Research Output Journal of Public Health and Medicine 6(1):125-131, 2026

ROJPHM **ISSN ONLINE: 1115-9715**

https://rojournals.org/roj-public-health-and-medicine/ **ISSN PRINT: 1115-6147**

https://doi.org/10.59298/ROJPHM/2026/61125131

Thermogenic Failure: How Impaired Brown and Beige Adipose Tissue Links Obesity to Diabetes Progression

Alberta Jeanne N.

School of Applied Health Sciences Kampala International University Uganda

ABSTRACT

Brown adipose tissue (BAT) and beige adipocytes dissipate energy as heat and act as metabolic sinks for glucose and lipids. Their activation improves insulin sensitivity, lowers ectopic fat, and protects against cardiometabolic disease. In obesity, however, thermogenic capacity declines due to impaired BAT recruitment, defective browning of white adipose tissue (WAT), mitochondrial dysfunction, and chronic inflammation, a state of "thermogenic failure." This failure reduces whole-body energy expenditure and promotes positive energy balance, but also removes a critical buffer that normally clears circulating nutrients and releases beneficial cytokines, thereby accelerating insulin resistance and type 2 diabetes (T2D). This review synthesizes current evidence on thermogenic fat in human and experimental obesity and its role in diabetes progression. We outline developmental and functional differences between classical brown and beige adipocytes, then examine how obesity disrupts sympathetic innervation, adrenergic signaling, mitochondrial integrity, and cellular composition within thermogenic depots. We next discuss how loss of thermogenic and endocrine functions of BAT/beige fat worsens hepatic steatosis, muscle insulin resistance, β-cell stress, and cardiovascular risk. Finally, we review lifestyle, surgical, and pharmacologic interventions that restore or substitute thermogenic activity and highlight key questions for translating BAT/beige biology into durable therapies for obesity-driven diabetes.

Keywords: brown adipose tissue; beige fat; thermogenesis; obesity; type 2 diabetes

INTRODUCTION

The rediscovery of metabolically active BAT in adult humans overturned the long-held view that thermogenic fat was relevant only to infants and small mammals. Imaging and biopsy studies now show BAT depots in the cervical, supraclavicular, paravertebral and perirenal regions, composed of multilocular, UCP1-positive adipocytes with dense mitochondria specialized for non-shivering thermogenesis[1]. In addition, beige (or brite) adipocytes can arise within WAT depots in response to cold, β-adrenergic stimulation, exercise, and certain hormones or nutrients, providing an inducible thermogenic reserve[1].

BAT and beige fat contribute to whole-body energy expenditure by uncoupling mitochondrial respiration from ATP synthesis via UCP1, dissipating the proton gradient as heat. Beyond heat production, thermogenic adipocytes act as avid consumers of glucose and lipids, improving postprandial substrate clearance and reducing triglyceride-rich lipoproteins[2]. Rodent models with enhanced BAT mass or WAT browning show resistance to diet-induced obesity and improved insulin sensitivity, while genetic or surgical ablation of thermogenic depots exaggerates weight gain and metabolic dysfunction[2].

Human studies support similar protective roles. Individuals with higher BAT activity (often assessed by ^18F-FDG PET/CT) tend to have lower BMI, less visceral adiposity, better insulin sensitivity, and reduced prevalence of cardiometabolic disease[3]. Cold acclimation can increase BAT glucose uptake and promote WAT browning, modestly improving insulin sensitivity in people with obesity and T2D, although the magnitude is variable and influenced by age, sex, and genetics[3].

Yet, paradoxically, obesity itself is associated with reduced detectable BAT and impaired beige fat biogenesis. Large imaging cohorts show that BAT prevalence and activity decline with increasing BMI, aging, and central adiposity[4]. Thermogenic depots in obese rodents and humans show fibrosis, lipid overload, reduced UCP1 expression, and blunted responses to cold or β-adrenergic stimulation[5]. Beige adipocyte precursors in WAT acquire senescent features and become less responsive to browning stimuli in obese and aged settings[5].

