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Adipose Tissue Immunometabolism as a Unifying Driver of Obesity and Type 2 Diabetes

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ABSTRACT

Adipose tissue is now recognized as an immune organ as much as a fat depot. In obesity, expansion and stress of white adipose tissue (WAT) drive a coordinated rewiring of immune and metabolic pathways "immunometabolism" that links weight gain to insulin resistance and type 2 diabetes (T2D). Lean adipose tissue is enriched in type 2 immune cells (M2-like macrophages, eosinophils, ILC2s, regulatory T cells), which support insulin sensitivity, lipolysis, and thermogenesis. With chronic overnutrition, hypertrophic adipocytes become hypoxic, stressed, and dying; chemokines and lipotoxic signals recruit and reprogram myeloid and lymphoid cells toward pro-inflammatory, glycolysis-dependent phenotypes, forming crown-like structures (CLS) and amplifying cytokine production. Adipose tissue macrophages (ATMs) emerge as central hubs controlling lipid handling, mitochondrial function, thermogenesis, and systemic glucose homeostasis. This review synthesizes current knowledge on adipose tissue immunometabolism as a unifying driver of obesity and T2D. We outline the cellular landscape of adipose immune cells, their metabolic programs, and how obesogenic cues reshape ATM, T-cell, and innate lymphoid cell states. We then discuss how these immunometabolic shifts impair adipocyte biology, disrupt endocrine outputs, and propagate systemic insulin resistance and β-cell stress. Protective pathways involving brown and beige fat, type 2 immunity, and mitochondrial crosstalk are contrasted with inflammatory circuits. Finally, we examine evidence that lifestyle, weight loss, and pharmacologic therapies can remodel adipose immunometabolism, and highlight emerging immunometabolic targets and biomarkers for precision treatment of obesity-driven T2D.

Keywords: adipose tissue; immunometabolism; macrophages; obesity; type 2 diabetes

INTRODUCTION

The classic view of adipose tissue as a passive energy store has been overturned. White adipose tissue (WAT) is now understood as a dynamic endocrine and immune organ, integrating nutrient availability with systemic metabolism through adipokines, lipids, and cytokines. In obesity, WAT expansion is not simply a matter of extra fat; it triggers profound remodeling of stromal, vascular, and immune compartments that collectively drive insulin resistance and T2D[1–3].

Lean WAT contains adipocytes, preadipocytes, adipose stem cells (ASCs), endothelial cells, fibroblasts, sympathetic fibers, and a rich immune infiltrate. Innate and adaptive immune cells including tissue-resident macrophages, eosinophils, mast cells, type 2 innate lymphoid cells (ILC2s), NK/NKT cells, B cells, $CD4^+$ and $CD8^+$ T cells, and a specialized pool of regulatory T cells (Tregs) participate in tissue development, vascularization, extracellular matrix (ECM) homeostasis, and thermoregulation[4, 5]. In the lean state, this milieu is skewed toward "type 2" immunity: alternatively activated macrophages, IL-4/IL-13–producing ILC2s, eosinophils, and Tregs; together they maintain insulin sensitivity, promote beige adipogenesis, and restrain inflammation[6].

Immunometabolism how metabolic pathways shape immune cell function and how immune signals alter cellular metabolism offers a conceptual framework linking obesity to T2D. In immune cells, activation states (e.g., pro- vs anti-inflammatory) are tightly coupled to metabolic programs such as glycolysis, oxidative phosphorylation (OXPHOS), fatty acid oxidation (FAO), and glutaminolysis. Pro-inflammatory, "M1-like" macrophages rely heavily on aerobic glycolysis and disrupted tricarboxylic acid (TCA) flux, whereas "M2-like" macrophages favor OXPHOS and FAO. Similar metabolic imprinting occurs in T cells, with effector subsets using glycolysis and memory/Treg cells relying more on OXPHOS and FAO[7–9].

In obesity, chronic nutrient excess, adipocyte hypertrophy, and hypoxia create a microenvironment rich in FFAs, cholesterol, ceramides, ROS, and damage-associated molecular patterns (DAMPs). These signals activate pattern-recognition receptors (e.g., TLR4) and stress pathways (NF-κB, JNK, inflammasomes) in adipocytes and resident immune cells[10]. Adipocytes upregulate chemokines such as CCL2 and CCL5, recruiting

monocytes and T cells; ASCs can also secrete CCL5 in response to TNF-α via NF-κB, promoting early T-cell infiltration[11].

Macrophage accumulation is a hallmark of obese WAT. In lean tissue, resident ATMs support lipid buffering and tissue remodeling. With progressive obesity, large numbers of monocyte-derived macrophages infiltrate and adopt metabolically activated, inflammatory phenotypes that surround dying adipocytes in crown-like structures (CLS). These CLS macrophages exhibit high glycolytic flux, increased lipid uptake, and robust secretion of TNF-α, IL-1β, IL-6, and chemokines that propagate local and systemic inflammation[12]. The density of CLS strongly correlates with insulin resistance and cardiometabolic risk in humans.

