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Regulation of Energy Metabolism in Mammals: The Role of Brown Adipose Tissue

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Abstract Energy metabolism in mammals is a complex process regulated by various tissues and organs, with brown adipose tissue (BAT) playing a crucial role. BAT is essential for thermogenesis, regulation of body weight, and the overall energy balance in mammals. This study provides a comprehensive overview of the structure, function, and distribution of BAT, as well as the molecular mechanisms underlying its activation. The role of BAT in energy metabolism, particularly in thermogenesis and the regulation of glucose and lipid metabolism, is discussed in detail. Furthermore, this study explore the genetic, epigenetic, hormonal, and environmental factors that regulate BAT activity, highlighting key signaling pathways. A case study on BAT's role in obesity and metabolic diseases is presented, including methods for detecting BAT, its potential as a therapeutic target, and relevant clinical trials. Comparative analyses of BAT function across different mammalian species offer insights into its evolutionary significance. This study concludes with a discussion on future directions in BAT research, emphasizing the potential for BAT-targeted therapies and advances in imaging techniques, and underscores the importance of BAT in maintaining energy homeostasis and its therapeutic potential in managing metabolic diseases.

Keywords Brown adipose tissue; Energy metabolism; Thermogenesis; Obesity; Metabolic diseases

1 Introduction

Energy metabolism in mammals encompasses a complex array of chemical processes that manage the uptake, conversion, storage, and breakdown of nutrients to maintain metabolic homeostasis. This intricate system is tightly regulated to adapt to environmental cycles, such as the day-night rhythm, through endogenous circadian clocks (Heyde et al., 2021). Adipose tissues, including white adipose tissue (WAT) and brown adipose tissue (BAT), play pivotal roles in this regulation. WAT primarily stores energy in the form of triglycerides, which can be mobilized during periods of energy deficit (Luo and Liu, 2016). In contrast, BAT is specialized in energy expenditure through nonshivering thermogenesis, a process that generates heat by burning calories (Wang et al., 2021).

Brown adipose tissue (BAT) is crucial for maintaining body temperature and overall energy balance in mammals. Unlike WAT, which stores energy, BAT dissipates energy as heat, a process essential for thermoregulation and metabolic homeostasis (Townsend and Tseng, 2014). BAT's ability to utilize various energy substrates, including lipids and glucose, makes it a significant player in whole-body metabolism (Choe et al., 2016). Recent studies have highlighted BAT's potential in combating obesity and metabolic disorders due to its unique capacity to burn calories and improve insulin sensitivity (Mottillo et al., 2016). The dynamic and flexible metabolism of BAT supports its role as an "energy sink," making it a promising target for therapeutic strategies against obesity and related conditions (Poekes et al., 2015).

This study elucidates the regulatory mechanisms of energy metabolism in mammals, with a particular focus on the role of brown adipose tissue (BAT). By exploring the metabolic pathways and functions of BAT, this study seeks to understand how this tissue contributes to overall energy homeostasis and its potential therapeutic applications in treating obesity and metabolic disorders. Through a comprehensive review of recent findings, this study intends to highlight the significance of BAT in energy regulation and its interaction with other metabolic tissues.

2 Overview of Brown Adipose Tissue (BAT)

Brown adipose tissue (BAT) is a specialized form of fat tissue that plays a crucial role in thermogenesis and energy metabolism in mammals. Unlike white adipose tissue (WAT), which stores energy, BAT dissipates energy as heat, contributing to the maintenance of body temperature and overall energy homeostasis.

2.1 Structure and function of BAT

BAT is characterized by its high density of mitochondria, which contain uncoupling protein 1 (UCP1). UCP1 is essential for the thermogenic function of BAT, as it uncouples oxidative phosphorylation from ATP production, allowing the energy to be released as heat instead (Sidossis and Kajimura, 2015). This process, known as non-shivering thermogenesis, is particularly important in newborns and hibernating animals, where it helps to prevent hypothermia (Tews and Wabitsch, 2021). Additionally, BAT can utilize various substrates, including lipids, glucose, and amino acids, to fuel its thermogenic activity, making it a dynamic and flexible tissue in terms of metabolic function (Wang et al., 2021).

2.2 Distribution of BAT in mammals

The distribution of BAT varies among different species and life stages. In humans, BAT is predominantly found in infants, with significant depots located in the cervical-supraclavicular regions, around the spine, and near the kidneys (Lee et al., 2013). While the relative mass of BAT declines with age, recent studies have shown that metabolically active BAT persists in some adults, particularly in the cervical and supraclavicular regions (Yuko and Saito, 2021). The presence and activity of BAT in adults are influenced by factors such as cold exposure, which can induce the browning of white adipose tissue, leading to the formation of beige adipocytes that share functional similarities with classical brown adipocytes (Kajimura et al., 2015).

