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Nanotechnology-Enabled Personalized Medicine: Integrating Genetic, Epigenetic, and Metabolic Insights in Obesity and Type 2 Diabetes

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ABSTRACT

Obesity and type 2 diabetes are heterogeneous, network-level disorders arising from the interplay of genetic variation, epigenetic remodeling, environmental exposures, and metabolic rewiring across adipose tissue, liver, skeletal muscle, gut, and pancreatic islets. Precision therapy requires not only stratifying patients by molecular drivers but also delivering interventions to the right tissue compartments with timing that reflects circadian and behavioral rhythms. Nanotechnology offers an enabling bridge between molecular diagnosis and actionable, patient-tailored treatment. Engineered nanoparticles like lipidic, polymeric, inorganic, or hybrid, can encapsulate diverse payloads, including small molecules, peptides, nucleic acids, and genome or epigenome editors, while incorporating ligands that target organ- and cell-specific receptors or microenvironmental cues. Meanwhile, minimally invasive diagnostics that harness circulating exosomes, cell-free nucleic acids, and metabolomic signatures can guide endotype discovery and longitudinal monitoring. This review outlines a framework for nanotechnology-enabled personalized medicine in obesity and type 2 diabetes that integrates genomics, epigenomics, and metabolomics with smart delivery systems. We examine patient stratification using polygenic risk and epigenetic clocks, design rules for targeted and stimuli-responsive nanocarriers, and strategies for aligning pharmacokinetics with metabolic states. Preclinical and emerging clinical evidence indicate that matching payload and carrier to molecular endotypes can amplify efficacy while reducing systemic exposure. We further discuss safety, manufacturability, regulatory science, and health equity considerations that determine feasibility at scale. By coupling molecular insight to programmable delivery, nanomedicine can move care beyond one-size-fits-all glycemic control toward durable network reprogramming tailored to each patient's biological context.

INTRODUCTION

Obesity and type 2 diabetes (T2D) are not uniform diseases but convergent phenotypes produced by distinct combinations of susceptibility alleles, developmental and lifestyle exposures, microbiome configurations, and cumulative metabolic stress[1–3]. Genome-wide association studies implicate loci involved in adipogenesis, insulin secretion, and neuronal regulation of appetite; yet the penetrance of these variants is shaped by epigenetic marks established during development and remodeled by diet, inflammation, and circadian disruption[4, 5]. Epigenetic modifications in adipocytes, hepatocytes, myocytes, and islet cells alter chromatin accessibility and transcriptional networks that determine lipid handling, mitochondrial biogenesis, and stimulus–secretion coupling[6,7]. Parallel changes in metabolites and signaling lipids such as branched-chain amino acids, acylcarnitines, ceramides, bile acids, and short-chain fatty acids orchestrate interorgan communication, amplifying insulin resistance and β-cell stress[8]. As a result, two individuals with similar body mass indices can harbor divergent molecular drivers: one dominated by hepatosteatosis and lipotoxic signaling, another by adipose inflammation and impaired adipogenesis, and a third by β-cell fragility despite modest insulin resistance[8].

Precision medicine aims to detect and act upon this heterogeneity, but translation has lagged for three reasons [9]. First, most therapies are delivered systemically and act broadly rather than correcting the dysregulated

nodes within specific tissues. Second, conventional pharmacokinetics rarely align with biological rhythms or meal-related dynamics that govern glucose flux and hormone secretion[10]. Third, diagnostic classification has often been limited to glycemic indices and crude clinical variables, falling short of the molecular resolution needed to guide intervention. Nanotechnology offers solutions at each bottleneck. Engineered nanoparticles can ferry fragile or hydrophobic payloads to selected tissues by exploiting receptor–ligand interactions and disease-altered microenvironments, release cargo in response to pH, redox, enzymatic, or mechanical cues, and thereby reshape exposure–response relationships[11]. In parallel, nanoscale diagnostics, including analyses of circulating extracellular vesicles and cell-free nucleic acids, enable noninvasive sampling of tissue states over time and may act as both biomarkers and therapeutic targets[12].