This shift from a thermogenically competent to a "failed" thermogenic phenotype has dual consequences. First, reduced energy expenditure and nutrient combustion favor positive energy balance and further weight gain. Second, loss of thermogenic sinks for glucose and lipids increases the burden on liver, muscle, and β-cells, promoting ectopic lipid accumulation, insulin resistance, and glucolipotoxic stress[6].

Thermogenic adipose tissue also functions as an endocrine organ. BAT and beige fat secrete "batokines" peptides, lipids, and metabolites such as FGF21, NRG4, IL-6, and specific acylcarnitines that influence hepatic lipid metabolism, muscle oxidative capacity, vascular function, and appetite regulation[7]. Impairment of this secretory function likely contributes to diabetes progression independently of heat production per se. Indeed, some UCP1-independent pathways (e.g., creatine cycling, Ca^{2+} cycling, futile substrate cycles) and batokine actions may mediate metabolic benefits even when classical thermogenesis is limited[7].

The concept of "thermogenic failure" therefore extends beyond simple loss of UCP1. It encompasses:

- defective development and maintenance of BAT depots;
- reduced recruitment and activation of beige adipocytes in WAT;
- mitochondrial structural and functional abnormalities;
- altered innervation and impaired sympathetic–adipocyte signaling;
- inflammatory and fibrotic remodeling of thermogenic niches;
- and disruption of batokine networks[8].

Critically, these defects do not arise in isolation. Chronic overnutrition, inactivity, and hyperglycemia drive systemic mitochondrial dysfunction and low-grade inflammation, which in turn damage thermogenic adipocytes[9, 10]. Conversely, early preservation or restoration of thermogenic capacity via cold exposure, exercise, diet, or pharmacologic agents—can attenuate obesity and improve glycemic control in preclinical models, and shows promising though modest effects in humans[9].

This review focuses on thermogenic failure as a mechanistic bridge between obesity and diabetes progression. Section 2 reviews the developmental origin and core biology of brown and beige adipocytes. Section 3 details how obesity disrupts thermogenic adipose tissue at cellular, mitochondrial, and neural levels. Section 4 explains how these defects propagate insulin resistance and β-cell stress. Section 5 covers BAT/beige endocrine functions. Section 6 summarizes current and emerging strategies to rescue thermogenesis. Section 7 outlines translational challenges and research priorities for leveraging thermogenic fat in obesity-driven T2D.

2. Brown vs Beige Adipocytes: Development, Regulation, and Function

Classical brown adipocytes originate from $Myf5^{+}$ mesodermal precursors shared with skeletal muscle, whereas beige adipocytes arise within WAT from $Myf5^{-}$ progenitors or via transdifferentiation of mature white adipocytes[11]. Brown adipocytes are abundant in interscapular depots in rodents and specific cervical/supraclavicular sites in humans; beige adipocytes appear mainly in subcutaneous depots upon stimulation[11]. Both cell types are rich in mitochondria and express UCP1, but they differ in gene signatures and regulatory inputs. Brown adipogenesis is driven by PRDM16, PGC-1α, EBF2, and BMP7, along with sympathetic innervation and thyroid hormones. Beige adipogenesis involves PRDM16, PPARγ, PGC-1α and is promoted by chronic cold, exercise, β3-agonists, and batokines such as FGF21 and irisin[12].

Functionally, BAT provides rapid, robust thermogenesis in response to cold or diet ("diet-induced thermogenesis"), while beige adipocytes offer more flexible, depot-specific thermogenic capacity. Both contribute to glucose and lipid disposal: cold-activated BAT uses glucose, NEFAs, and lipoprotein-derived triglycerides as fuels, protecting against hyperglycemia and hyperlipidemia[13, 14]. Beige fat can similarly enhance glucose uptake and increase local oxidative metabolism when activated. Thermogenic output is regulated by sympathetic nervous system (SNS) activity through β-adrenergic receptors (β1/β2/β3) on adipocytes. NE binding triggers cAMP–PKA signaling, lipolysis, and induction of thermogenic genes via PGC-1α and related transcriptional networks. Thyroid hormones, natriuretic peptides, sex steroids, and certain nutrients (e.g., capsaicin, ω-3 fatty acids) modulate this cascade[14].