2.3 Molecular mechanisms of BAT activation

The activation of BAT is primarily regulated by the sympathetic nervous system through the release of norepinephrine, which binds to adrenergic receptors on brown adipocytes, triggering a cascade of intracellular events that lead to the activation of UCP1 and subsequent heat production (Figure 1) (Bienboire-Frosini et al., 2023). Additionally, several neurotrophic factors, known as batokines, such as NGF, NRG4, and S100b, play a role in the remodeling and sympathetic innervation of BAT, enhancing its thermogenic capacity (Robertson et al., 2023). Moreover, BAT secretes various paracrine and endocrine factors that influence systemic metabolism, suggesting that BAT functions as a metabolic regulator beyond its thermogenic role (Schéele and Wolfrum, 2019).

The study of Bienboire-Frosini et al. (2023) illustrates the complex biochemical process by which brown adipose tissue (BAT) in mammals produces heat, particularly in response to cold environments. It shows the role of the sympathetic nervous system in activating BAT through the release of norepinephrine (NE), which binds to β3-adrenergic receptors (β3-AR) on brown fat cells. This triggers a cascade of events involving cAMP, PKA, and various transcription factors that ultimately increase the expression of UCP1 in mitochondria. UCP1 plays a key role in the production of heat through the process of non-shivering thermogenesis, utilizing fatty acids as fuel.

In summary, BAT is a critical tissue for thermogenesis and energy metabolism in mammals. Its structure, distribution, and activation mechanisms are finely tuned to meet the thermogenic demands of the organism, making it a potential target for therapeutic strategies aimed at combating obesity and metabolic disorders.

3 Role of BAT in energy metabolism

3.1 Thermogenesis and heat production

Brown adipose tissue (BAT) is specialized in expending energy through non-shivering thermogenesis, a process that produces heat by uncoupling protein 1 (UCP1)-dependent and UCP1-independent mechanisms (Shinde et al., 2021). This thermogenic capability allows BAT to burn calories through uncoupled respiration, producing heat to maintain body temperature, a feature that makes BAT a unique "energy sink" in mammals (Wang et al., 2021). The activation of BAT, particularly through cold exposure, leads to increased utilization of circulating blood glucose and fatty acids, contributing to thermogenesis and energy expenditure. This process is crucial for maintaining

body temperature and has been proposed as a potential therapeutic strategy for combating obesity by increasing energy expenditure (Maliszewska and Krętowski, 2021).