Adipose immunometabolism is not restricted to myeloid cells. Obesity reshapes the T-cell compartment, reducing tissue Tregs and ILC2s while expanding Th1, Th17, and cytotoxic $CD8^+$ T cells that secrete IFN-γ and other pro-inflammatory mediators. These lymphocytes further polarize ATMs toward inflammatory states and impair β-adrenergic signaling to adipocytes, dampening lipolysis and thermogenesis. Regulatory T cells in visceral adipose tissue (VAT) display unique transcriptional and metabolic programs, including cholesterol metabolism signatures that are crucial for their maintenance and anti-inflammatory function; obesity disrupts these pathways, aggravating VAT inflammation and insulin resistance[13, 14].

Concurrently, adipocyte intrinsic metabolism is altered. Mitochondrial biogenesis and respiration decline, lipid droplet dynamics are impaired, and ER stress and oxidative stress increase. ATMs and other immune cells respond to these changes and, in turn, enforce them via cytokines, catecholamine metabolism, and direct organelle exchange. For example, ATMs can take up mitochondria from adipocytes; disruption of this mitochondrial transfer worsens obesity and insulin resistance, highlighting bidirectional metabolic crosstalk[14–16].

The net effect is a vicious cycle: hypertrophic, hypoxic adipocytes drive inflammatory immune activation; immune cells adopt pathologic metabolic programs that further impair adipocyte function and endocrine outputs (adiponectindecrease, leptin increase, resistin increase, pro-inflammatory adipokines increase). These changes inhibit insulin signaling in adipose tissue, promote ectopic lipid deposition in liver and muscle, and increase flux of FFAs and cytokines to the systemic circulation, ultimately contributing to whole-body insulin resistance and β-cell overwork[17, 18].

Thus, adipose tissue immunometabolism offers a unified view of obesity and T2D: disease progression reflects progressive failure of immune–metabolic cooperation within WAT. The following sections dissect the cellular players, metabolic rewiring, systemic consequences, and therapeutic opportunities emerging from this perspective.

2. Cellular Landscape of Adipose Tissue Immunometabolism

Adipose tissue harbors one of the body's most diverse immune ecosystems. In lean WAT, resident ATMs, eosinophils, ILC2s, mast cells, NK/NKT cells, B cells, and multiple T-cell subsets form a network that actively maintains tissue homeostasis[19].

Adipose tissue macrophages (ATMs)

Lean ATMs are mostly tissue-resident and display an alternatively activated, M2-like phenotype characterized by expression of CD206, CD163, and genes associated with FAO and OXPHOS. They clear debris, remodel ECM, and buffer lipids by taking up FA and cholesterol from adipocytes. In obesity, ATM composition changes dramatically: recruited monocyte-derived macrophages accumulate, forming heterogeneous subpopulations including metabolically activated (MMe), lipid-associated macrophages (LAMs, often $TREM2^+$), and $CD9^+$ macrophages concentrated in CLS. These subsets show high glycolysis, lipid handling, and inflammatory transcriptional signatures[2, 20].

T cells and B cells

Lean VAT is enriched in Tregs with distinct TCR repertoires and transcriptional programs, including PPARγ and ST2 expression, that support anti-inflammatory cytokine production and metabolic control. Obesity reduces these Tregs and increases IFN-γ–producing Th1 and cytotoxic $CD8^+$ T cells that promote ATM inflammation. B cells also shift toward pro-inflammatory phenotypes, producing pathogenic antibodies and cytokines that exacerbate insulin resistance[13].

Innate lymphoid and granulocytic cells

ILC2s, supported by IL-33 from stromal and endothelial cells, produce IL-5 and IL-13, fostering eosinophil survival and M2-like macrophage polarization; they also directly promote beige adipogenesis and thermogenesis. Eosinophils supply IL-4/IL-13, reinforcing type 2 immunity. Neutrophils and pro-inflammatory mast cells, by contrast, increase early in obesity and contribute to insulin resistance via elastase, proteases, and cytokines[21, 22].

Adipose stem and stromal cells

ASCs regulate immune infiltration by producing chemokines such as CCL5 in response to TNF-α, driving early T-cell recruitment and setting the stage for chronic inflammation. Perivascular cells, fibroblasts, and endothelial cells also express adhesion molecules and cytokines that shape immune composition and niche-specific immunometabolism[23].This cellular complexity underscores that adipose immunometabolism is not simply

"macrophage inflammation" but an emergent property of many immune–stromal interactions, tuned by nutrient status and adipocyte health.

3. Immunometabolic Reprogramming of Adipocytes and ATMs in Obesity

Obesity drives coordinated metabolic rewiring of both adipocytes and ATMs.