Human data confirm that BAT activation increases whole-body energy expenditure and improves insulin-stimulated glucose disposal, although the quantitative contribution in adults is smaller than in rodents and varies widely among individuals[15]. Importantly, thermogenic adipocytes also produce batokines that act systemically, meaning their metabolic influence exceeds their mass or immediate heat output[15]. Thus, brown and beige adipocytes collectively form a thermogenic and endocrine organ that supports energy balance and insulin sensitivity. Thermogenic failure in obesity should be viewed as a breakdown in this integrated system rather than simple loss of UCP1 expression.

3. Mechanisms of Thermogenic Failure in Obesity

Obesity induces structural and functional changes that blunt thermogenic adipose tissue.

1.**Sympathetic and receptor defects;** In obesity, SNS tone may be globally elevated yet regionally ineffective. Chronic overnutrition and hyperleptinemia can desensitize β-adrenergic pathways in adipose tissue, reducing cAMP responses and UCP1 induction despite adequate NE[16]. Downregulation or uncoupling of β3-adrenergic receptors, impaired NE reuptake, and altered local catecholamine metabolism by immune cells further weaken thermogenic signaling.

2. **Mitochondrial dysfunction:** Thermogenic adipocytes depend on intact mitochondrial networks. Obesity is associated with swollen mitochondria, reduced cristae density, lower respiratory capacity, and increased ROS production in BAT and beige depots[17, 18]. These defects reduce UCP1-mediated proton leak and can trigger mitophagy or cell death. Systemic nutrient excess and lipotoxicity exacerbate mitochondrial damage via ceramides, DAGs, and chronic oxidative stress.

3. **Inflammation and fibrosis:** Thermogenic depots become infiltrated by pro-inflammatory macrophages and T cells in obesity, mirroring changes in WAT. Cytokines such as TNF-α and IL-1β suppress thermogenic gene programs, reduce PGC-1α expression, and promote ECM deposition and fibrosis, physically constraining adipocyte plasticity and perfusion[19].

4. **Impaired beige recruitment and progenitor senescence;** Obesity and aging drive senescent signatures in beige adipocyte progenitors, including DNA damage responses, cell-cycle arrest, and SASP factor secretion. These changes reduce responsiveness to browning stimuli and may actively inhibit neighboring cells[20].

5. **Endocrine and environmental antagonists;** Hyperinsulinemia, glucocorticoid excess, and certain endocrine disruptors can inhibit UCP1 expression and browning. Sleep disruption and thermoneutral indoor environments reduce cold-induced SNS activity, limiting endogenous BAT stimulation[20, 21]. These mechanisms converge to reduce BAT volume, diminish beige capacity, and blunt acute thermogenic responses—establishing a state of thermogenic failure that both reflects and reinforces obesity.

4. From Thermogenic Failure to Diabetes Progression

How does impaired thermogenic fat accelerate the transition from obesity to T2D?

Reduced nutrient clearance and ectopic fat: Active BAT/beige fat efficiently clears circulating triglyceride-rich lipoproteins and glucose, limiting substrate overflow to liver and muscle. In thermogenic failure, this buffer is lost, promoting hepatic steatosis and intramyocellular lipid accumulation key drivers of hepatic and muscle insulin resistance[20].

Lower energy expenditure and weight gain: Even modest reductions in adaptive thermogenesis can shift energy balance toward weight gain over years. Increased fat mass further aggravates insulin resistance through adipose inflammation, adipokine dysregulation, and lipotoxicity, creating a self-reinforcing loop[22].

Loss of batokine signalling: Thermogenic adipocytes secrete batokines such as FGF21 and NRG4 that enhance hepatic FAO, suppress de novo lipogenesis, and improve systemic insulin sensitivity[23]. Reduced batokine output in thermogenic failure may remove these protective endocrine signals, contributing to worsening dyslipidemia and hyperglycemia.