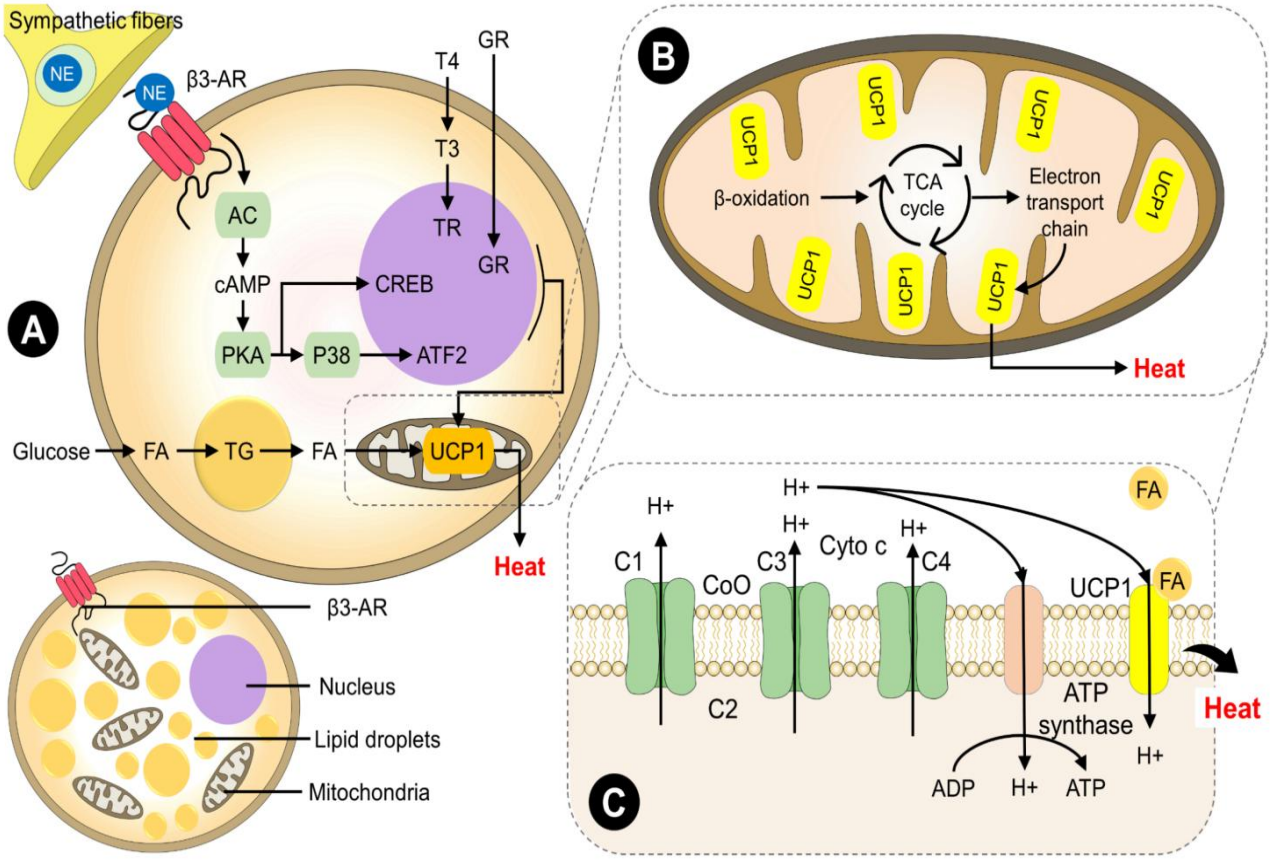

Figure 1 Characteristics and activation of the brown adipose tissue in mammals (Adopted from Bienboire-Frosini et al., 2023)

Image caption: When mammals are exposed to cold environments, it activates the sympathetic nervous system and the consequent release of catecholamines, notably NE from the adrenal glands. NE binds to β3-AR located in BAT to start a series of biochemical reactions to produce heat. cAMP production by AC results in the activation of the PKA, a protein that promotes lipolysis and thermogenesis through CREB, P38, and ATF2. Thyroid hormones (T4 and T3) also participate in gene expression and TG uptake, as well as GR and glucose. The conversion of TG to FA is used by the mitochondria to produce heat. In the mitochondria's membrane, UCP1 receptors and cytochrome c participate in thermogenesis following β-oxidation, the TCA cycle, and the electron transport chain mechanism for thermogenesis. (A) Schematic deposit of BAT; AC: adenylyl cyclase; ATF2: activating transcription factor 2. (B) Mitochondria close-up; β3-AR: beta3-adrenergic receptor. (C) Mitochondrial membrane; cAMP: cyclic AMP; CREB: cAMP response element-binding protein; GR: glucocorticoid; FA: fatty acids; NE: norepinephrine; PKA: protein kinase A; T3/T4: thyroid hormone; TG: triglyceride; UCP1: uncoupling protein 1 (Adopted from Bienboire-Frosini et al., 2023)

3.2 Regulation of body weight and energy balance

BAT plays a significant role in regulating body weight and energy balance. The ability of BAT to dissipate energy through thermogenesis makes it a promising target for obesity treatment. Studies have shown that BAT activation can lead to a reduction in body weight and fat mass. For instance, BAT transplantation in mice resulted in improved glucose tolerance, increased insulin sensitivity, lower body weight, and decreased fat mass (Stanford et al., 2013). Additionally, the presence of thermogenically active BAT depots in humans has been associated with lower body mass index (BMI) and visceral adiposity, suggesting an inverse relationship between BAT activity and obesity (Figure 2) (Takeda et al., 2023). The potential of BAT to modulate energy balance and body weight highlights its importance in metabolic homeostasis and obesity prevention (Sidossis and Kajimura, 2015).

The study of Takeda et al. (2023) compares the metabolic differences between lean and obese individuals, focusing on the activity of brown adipose tissue (BAT). In lean individuals, BAT is active and helps burn calories through thermogenesis, contributing to weight maintenance. In contrast, obesity is associated with reduced BAT

activity, leading to decreased thermogenesis and increased lipid accumulation. The image highlights the role of specific obesity-associated factors that negatively impact BAT function. Modulating these factors through pharmacological interventions could potentially restore BAT activity, offering a therapeutic approach to managing obesity and related metabolic disorders.