Adipocyte metabolic stress

With chronic caloric excess, adipocytes enlarge (hypertrophy) and, in visceral depots, outstrip local vascular supply, leading to hypoxia and fibrosis. Hypoxic and stressed adipocytes accumulate saturated FAs, ceramides, and DAGs, activate HIF-1α, ER stress pathways, and produce ROS. They secrete CCL2, CCL5, CXCL chemokines, TNF-α, IL-6, and lipids that recruit and activate immune cells. Adipocyte mitochondrial biogenesis and OXPHOS decline, limiting FAO and increasing lipid spillover to liver and muscle[24, 25].

ATM metabolic polarization

In lean WAT, ATMs rely more on FAO and OXPHOS, supporting tissue remodeling and efferocytosis with low inflammatory output. Obesity pushes ATMs toward glycolysis-dominant, MMe-like states. Lipid uptake via CD36 and scavenger receptors, engagement of TLR4 by FFAs and LPS, and exposure to IFN-γ and TNF-α activate NF-κB and inflammasomes, promoting transcription of IL-1β, IL-6, TNF-α, and chemokines. Metabolic intermediates (succinate, citrate) feedback to stabilize HIF-1α and drive inflammatory gene expression, while mitochondrial dysfunction further skews toward glycolysis[19, 26].

ATMs also control adipocyte metabolism through multiple mechanisms:

i. **Lipid buffering:** By taking up excess lipids from adipocytes and dead cells, ATMs influence local lipotoxicity but may become foam-cell–like, reinforcing inflammation.
ii. **Cytokine signaling:** ATM-derived TNF-α, IL-1β, and IL-6 inhibit insulin signaling in adipocytes via serine phosphorylation of IRS proteins and suppression of GLUT4.
iii. **Catecholamine handling:** ATMs can uptake and degrade catecholamines, dampening β-adrenergic signaling and reducing lipolysis and thermogenesis.
iv. **Organelle transfer:** Mitochondrial transfer from adipocytes to ATMs modulates both cell types; defective transfer is linked to metabolic deterioration[16, 22].

Beyond M1/M2

Omics studies highlight that the simple M1/M2 dichotomy is insufficient in obese WAT. Single-cell sequencing reveals multiple ATM states, including LAMs expressing TREM2 and genes involved in lipid catabolism and lysosomal function, as well as subsets associated with fibrosis or thermogenesis control. This heterogeneity reflects nuanced immunometabolic programs tailored to specific micro-niches (CLS vs interstitial regions vs perivascular areas)[14, 27]. Thus, obesity does not just increase ATM number; it shifts their metabolic wiring and specialization, creating a mosaic of immunometabolic states that collectively disrupt adipose and systemic homeostasis.

4. From Adipose Inflammation to Systemic Insulin Resistance and T2D

Adipose tissue immunometabolism drives systemic insulin resistance through several interconnected mechanisms.

Autocrine/paracrine insulin resistance in adipose tissue

Pro-inflammatory cytokines from ATMs and T cells (TNF-α, IL-1β, IL-6, IFN-γ) impair insulin signaling in adipocytes by activating JNK and IKKβ, promoting serine phosphorylation and degradation of IRS1/2, and reducing GLUT4 expression. Locally, this blunts insulin-stimulated glucose uptake and suppresses antilipolytic signaling, increasing lipolysis and FFA release[2].

FFA and cytokine flux to liver and muscle

Excess FFAs delivered to liver promote steatosis, VLDL overproduction, and hepatic insulin resistance via DAG–PKCε activation. Skeletal muscle exposed to elevated FFAs and inflammatory cytokines accumulates lipid intermediates, impairing insulin signaling and glucose disposal. Thus, dysfunctional WAT becomes a source of lipids and inflammatory mediators that propagate insulin resistance across organs[28, 29].

Endocrine adipokine imbalance

Obese, inflamed WAT produces less adiponectin (insulin-sensitizing, anti-inflammatory) and more leptin, resistin, and pro-inflammatory adipokines[10]. Reduced adiponectin impairs FAO in liver and muscle and promotes vascular inflammation, while hyperleptinemia with leptin resistance affects appetite regulation and immune activation[30, 31].

Crosstalk with pancreatic islets

Cytokines and lipids from WAT reach pancreatic islets, where they promote β-cell stress, dedifferentiation, and apoptosis. Chronic hyperinsulinemia driven by peripheral insulin resistance further stresses β-cells. Adipose-derived exosomes carrying miRNAs and proteins can directly modulate β-cell gene expression and survival. Together, these signals couple adipose immunometabolism to β-cell failure and overt T2D[32–34].

Vascular and systemic inflammation

Inflamed WAT releases IL-6, TNF-α, and acute-phase mediators that act on liver and endothelium, driving CRP production and vascular dysfunction. Endothelial insulin resistance, reduced NO bioavailability, and

increased adhesion molecule expression promote atherosclerosis, explaining why obesity and T2D are tightly linked to cardiovascular disease[35].

In sum, adipose tissue immunometabolism acts as an upstream "organ-level driver" of metabolic syndrome, integrating local immune–metabolic dysfunction with whole-body insulin resistance, β-cell stress, and vascular disease.