Mitochondrial-inflammation axis: Mitochondrial dysfunction in thermogenic fat can generate ROS and DAMPs that propagate local and systemic inflammation. Chronic inflammatory signaling in the liver, muscle, and islets impairs insulin signaling and β-cell survival[24].

Impact on β-cell workload: As peripheral insulin resistance rises, β-cells must increase insulin secretion to maintain euglycemia. In the absence of thermogenic sinks, glucose excursions are larger and lipid exposure is higher, increasing β-cell stress, promoting dedifferentiation, and ultimately accelerating β-cell failure and overt T2D[24]. Clinical observations are consistent: individuals with detectable BAT have lower odds of T2D and fewer complications, even after adjustment for BMI; conversely, BAT-negative status correlates with higher fasting glucose and insulin resistance[24]. Collectively, these data support thermogenic failure as an important, though not exclusive, driver of diabetes progression in obesity.

5. Endocrine and Paracrine Roles of Thermogenic Adipose Tissue

Thermogenic fat exerts systemic effects that go beyond heat:

Batokines and lipid mediators: BAT and beige fat secrete FGF21, NRG4, IL-6, and lipids such as 12,13-diHOME, which enhance muscle FA uptake, increase hepatic FAO, and improve glucose tolerance[25]. These factors also modulate vascular tone and inflammation, suggesting roles in cardiometabolic protection.

Crosstalk with muscle and liver: BAT activation increases skeletal muscle oxidative capacity and mitochondrial gene expression, possibly through batokines and altered substrate flux[25–27]. NRG4 from BAT suppresses hepatic lipogenesis and may slow progression of metabolic-associated steatotic liver disease (MASLD).

Local paracrine effects in WAT depots: Beige adipocytes within WAT can influence neighboring white adipocytes, immune cells, and vasculature via paracrine factors, improving local insulin sensitivity and limiting fibrosis. Conversely, thermogenic failure in these niches may shift the balance toward inflammatory, fibrotic remodeling[28–31].

Neuroendocrine feedback: BAT communicates with the CNS through sensory innervation and circulating signals, feeding back on appetite and sympathetic outflow. Rodent studies suggest that BAT activation can influence hypothalamic circuits to restrain food intake and improve glucose homeostasis[32]. Thus, thermogenic failure not only reduces heat production and substrate oxidation but also disrupts a complex endocrine network that normally counterbalances the metabolic stress of overnutrition.

6. Restoring Thermogenesis: Lifestyle, Surgical, and Pharmacologic Strategies

Cold exposure and lifestyle: Repeated mild cold exposure (e.g., 14–17 °C for several hours/day) increases BAT activity and can induce WAT browning in humans, improving insulin sensitivity and postprandial glucose disposal, though effects are modest and require adherence[33]. Exercise promotes beige fat via myokines (irisin, IL-6), natriuretic peptides, and improved mitochondrial function. Healthy sleep and thermoregulation patterns may support endogenous BAT activation[33].

Bariatric and metabolic surgery: Bariatric surgery improves thermogenic capacity indirectly by reducing adiposity, inflammation, and lipotoxicity, and directly via changes in bile acids, gut hormones, and SNS activity that favor BAT activation and WAT browning. Post-surgery patients often show increased cold-induced thermogenesis and improved BAT imaging signals alongside rapid remission of T2D[34].

β3-adrenergic agonists and sympathomimetics: Selective β3-agonists (e.g., mirabegron) increase BAT glucose uptake and energy expenditure in humans but may raise heart rate and blood pressure at doses required for metabolic effects[35]. Refining dose, delivery, and receptor selectivity or using peripherally restricted agents may improve the risk–benefit ratio.

Hormonal and peptide therapies: FGF21 analogs, GLP-1/GIP agonists, and thyroid hormone receptor β agonists enhance thermogenic gene expression and browning in preclinical models and may partly act through BAT/beige recruitment in humans[36–38]. Their strong weight-loss and glycemic effects make it difficult to isolate BAT-specific contributions, but they illustrate how systemic endocrine manipulation can secondarily rescue thermogenesis.

Mitochondrial and metabolic modulators: Compounds that enhance mitochondrial biogenesis, improve electron transport, or reduce ROS (e.g., PGC-1α activators, targeted antioxidants) may restore thermogenic capacity when combined with adrenergic stimulation[39].

