signaling through oxidative modification of BMP receptors and Smad proteins, mitochondrial dysfunction, and altered hepcidin regulation, collectively compromising hair follicle activation and regeneration [61].

Transforming growth factor- β (TGF- β) is a major inducer of catagen through activation of Smad2/3 signaling and upregulation of pro-apoptotic Bcl-2 family proteins. Iron deficiency, together with IL-6/STAT3-mediated hepcidin induction, reduces iron availability and sensitizes follicular cells to TGF- β -mediated apoptosis. These events are accompanied by loss of mitochondrial membrane potential, reduced expression of anti-apoptotic Bcl-2, and accelerated follicular regression [62], [63].

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ISSN 2760-490X (Online)

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Sonic hedgehog (Shh) and Notch signalling are shown to play a fundamental role in hair follicle morphogenesis and dermal papilla maturation, but how they actually regulate cell fate determination is still unclear. Therefore, it is the aim of this study to investigate the mode of action of Shh and Notch-regulated mitochondrial function on cellular energy metabolism, especially how mitochondrial function can affect the cellular NAD^+/NADH balance, which in turn provides ATP to fuel Notch-dependent differentiation. To understand whether mitochondrial dysfunction due to iron deficiency can promote hair follicle cycling, not only the effects of mitochondrial function on cell metabolic fate was studied but also whether dietary iron deficiency can impact the overall cellular redox state and thereby affect the overall health and viability of vehicles by increasing reactive oxygen species (ROS). [64], [65].

5.5 Potential Role of Ferroptosis in Follicular Damage

Ferroptosis, a type of regulated cell death identified recently, is characterized by the accumulation of lipid hydroperoxides in an iron-dependent manner. The term ferroptosis is derived from the Latin word “ferrum,” meaning iron, and the Greek word “ptosis,” meaning falling. The iron-dependent accumulation of lipid hydroperoxides is primarily caused by, glutathione (GSH) depletion, impaired GPX4 activity, and oxidative stress caused by Fenton reactions []. In ferroptosis, lipid peroxidation results in the accumulation of toxic lipid hydroperoxides, causing cell damage that may eventually lead to necrosis in cells, while apoptosis only manifests near the end of the cells death process. Ferroptosis is characterized by mitochondrial remodeling by inhibiting complex I and II of the electron transport chain. This disruption of the electron supply and electron transport chain coupled with the build up of iron ions induces the Fe^{2+} ions to catalyse mitochondrial lipid

Eureka Journal of Physical and Chemical Research (EJPCR)

ISSN 2760-490X (Online)

Volume 2, Issue 8, August 2026



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peroxidation leading to excess generation of lipid peroxides which results in oxidative stress throughout the cell. [29], [35].

The metabolic processes of iron and its role as a leading cause of free radicals production and oxidative stress comprise an important component of the pathophysiology of neurodegenerative disorders such as Alzheimer's disease and Huntington's disease. These disorders share common features such as excessive levels of reactive oxygen species and increased lipoperoxidation, both of which lead to ferroptosis. Ferroptosis also serves important functions in hair follicle biology, where its modulation is necessary for various hair follicle morphogenetic events. This connection between iron metabolism and oxidative stress supports the involvement of ferroptosis in the pathophysiology of neurodegenerative disorders and the regulation of directed cellular plasticity during hair follicle morphogenesis, both systems of which may have originated billions of years ago, and together comprise a structured and functionally united network of biomechanical and biochemical processes. degeneration of melanocytes contributes to hair graying. Iron deficiency-associated oxidative stress may promote lipid peroxidation and melanocyte injury, suggesting that ferroptosis could represent a potential mechanism underlying pigment loss and hair follicle dysfunction [29], [35].

Although the role of ferroptosis in iron deficiency-associated alopecia has not been fully established, targeting ferroptosis-related pathways may represent a promising therapeutic strategy for preventing hair graying and mitigating hair follicle degeneration associated with disrupted iron homeostasis [29], [35].

6. Clinical Evidence and Diagnostic Limitations

Iron plays a multifunctional role in biological systems. Within the cell, iron is shuttled back and forth between various cellular compartments, resulting in

Eureka Journal of Physical and Chemical Research (EJPCR)

ISSN 2760-490X (Online)

Volume 2, Issue 8, August 2026



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distinct iron kinetics. Thus, cellular iron distribution, as well as the dynamics of the cellular iron pool over time, can be controlled with iron and metal chelators. At certain pools of iron, iron can exert toxic functions by generating excessive reactive oxygen species through various mechanisms such as the Fenton reaction. The accumulation of labile iron can precipitate the depletion of stored iron in ferritin, which can compromise antioxidant defenses and facilitate redox cycling of iron. As a consequence, cellular lipid peroxidation can occur, leading to ferroptosis, an iron-dependent form of regulated cell death. The specific kinetics of iron within a cell/cell-type, therefore, affects iron-dependent cellular mechanisms, including cellular damage and cell death. [29, 35] (**Fig. 3**).

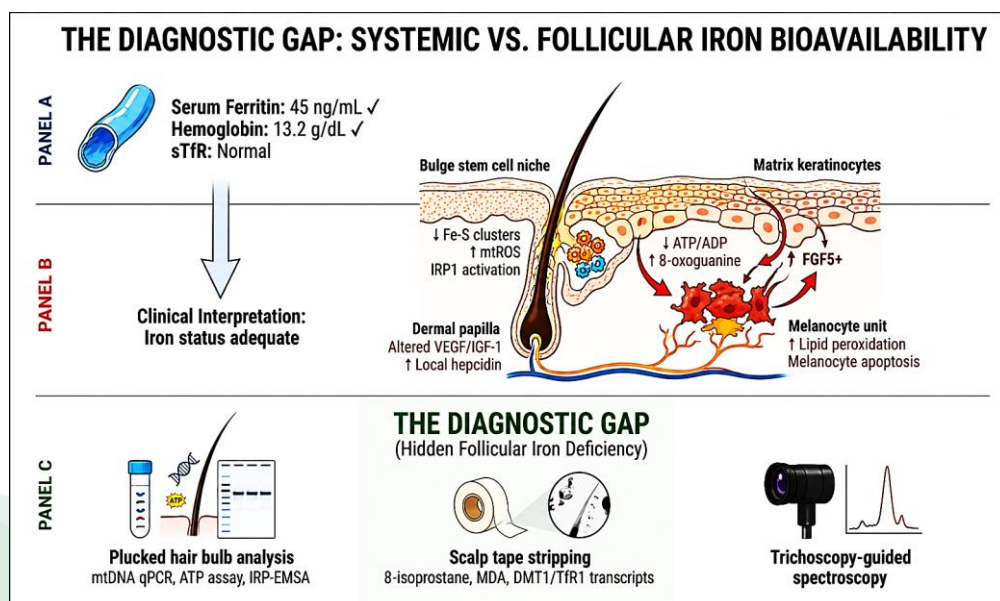


Figure 3. Diagnostic gap between systemic iron markers and follicular iron bioavailability.