5. Brown/Beige Fat, Type 2 Immunity and Protective Immunometabolism

Not all adipose immunometabolism is detrimental. Brown adipose tissue (BAT) and beige adipocytes in WAT depots exemplify immunometabolic programs that protect against obesity and T2D.

Immune control of thermogenesis

BAT and beige fat use UCP1-dependent and UCP1-independent mechanisms (Ca^{2+} cycling, creatine and TAG/FA cycling) to dissipate energy as heat and enhance glucose and lipid clearance. Immune cells, especially alternatively activated macrophages, eosinophils, ILC2s, and select T-cell subsets, actively regulate these thermogenic programs[36].

Cold exposure and β-adrenergic stimulation promote type 2 immune responses in adipose tissue: ILC2s and eosinophils produce IL-5/IL-13; macrophages adopt M2-like states; Tregs accumulate; collectively these cells support beige adipogenesis and UCP1 expression. Conversely, obesity blunts these circuits, reducing thermogenic capacity.

Adipose Tregs and ILC2s as metabolic guardians

VAT Tregs and ILC2s represent specialized immunometabolic regulators. VAT Tregs depend on PPARγ and cholesterol metabolism pathways (e.g., SREBF2-driven programs) to survive and function; they suppress local inflammation and normalize metabolic parameters. Obesity reduces or reshapes these Tregs, tipping the balance toward inflammatory T cells and ATMs. ILC2s respond to IL-33 and other alarmins, promoting beige adipocyte differentiation and maintaining insulin sensitivity; their loss in obesity contributes to thermogenic failure[37].

Macrophages in BAT and beige fat

In BAT and beige depots, macrophages can either enhance or impair thermogenesis depending on polarization and niche. M2-like macrophages support sympathetic signaling, protect mitochondria, and clear lipids, whereas inflammatory macrophages can degrade catecholamines and secrete cytokines that suppress thermogenic gene expression. Recent work highlights that macrophage-derived signals and organelle interactions are integral to long-term thermogenic adaptations[9, 38].

These observations suggest that "beneficial immunometabolism" type 2 immune tone, Treg/ILC2 enrichment, M2-like ATMs, robust mitochondrial function can counteract obesity and preserve insulin sensitivity. Strategies that restore or mimic these protective immune circuits (e.g., IL-33 agonism, Treg/ILC2 expansion, targeted macrophage reprogramming) are emerging as potential therapies to treat obesity-driven T2D by enhancing energy expenditure and resolving inflammation.

6. Remodeling Adipose Immunometabolism: Weight Loss, Lifestyle and Pharmacologic Interventions

A central translational question is how plastic adipose immunometabolism is—and to what extent it can be reset by interventions.

Weight loss and lifestyle change

Caloric restriction and weight loss improve insulin sensitivity and reduce adipose inflammation. Human and animal studies show decreased ATM content, reduced CLS, and partial repolarization toward less inflammatory macrophage states. Treg and ILC2 levels can recover, and expression of thermogenic genes and mitochondrial function in adipocytes improves. Single-cell analyses indicate that caloric restriction after obesity promotes emergence of distinct macrophage subsets associated with tissue repair and improved metabolism[39].

Physical activity also remodels adipose immunometabolism, reducing inflammatory cytokines and improving adipocyte mitochondrial function. Diet composition modulates immune tone: fiber-derived SCFAs and polyphenols exhibit HDAC-inhibitory and anti-inflammatory effects; omega-3 FAs can shift macrophage and T-cell phenotypes toward resolving states[39, 40].

Bariatric surgery

Bariatric surgery induces rapid and profound improvements in glycemia and insulin sensitivity that outpace weight loss alone. Post-surgery adipose tissue shows reduced ATM infiltration, fewer CLS, improved vascularization, and increased markers of beige adipogenesis. Immune cell composition shifts toward less inflammatory profiles, though some immunometabolic scars persist, particularly in long-standing obesity[28].

Antidiabetic pharmacotherapies

Metformin reduces hepatic glucose production but also exerts anti-inflammatory and immunometabolic effects in adipose tissue, partly via AMPK activation. GLP-1 receptor agonists and dual/triple incretin agonists promote weight loss, decrease WAT inflammation, and enhance thermogenesis in brown/beige fat. SGLT2 inhibitors improve adipose morphology and reduce inflammatory markers, potentially via shifts in fuel utilization and adipokine profiles. These drugs may indirectly reprogram adipose immunometabolism, although detailed immune–metabolic mapping is ongoing[35, 41].

Limits of reversibility

Not all changes fully revert. Long-duration obesity is associated with persistent fibrosis, ECM remodeling, and altered stromal niches that maintain inflammatory immune states despite weight loss. Early-life obesity or high-

fat diet exposure may imprint long-lasting immunometabolic programs in ATMs and T cells[33]. Thus, timing, magnitude, and durability of intervention critically determine how far adipose immunometabolism can be normalized, reinforcing the value of early and sustained treatment[42].