Overall, existing interventions can partially reverse thermogenic failure but rarely fully normalize BAT/beige function in long-standing obesity, underscoring the need for earlier prevention and more precise BAT-targeted therapies.

7. Therapeutic Horizons and Research Priorities

Given its central role in energy and glucose homeostasis, thermogenic adipose tissue is an

Biomarkers and imaging

Advanced PET tracers, MRI techniques, and infrared thermography are improving BAT detection and functional assessment. Blood-based markers (batokines, acylcarnitines, thermogenic gene transcripts in circulating cells) may allow less invasive monitoring[40]. Combining imaging with multi-omic profiling of adipose biopsies can define "thermogenic signatures" to stratify patients and track response to interventions.

Precision activation and cell engineering

Emerging approaches include: Depot-targeted delivery of β3-agonists or gene therapies; CRISPR-based editing of key thermogenic regulators (e.g., PRDM16, UCP1, m6A machinery) in adipocyte precursors;[41], and cell-based therapies using ex vivo–engineered beige adipocytes or progenitors implanted into metabolically active depots.

Integration with current T2D care

In practice, thermogenic strategies will likely complement GLP-1/GIP agonists, SGLT2 inhibitors, and insulin sensitizers, rather than replace them. BAT/beige activation may be particularly valuable for patients with residual obesity, high ectopic fat, or specific thermogenic deficits identifiable via imaging or biomarkers[41].

Future directions

Priority areas include: Dissecting depot-specific roles of BAT vs beige fat in humans; clarifying batokine networks and their receptors; mapping how early-life nutrition and temperature exposure program lifetime thermogenic capacity; and designing trials where BAT activation is a pre-specified primary endpoint linked to glycemic and cardiovascular outcomes.

CONCLUSION

In summary, thermogenic failure is an under-appreciated mechanism connecting obesity to diabetes progression. Preserving or restoring brown and beige adipose tissue function—thermogenic and endocrine—offers a promising avenue to blunt this progression. The challenge now is to convert mechanistic insight into safe, scalable, and personalized interventions that can be integrated into the comprehensive management of obesity-driven T2D.

REFERENCES

1. Sidossis, L., Kajimura, S.: Brown and beige fat in humans: thermogenic adipocytes that control energy and glucose homeostasis. J. Clin. Invest. 125, 478–486 (2015). https://doi.org/10.1172/JCI78362