Personalized nanotherapy begins with endotyping, the process of partitioning patients into biologically coherent subgroups based on integrated omics and clinical features. Polygenic risk scores stratify baseline predisposition to obesity or β-cell dysfunction, while DNA methylation clocks and locus-specific methylation patterns reflect cumulative environmental exposures and predict cardiometabolic outcomes[13]. Transcriptomic and proteomic data resolve inflammatory and metabolic pathway activity in circulation; metabolomics detects substrate selection and mitochondrial function; and exosomal small RNA profiles hint at tissue-specific signaling. Layered atop these measurements are dynamic readouts from continuous glucose monitoring, indirect calorimetry, and wearable sensors that capture circadian and behavioral context[14]. Together, they produce a map of actionable liabilities, excess hepatic lipogenesis, impaired adipose expandability, muscle mitochondrial inflexibility, and islet ER stress that can be matched to nano-enabled payloads.

Designing the right carrier–payload pair is as important as selecting the mechanism. Lipid nanoparticles excel at delivering nucleic acids with endosomal escape, polymeric and hybrid systems control release kinetics for small molecules and peptides, and membrane-cloaked or ligand-decorated platforms improve homing and cellular uptake[15]. Formulations can be tuned to exploit fenestrated hepatic sinusoids, inflamed adipose microvasculature, or islet endothelium, while microenvironment-sensitive chemistries trigger release where pH, reactive oxygen species, or enzymes are pathologically altered. Chronotherapeutic strategies synchronize dosing with feeding or sleep–wake cycles to enhance efficacy and minimize adverse effects. Crucially, these pharmacologic advances must be balanced against safety, manufacturability, and equity: repeated dosing in obese, inflamed hosts can accelerate clearance or complement activation; cGMP processes must deliver tight control of size, charge, composition, and ligand density; and access must be broadened through cost-conscious excipient choices and scalable assembly[16].

This review presents a cohesive framework that integrates genetic, epigenetic, and metabolic insights with nanotechnology design to enable personalized therapy in obesity and T2D. We begin with patient stratification methods that translate omics into endotypes. We then outline core nanocarrier platforms and their engineering levers for organ- and cell-specific delivery. Next, we discuss stimuli-responsive designs that align release with local biology and circadian timing, and we survey payloads from small molecules to genome and epigenome editors paired to dominant endotypes. We consider evidence from preclinical models and early human studies where matching the mechanism to endotype enhances outcomes. Finally, we examine safety, regulatory pathways, manufacturability, and ethical and equity considerations essential for translation. The goal is to move beyond abstract enthusiasm toward practical blueprints that clinicians and developers can deploy in real-world care.

2. Patient Endotyping: From Polygenic Risk and Epigenetic Clocks to Circulating Vesicles

Personalized nanotherapy for obesity and T2D begins with a rigorous partitioning of patients into molecularly coherent endotypes. Polygenic risk scores capture the cumulative effects of common variants across loci that influence insulin secretion, adipocyte differentiation, central appetite regulation, and lipid handling[17]. While the absolute risk explained may be modest, polygenic profiling identifies individuals whose metabolic trajectories are more likely to depend on β-cell fragility versus adipose expandability or hepatic lipogenesis. Yet genetics alone is insufficient because environmental exposures and developmental history imprint durable epigenetic signatures[17]. DNA methylation clocks estimate biological age acceleration associated with obesity and metabolic syndrome, while locus-specific methylation at enhancers near lipid metabolism or endoplasmic reticulum stress genes correlates with hepatic steatosis or islet dysfunction. Histone modification patterns and chromatin accessibility in blood-derived cells can act as proxies for tissue states, especially when integrated with transcriptomic modules reflective of inflammation and mitochondrial activity[18, 19].

Circulating biomarkers extend this map. Plasma proteomics detects hepatokines, adipokines, and myokines that report interorgan crosstalk; metabolomics profiles acylcarnitines, ceramides, bile acids, and branched-chain amino acids that index substrate selection and oxidative flux[20]. Critically, extracellular vesicles, including exosomes, carry tissue-stamped microRNAs, long noncoding RNAs, and proteins, enabling noninvasive surveillance of hepatic lipogenesis, adipose inflammation, skeletal muscle mitochondrial capacity, and islet stress. Vesicle surface proteins can indicate cell-of-origin, allowing multi-tissue deconvolution that guides targeting. Longitudinal sampling reveals endotype stability or drift during weight loss, pharmacotherapy, or lifestyle changes, providing opportunities to adapt payloads and carriers over time[20].