Eureka Journal of Physical and Chemical Research (EJPCR)

ISSN 2760-490X (Online)

Volume 2, Issue 8, August 2026



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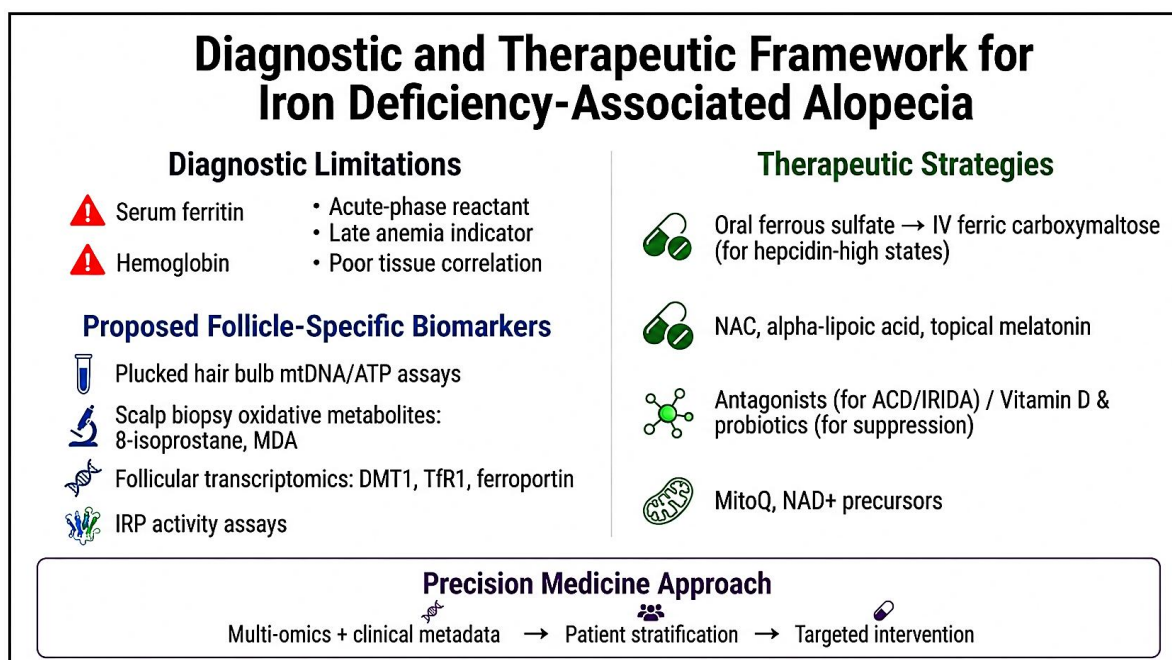


Figure 4. Diagnostic and therapeutic framework for iron deficiency-associated alopecia.

The mammalian skin contains the very versatile appendages known as hair follicles (HFs). A unique aspect of HFs is their cyclical regeneration and subsequent involution. HFs continue to develop throughout the life span of mammals and undergo cycles of growth (anagen), regression (catagen), and rest (telogen), with prompt resumption of growth after the rest period. In the bulge niche of the HF, which contains hair follicular stem cells, the Wnt/-catenin and Sonic Hedgehog (Shh) pathways are both involved, which indicates the signaling pathways involved in HF development and maintenance, as an active hair cycle indicates a normal HF. Specialized signaling centers such as the dermal papilla have also been recognized as

Eureka Journal of Physical and Chemical Research (EJPCR)

ISSN 2760-490X (Online)

Volume 2, Issue 8, August 2026



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important components to induce HF development. Recent discoveries suggest that specialized dermal papilla signaling induces epithelial proliferation and that various other dermal components may participate in termed dermal signals. [5, 40] (Fig. 4).

6.1 Epidemiological Associations

Iron is an essential component of hemoglobin in erythrocytes, which is why its deficiency can lead to anemia in cases of severe iron-deficient states. It also has clinical evidence linking it to many other metabolic processes, including hair loss. Several studies have established that iron deficiency, as evidenced by low serum ferritin concentrations (<40 ng/mL), is most commonly associated with diffuse telogen effluvium. They have also demonstrated the effectiveness of iron supplementation in reversing hair loss when low serum ferritin concentrations have been confirmed. The evidence linking iron deficiency with hair loss caused by alopecia areata remains more controversial due to conflicting findings. Iron and its deficiency lead to several molecular mechanisms that promote growth and survival of hair follicles and hair, and it is possible that these pathways may be impaired in the presence of iron deficiency. The link between iron and androgenetic alopecia remains still farther from being established. [75].

The timeline for clinical improvement and hair regrowth in individuals with iron deficiency and telogen effluvium is discussed. In individuals with iron deficiency, clinical improvement may occur within weeks of initiating treatment. However, measurable hair regrowth can require a longer time frame of at least 3–6 months. The hair growth cycle is the explanation for this time frame, requiring an adequate number of hair follicles to re-enter anagen or the growing phase. Furthermore, the effects of iron deficiency on hair

Eureka Journal of Physical and Chemical Research (EJPCR)

ISSN 2760-490X (Online)

Volume 2, Issue 8, August 2026



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shedding appear to be milder than those from other causes of telogen effluvium, such as severe stressful events or illness that precipitate significant and ongoing hair shedding. Therefore, the timeline for clinical improvement and hair regrowth can be more favorable than for other causes of telogen effluvium. [76].

6.2 Limitations of Conventional Biomarkers

Currently, the assessment of iron status in clinical practice is mostly based on serum ferritin and hemoglobin. These indicators have major drawbacks when it comes to hair follicle pathology. Serum ferritin is an acute-phase reactant; inflammatory states, infections, neoplasia, and liver disease may raise serum ferritin levels even with depleted tissue iron stores. This situation might create a false impression of normal functional iron status [71]. On the other hand, serum ferritin does not always indicate the availability of intracellular iron in highly metabolic tissues.

Hemoglobin concentration can be used for diagnosing anemia but is known as a late marker for iron deficiency. It has been suggested that hair follicle dysfunction happens before overt anemia develops since the high metabolic demands of the follicle would make it sensitive to early depletion of iron long before there was any compromise to erythropoiesis. Soluble transferrin receptor (sTfR) and sTfR/log(ferritin) index are more sensitive measures of tissue iron deficiency; however, they are not routinely assessed in dermatological practice [72].