2. Ikeda, K., Yamada, T.: UCP1 Dependent and Independent Thermogenesis in Brown and Beige Adipocytes. Front. Endocrinol. 11, 498 (2020). https://doi.org/10.3389/fendo.2020.00498
3. Wibmer, A.G., Becher, T., Eljalby, M., Crane, A., Andrieu, P.C., Jiang, C.S., Vaughan, R., Schöder, H., Cohen, P.: Brown adipose tissue is associated with healthier body fat distribution and metabolic benefits independent of regional adiposity. Cell Rep. Med. 2, 100332 (2021). https://doi.org/10.1016/j.xcrm.2021.100332
4. Kulterer, O.C., Herz, C.T., Prager, M., Schmöltzer, C., Langer, F.B., Prager, G., Marculescu, R., Kautzky-Willer, A., Hacker, M., Haug, A.R., Kiefer, F.W.: Brown Adipose Tissue Prevalence Is Lower in Obesity but Its Metabolic Activity Is Intact. Front. Endocrinol. 13, 858417 (2022). https://doi.org/10.3389/fendo.2022.858417
5. Brandão, B.B., Poojari, A., Rabiee, A.: Thermogenic Fat: Development, Physiological Function, and Therapeutic Potential. Int. J. Mol. Sci. 22, 5906 (2021). https://doi.org/10.3390/ijms22115906
6. Roberts, L.D., Boström, P., O'Sullivan, J.F., Schinzel, R.T., Lewis, G.D., Dejam, A., Lee, Y.-K., Palma, M.J., Calhoun, S., Georgiadi, A., Chen, M.-H., Ramachandran, V.S., Larson, M.G., Bouchard, C., Rankinen, T., Souza, A.L., Clish, C.B., Wang, T.J., Estall, J.L., Soukas, A.A., Cowan, C.A., Spiegelman, B.M., Gerszten, R.E.: β-Aminoisobutyric Acid Induces Browning of White Fat and Hepatic β-Oxidation and Is Inversely Correlated with Cardiometabolic Risk Factors. Cell Metab. 19, 96–108 (2014). https://doi.org/10.1016/j.cmet.2013.12.003
7. Wang, S., Liu, Y., Chen, J., He, Y., Ma, W., Liu, X., Sun, X.: Effects of multi-organ crosstalk on the physiology and pathology of adipose tissue. Front. Endocrinol. 14, 1198984 (2023). https://doi.org/10.3389/fendo.2023.1198984
8. Yin, X., Chen, Y., Ruze, R., Xu, R., Song, J., Wang, C., Xu, Q.: The evolving view of thermogenic fat and its implications in cancer and metabolic diseases. Signal Transduct. Target. Ther. 7, 324 (2022). https://doi.org/10.1038/s41392-022-01178-6
9. Hernández-Aguilera, A., Rull, A., Rodríguez-Gallego, E., Riera-Borrull, M., Luciano-Mateo, F., Camps, J., Menéndez, J.A., Joven, J.: Mitochondrial Dysfunction: A Basic Mechanism in Inflammation-Related Non-Communicable Diseases and Therapeutic Opportunities. Mediators Inflamm. 2013, 135698 (2013). https://doi.org/10.1155/2013/135698
10. Obasi, D.C., Abba, J.N., Aniokete, U.C., Okoroh, P.N., Akwari, A.Ak.: Evolving Paradigms in Nutrition Therapy for Diabetes: From Carbohydrate Counting to Precision Diets. Obes. Med. 100622 (2025). https://doi.org/10.1016/j.obmed.2025.100622
11. Ikeda, K., Maretich, P., Kajimura, S.: The common and distinct features of brown and beige adipocytes. Trends Endocrinol. Metab. TEM. 29, 191–200 (2018). https://doi.org/10.1016/j.tem.2018.01.001
12. Ghesmati, Z., Rashid, M., Fayezi, S., Gieseler, F., Alizadeh, E., Darabi, M.: An update on the secretory functions of brown, white, and beige adipose tissue: Towards therapeutic applications. Rev. Endocr. Metab. Disord. 25, 279–308 (2024). https://doi.org/10.1007/s11154-023-09850-0
13. Mukherjee, J., Baranwal, A., Schade, K.N.: Classification of Therapeutic and Experimental Drugs for Brown Adipose Tissue Activation: Potential Treatment Strategies for Diabetes and Obesity. Curr. Diabetes Rev. 12, 414–428 (2016). https://doi.org/10.2174/1573399812666160517115450
14. Lizcano, F.: The Beige Adipocyte as a Therapy for Metabolic Diseases. Int. J. Mol. Sci. 20, 5058 (2019). https://doi.org/10.3390/ijms20205058
15. Marlatt, K.L., Ravussin, E.: Brown Adipose Tissue: An Update on Recent Findings. Curr. Obes. Rep. 6, 389–396 (2017). https://doi.org/10.1007/s13679-017-0283-6
16. Thorp, A.A., Schlaich, M.P.: Relevance of Sympathetic Nervous System Activation in Obesity and Metabolic Syndrome. J. Diabetes Res. 2015, 341583 (2015). https://doi.org/10.1155/2015/341583
17. Chouchani, E.T., Kazak, L., Spiegelman, B.M.: Mitochondrial reactive oxygen species and adipose tissue thermogenesis: Bridging physiology and mechanisms. J. Biol. Chem. 292, 16810–16816 (2017). https://doi.org/10.1074/jbc.R117.789628
18. Alum, E.U.: Metabolic memory in obesity: Can early-life interventions reverse lifelong risks? Obes. Med. 55, 100610 (2025). https://doi.org/10.1016/j.obmed.2025.100610
19. Mandal, M., Mamun, M.A.A., Rakib, A., Singh, U.P.: High-fat diet-induced adipose tissue-resident macrophages, T cells, and dendritic cells modulate chronic inflammation and adipogenesis during obesity. Front. Immunol. 16, 1524544 (2025). https://doi.org/10.3389/fimmu.2025.1524544
20. Narasimhan, A., Flores, R.R., Camell, C.D., Bernlohr, D.A., Robbins, P.D., Niedernhofer, L.J.: Cellular Senescence in Obesity and Associated Complications: a New Therapeutic Target. Curr. Diab. Rep. 22, 537–548 (2022). https://doi.org/10.1007/s11892-022-01493-w
21. Alum, E.U.: Circadian nutrition and obesity: timing as a nutritional strategy. J. Health Popul. Nutr. 44, 367 (2025). https://doi.org/10.1186/s41043-025-01102-y