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Dynamic physiological measurements amplify resolution. Continuous glucose monitoring quantifies postprandial excursions and nocturnal stability, separating patients with predominant hepatic insulin resistance from those with impaired first-phase insulin secretion. Indirect calorimetry and wearable sensors infer metabolic flexibility and chronotype; disruptions in sleep timing and meal regularity correlate with epigenetic and endocrine changes that can be therapeutically targeted[21]. Together, these layers position each patient on a multi-dimensional landscape of liabilities: a hepatosteatotic–inflammatory endotype with elevated ceramides and FXR signaling; an adipose-inflammation endotype marked by vesicular microRNAs that suppress insulin signaling; a β-cell–fragility endotype with exosomal signatures of endoplasmic reticulum stress and reduced identity factors; or mixed phenotypes that demand combination therapy[21].

The purpose of endotyping is not taxonomy but action. A hepatosteatosis-dominant profile points toward payloads that reduce de novo lipogenesis, enhance fatty acid oxidation, or modulate bile-acid pathways, delivered via carriers tuned for hepatic uptake[22]. An adipose-limited expandability endotype favors anti-inflammatory and adipogenesis-supporting cargos with depots that navigate inflamed microvasculature[22]. A β-cell–fragile endotype benefits from islet-targeted antioxidants, calcium-handling modulators, or nucleic acids that reinforce identity. Importantly, endotypes exist along continua and evolve with interventions; thus, diagnostic platforms must be repeatable and affordable, with turnaround times that support clinical decision-making. Machine learning models integrating omics and clinical data can propose endotypes with probability scores and suggested therapeutic modules, which can then be tested and refined within adaptive care pathways.

3. Carrier Design: Lipid, Polymeric, and Hybrid Platforms for Organ- and Cell-Specific Delivery

Selecting the appropriate nanocarrier is central to matching therapy to endotype. Lipid nanoparticles, including ionizable compositions, offer efficient encapsulation and cytosolic delivery of nucleic acids. By tuning ionizable lipid pK_a, helper lipid ratios, and PEG–lipid desorption kinetics, these carriers stabilize in circulation, then protonate within endosomes to promote escape[23–26]. For hepatic targeting, exploiting endogenous apolipoprotein adsorption engages LDL receptors on hepatocytes; for adipose or islets, exogenous ligands are appended to steer binding amid distinct vascular and interstitial environments. Liposomes, with phospholipid bilayers and adjustable cholesterol content, excel at carrying hydrophobic small molecules and peptides, providing controlled release and fusogenic options that enhance intracellular access[27, 28].

Polymeric nanoparticles such as PLGA and PEG–PLGA offer mechanical robustness and programmable degradation, ideal for sustained release of small molecules or proteins in tissues where prolonged, low-level exposure outperforms peaks[29–31]. Surface PEGylation and zwitterionic coatings reduce opsonization; incorporation of targeting moieties via click chemistry allows precise ligand densities[32]. Polysaccharide systems like chitosan add mucoadhesion and transient tight-junction opening for oral delivery, while hyaluronic acid coatings engage CD44 in inflamed adipose tissue. Hybrid architectures unite the strengths of both worlds: lipid–polymer hybrids present a fluid lipid shell for membrane interactions and ligand display atop a polymeric core that governs release kinetics and storage stability, enabling multi-compartment loading for complex regimens[32].

Carrier physicochemistry must reflect tissue microanatomy. For liver, sizes of 70–120 nm traverse fenestrated sinusoids and avoid rapid renal clearance; neutral to slightly negative zeta potentials limit complement activation. In adipose depots, decreased stiffness and near-neutral charge facilitate extravasation through inflamed microvasculature, while peptides targeting prohibitin or neuropilin-1 enrich uptake by adipocytes and macrophages [33]. Islet delivery benefits from endothelial ligands that mediate transcytosis and from niche-anchoring motifs responsive to zinc-rich perivascular spaces. Protein corona management is increasingly decisive: carriers with tailored lipid headgroups or preadsorbed selective proteins maintain ligand accessibility and avoid macrophage capture, preserving targeting fidelity in obese, inflamed hosts[34].

Finally, manufacturability and safety constrain design space. Continuous-flow microfluidic assembly yields tight polydispersity and reproducible encapsulation across scales, while high-pressure homogenization supports solid lipid systems[35]. Excipient selection favors pharmacopeial lipids and biodegradable polymers with track records in parenteral and oral use. Critical quality attributes, such as size, polydispersity, surface charge, composition, ligand density, encapsulation efficiency, and release kinetics, must be linked to potency assays aligned with mechanism, ensuring that batch-to-batch variation remains within clinically meaningful limits[35]. Carrier choice thus emerges from a matrix that balances payload needs, target tissue biology, dosing route and schedule, safety margins, and industrial feasibility.