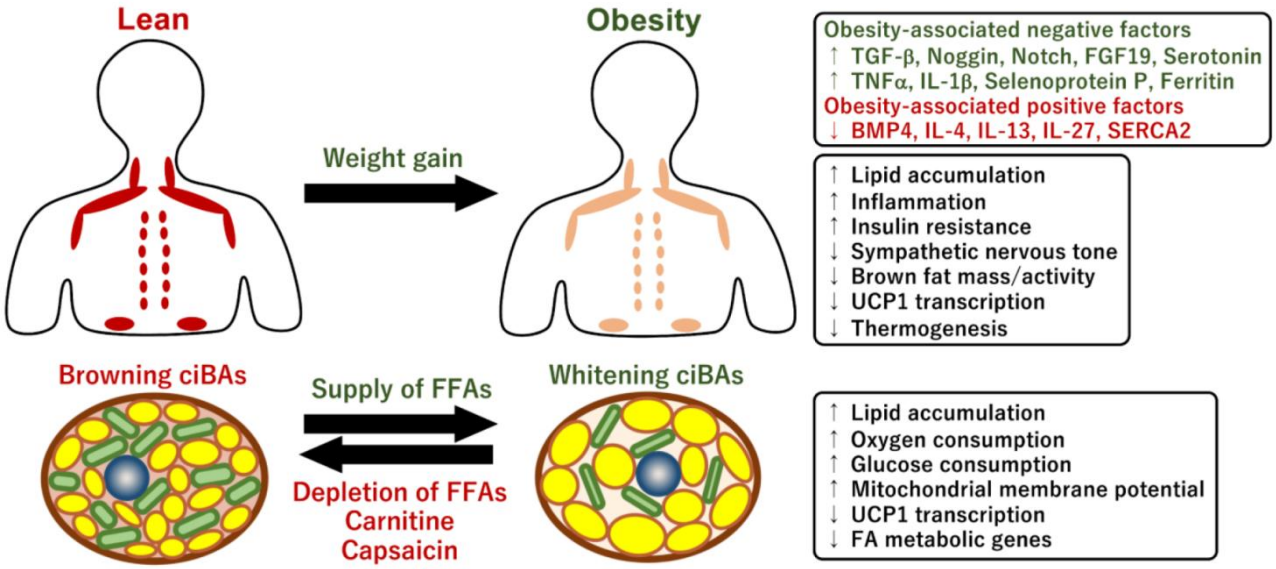

Figure 2 Obesity-associated metabolic differences in human individuals and the brown adipocyte model (Adopted from Takeda et al., 2023)

Image caption: Obese human individuals exhibit the repression of BAT mass and activity and lower BAT uptake of blood glucose and free fatty acids compared with those in lean individuals. Mechanistically, the repression is caused by obesity-associated factors that positively and negatively modulate adipocyte browning, de novo brown adipogenesis, UCP1 expression and activity, and adrenergic responses. The amount of the negative factors, such as TGF-β, Noggin, Notch, TNFα, and selenoprotein P, increases under obese conditions, whereas the amount of the positive factors such as BMP4 and Il-27 decreases. The pharmacological modulation of the metabolic pathways involved in these obesity-associated factors may provide therapeutic intervention in the management of obesity and metabolic diseases through brown fats. During the culture of the chemical compound-induced brown/beige adipocytes (ciBAs), the increase in free fatty acids (FFAs) in the culture medium induces white adipocyte-like phenotypes of ciBAs in terms of UCP1 expression and lipid metabolism, which may reflect BAT under obese conditions. In contrast, the depletion of FFAs or prolonged treatment with either carnitine or capsaicin causes the browning process of ciBAs, which may reflect BAT under lean conditions (Adopted from Takeda et al., 2023)

3.3 Impact of BAT on glucose and lipid metabolism

BAT significantly influences glucose and lipid metabolism. It has been shown to improve glucose homeostasis and insulin sensitivity. For example, BAT transplantation in mice led to increased insulin-stimulated glucose uptake in various tissues, including endogenous BAT, white adipose tissue (WAT), and heart muscle, but not skeletal muscle. This indicates that BAT plays a crucial role in regulating glucose metabolism. Furthermore, BAT activation has been linked to enhanced lipid metabolism. Studies have demonstrated that BAT activation increases whole-body lipolysis, triglyceride-free fatty acid (FFA) cycling, FFA oxidation, and adipose tissue insulin sensitivity (Chondronikola et al., 2016). The ability of BAT to utilize glucose and lipids for thermogenesis and its potential endocrine functions, such as the secretion of regulatory molecules like IL-6, further underscore its role in maintaining metabolic homeostasis and combating metabolic diseases (Villarroya et al., 2017; Carpentier et al., 2018).

4 Regulation of BAT Activity

4.1 Genetic and epigenetic regulation

The regulation of brown adipose tissue (BAT) activity is significantly influenced by genetic and epigenetic factors. Genetic determinants play a crucial role in the distribution, amount, and efficiency of BAT, particularly in newborn mammals, where these factors are vital for thermoregulation and survival (Bienboire-Frosini et al., 2023).