7. Therapeutic Targets, Biomarkers and Future Directions

Viewing obesity and T2D through the lens of adipose immunometabolism opens new therapeutic and diagnostic avenues.

Cellular and molecular targets

ATMs are prime targets. Approaches include blocking chemokine axes (e.g., CCL2–CCR2, CCL5–CCR5) to reduce monocyte recruitment, inhibiting TLR4 or inflammasomes, or reprogramming ATMs toward lipid-handling, pro-resolving phenotypes (e.g., via PPARγ agonism, omega-3 derivatives, or selective metabolic modulators). Trials must balance efficacy with preservation of host defense[43].

Enhancing protective immune circuits is another strategy: IL-33 or related pathways to expand adipose Tregs and ILC2s; adoptive or in situ boosting of VAT Tregs; or interventions that promote type 2 immunity and beige adipogenesis without provoking allergy or fibrosis. Targeting immune cell metabolism (e.g., glycolysis in inflammatory ATMs, cholesterol metabolism in VAT Tregs) offers precision leverage points to reshape function without global immunosuppression[43].

Immunometabolic biomarkers

Adipose immunometabolism may be tracked via circulating markers: adipokines (adiponectin, leptin), inflammatory cytokines, chemokines, and soluble receptors; exosomal miRNAs and proteins derived from adipocytes or ATMs; or cell-free mitochondrial DNA. Imaging or biopsy-based quantification of CLS and specific ATM/T-cell subsets, combined with single-cell transcriptomics, could stratify patients by "immunometabolic stage," informing prognosis and treatment choice[44].

Integrated and personalized interventions

Future care of obesity-driven T2D will likely combine weight-loss strategies, metabolic drugs, and immunometabolic modulators tailored to depot-specific and patient-specific immune signatures. For example, individuals with ATM-dominant inflammatory profiles might benefit most from macrophage-targeted therapies, while those with profound loss of VAT Tregs/ILC2s may respond to IL-33/Treg-centric approaches. Longitudinal multi-omic profiling of adipose tissue and blood in intervention trials will be essential to define such endotypes[45].

Key research priorities include:

- mapping depot- and sex-specific immunometabolic networks;
- defining early-life windows when adipose immune programming is most plastic;
- understanding crosstalk with gut microbiota, liver, and pancreas;
- and developing safe tools to manipulate immune cell metabolism in humans.

CONCLUSION

In conclusion, adipose tissue immunometabolism provides a unifying mechanistic bridge between obesity and T2D. It explains how chronic nutrient excess is translated into persistent immune activation, adipocyte dysfunction, and systemic insulin resistance—but also reveals endogenous protective circuits that can be harnessed. Targeting this immune–metabolic interface offers promising paths to not only treat, but potentially prevent or reverse, obesity-driven T2D.

REFERENCES

1. Abbasi, M., Boka, D.A., DeLoit, H.: Nanomaterial-Enhanced Microneedles: Emerging Therapies for Diabetes and Obesity. Pharmaceutics. 16, 1344 (2024). https://doi.org/10.3390/pharmaceutics16101344
2. Acevedo-Román, A., Pagán-Zayas, N., Velázquez-Rivera, L.I., Torres-Ventura, A.C., Godoy-Vitorino, F.: Insights into Gut Dysbiosis: Inflammatory Diseases, Obesity, and Restoration Approaches. Int. J. Mol. Sci. 25, 9715 (2024). https://doi.org/10.3390/ijms25179715
3. Allocca, S., Monda, A., Messina, A., Casillo, M., Sapuppo, W., Monda, V., Polito, R., Di Maio, G., Monda, M., La Marra, M.: Endocrine and Metabolic Mechanisms Linking Obesity to Type 2 Diabetes: Implications for Targeted Therapy. Healthcare. 13, 1437 (2025). https://doi.org/10.3390/healthcare13121437
4. Hayward, S.L., Wilson, C.L., Kidambi, S.: Hyaluronic acid-conjugated liposome nanoparticles for targeted delivery to CD44 overexpressing glioblastoma cells. Oncotarget. 7, 34158–34171 (2016). https://doi.org/10.18632/oncotarget.8926
5. Uti, D.E., Omang, W.A., Alum, E.U., Ugwu, O.P.-C., Wokoma, M.A., Oplekwu, R.I., Atangwho, I.J., Egbung, G.E.: Combined Hyaluronic Acid Nanobioconjugates Impair CD44-Signaling for Effective Treatment Against Obesity: A Review of Comparison with Other Actors. Int. J. Nanomedicine. 20, 10101–10126 (2025). https://doi.org/10.2147/IJN.S529250
6. Alum, E.U., Izah, S.C., Betiang, P.A., Paul-Chima Ugwu, O., Ainebyoona, C., Uti, D.E., Echegu, D.A., Alum, B.N.: The Ketogenic Diet in Obesity Management: Friend or Foe? Cell Biochem. Biophys. (2025). https://doi.org/10.1007/s12013-025-01878-0