4. Stimuli-Responsive and Chronotherapeutic Delivery: Aligning Exposure with Biology

Obesity and T2D are characterized by rhythmic fluctuations in hormones, substrate use, and tissue perfusion, as well as microenvironmental abnormalities such as acidosis, oxidative stress, and heightened protease activity[36–38]. Stimuli-responsive nanocarriers exploit these features to synchronize release with therapeutic windows. pH-labile lipids and polymers accelerate cargo discharge in acidic endosomes or inflamed extracellular spaces, while redox-sensitive linkers cleave in glutathione-rich cytosol to free small molecules or nucleic acids. Reactive oxygen species–responsive moieties disassemble in oxidative milieus, positioning antioxidants or mitochondrial modulators precisely where stress is greatest[39–41]. Enzyme-cleavable coatings respond to matrix metalloproteinases enriched in inflamed adipose tissue, enhancing local deposition and uptake.

Mechanically responsive constructs attune release to shear stress patterns in hepatic sinusoids or microvascular beds, aligning exposure with perfusion.

Chronotherapeutic design layers time onto place. Insulin sensitivity and β-cell responsiveness vary across the day; meal timing reshapes bile-acid cycles and incretin responses; sleep disruption impairs glucose tolerance[42]. Carriers can be tuned to produce predawn or preprandial plateaus for agents that buffer hepatic glucose output, or mealtime pulses for β-cell supportive cargos that augment first-phase insulin secretion. Oral systems with enteric coatings and colonic release harness bile-acid and microbial rhythms to modulate FXR/TGR5 signaling and short-chain fatty acid production. Subcutaneous depots formed by in situ–gelling polymers or slow-dissolving lipid matrices deliver near-zero-order kinetics, reducing peaks and improving adherence[42].

Real-time adaptation is a frontier enabled by digital biomarkers. Continuous glucose traces and wearable-derived activity and sleep metrics can feed control algorithms that recommend dosing windows or adjust depot intervals[43]. On the diagnostic side, longitudinal profiling of circulating exosomal microRNAs or cell-free DNA methylation patterns detects shifts in tissue stress or inflammation, prompting changes in payload composition or targeting ligands. Closed-loop paradigms distinct from automated insulin delivery could modulate the timing of nanotherapy to sustain network reprogramming with minimal drug burden[43]. Safety remains paramount: stimuli-responsive elements must not promote off-target release in sensitive tissues, and chronotherapeutic schedules must consider variability in routines and shift work. With these safeguards, aligning exposure with biology can magnify effect sizes and compress the dose needed to achieve durable benefit.

5. Payloads Mapped to Endotypes: Small Molecules, RNA, and Epigenome Editing

The value of personalized nanomedicine lies in pairing the right mechanism to the patient's dominant liabilities and delivering it precisely. In hepatosteatosis-dominant endotypes, small molecules that inhibit de novo lipogenesis, activate AMPK, or promote fatty acid oxidation can be encapsulated in lipid or hybrid carriers that favor hepatocyte uptake through apolipoprotein-mediated pathways or GalNAc-like ligands[44]. In adipose-inflammation endotypes, payloads that suppress NF-κB and NLRP3 activation, promote adipogenesis and beige remodeling, or modulate macrophage polarization can be packaged in soft, matrix-responsive carriers equipped with adipose endothelial ligands[45]. For β-cell–fragility endotypes, cargos that stabilize mitochondrial ATP production, tune ER stress sensors, correct calcium oscillations, or reinforce identity factor networks can be delivered in islet-targeted carriers that combine endothelial transcytosis with β-cell receptor binding[45].

Nucleic acid therapeutics expand precision. siRNAs and antisense oligonucleotides reduce expression of stress kinases, lipid synthesis drivers, or negative regulators of insulin signaling; microRNA mimics or sponges rebalance gene networks toward oxidative metabolism or β-cell identity; mRNAs transiently express protective factors such as antioxidant enzymes or transcriptional coactivators[46]. Ionizable lipid nanoparticles enable these cargos with efficient endosomal escape, while chemical modifications stabilize oligonucleotides and limit innate immune sensing. Epigenome editors like CRISPR-dCas9 fused to DNA methylation or histone-modifying domains offer durable resetting of regulatory elements controlling adipocyte differentiation, hepatic lipogenesis, or β-cell transcriptional identity. Because permanence raises safety stakes, tissue targeting and tightly regulated expression cassettes become essential, and reversible editors or base editors with narrow editing windows may be preferable in early deployments[46].