Key thermogenic transcriptional factors such as uncoupling protein 1 (UCP1), nuclear respiratory factor 1 (NRF1), and peroxisome-proliferator-activated receptor gamma coactivator 1-alpha (PGC1-α) are essential for BAT function and are regulated at the genetic level. Additionally, the developmental lineage of brown adipocytes and their unique energy utilization mechanisms are influenced by genetic factors, which are critical for designing therapeutic interventions for metabolic disorders (Shinde et al., 2021).

4.2 Hormonal influences (e.g., thyroid hormones, insulin, leptin)

Hormonal regulation is another pivotal aspect of BAT activity. Thyroid hormones, insulin, and leptin are among the key hormones that influence BAT thermogenesis and energy expenditure. Thyroid hormones, for instance, have been shown to activate BAT and enhance thermogenesis, which can potentially aid in weight loss (Perez et al., 2022). Insulin sensitivity and glucose metabolism are also significantly improved by BAT activity, as evidenced by the upregulation of insulin-stimulated glucose uptake in BAT and other tissues following BAT transplantation (Stanford et al., 2013). Furthermore, leptin, an adipokine, plays a role in energy balance and can influence BAT activity, contributing to overall metabolic homeostasis (Heyde et al., 2012).

4.3 Environmental factors (e.g., temperature, diet)

Environmental factors such as temperature and diet are crucial in regulating BAT activity. Cold exposure is a well-documented activator of BAT thermogenesis, as it stimulates the sympathetic nervous system to increase BAT activity and energy expenditure (Carpentier et al., 2018; Sidossis and Kajimura, 2015). This process, known as non-shivering thermogenesis, is essential for maintaining body temperature in cold environments. Dietary factors also influence BAT activity; for example, certain nutrients and compounds like capsinoids and caffeine can activate BAT and promote thermogenesis. The interplay between environmental cues and BAT activity underscores the adaptive nature of this tissue in response to external stimuli.

4.4 Signaling pathways involved in BAT regulation

Several signaling pathways are involved in the regulation of BAT activity. The AMP-activated protein kinase (AMPK) pathway and fibroblast growth factor 21 (FGF21) are critical molecular markers that enhance BAT thermogenic activity and energy expenditure (Ziqubu et al., 2023). The central nervous system (CNS) also plays a significant role in regulating BAT through sympathetic nerve activity, which is crucial for thermogenesis and energy balance (Morrison et al., 2014). Additionally, the circadian regulation of energy metabolism involves intricate signaling pathways that synchronize BAT activity with the body's internal clock, further highlighting the complexity of BAT regulation.

In summary, the regulation of BAT activity is a multifaceted process involving genetic and epigenetic factors, hormonal influences, environmental factors, and intricate signaling pathways. Understanding these regulatory mechanisms is essential for leveraging BAT as a therapeutic target for metabolic disorders and improving overall energy metabolism in mammals.

5 Case Study: BAT Activity in Mammals

5.1 Methods for detecting and measuring bat in mammals

Brown adipose tissue (BAT) activity in mammals can be detected and measured using various advanced imaging techniques. Positron emission tomography coupled with computed tomography (PET/CT) using the glucose tracer 18-fluorodeoxyglucose (18FDG) is the gold standard for quantifying BAT activity. This method allows for the visualization of metabolically active BAT by tracking glucose uptake, which is indicative of BAT's thermogenic activity (Carpentier et al., 2018). Additionally, other methods such as measuring nonesterified fatty acids (NEFA), chylomicron-triglycerides (TG), oxygen consumption, and intracellular TG levels have been employed to quantify energy substrate metabolism in BAT. These techniques provide a comprehensive understanding of BAT's role in energy expenditure and its potential as a therapeutic target.

5.2 BAT's role in obesity and metabolic diseases

BAT plays a crucial role in regulating energy expenditure and maintaining metabolic homeostasis. It is known for its ability to burn calories through non-shivering thermogenesis, a process mediated by uncoupling protein 1

(UCP1) (Wang et al., 2021). This thermogenic activity makes BAT an attractive target for combating obesity and related metabolic diseases. Studies have shown that individuals with higher BAT activity tend to have lower body mass index (BMI), improved insulin sensitivity, and better glucose metabolism (Singh et al., 2021). Conversely, reduced BAT activity is associated with obesity and metabolic complications such as insulin resistance and type 2 diabetes (T2D) (Maliszewska and Krętowski, 2021). Therefore, enhancing BAT activity could be a promising strategy for treating obesity and its associated disorders.