Follicle-specific biomarkers have yet to be developed but should meet an urgent clinical need. Some potential candidates include: (i) markers of mitochondrial function, such as mtDNA copy number and ATP production rates, measured in plucked hair bulbs; (ii) metabolites indicating oxidative

Eureka Journal of Physical and Chemical Research (EJPCR)

ISSN 2760-490X (Online)

Volume 2, Issue 8, August 2026



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stress, such as 8-isoprostanes and malondialdehyde from scalp biopsies; (iii) assays for activities of iron regulatory proteins; and (iv) transcriptomic profiling of follicular iron transporters including DMT1, ferroportin, and TfR1 [73]. A rigorous integration of molecular metrics with conventional hematological parameters may open new cooperative avenues with a scientific rigor aimed to develop a well-sustained ecosystem to constant improvement of the precision diagnostics of alopecia situations such as those related to iron deficiency.

7. Proposed Unified Mechanistic Model

Iron deficiency is the most prevalent nutritional deficiency and one of the top causes of hair loss. The suspicion of an association between iron levels and hair loss has existed for centuries, although it has only recently become a topic of scientific discussion. Several nonrandomized studies on small populations (mostly among women) have demonstrated an association between hair loss and low serum iron, ferritin, or hemoglobin levels. However, the precise mechanism by which iron deficiency alters hair follicle function remains unclear. Hair follicles are actively cycling structures that undergo periodic phases of growth (anagen), regression (catagen), and rest (telogen). Much of the high cellular activity during the anagen phase is fueled by aerobic respiration through mitochondrial oxidative phosphorylation, which produces most cellular ATP. Mitochondrial bioenergetics are intimately linked to cellular iron metabolism. Iron deficiency inhibits mitochondrial respiration due to the reduced availability of its most important components: heme and iron-sulfur clusters. This disruption decreases ATP production, leading to increased AMP levels and the activation of AMP-activated protein kinase (AMPK). AMPK acts as a cellular energy sensor, inhibiting energy-intensive

Eureka Journal of Physical and Chemical Research (EJPCR)

ISSN 2760-490X (Online)

Volume 2, Issue 8, August 2026



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processes (e.g., lipogenesis, protein synthesis) and instead promoting catabolic pathways (e.g., glucose and fatty acid oxidation) to restore ATP levels. In the case of iron deficiency, activated AMPK inhibits cell cycle progression and causes cell cycle arrest in hair follicle progenitor cells, leading to hair follicle miniaturization and impaired regeneration. Further elucidation of the role of iron homeostasis in hair follicle biology may lead to novel therapeutic strategies based on site-specific iron supplementation. [22], [27], [36]. (Fig. 5).

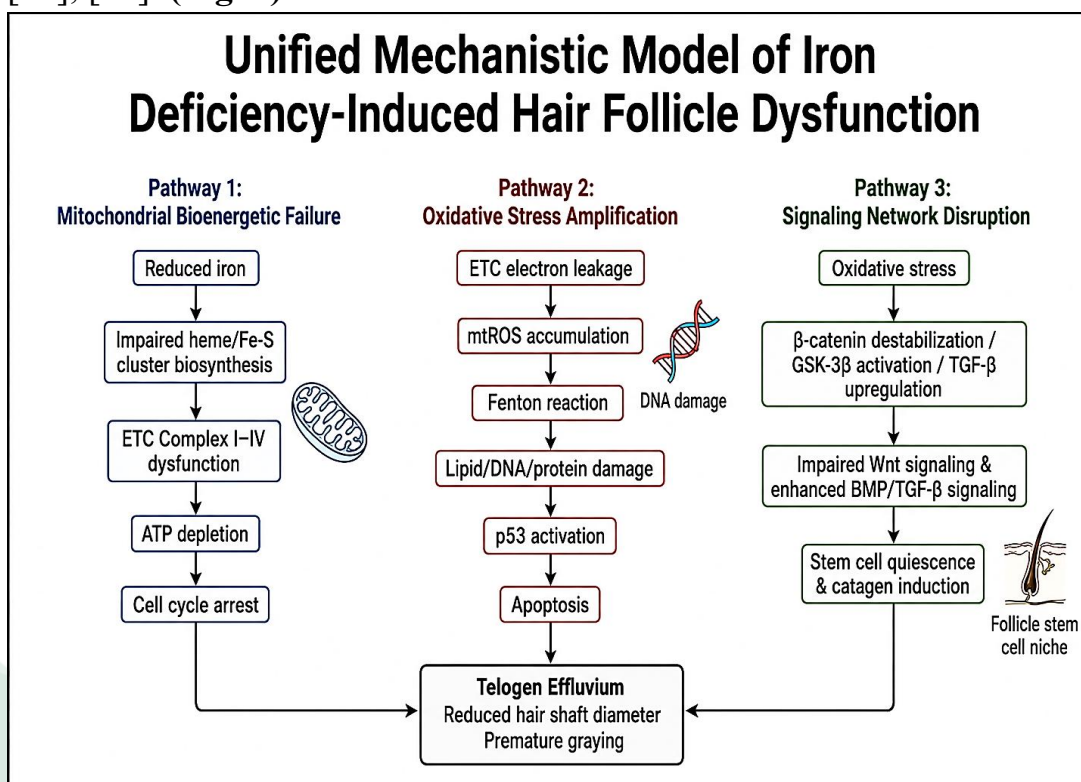


Figure 5. Unified mechanistic model linking iron deficiency to mitochondrial bioenergetic failure, oxidative stress, signaling disruption, and follicular dysfunction.

Eureka Journal of Physical and Chemical Research (EJPCR)

ISSN 2760-490X (Online)

Volume 2, Issue 8, August 2026



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Evidence suggests hair loss due to iron deficiency may be driven via telogen effluvium. Iron is a crucial co-factor for mitochondrial oxidative phosphorylation and ATP production in the electron transport chain and, therefore, integral for the health of hair follicles. Iron is also necessary for heme biosynthesis, and therefore iron deficiency leads to mitochondrial dysfunction and oxidative stress in follicle cells that can result in premature differentiation and apoptosis, leading to a reduction in hair shaft production. Consequently, the anagen maintenance stage of the hair cycle is severely impaired. For this reason, iron deficiency can indeed lead to reduced hair shaft production and loss from the body. [22], [27], [36].