Combination payloads unlock polypharmacology. Co-loading a small-molecule AMPK activator with an siRNA to lipogenic transcription factors in a single hepatocyte-targeted carrier can achieve synergy at lower doses than either alone[47]. Pairing β-cell antioxidants with microRNA mimics that restore identity can produce immediate functional rescue followed by durable stabilization. Sequencing strategies may deploy hepatic and adipose therapies first to relieve β-cell secretory pressure, then add β-cell–focused editing once systemic stress declines. Potency assays must mirror these mechanisms: hepatic fat by proton MR spectroscopy, adipose inflammation by imaging and cytokine panels, muscle oxidative indices by indirect calorimetry, β-cell function by mixed-meal tolerance tests and C-peptide deconvolution, and molecular readouts via circulating vesicle cargo[47]. The ultimate goal is not merely glycemic improvement but network-level remodeling measurable across omics and physiology.

6. Evidence and Case Studies: Matching Mechanism, Carrier, and Endotype

Proof-of-concept studies demonstrate that aligning the mechanism and carrier to the endotype amplifies therapeutic benefit in obese and diabetic models[48]. In steatohepatitis-biased phenotypes, hepatocyte-directed lipid nanoparticles delivering siRNA against lipogenic enzymes reduce hepatic triglyceride content and improve insulin sensitivity more effectively than equivalent free oligonucleotides, with parallel declines in aminotransferases and inflammatory markers[49]. When co-loaded with small-molecule AMPK activators, these systems produce additive reductions in de novo lipogenesis and improvements in glucose tolerance, validating the polypharmacology strategy. In adipose-inflammation models, chitosan-coated or zwitterionic hybrid nanoparticles decorated with adipose endothelial ligands concentrate anti-inflammatory payloads within depots, reducing crown-like structures and restoring insulin-stimulated glucose uptake in adipocytes, while also shifting macrophage polarization toward reparative states[49].

Islet-focused interventions provide complementary evidence. Ionizable lipid nanoparticles engineered for islet transcytosis and β-cell receptor engagement deliver microRNA mimics or siRNAs that restore stimulus–secretion coupling, normalize calcium oscillations, and preserve insulin content at lower systemic exposures than non-targeted formulations[50]. Liposomal antioxidants or ER stress modulators targeted to islets reduce unfolded protein response markers and improve first-phase insulin secretion during hyperglycemic clamps. These gains are magnified when peripheral insulin resistance is concurrently alleviated by hepatic or adipose-directed nanotherapies, suggesting a systems approach where relieving β-cell pressure and correcting substrate flux in parallel yields durable control[50].

Human data are emergent but encouraging in adjacent domains. Lipid nanoparticles have established safety and translatability for nucleic acids in the liver, and oral lipid systems have improved bioavailability for hydrophobic anti-inflammatory compounds[51]. Botanical-derived payloads formulated as phytosomes or nanostructured lipids have shown improved pharmacokinetics and glycemic effects in small trials. While direct, islet-targeted nanotherapies have yet to be widely tested in humans, the translational mechanics, carrier safety, manufacturing, and regulatory pathways are converging[51]. Early-phase studies can leverage enriched endotypes identified by omics and continuous glucose phenotypes, deploying hepatic or adipose therapies with clear pharmacodynamic biomarkers such as intrahepatic triglyceride, adipose inflammation imaging, and CGM-derived variability. As platforms mature, β-cell–targeted payloads may enter trials with sensitive readouts like mixed-meal C-peptide and exosomal β-cell microRNA panels.

Collectively, these case studies support a thesis: the right patient–mechanism–carrier match converts modest pharmacology into clinically meaningful benefit at lower doses and with fewer adverse effects. Importantly, negative or equivocal results often reflect mismatches in payloads delivered to the wrong tissue, carriers neutralized by protein coronas in inflamed hosts, or dosing schedules out of sync with biology, underscoring the need for rational design anchored in endotyping and delivery science. Iterative cycles that update endotype assignments and adjust carriers or payloads based on longitudinal biomarkers will be central to realizing the promise of nanotechnology-enabled personalized medicine.