5.3 Therapeutic approaches targeting BAT in mammalian health

Several therapeutic approaches have been explored to activate BAT and enhance its thermogenic capacity. Pharmacological agents such as β-agonists, capsinoids, thyroid hormone, sildenafil, and caffeine have been investigated for their potential to stimulate BAT activity and promote weight loss (Perez et al., 2022). Metformin, a widely used anti-diabetic drug, has also been shown to enhance BAT thermogenic activity by upregulating key thermogenic transcriptional factors and molecular markers involved in glucose metabolism and energy regulation (Figure 3) (Ziqubu et al., 2023). Additionally, cold exposure has been consistently demonstrated to activate BAT and induce thermogenesis, although its long-term feasibility as a therapy remains uncertain. Targeting AMP-activated protein kinase (AMPK) in BAT has emerged as another promising strategy, as it plays a significant role in regulating BAT's metabolic activity and non-shivering thermogenesis (Desjardins and Steinberg, 2018). These therapeutic approaches hold potential for improving metabolic health by increasing energy expenditure and reducing obesity-related complications.

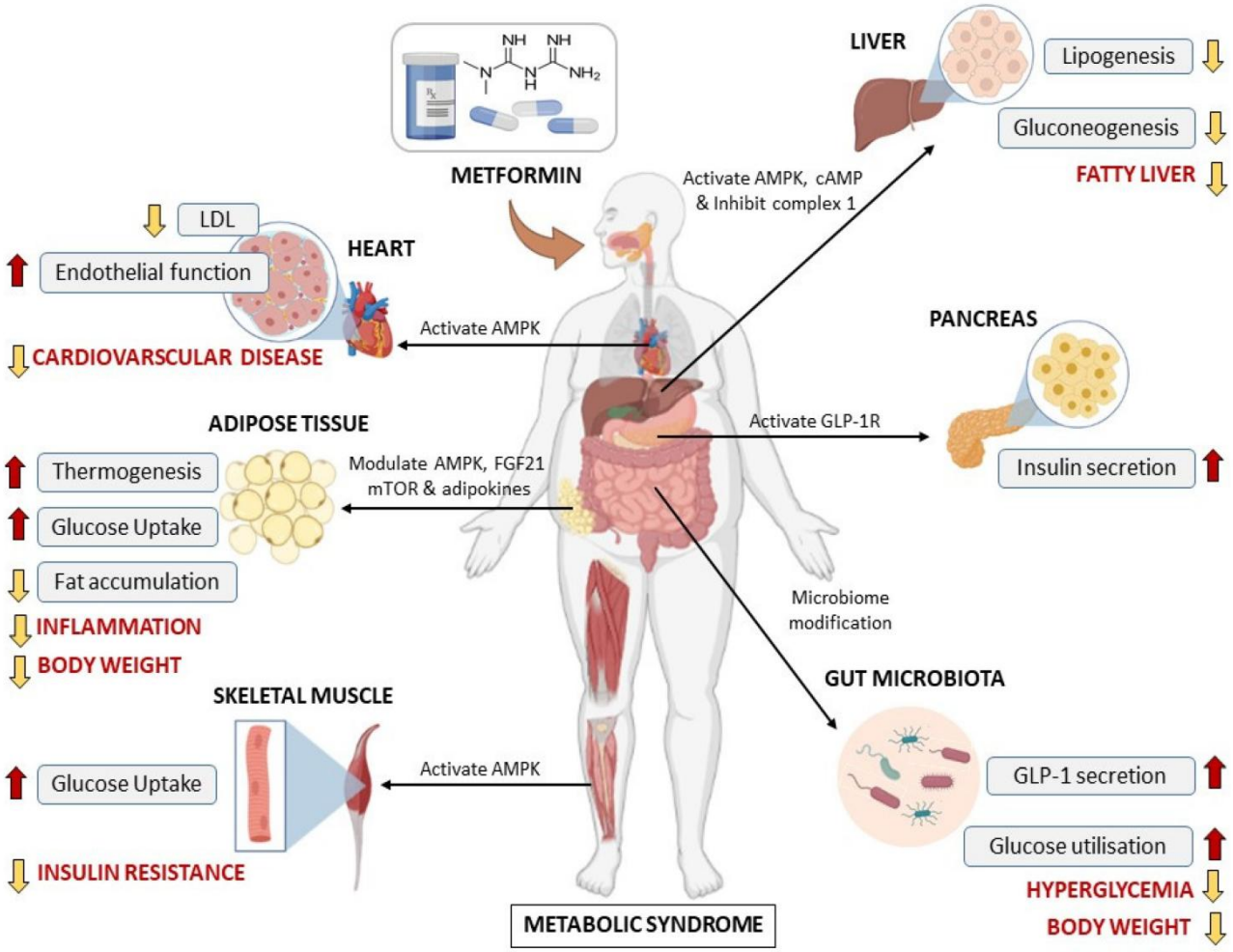

Figure 3 An overview of the most prominent mechanisms of action and impact of metformin on different metabolic diseases in conditions of metabolic syndrome (Adopted from Ziqubu et al., 2023)