7. Hill, A.A., Anderson-Baucum, E.K., Kennedy, A.J., Webb, C.D., Yull, F.E., Hasty, A.H.: Activation of NF-κB drives the enhanced survival of adipose tissue macrophages in an obesogenic environment. Mol. Metab. 4, 665–677 (2015). https://doi.org/10.1016/j.molmet.2015.07.005
8. Mussbacher, M., Derler, M., Basílio, J., Schmid, J.A.: NF-κB in monocytes and macrophages – an inflammatory master regulator in multitalented immune cells. Front. Immunol. 14, 1134661 (2023). https://doi.org/10.3389/fimmu.2023.1134661
9. Tang, Y., Chen, O., Dong, B., Liu, L., Ying, W., Liu, H.: Nanomaterials for the treatment and monitoring of obesity: Targeting adipose tissue macrophages. Acta Biomater. S1742-7061(25)00719–6 (2025). https://doi.org/10.1016/j.actbio.2025.09.052
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. Uti, D.E., Atangwho, I.J., Omang, W.A., Alum, E.U., Obeten, U.N., Udeozor, P.A., Agada, S.A., Bawa, I., Ogbu, C.O.: Cytokines as key players in obesity low grade inflammation and related complications. Obes. Med. 54, 100585 (2025). https://doi.org/10.1016/j.obmed.2025.100585
12. Prabhu, S., Deng, H., Cross, T.-W.L., Shahoei, S.H., Konopka, C.J., Medina, N.G., Applegate, C.C., Wallig, M.A., Dobrucki, L.W., Nelson, E.R., Smith, A.M., Swanson, K.S.: Nanocarriers Targeting Adipose Macrophages Increase Glucocorticoid Anti-Inflammatory Potency to Ameliorate Metabolic Dysfunction. Biomater. Sci. 9, 506–518 (2021). https://doi.org/10.1039/d0bm01142h
13. Barber, T.M., Kyrou, I., Randeva, H.S., Weickert, M.O.: Mechanisms of Insulin Resistance at the Crossroad of Obesity with Associated Metabolic Abnormalities and Cognitive Dysfunction. Int. J. Mol. Sci. 22, 546 (2021). https://doi.org/10.3390/ijms22020546
14. Czech, M.P.: Mechanisms of insulin resistance related to white, beige, and brown adipocytes. Mol. Metab. 34, 27–42 (2020). https://doi.org/10.1016/j.molmet.2019.12.014
15. Li, Z., Zhang, Z., Ke, L., Sun, Y., Li, W., Feng, X., Zhu, W., Chen, S.: Resveratrol promotes white adipocytes browning and improves metabolic disorders in Sirt1-dependent manner in mice. FASEB J. Off. Publ. Fed. Am. Soc. Exp. Biol. 34, 4527–4539 (2020). https://doi.org/10.1096/fj.201902222R
16. Schachner-Nedherer, A.-L., Fuchs, J., Vidakovic, I., Höller, O., Schratter, G., Almer, G., Fröhlich, E., Zimmer, A., Wabitsch, M., Kornmueller, K., Prassl, R.: Lipid Nanoparticles as a Shuttle for Anti-Adipogenic miRNAs to Human Adipocytes. Pharmaceutics. 15, 1983 (2023). https://doi.org/10.3390/pharmaceutics15071983
17. Sikur, N., Böröczky, C., Paszternák, A., Gyöngyössy, R., Szökő, É., Varga, K., Tábi, T.: Resveratrol and Its Derivatives Diminish Lipid Accumulation in Adipocytes In Vitro—Mechanism of Action and Structure–Activity Relationship. Nutrients. 16, 3869 (2024). https://doi.org/10.3390/nu16223869
18. Wu, Y., Ma, J., Chen, J., Liu, X., Wang, Z., Luo, L., Sun, C.: Ablation of CD44 Attenuates Adipogenesis in White Adipocytes via the Tryptophan 5-Hydroxylase 2/5-Hydroxytryptamine Axis to Protect Mice from High-Fat Diet–Induced Obesity. Am. J. Pathol. 195, 247–264 (2025). https://doi.org/10.1016/j.ajpath.2024.10.005
19. de Sousa Neto, I.V., Durigan, J.L.Q., da Silva, A.S.R., de Cássia Marqueti, R.: Adipose Tissue Extracellular Matrix Remodeling in Response to Dietary Patterns and Exercise: Molecular Landscape, Mechanistic Insights, and Therapeutic Approaches. Biology. 11, 765 (2022). https://doi.org/10.3390/biology11050765
20. Chrastina, M., Poništ, S., Tóth, J., Czigle, S., Pašková, Ľ., Vyletelová, V., Švík, K., Bauerová, K.: Combination Therapy of Carnosic Acid and Methotrexate Effectively Suppressed the Inflammatory Markers and Oxidative Stress in Experimental Arthritis. Molecules. 27, 7115 (2022). https://doi.org/10.3390/molecules27207115
21. Carpentier, A.C., Blondin, D.P., Virtanen, K.A., Richard, D., Haman, F., Turcotte, É.E.: Brown Adipose Tissue Energy Metabolism in Humans. Front. Endocrinol. 9, (2018). https://doi.org/10.3389/fendo.2018.00447
22. Chen, J.-Y., Peng, S.-Y., Cheng, Y.-H., Lee, I.-T., Yu, Y.-H.: Effect of Forskolin on Body Weight, Glucose Metabolism and Adipocyte Size of Diet-Induced Obesity in Mice. Anim. Open Access J. MDPI. 11, 645 (2021). https://doi.org/10.3390/ani11030645
23. Umoru, G.U., Atangwho, I.J., David-Oku, E., Uti, D.E., Agwupuye, E.I., Obeten, U.N., Maitra, S., Subramaniyan, V., Wong, L.S., Aljarba, N.H., Kumarasamy, V.: Tetracarpidium conophorum nuts (African walnuts) up-regulated adiponectin and PPAR-γ expressions with reciprocal suppression of TNF-α gene in obesity. J. Cell. Mol. Med. 28, e70086 (2024). https://doi.org/10.1111/jcmm.70086
24. Clark, M., Thomaseth, K., Dirikolu, L., Ferguson, D.C., Hoenig, M.: Effects of Pioglitazone on Insulin Sensitivity and Serum Lipids in Obese Cats. J. Vet. Intern. Med. 28, 166–174 (2014). https://doi.org/10.1111/jvim.12255
25. Keathley, J., Garneau, V., Marcil, V., Mutch, D.M., Robitaille, J., Rudkowska, I., Sofian, G.M., Desroches, S., Vohl, M.-C.: Nutrigenetics, omega-3 and plasma lipids/lipoproteins/apolipoproteins with evidence