Impaired heme synthesis is an essential mechanism of mitochondrial dysfunction, which is attributed to several human diseases. Compromised mitochondrial respiratory complexes in various cell types cause increased electron leakage and excessive mitochondrial reactive oxygen species, leading to elevated oxidative stress and subsequent lipid, protein, and DNA damage. Mitochondrial dysfunction can also contribute to cell death through apoptosis, which is associated with the severe loss of follicular melanocytes. This is because oxidative stress causes the apoptosis of follicular melanocytes, leading to diffuse hair shedding, decreased hair shaft diameter, hair graying, and even alopecia areata. Thus, conditions that impair heme synthesis can lead to diffuse hair loss, in addition to other symptoms, based on mitochondrial function. Elevated mitochondrial reactive oxygen species are generated due to compromised mitochondrial complexes leading to mitochondrial dysfunction, which causes diminished mitochondrial function. [29], [35], [55].

Mitochondrial dysfunction disrupts the ratios of NAD^+/NADH and ATP/AMP , leading to altered activity of AMPK, Sirtuins, and mTOR which

Eureka Journal of Physical and Chemical Research (EJPCR)

ISSN 2760-490X (Online)

Volume 2, Issue 8, August 2026



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suppress Wnt/ β -catenin-mediated stem cell activation and enhance the TGF- β signaling pathway to promote telogen retention and impair hair follicle regeneration, linking this event to hair loss, as shown in studies by Wang et al. and Choi et al. Therefore, mitochondrial dysfunction can be a cause of iron deficiency. Insufficient iron can result in impaired ATP production and Aoxidative phosphorylation, leading to increased reactive oxygen species (ROS) and metabolic imbalance. Researchers have also elucidated that the transfer of iron in the body is regulated by iron-regulatory proteins (IRPS), including IRP1 and IRP2, and several heme-dependent transcription factors. Mitochondrial dysfunction contributes to impaired hair follicle stem cell activation and hair loss-associated iron deficiency. Elevated oxidative stress, caused by abnormal iron metabolism, is also thought to be involved in disorders associated with iron deficiency.

Iron deficiency causes excessive oxidative stress, exacerbating iron metabolism and potentially disrupting stem cell activation. The abovementioned possibilities indicate that iron deficiency is involved in hair loss. [42], [60], [62], [63]

8. Therapeutic Implications and Future Directions

In patients with non-anemic iron deficiency and hair loss, a multi-pronged treatment approach can be effective in addressing the deficiency and promoting hair growth. Oral or intravenous iron repletion will help replace the iron deficiency. However, standalone iron therapy may not produce the best results in iron replete patients with elevated hepcidin levels that are induced by inflammation or in response to other factors, such as excess body fat. Pioneering work has been done in modulating the hepcidin pathway using investigational Mini hepcidins to enhance iron absorption and utilization.

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ISSN 2760-490X (Online)

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Other strategies involve block hepcidin activity to enhance iron availability to the body and hair follicles. Deficiency of vitamin D can increase hepcidin activity and reduce the efficacy of iron therapy. Leucine-rich peptide 2 (LRP2) serves as a receptor for circulating vitamin D to translocate it into cells. Supplementation in patients with non-anemic iron deficiency and hair loss may enhance iron therapy efficacy and increase the amount of hair regrowth.. [76, 81] (Fig. 6).

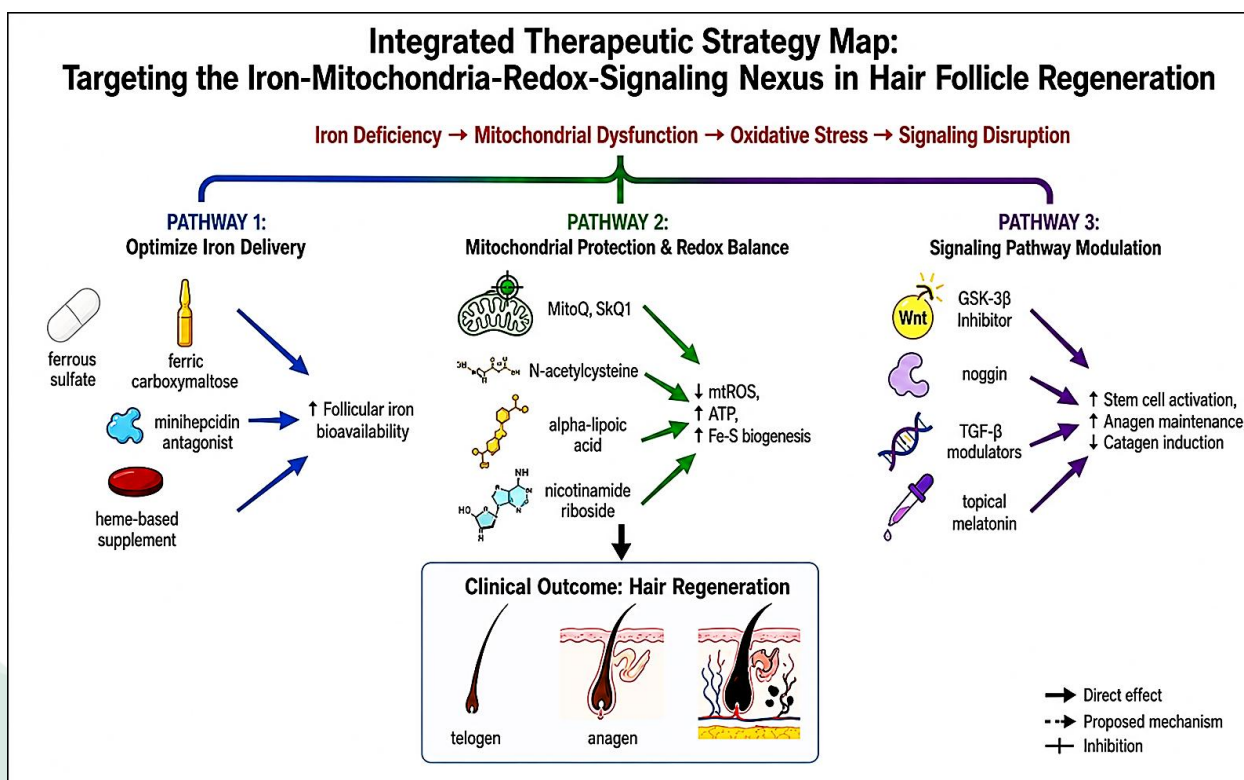


Figure 6. Integrated therapeutic strategy map targeting iron delivery, mitochondrial protection, redox balance, and follicular signaling pathways.