22. Chait, A., den Hartigh, L.J.: Adipose Tissue Distribution, Inflammation and Its Metabolic Consequences, Including Diabetes and Cardiovascular Disease. Front. Cardiovasc. Med. 7, (2020). https://doi.org/10.3389/fcvm.2020.00022
23. Lee, E., Korf, H., Vidal-Puig, A.: An adipocentric perspective on the development and progression of non-alcoholic fatty liver disease. J. Hepatol. 78, 1048–1062 (2023). https://doi.org/10.1016/j.jhep.2023.01.024
24. Choi, W., Woo, G.H., Kwon, T.-H., Jeon, J.-H.: Obesity-Driven Metabolic Disorders: The Interplay of Inflammation and Mitochondrial Dysfunction. Int. J. Mol. Sci. 26, 9715 (2025). https://doi.org/10.3390/ijms26199715
25. Yang, F.T., Stanford, K.I.: Batokines: Mediators of Inter-Tissue Communication (a Mini-Review). Curr. Obes. Rep. 11, 1–9 (2022). https://doi.org/10.1007/s13679-021-00465-7
26. Cavagna, L., Seminari, E., Zanframundo, G., Gregorini, M., Di Matteo, A., Rampino, T., Montecucco, C., Pelenghi, S., Cattadori, B., Pattonieri, E.F., Vitulo, P., Bertani, A., Sambataro, G., Vancheri, C., Biglia, A., Bozzalla-Cassione, E., Bonetto, V., Monti, M.C., Ticozzelli, E., Turco, A., Oggionni, T., Corsico, A., Bertuccio, F., Zuccaro, V., Codullo, V., Morosini, M., Marena, C., Gnecchi, M., Pellegrini, C., Meloni, F.: Calcineurin Inhibitor-Based Immunosuppression and COVID-19: Results from a Multidisciplinary Cohort of Patients in Northern Italy. Microorganisms. 8, 977 (2020). https://doi.org/10.3390/microorganisms8070977
27. Colson, C., Batrow, P.-L., Gautier, N., Rochet, N., Ailhaud, G., Peiretti, F., Amri, E.-Z.: The Rosmarinus Bioactive Compound Carnosic Acid Is a Novel PPAR Antagonist That Inhibits the Browning of White Adipocytes. Cells. 9, 2433 (2020). https://doi.org/10.3390/cells9112433
28. Abed, H.F., Abuwatfa, W.H., Husseini, G.A.: Redox-Responsive Drug Delivery Systems: A Chemical Perspective. Nanomaterials. 12, 3183 (2022). https://doi.org/10.3390/nano12183183
29. Aremu, T.O., Oluwole, O.E., Adeyinka, K.O., Schommer, J.C.: Medication Adherence and Compliance: Recipe for Improving Patient Outcomes. Pharm. J. Pharm. Educ. Pract. 10, 106 (2022). https://doi.org/10.3390/pharmacy10050106
30. Ariyanto, E.F., Wirajati, F., Rahman, P.H., Berbudi, A., Rohmawaty, E.: Mechanism of action of Indonesian medicinal plants in inhibiting 3T3-L1 adipocyte differentiation: A review. J. Appl. Pharm. Sci. 13, 050–057 (2023). https://doi.org/10.7324/JAPS.2023.6711
31. Chaturvedi, S., Gupta, P.: Chapter 8 - Plant secondary metabolites for preferential targeting among various stressors of metabolic syndrome. In: Atta-ur-Rahman (ed.) Studies in Natural Products Chemistry. pp. 221–261. Elsevier (2021)