evaluation using the GRADE approach: a systematic review. BMJ Open. 12, e054417 (2022). https://doi.org/10.1136/bmjopen-2021-054417
26. Auger, C., Kajimura, S.: Adipose Tissue Remodeling in Pathophysiology. Annu. Rev. Pathol. Mech. Dis. 18, 71–93 (2023). https://doi.org/10.1146/annurev-pathol-042220-023633
27. Schirinzi, V., Poli, C., Berteotti, C., Leone, A.: Browning of Adipocytes: A Potential Therapeutic Approach to Obesity. Nutrients. 15, 2229 (2023). https://doi.org/10.3390/nu15092229
28. Divella, R., De Luca, R., Abbate, I., Naglieri, E., Daniele, A.: Obesity and cancer: the role of adipose tissue and adipo-cytokines-induced chronic inflammation. J. Cancer. 7, 2346–2359 (2016). https://doi.org/10.7150/jca.16884
29. Tsuda, K., Yamanaka, K., Kitagawa, H., Akeda, T., Naka, M., Niwa, K., Nakanishi, T., Kakeda, M., Gabazza, E.C., Mizutani, H.: Calcineurin Inhibitors Suppress Cytokine Production from Memory T Cells and Differentiation of Naïve T Cells into Cytokine-Producing Mature T Cells. PLOS ONE. 7, e31465 (2012). https://doi.org/10.1371/journal.pone.0031465
30. Zou, H., Zhang, M., Zhu, X., Zhu, L., Chen, S., Luo, M., Xie, Q., Chen, Y., Zhang, K., Bu, Q., Wei, Y., Ye, T., Li, Q., Yan, X., Zhou, Z., Yang, C., Li, Y., Zhou, H., Zhang, C., You, X., Zheng, G., Zhao, G.: Ginsenoside Rb1 Improves Metabolic Disorder in High-Fat Diet-Induced Obese Mice Associated With Modulation of Gut Microbiota. Front. Microbiol. 13, (2022). https://doi.org/10.3389/fmicb.2022.826487
31. Sharma, D., Arora, S., Banerjee, A., Singh, J.: Improved insulin sensitivity in obese-diabetic mice via chitosan Nanomicelles mediated silencing of pro-inflammatory Adipocytokines. Nanomedicine Nanotechnol. Biol. Med. 33, 102357 (2021). https://doi.org/10.1016/j.nano.2020.102357
32. Araujo-Abad, S., Berna, J.M., Lloret-Lopez, E., López-Cortés, A., Saceda, M., de Juan Romero, C.: Exosomes: from basic research to clinical diagnostic and therapeutic applications in cancer. Cell. Oncol. 48, 269–293 (2025). https://doi.org/10.1007/s13402-024-00990-2
33. 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
34. Fawzy, M.P., Hassan, H.A.F.M., Amin, M.U., Preis, E., Bakowsky, U., Fahmy, S.A.: Deploying nucleic acids-loaded plant-derived exosomes as green nano gadget in cancer gene therapy. Mater. Adv. 6, 1230–1261 (2025). https://doi.org/10.1039/D4MA01189A
35. La Sala, L., Carlini, V., Macas-Granizo, M.B., Trabucchi, E., Pontiroli, A.E., Berra, C., Naselli, A., D'Anzeo, M., Porta, A., Martin Delgado, J., Vianello, E., Dozio, E., Corsi Romanelli, M., Drago, L.: The eternal struggle between titans: Fecal microbiota transplant (FMT) versus metformin in type 2 diabetes (T2D) gut dysmotility. J. Adv. Res. (2025). https://doi.org/10.1016/j.jare.2025.09.021
36. Ikeda, K., Yamada, T.: UCP1 Dependent and Independent Thermogenesis in Brown and Beige Adipocytes. Front. Endocrinol. 11, (2020). https://doi.org/10.3389/fendo.2020.00498