Image caption: AMPK: AMP-activated protein kinase, cAMP: cyclic adenosine monophosphate, FGF21: fibroblast growth factor 21, GLP-1R: glucagon-like peptide 1 receptor, LDL: low-density lipoprotein (Adopted from Ziqubu et al., 2023)

The study of Ziqubu et al. (2023) illustrates the multifaceted effects of metformin on various tissues in the context of metabolic syndrome. Metformin acts primarily by activating AMPK, which helps reduce glucose production in the liver, enhances insulin sensitivity in skeletal muscles, and decreases fat accumulation in adipose tissue. Additionally, metformin improves cardiovascular health by lowering LDL levels and enhancing endothelial function. It also positively impacts the gut microbiota, leading to improved glucose utilization and reduced hyperglycemia and body weight. Overall, metformin addresses several key aspects of metabolic syndrome, making it a widely used therapeutic agent.

5.4 Case examples and clinical trials

Several clinical trials have investigated the effects of various interventions on BAT activity and their potential therapeutic benefits. For instance, a systematic review of clinical trials testing the impact of agents such as β-agonists, capsinoids, and cold exposure on BAT activation revealed significant heterogeneity in the duration of interventions and metrics used to estimate thermogenesis and energy expenditure. Despite the observed activation of BAT, the studies did not consistently correlate with significant weight loss, highlighting the need for further research to determine the long-term efficacy and safety of these interventions. Another study demonstrated that BAT transplantation in mice improved glucose tolerance, increased insulin sensitivity, and reversed high-fat diet-induced insulin resistance, suggesting a potential role for BAT in regulating glucose homeostasis and insulin sensitivity (Stanford et al., 2013). These findings underscore the therapeutic potential of targeting BAT for treating metabolic diseases and warrant further investigation in larger, well-designed clinical trials.

6 Comparative Analysis: BAT in Different Mammals

6.1 Differences in BAT function across species

Brown adipose tissue (BAT) plays a crucial role in thermogenesis and energy metabolism across various mammalian species. However, the function and efficiency of BAT can vary significantly. For instance, in neonatal mammals, BAT is essential for preventing hypothermia by activating biochemical and endocrine processes in response to cold stress. The presence and activation of BAT, as well as its location and thermogenic response, depend on both intrinsic and extrinsic factors unique to each species (Bienboire-Frosini et al., 2023). In small mammalian hibernators, BAT has evolved to have a high capacity for heat production, which is critical for rewarming from hypothermic torpor during hibernation (Ballinger and Andrews, 2018). In contrast, adult humans have been found to possess metabolically active BAT, which plays a role in energy expenditure and glucose homeostasis, although its prevalence and activity decrease with age and higher body mass index.

6.2 Evolutionary perspectives on BAT

The evolutionary history of BAT and its thermogenic function is deeply rooted in the adaptation of mammals to diverse ecological niches. The presence of mitochondrial uncoupling protein 1 (UCP1) in BAT is a key evolutionary trait that enables adaptive thermoregulation through heat production. Studies on non-model organisms have broadened our understanding of BAT regulation and its physiological roles, highlighting the unique evolutionary adaptations of BAT in different species (Jastroch et al., 2018). For example, the ability of small mammalian hibernators to use BAT for rewarming from torpor is a specialized adaptation that has uncovered new molecular mechanisms and potential strategies for biomedical applications. The comparative biology of BAT across species provides insights into conserved and specialized functional changes, emphasizing the importance of considering species diversity, ecology, and evolution in BAT research.

6.3 Comparative case studies

Several case studies illustrate the diverse roles and adaptations of BAT in different mammals. In neonatal mammals, BAT is vital for thermogenesis and preventing hypothermia, with its distribution, amount, and efficiency varying among species. In small mammalian hibernators, BAT's high thermogenic capacity is crucial for survival during hibernation, with recent research uncovering the molecular pathways involved in BAT regulation and function. In adult humans, the rediscovery of metabolically active BAT has led to a renewed interest in its potential therapeutic applications for obesity and metabolic disorders. Human BAT activity has been shown to correlate positively with energy expenditure during cold exposure and negatively with age and body

mass index, suggesting its role in regulating energy metabolism and thermogenesis (Lee et al., 2013). These case studies highlight the importance of BAT in different physiological contexts and its potential for therapeutic interventions across species.

By examining the differences in BAT function, evolutionary perspectives, and comparative case studies, we gain a comprehensive understanding of the role of BAT in regulating energy metabolism in mammals. This knowledge can inform future research and potential therapeutic strategies for metabolic disorders.