Eureka Journal of Physical and Chemical Research (EJPCR)

ISSN 2760-490X (Online)

Volume 2, Issue 8, August 2026



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Iron deficiency is a common cause of hair loss, which can be effectively treated by iron replacement therapy. In patients with iron deficiency hair loss due to pharmacological impairment, we recommend switching to an oral ferrous sulfate compound as the first-line treatment. Gastrointestinal side effects are the most commonly reported adverse events in these patients, and they are usually mild and infrequently result in treatment discontinuation. However, in patients who cannot tolerate oral iron therapy or require faster repletion, alternative agents such as intravenous iron (also known as parenteral iron) are available. While intravenous iron products have been shown to achieve similarly high serum iron levels and ferritin indices, clinical studies investigating their role in treating iron deficiency hair loss are lacking. Antioxidant therapies may play a key role in maximizing the clinical benefits of iron replacement therapy. While various antioxidants have been studied for hair loss, the most studied agents include N-acetylcysteine and α -lipoic acid. In addition, topical melatonin has also gained traction as a therapeutic option following, we reported its role in regulating various mechanisms of hair growth and hair loss. There is limited clinical evidence regarding the use of antioxidants for treating iron deficiency-associated hair loss, but these agents have demonstrated potential to improve hair growth in the setting of other hair loss disorders. Overall, additional clinical studies targeting iron deficiency hair loss with adjunctive antioxidant therapies are needed to better elucidate their impact on hair growth. [76], [81].

Hepcidin is a small, 25-amino-acid-long peptide secreted by the liver that is responsible for controlling the body's iron balance through its influence on iron bioavailability. Iron, while a vital nutrient, can easily become toxic to cells if present in excess. The human body has no active means to excrete this transition metal, and thus iron metabolism is regulated mainly through the

Eureka Journal of Physical and Chemical Research (EJPCR)

ISSN 2760-490X (Online)

Volume 2, Issue 8, August 2026



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adjustment of its uptake by enterocytes in the gut and the reticuloendothelial system, where iron is retrieved from old erythrocytes. Hepcidin regulates the expression and function of the iron transporter ferroportin, which promotes iron absorption in the gut as well as iron release from systemic stores, thus making hepcidin the main systemic regulator of iron homeostasis. Hepcidin expression is regulated by a variety of signals, including the iron supply itself, erythropoiesis (the simultaneous production of red blood cells), oxygen availability, inflammation, and sometimes, in pathological conditions, also by the estrogen signaling pathway. In order to regulate the body's intracellular and systemic iron levels and the corresponding development of organs and tissues, hepcidin expression must be properly controlled. Of note, many signaling molecules are discovered and characterized by investigators, but not all of them act as hepcidin regulators. Other hepcidin antagonists, such as vitamin D, testosterone, and probiotics, are likely to be attractive candidates for therapeutic strategies for hair loss, notably greater iron absorption.

Mitochondrial dysfunction is also a viable target. In this context, compounds like MitoQ, SkQ1, and even nicotinamide riboside can be explored, which have been shown to efficiently protect the follicles from some noxious stimuli and potentially improve iron absorption as well. [76], [81].

Research on hair follicle stem cells has revived interest in hair biology, with cellular and molecular strategies providing fresh insights into hair follicle homeostasis, disorders and therapeutic development. However, significant knowledge gaps remain in understanding the role of oxidative stress with respect to iron metabolism, owing to their limited access in vivo and pre-clinical models. Conducting clinical observations with the use of non-invasive, innovative methodologies such as trichoscopy-guided scalp biopsy, hair metabolomics and scalp tape-stripping, are essential in building a

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ISSN 2760-490X (Online)

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comprehensive knowledge base to prioritize novel therapeutic intervention strategies to target iron deficiency-induced hair follicle dysfunction.

Precision medicine continues to rise in momentum across the field of dermatology and dermatopathology that according to the National Library of Medicine can be defined as an approach to disease treatment and prevention that considers the variability in the patient's genes, environment and lifestyle. Significant progress in molecular diagnostics with the advancement of systems biology projects (e.g. the human genome and proteome) have spurred the need for mechanistic research to further our understanding of hair biology and hair follicle stem cell niches; comprehensively building a knowledge base, and cataloging non-genetic change that mediate these hair cells. The future of micromorphological evaluations and hair follicle histopathology lie in the identification of iron metabolism and oxidative stress as candidate biomarkers and therapeutic targets. The association between these processes and hair follicle homeostasis, development and degeneration presents a novel avenue for therapeutic development through precision medicine. [73], [76], [81].

9. Limitations of Current Evidence

Although several clinical studies have examined the relationship between iron deficiency and abnormal hair follicles, there are some limitations in the studies reviewed. First, the studies were observational and often included a small sample size, which makes it difficult to establish a causal relationship between iron deficiency and alopecia. Second, there was no long-term follow-up to evaluate the dermatological clinical course, which is necessary to determine the correlation between the amelioration of hair loss symptoms and

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ISSN 2760-490X (Online)

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serum ferritin levels or the effect of iron supplementation in the management of heritable and non-heritable alopecia. Third, the cutoff values of ferritin involved in the definition of iron deficiency were not linear. Diagnostic bias was also suspected. For instance, in some studies, it is possible that patients with alopecia, but with iron stores, are misdiagnosed as not being iron deficient. Finally, serum ferritin concentrations can be affected by several comorbidities, which can lead to complications between iron deficiency and hair loss. In conclusion, further research is needed to clarify the relationship between these two. [71], [72].

As iron deficiency is a widely recognized cause of hair loss, practitioners need to know which patients should be tested for iron deficiency and whether oral or parenteral iron replacement is indicated. Several criteria have been proposed in the literature, but none have been validated or proven to be reproducible. Iron saturation, ferritin levels, complete blood counts, and transferrin levels can be tested, but each has significant gaps that could lead to misdiagnoses. There are currently no validated follicle-specific biomarkers to assess iron deficiency inside the hair follicle, so these systemic biomarkers are primarily relied upon. However, systemic biomarkers do not evaluate follicular iron metabolism and do not provide a reliable measure of iron availability in the hair follicle.

An advanced investigation into the precise mechanism of iron-related hair loss and the identification of reliable assays for follicular iron availability is required. Multi-omics technologies show significant promise to decipher the intricate interplay between iron metabolism and hair follicle physiology and pathophysiology, which could pave the way for tailored therapeutic products or effective dietary recommendations to address iron deficiency-related hair loss. However, the art and science of hair restoration should be integrated into

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ISSN 2760-490X (Online)

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systems biology to feed burgeoning multi-omics data into systems biology modeling and uncover enhanced treatments for these unique conditions. To achieve this, further work to develop standardized diagnostic criteria and clinical trial protocols specific for investigating the precise pathology of hair loss disorders is a priority. [73], [76], [81].