37. Zhen, Y., Shu, W., Hou, X., Wang, Y.: Innate Immune System Orchestrates Metabolic Homeostasis and Dysfunction in Visceral Adipose Tissue During Obesity. Front. Immunol. 12, (2021). https://doi.org/10.3389/fimmu.2021.702835
38. Mohaghegh, N., Ahari, A., Buttles, C., Davani, S., Hoang, H., Huang, Q., Huang, Y., Hosseinpour, B., Abbasgholizadeh, R., Cottingham, A.L., Farhadi, N., Akbari, M., Kang, H., Khademhosseini, A., Jucaud, V., Pearson, R.M., Hassani Najafabadi, A.: Simvastatin-Loaded Polymeric Nanoparticles: Targeting Inflammatory Macrophages for Local Adipose Tissue Browning in Obesity Treatment. ACS Nano. 18, 27764–27781 (2024). https://doi.org/10.1021/acsnano.4c10742
39. Barquissau, V., Léger, B., Beuzelin, D., Martins, F., Amri, E.-Z., Pisani, D.F., Saris, W.H.M., Astrup, A., Maoret, J.-J., Iacovoni, J., Déjean, S., Moro, C., Viguerie, N., Langin, D.: Caloric Restriction and Diet-Induced Weight Loss Do Not Induce Browning of Human Subcutaneous White Adipose Tissue in Women and Men with Obesity. Cell Rep. 22, 1079–1089 (2018). https://doi.org/10.1016/j.celrep.2017.12.102
40. Montefusco, L., D'Addio, F., Loretelli, C., Ben Nasr, M., Garziano, M., Rossi, A., Pastore, I., Plebani, L., Lunati, M.E., Bolla, A.M., Porta, M.D., Piuri, G., Rocchio, F., Abdelsalam, A., Assi, E., Barichella, M., Maestroni, A., Usuelli, V., Loreggian, L., Muzio, F., Zuccotti, G.V., Cazzola, R., Fiorina, P.: Anti-inflammatory effects of diet and caloric restriction in metabolic syndrome. J. Endocrinol. Invest. 44, 2407–2415 (2021). https://doi.org/10.1007/s40618-021-01547-y
41. Dutta, S., Shah, R.B., Singhal, S., Dutta, S.B., Bansal, S., Sinha, S., Haque, M.: Metformin: A Review of Potential Mechanism and Therapeutic Utility Beyond Diabetes. Drug Des. Devel. Ther. 17, 1907–1932 (2023). https://doi.org/10.2147/DDDT.S409373
42. Basso, P.J., Schcolnik-Cabrera, A., Zhu, M., Strachan, E., Clemente-Casares, X., Tsai, S.: Weight Loss-Associated Remodeling of Adipose Tissue Immunometabolism. Obes. Rev. 26, e13975 (2025). https://doi.org/10.1111/obr.13975
43. Guo, S., Zhang, Q., Guo, Y., Yin, X., Zhang, P., Mao, T., Tian, Z., Li, X.: The role and therapeutic targeting of the CCL2/CCR2 signaling axis in inflammatory and fibrotic diseases. Front. Immunol. 15, 1497026 (2025). https://doi.org/10.3389/fimmu.2024.1497026

44. Rakab, M.S., Asada, M.C., Mirza, I., Morsy, M.H., Mostafa, A., Bianco, F.M., Ali, M.M., Hassan, C., Masrur, M.A., Layden, B.T., Mahmoud, A.M.: Adiposome Proteomics Uncover Molecular Signatures of Cardiometabolic Risk in Obese Individuals. Proteomes. 13, 39 (2025). https://doi.org/10.3390/proteomes13030039
45. Li, Y., Yang, H., Zhang, X., He, X., Liuli, A., Li, R., Han, X., Li, Y., Gao, P.: Integrated proteomic and metabolomic profiling identifies distinct molecular signatures and metabolic pathways associated with obesity and potential targets for anti-obesity therapies. Front. Endocrinol. 16, 1625501 (2025). https://doi.org/10.3389/fendo.2025.1625501

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