7. Safety, Manufacturing, Regulation, and Equity: Making Personalization Practical

Translation requires that individualized nanotherapies be not only effective but safe, manufacturable, and accessible. Safety considerations in obese, inflamed populations include complement activation–related pseudoallergy, accelerated blood clearance upon repeat dosing, and altered biodistribution due to reticuloendothelial activation and organ steatosis[52]. Selecting pharmacopeial lipids, biodegradable polymers, and zwitterionic or low-density PEG coatings reduces innate immune activation; tuning ionizable lipid pK_a balances endosomal escape with extracellular safety; and degradable chemistries limit tissue accumulation. Toxicology should be performed in metabolically diseased models using repeated dosing to reveal clearance dynamics and organ-specific liabilities[52]. For genetic and epigenetic payloads, high-fidelity editors, tissue-restricted expression, and reversible designs mitigate the risk of off-target or permanent changes.

Manufacturability centers on continuous-flow microfluidic assembly and high-pressure homogenization that produce tight size distributions and reproducible encapsulation at scale. Process analytical technologies, real-time particle sizing, composition assays by LC–MS, ligand density quantification, and release profiling link critical quality attributes to potency assays that reflect mechanism, such as hepatocyte lipogenesis suppression or β-cell glucose-stimulated insulin secretion[53]. Stability programs define shelf life with lyophilization and cryoprotectants for logistical resilience. Regulatory pathways can build on precedents for lipid nanoparticles, oligonucleotides, and botanical drugs, but personalized combinations will require adaptive frameworks that allow modular swapping of ligands or payloads within validated carrier backbones[53]. Companion diagnostics—omics panels and vesicle-based biomarkers must achieve analytical validity, clinical validity, and utility to justify their role in selection and monitoring.

Equity is both an ethical imperative and a practical necessity. Polygenic scores and epigenetic clocks must be trained and validated across ancestries to avoid perpetuating disparities. Cost-sensitive carrier choices and scalable processes reduce price barriers; oral or infrequent subcutaneous dosing with simple storage broadens access beyond specialized centers. Federated learning on de-identified, diverse datasets can refine endotyping without centralizing sensitive information, while clear consent and data governance preserve trust. Patient-centric design, palatable formulations, minimal clinic visits, digital tools that translate complex biomarker feedback into simple guidance support adherence and sustained benefit.

CONCLUSION

In sum, making personalization practical demands a systems mindset that integrates safety engineering, industrial rigor, regulatory alignment, and social responsibility. When these elements align, nanotechnology-enabled personalized medicine can move from bespoke promise to a reproducible, equitable standard for managing obesity and T2D—delivering the right mechanism, at the right dose, to the right tissue, at the right time, for the right person.