10. Conclusion

Iron deficiency is a systemic metabolic issue, resulting in a range of chronic clinical conditions due to its effects on cellular energy production and oxidative stress, as well as the inability to effectively heal injured tissues. This systemic nature of iron metabolism is exemplified during the growth of hair follicles (HFs), which when compared with other epidermal-derived tissues, have increased sensitivity to iron metabolism due to their dependence on mitochondrial dependent ATP production. Iron is also essential for the function of ribonucleotide reductase, a key enzyme involved in nucleic acid synthesis and thus, cell proliferation. In addition, iron is at the center of a range of biological processes (such as oxidative stress-mediated signalling and reactive oxidative species production) which are crucial to the normal cycling of HFs. In iron-deficient conditions, the regulation of HO-1, a key enzyme involved in the metabolic conversion of heme degradation, is misregulated leading to disrupted metabolic homeostasis and cell survival. Given the complex effects of iron deficiency on HF function and the systemic nature of this disorder, the need for better diagnostic biomarkers is paramount in order to provide a more robust diagnosis of systemic iron status and its tissue-specific impacts on HFs. Current serum biomarkers for iron deficiency such as ferritin are inadequate tests of systemic iron status, and moreover, are not tissue-specific, excessively variable and confounded by a wide range of

Eureka Journal of Physical and Chemical Research (EJPCR)

ISSN 2760-490X (Online)

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biological parameters. This wide range of factors that can influence the efficacy of iron biomarkers complicates the accurate determination and diagnosis of iron deficiency. Remarkably, this systemic nature of iron metabolism and its tissue specific impact on HFs is poorly understood and this gap in our understanding is likely due to the absence of an integrated systems biology approach which combine the use of high-throughput sequencing of tissue specimens obtained from adult and neonatal HF as well as precociously and abnormally cycling HFs. Given the complex nature of hair cycling and the systemic metabolism of iron, a systems biology approach is likely to provide insight into the complex molecular processes driving aberrant iron and metabolic homeostasis in HFs – potentially leading to tissue-specific biomarkers of iron deficiency. Furthermore, a detailed understanding of the complex metabolic pathways dependent on iron metabolism would provide novel insights into how HFs respond to and efficiently utilize the iron they require for their normal cycling – creating the potential to develop new therapies for the treatment of hair loss associated with iron deficiency via precision diagnostics and personalized treatments.

Declarations

Ethics declaration: Not applicable.

Funding: The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Eureka Journal of Physical and Chemical Research (EJPCR)

ISSN 2760-490X (Online)

Volume 2, Issue 8, August 2026



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<https://eurekaopenaccess.com/index.php/1>

References

- [1] Kassebaum NJ, Jasrasaria R, Naghavi M, et al. A systematic analysis of global anemia burden from 1990 to 2010. *Blood*. 2014;123(5):615-24.
- [2] Stevens GA, Finucane MM, De-Régil LM, et al. Global, regional, and national trends in haemoglobin concentration and prevalence of total and severe anaemia in children and pregnant and non-pregnant women for 1995–2011: a systematic analysis of population-representative data. *Lancet Glob Health*. 2013;1(1): e16-25.
- [3] Malkud S. A clinicopathological and dermoscopic study of non-cicatricial alopecia. *Int J Trichology*. 2015;7(1):23.
- [4] Park SY, Na SY, Kim JH, et al. Iron plays a certain role in patterned hair loss. *J Korean Med Sci*. 2013;28(6):934-8.
- [5] Schneider MR, Schmidt-Ullrich R, Paus R. The hair follicle as adynamic mini organ. *Curr Biol*. 2009;19(3): R132-42.
- [6] Alonso L, Fuchs E. The hair cycle. *J Cell Sci*. 2006;119(3):391-3.
- [7] Bothwell TH, Charlton RW, Cook JD, Finch CA. Iron metabolism in man. Oxford: Blackwell Scientific; 1979.
- [8] Arosio P, Levi S. Cytosolic and mitochondrial ferritins in the regulation of cellular iron homeostasis and oxidative damage. *Biochim Biophys Acta*. 2010;1800(8):783-92.
- [9] Nemeth E, Tuttle MS, Powelson J, et al. Heparin regulates cellular iron efflux by binding to ferroportin and inducing its internalization. *Science*. 2004;306(5704):2090-3.
- [10] De Domenico I, Ward DM, Kaplan J. Heparin regulation: ironing out the details. *J Clin Invest*. 2007;117(7):1755-8.
- [11] Ganz T. Heparin and iron regulation, 10 years later. *Blood*. 2011;117(17):4425-33.

Eureka Journal of Physical and Chemical Research (EJPCR)

ISSN 2760-490X (Online)

Volume 2, Issue 8, August 2026



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<https://eurekaopenaccess.com/index.php/1>

- [12] Kautz L, Jung G, Valore EV, et al. Identification of erythroferrone as an erythroid regulator of iron metabolism. *Nat Genet.* 2014;46(7):678-84.
- [13] Peyssonnaud C, Zinkernagel AS, Schuepbach RA, et al. Regulation of iron homeostasis by the hypoxia-inducible transcription factors (HIFs). *J Clin Invest.* 2007;117(7):1926-32.
- [14] Wrighting DM, Andrews NC. Interleukin-6 induces hepcidin expression through STAT3. *Blood.* 2006;108(9):3204-9.
- [15] Hentze MW, Muckenthaler MU, Galy B, Camaschella C. Two to tango: regulation of mammalian iron metabolism. *Cell.* 2010;142(1):24-38.
- [16] Weiss G, Goodnough LT. Anemia of chronic disease. *N Engl J Med.* 2005;352(10):1011-23.
- [17] Finberg KE, Heeney MM, Campagna DR, et al. Mutations in TMPRSS6 cause iron-refractory iron deficiency anemia (IRIDA). *Nat Genet.* 2008;40(5):569-71.
- [18] Hentze MW, Kuhn LC. Molecular control of vertebrate iron metabolism: mRNA-based regulatory circuits operated by iron, nitric oxide, and oxidative stress. *Proc Natl Acad Sci USA.* 1996;93(16):8175-82.
- [19] Recalcati S, Minotti G, Cairo G. Iron regulatory proteins: from molecular mechanisms to drug development. *Antioxid Redox Signal.* 2010;13(10):1593-616.
- [20] Pantopoulos K, Hentze MW. Activation of iron regulatory protein-1 by oxidative stress in vitro. *Proc Natl Acad Sci USA.* 1998;95(18):10559-63.
- [21] Cairo G, Recalcati S, Mantovani A, Locati M. Iron trafficking and metabolism in macrophages: contribution to the polarized phenotype. *Trends Immunol.* 2011;32(6):241-7.
- [22] Sheftel AD, Stehling O, Lill R. Iron-sulfur proteins in health and disease. *Trends Endocrinol Metab.* 2010;21(5):302-14.