32. Till, A., Fries, C., Fenske, W.K.: Brain-to-BAT - and Back?: Crosstalk between the Central Nervous System and Thermogenic Adipose Tissue in Development and Therapy of Obesity. Brain Sci. 12, 1646 (2022). https://doi.org/10.3390/brainsci12121646
33. Ka, I., J, B., M, C., M, W., Oc, H., M, M., J, H., C, S., L, R., A, W., Ar, H., Fw, K., H, L., Sm, S.: Cold-Induced Brown Adipose Tissue Activity Alters Plasma Fatty Acids and Improves Glucose Metabolism in Men. J. Clin. Endocrinol. Metab. 102, (2017). https://doi.org/10.1210/jc.2017-01250
34. Latteri, S., Sofia, M., Puleo, S., Di Vincenzo, A., Cinti, S., Castorina, S.: Mechanisms linking bariatric surgery to adipose tissue, glucose metabolism, fatty liver disease and gut microbiota. Langenbecks Arch. Surg. 408, 101 (2023). https://doi.org/10.1007/s00423-023-02821-8
35. Bs, F., H, M., B, Z., Al, C., Hj, V., Rh, E.K., Zr, J., Pm, W., J, C., Aj, M., Pg, S., Ee, D.-V., Pa, K.: The β3-adrenergic receptor agonist mirabegron improves glucose homeostasis in obese humans. J. Clin. Invest. 130, (2020). https://doi.org/10.1172/JCI134892
36. Arow, Z., Hornik-Lurie, T., Hilu, R., Giladi, E., Arnson, Y., Vaknin-Assa, H., Assali, A., Pereg, D.: SGLT2 inhibitors and GLP-1 receptor agonists: impact on mortality in diabetic patients with cardiovascular disease. Cardiovasc. Diabetol. 24, 353 (2025). https://doi.org/10.1186/s12933-025-02874-7
37. Chai, S., Niu, Y., Liu, F., Wu, S., Yang, Z., Sun, F.: Comparison of GLP-1 Receptor Agonists, SGLT-2 Inhibitors, and DPP-4 Inhibitors as an Add-On Drug to Insulin Combined With Oral Hypoglycemic Drugs: Umbrella Review. J. Diabetes Res. 2024, 8145388 (2024). https://doi.org/10.1155/2024/8145388
38. Liu, Q.K.: Mechanisms of action and therapeutic applications of GLP-1 and dual GIP/GLP-1 receptor agonists. Front. Endocrinol. 15, 1431292 (2024). https://doi.org/10.3389/fendo.2024.1431292
39. Abu Shelbayeh, O., Arroum, T., Morris, S., Busch, K.B.: PGC-1α Is a Master Regulator of Mitochondrial Lifecycle and ROS Stress Response. Antioxidants. 12, 1075 (2023). https://doi.org/10.3390/antiox12051075
40. Kordić, M., Dugandžić, J., Ratko, M., Habek, N., Dugandžić, A.: Infrared Thermography for the Detection of Changes in Brown Adipose Tissue Activity. J. Vis. Exp. JoVE. (2022). https://doi.org/10.3791/64463
41. Mao, L., Lu, J., Hou, Y., Nie, T.: Directly targeting PRDM16 in thermogenic adipose tissue to treat obesity and its related metabolic diseases. Front. Endocrinol. 15, (2024). https://doi.org/10.3389/fendo.2024.1458848

CITE AS: Alberta Jeanne N. (2026). Thermogenic Failure: How Impaired Brown and Beige Adipose Tissue Links Obesity to Diabetes Progression. Research Output Journal of Public Health and Medicine 6(1):125-131. https://doi.org/10.59298/ROJPHM/2026/61125131