7 Future Directions in BAT Research

7.1 Potential for BAT-targeted therapies

Brown adipose tissue (BAT) has emerged as a promising target for therapeutic interventions aimed at combating obesity and metabolic disorders. The unique ability of BAT to expend energy through non-shivering thermogenesis makes it an attractive candidate for increasing energy expenditure and improving metabolic health. Recent studies have highlighted the potential of pharmacological agents, such as metformin, to enhance BAT activity and promote weight loss, improve insulin sensitivity, and regulate glucose metabolism by upregulating key thermogenic markers like UCP1, NRF1, and PGC1-α (Ziqubu et al., 2023). Additionally, the endocrine functions of BAT, which influence glucose and lipid homeostasis, further underscore its therapeutic potential (Shinde et al., 2021; Yuko and Saito, 2021). Future research should focus on identifying and optimizing BAT activators, understanding the molecular mechanisms underlying BAT thermogenesis, and exploring the long-term effects of BAT-targeted therapies on metabolic health.

7.2 Advances in BAT imaging and measurement techniques

The accurate measurement and imaging of BAT are crucial for advancing our understanding of its role in energy metabolism and for developing effective therapies. Positron emission tomography coupled with computed tomography (PET/CT) using the glucose tracer 18FDG has been the gold standard for detecting metabolically active BAT in humans (Carpentier et al., 2018). However, this method primarily reflects BAT's glucose metabolism rather than its thermogenic activity. Recent advances have introduced methods to measure various energy substrates, such as nonesterified fatty acids, chylomicron-triglycerides, and oxygen, providing a more comprehensive assessment of BAT's metabolic activity. Additionally, the development of integrated whole-body in vivo methods could offer more accurate quantification of BAT's contribution to total energy expenditure. Future research should aim to refine these imaging techniques and develop new methods that can more precisely measure BAT activity and its impact on systemic metabolism.

7.3 Challenges and opportunities in BAT research

Despite the promising potential of BAT in metabolic health, several challenges remain. One major challenge is the variability in BAT activity among individuals, influenced by factors such as age, body mass index (BMI), and environmental conditions (Singh et al., 2021). Additionally, the exact mechanisms by which BAT influences systemic metabolism and its interactions with other tissues are not fully understood (Poekes et al., 2015). There is also a need for more research on the long-term safety and efficacy of BAT-targeted therapies. However, these challenges present opportunities for future research. Investigating the developmental lineages of brown and beige adipocytes, understanding the molecular control of BAT development, and exploring the endocrine functions of BAT could provide new insights into its role in metabolic regulation (Kajimura and Saito, 2014; Sidossis and Kajimura, 2015). Moreover, leveraging the heterogeneity of BAT and its ability to adapt to different metabolic demands could lead to personalized therapeutic strategies for obesity and related metabolic disorders.

In conclusion, while significant progress has been made in understanding BAT's role in energy metabolism, future research should focus on optimizing BAT-targeted therapies, advancing imaging techniques, and addressing the challenges in BAT research to fully harness its therapeutic potential.

8 Concluding Remarks

Brown adipose tissue (BAT) plays a crucial role in regulating energy metabolism in mammals through its thermogenic capabilities. Several studies have demonstrated that BAT activation can significantly increase energy

expenditure, particularly during cold exposure. For instance, cold-induced thermogenesis (CIT) is notably higher in individuals with metabolically active BAT, indicating a seasonal variation in energy expenditure linked to BAT activity. Additionally, BAT activation has been shown to enhance lipid metabolism, with increased whole-body lipolysis and fatty acid oxidation observed during cold exposure. Despite these promising findings, the impact of BAT activation on long-term weight loss remains uncertain, as many studies report significant heterogeneity in results and small sample sizes.

The activation of BAT has profound implications for mammalian energy metabolism. It serves as a critical mechanism for maintaining body temperature during cold exposure and contributes to overall energy balance by increasing energy expenditure. The ability of BAT to utilize various energy substrates, including lipids, glucose, and other metabolites, underscores its metabolic flexibility and importance in whole-body metabolic homeostasis. Furthermore, the presence of beige adipocytes, which can emerge in response to environmental cues such as chronic cold exposure, suggests potential therapeutic targets for obesity and related metabolic disorders. However, the clinical relevance of BAT activation for sustained weight loss and metabolic health requires further investigation, particularly in terms of long-term feasibility and safety.

In conclusion, BAT represents a vital component of mammalian energy metabolism, with its thermogenic activity playing a key role in regulating energy expenditure and maintaining metabolic homeostasis. While the potential of BAT activation as a therapeutic strategy for obesity and metabolic diseases is promising, more extensive and long-term studies are needed to fully understand its efficacy and safety. Future research should focus on developing integrated methods to quantify BAT's contribution to energy expenditure and exploring the molecular mechanisms underlying its activation and function. Understanding these aspects will be crucial for harnessing the full potential of BAT in metabolic health interventions.

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Conflict of Interest Disclosure

The authors affirm that this research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

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