Eureka Journal of Physical and Chemical Research (EJPCR)

ISSN 2760-490X (Online)

Volume 2, Issue 8, August 2026



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<https://eurekaopenaccess.com/index.php/1>

- [23] Lill R, Hoffmann B, Molik S, et al. The role of mitochondria in cellular iron-sulfur protein biogenesis and iron metabolism. *Biochim Biophys Acta*. 2012;1823(9):1491-508.
- [24] Shaw GC, Cope JJ, Li L, et al. Mitoferrin is essential for erythroid iron assimilation. *Nature*. 2006;440(7080):96-100.
- [25] Paradkar PN, Zumbrennen KB, Paw BH, et al. Regulation of mitochondrial iron import through differential turnover of mitoferrin 1 and mitoferrin 2. *Mol Cell Biol*. 2009;29(4):1007-16.
- [26] Chen W, Paradkar PN, Li L, et al. Abcb10 physically interacts with mitoferrin-1 (Slc25a37) to enhance its stability and function in the erythroid mitochondria. *Proc Natl Acad Sci USA*. 2009;106(38):16263-8.
- [27] Ye H, Jeong SY, Ghosh MC, et al. Glutaredoxin 5 deficiency causes sideroblastic anemia by specifically impairing heme biosynthesis and depleting cytosolic iron in human erythroblasts. *J Clin Invest*. 2010;120(5):1749-61.
- [28] Atamna H. Heme, iron, and the mitochondrial decay of ageing. *Ageing Res Rev*. 2004;3(3):303-18.
- [29] Chen X, Kang R, Kroemer G, Tang D. Iron metabolism in ferroptosis. *Front Cell Dev Biol*. 2020; 8:590226.
- [30] Winterbourn CC. Toxicity of iron and hydrogen peroxide: the Fenton reaction. *Toxicol Lett*. 1995; 82:969-74.
- [31] Arosio P, Elia L, Poli M. Ferritin, cellular iron storage and regulation. *IUBMB Life*. 2017;69(6):414-22.
- [32] Ferreira C, Bucchini D, Martin ME, et al. Early embryonic lethality of H ferritin gene deletion in mice. *J Biol Chem*. 2000;275(4):3021-4.
- [33] Shi H, Bencze KZ, Stemmler TL, Philpott CC. A cytosolic iron chaperone that delivers iron to ferritin. *Science*. 2008;320(5880):1207-10.

Eureka Journal of Physical and Chemical Research (EJPCR)

ISSN 2760-490X (Online)

Volume 2, Issue 8, August 2026



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<https://eurekaooa.com/index.php/1>

- [34] Yu M, Gai C, Li Z, et al. Targeted exosome-encapsulated erastin induced ferroptosis in triple negative breast cancer cells. *Cancer Sci.* 2019;110(10):3173-82.
- [35] Dixon SJ, Lemberg KM, Lamprecht MR, et al. Ferroptosis: an iron-dependent form of nonapoptotic cell death. *Cell.* 2012;149(5):1060-72.
- [36] Paus R, Cotsarelis G. The biology of hair follicles. *N Engl J Med.* 1999;341(7):491-7.
- [37] Ohyama M, Terunuma A, Tock CL, et al. Characterization and isolation of stem cell-enriched human hair follicle bulge cells. *J Clin Invest.* 2006;116(1):249-60.
- [38] Cotsarelis G. Epithelial stem cells: a folliculocentric view. *J Invest Dermatol.* 2006;126(7):1459-68.
- [39] Paus R, Foitzik K. In search of the 'hair cycle clock': a guided tour. *Differentiation.* 2004;72(9-10):489-511.
- [40] Driskell RR, Clavel C, Rendl M, Watt FM. Hair follicle dermal papilla cells at a glance. *J Cell Sci.* 2011;124(8):1179-82.
- [41] Slominski A, Paus R, Costantino R. Differential expression and activity of melanogenesis-related proteins during induced hair growth in mice. *J Invest Dermatol.* 1991;96(4):541-6.
- [42] Andl T, Reddy ST, Gaddapara T, Millar SE. WNT signals are required for the initiation of hair follicle development. *Dev Cell.* 2002;2(5):643-53.
- [43] Botchkarev VA, Botchkareva NV, Nakamura M, et al. Noggin is required for induction of the hair follicle growth phase in postnatal skin. *FASEB J.* 2001;15(12):2205-14.
- [44] Lindner G, Botchkarev VA, Botchkareva NV, et al. Analysis of apoptosis during hair follicle regression (catagen). *Am J Pathol.* 1997;151(6):1601.

Eureka Journal of Physical and Chemical Research (EJPCR)

ISSN 2760-490X (Online)

Volume 2, Issue 8, August 2026



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<https://eurekaopenaccess.com/index.php/1>

- [45] Paus R, Slominski A, Czarnecki BM. Is alopecia areata an autoimmune-response against melanogenesis-related proteins, exposed by abnormal MHC class I expression in the anagen hair bulb? *Yale J Biol Med*. 1993;66(6):541.
- [46] Muller-Rover S, Handjiski B, van der Veen C, et al. A comprehensive guide for the accurate classification of murine hair follicles in distinct hair cycle stages. *J Invest Dermatol*. 2001;117(1):3-15.
- [47] Paus R, Arck P. Neuroendocrine perspectives in alopecia areata: does stress play a role? *J Invest Dermatol*. 2014;134(5):1147-9.
- [48] Adachi K, Uno H. ATP in the hair follicle: its metabolism and function. *J Invest Dermatol*. 1969;52(3):262-8.
- [49] Atamna H, Killilea DW, Killilea AN, Ames BN. Heme deficiency may be a factor in the mitochondrial and neuronal decay of aging. *Proc Natl Acad Sci USA*. 2002;99(23):14807-12.
- [50] Rouault TA. Biogenesis of iron-sulfur clusters in mammalian cells: new insights and relevance to human disease. *Dis Model Mech*. 2012;5(2):155-64.
- [51] Hardie DG, Ross FA, Hawley SA. AMPK: a nutrient and energy sensor that maintains energy homeostasis. *Nat Rev Mol Cell Biol*. 2012;13(4):251-62.
- [52] Kakhlon O, Gruenbaum Y, Cabantchik ZI. Repression of the heavy ferritin chain increases the labile iron pool of human K562 cells. *Biochem J*. 2001;356(Pt 2):311-8.
- [53] Arck PC, Overall R, Spatz K, et al. Towards a 'free radical theory of graying': melanocyte apoptosis in the aging human hair follicle is an indicator of oxidative stress induced tissue damage. *FASEB J*. 2006;20(9):1567-9.
- [54] Klaunig JE, Kamendulis LM. The role of oxidative stress in carcinogenesis. *Annu Rev Pharmacol Toxicol*. 2004; 44:239-67.

Eureka Journal of Physical and Chemical Research (EJPCR)

ISSN 2760-490X (Online)

Volume 2, Issue 8, August 2026



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<https://eurekaopenaccess.com/index.php/1>

- [55] Wood JM, Decker H, Hartmann H, et al. Senile hair graying: H₂O₂-mediated oxidative stress affects human hair color by blunting methionine sulfoxide repair. *FASEB J.* 2009;23(7):2065-75.
- [56] Winterbourn CC, Kettle AJ, Hampton MB. Reactive oxygen species and neutrophil function. *Annu Rev Biochem.* 2016; 85:765-92.
- [57] Cohen LA, Gutierrez L, Weiss A, et al. Serum ferritin is derived primarily from macrophages through a nonclassical secretory pathway. *Blood.* 2010;116(9):1574-84.
- [58] Kidane TZ, Sauble E, Linder MC. Release of iron from ferritin requires lysosomal activity. *Am J Physiol Cell Physiol.* 2006;291(3):C445-55.
- [59] Levi S, Arosio P. Mitochondrial ferritin. *Int J Biochem Cell Biol.* 2004;36(10):1887-9.
- [60] Funayama N, Fagotto F, McCrea P, Gumbiner BM. Embryonic axis induction by the armadillo repeat domain of beta-catenin: evidence for intracellular signaling. *J Cell Biol.* 1995;128(5):959-68.
- [61] Babitt JL, Huang FW, Wrighting DM, et al. Bone morphogenetic protein signaling by hemojuvelin regulates hepcidin expression. *Nat Genet.* 2006;38(5):531-9.
- [62] Foitzik K, Lindner G, Mueller-Roeve S, et al. Control of murine hair follicle regression (catagen) by TGF-beta1 in vivo. *FASEB J.* 2000;14(5):752-60.
- [63] Yu PB, Hong CC, Sachidanandan C, et al. Dorsomorphin inhibits BMP signals required for embryogenesis and iron metabolism. *Nat Chem Biol.* 2008;4(1):33-41.
- [64] Chiang C, Swan RZ, Grachtchouk M, et al. Essential role for Sonic hedgehog during hair follicle morphogenesis. *Dev Biol.* 1999;205(1):1-9.

Eureka Journal of Physical and Chemical Research (EJPCR)

ISSN 2760-490X (Online)

Volume 2, Issue 8, August 2026



This article/work is licensed under CC by 4.0 Attribution

<https://eurekaooa.com/index.php/1>

- [65] Watt FM, Huck WTS. Role of the extracellular matrix in regulating stem cell fate. *Nat Rev Mol Cell Biol.* 2013;14(8):467-73.
- [66] Trost LB, Bergfeld WF, Calogeras E. The diagnosis and treatment of iron deficiency and its potential relationship to hair loss. *J Am Acad Dermatol.* 2006;54(5):824-44.
- [67] Rushton DH, Norris MJ, Dover R, Busuttill N. Causes of hair loss and the developments in hair rejuvenation. *Int J Cosmet Sci.* 2002;24(1):17-23.
- [68] Hard S. Non-anemic iron deficiency as an etiologic factor in diffuse loss of hair of the scalp in women. *Acta Derm Venereol.* 1963; 43:562-9.
- [69] Bhat YJ, Saqib NU, Hassan I. Iron deficiency in alopecia areata: a systematic review and meta-analysis. *J Dermatolog Treat.* 2021;32(7):726-31.
- [70] Kantor J, Kessler LJ, Brooks DG, Cotsarelis G. Decreased serum ferritin is associated with alopecia in women. *J Invest Dermatol.* 2003;121(5):985-8.
- [71] Wang W, Knovich MA, Coffman LG, Torti FM, Torti SV. Serum ferritin: past, present and future. *Biochim Biophys Acta.* 2010;1800(8):760-9.
- [72] Skikne BS, Punnonen K, Caldron PH, et al. Improved differential diagnosis of anemia of chronic disease and iron deficiency anemia: a prospective multicenter evaluation of soluble transferrin receptor and the sTfR/log ferritin index. *Am J Hematol.* 2011;86(11):923-7.
- [73] Ramos P, Hankins JS, Aygun B, et al. Adaptation of a nonhuman primate model of non-anemic iron deficiency for the evaluation of iron sources for the treatment of iron deficiency anemia. *Am J Hematol.* 2012;87(6):629-34.
- [74] Auerbach M, Ballard H. Clinical use of intravenous iron: administration, efficacy, and safety. *Hematology Am Soc Hematol Educ Program.* 2010; 2010:338-47.

Eureka Journal of Physical and Chemical Research (EJPCR)

ISSN 2760-490X (Online)

Volume 2, Issue 8, August 2026



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<https://eurekaopenaccess.com/index.php/1>

- [75] Tolkien Z, Stecher L, Mander AP, et al. Ferrous sulfate supplementation causes significant gastrointestinal side effects in women: a randomized clinical trial. PLoS One. 2015;10(2):e0117383.
- [76] Fischer TW, Slominski A, Zmijewski MA, et al. Melatonin as a major skin protectant: from free radical scavenging to DNA damage repair. Exp Dermatol. 2008;17(9):713-30.
- [77] Preza GC, Ruchala P, Pinon R, et al. Minihepcidins are rationally designed small peptides that mimic hepcidin activity in mice and may be useful for the treatment of iron overload. J Clin Invest. 2011;121(12):4880-8.
- [78] Bacchetta J, Zaritsky JJ, Sea JL, et al. Suppression of FGF-23 prevents hypophosphatemia and rickets in mice with Phex deficiency. J Am Soc Nephrol. 2009;20(11):2323-31.
- [79] Dev S, Babitt JL. Overview of iron metabolism in health and disease. Hemodial Int. 2017;21(Suppl 1):S6-S20.
- [80] Joost S, Annusver K, Jacob T, et al. Single-cell transcriptomics of traced epidermal and hair follicle stem cells reveals rapid adaptations during wound healing. Cell Rep. 2020;25(3):585-97.
- [81] Bacchetta J, Zaritsky JJ, Sea JL, et al. Suppression of iron-regulatory hormone hepcidin by vitamin D. J Am Soc Nephrol. 2014;25(3):564-572.
- [82] Zughaier SM, Alvarez JA, Sloan JH, et al. The role of vitamin D in regulating serum levels of hepcidin in humans. J Clin Transl Endocrinol. 2014;1(1):19-25.
- [83] Smith EM, Alvarez JA, Kearns MD, et al. High-dose vitamin D3 reduces circulating hepcidin concentrations: a pilot randomized trial. Nutr Res. 2017; 41:14-19.