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REFERENCES

1. Baliou, S., Apetroaei, M.-M., Hatzidaki, E., Kuzmin, S.V., Tzatzarakis, M.N., Arsene, A.L., Tsatsakis, A., Ioannou, P.: The Interplay Between Obesity and Type 2 Diabetes: Common Pathophysiological Mechanisms Contributing to Telomere Shortening. Life. 15, 873 (2025). https://doi.org/10.3390/life15060873
2. Cheng, L., Wang, J., Dai, H., Duan, Y., An, Y., Shi, L., Lv, Y., Li, H., Wang, C., Ma, Q., Li, Y., Li, P., Du, H., Zhao, B.: Brown and beige adipose tissue: a novel therapeutic strategy for obesity and type 2 diabetes mellitus. Adipocyte. 10, 48–65. https://doi.org/10.1080/21623945.2020.1870060
3. Ejemot-Nwadiaro, R.I., Betiang, P.A., Basajja, M., Uti, D.E.: Obesity and Climate Change: A Two-way Street with Global Health Implications. Obes. Med. 100623 (2025). https://doi.org/10.1016/j.obmed.2025.100623
4. Sandovici, I., Morais, T., Constância, M., Monteiro, M.P.: Epigenetic Changes Associated With Obesity-related Metabolic Comorbidities. J. Endocr. Soc. 9, bvaf129 (2025). https://doi.org/10.1210/jendso/bvaf129
5. Wen, W., Gu, S., Guo, F., Chen, Z., Yan, S., Mo, Z.: Dynamic Rendition of Adipose Genes Under Epigenetic Regulation: Revealing New Mechanisms of Obesity Occurrence. Curr. Issues Mol. Biol. 47, 540 (2025). https://doi.org/10.3390/cimb47070540
6. Handy, D.E., Castro, R., Loscalzo, J.: Epigenetic Modifications: Basic Mechanisms and Role in Cardiovascular Disease. Circulation. 123, 2145–2156 (2011). https://doi.org/10.1161/CIRCULATIONAHA.110.956839
7. Krämer, A.I., Handschin, C.: How Epigenetic Modifications Drive the Expression and Mediate the Action of PGC-1α in the Regulation of Metabolism. Int. J. Mol. Sci. 20, 5449 (2019). https://doi.org/10.3390/ijms20215449
8. Newgard, C.B.: Interplay between lipids and branched-chain amino acids in development of insulin resistance. Cell Metab. 15, 606–614 (2012). https://doi.org/10.1016/j.cmet.2012.01.024
9. Alum, E.U.: Optimizing patient education for sustainable self-management in type 2 diabetes. Discov. Public Health. 22, 44 (2025). https://doi.org/10.1186/s12982-025-00445-5
10. Thakor, A.S.: The Third Pillar of Precision Medicine — Precision Delivery. MedComm. 6, e70200 (2025). https://doi.org/10.1002/mco2.70200
11. Hartl, D., de Luca, V., Kostikova, A., Laramie, J., Kennedy, S., Ferrero, E., Siegel, R., Fink, M., Ahmed, S., Millholland, J., Schuhmacher, A., Hinder, M., Piali, L., Roth, A.: Translational precision medicine: an industry perspective. J. Transl. Med. 19, 245 (2021). https://doi.org/10.1186/s12967-021-02910-6
12. Wang, R.C., Wang, Z.: Precision Medicine: Disease Subtyping and Tailored Treatment. Cancers. 15, 3837 (2023). https://doi.org/10.3390/cancers15153837
13. Massa, C., Seliger, B.: Combination of multiple omics techniques for a personalized therapy or treatment selection. Front. Immunol. 14, 1258013 (2023). https://doi.org/10.3389/fimmu.2023.1258013
14. Cappon, G., Acciaroli, G., Vettoretti, M., Facchinetti, A., Sparacino, G.: Wearable Continuous Glucose Monitoring Sensors: A Revolution in Diabetes Treatment. Electronics. 6, 65 (2017). https://doi.org/10.3390/electronics6030065
15. Zheng, L., Bandara, S.R., Tan, Z., Leal, C.: Lipid nanoparticle topology regulates endosomal escape and delivery of RNA to the cytoplasm. Proc. Natl. Acad. Sci. U. S. A. 120, e2301067120. https://doi.org/10.1073/pnas.2301067120
16. Lee, Y., Field, J.M., Sehgal, A.: Circadian Rhythms, Disease and Chronotherapy. J. Biol. Rhythms. 36, 503–531 (2021). https://doi.org/10.1177/07487304211044301
17. Ghatan, S., van Rooij, J., van Hoek, M., Boer, C.G., Felix, J.F., Kavousi, M., Jaddoe, V.W., Sijbrands, E.J.G., Medina-Gomez, C., Rivadeneira, F., Oei, L.: Defining type 2 diabetes polygenic risk scores through colocalization and network-based clustering of metabolic trait genetic associations. Genome Med. 16, 10 (2024). https://doi.org/10.1186/s13073-023-01255-7
18. Chen, Y., Liang, R., Li, Y., Jiang, L., Ma, D., Luo, Q., Song, G.: Chromatin accessibility: biological functions, molecular mechanisms and therapeutic application. Signal Transduct. Target. Ther. 9, 340 (2024). https://doi.org/10.1038/s41392-024-02030-9
19. Ikpozu, E.N., Offor, C.E., Igwenyi, I.O., Obaroh, I.O., Ibiam, U.A., Ukaidi, C.U.A.: RNA-based diagnostic innovations: A new frontier in diabetes diagnosis and management. Diab. Vasc. Dis. Res. 22, 14791641251334726 (2025). https://doi.org/10.1177/14791641251334726
20. de Oliveira Dos Santos, A.R., de Oliveira Zanuso, B., Miola, V.F.B., Barbalho, S.M., Santos Bueno, P.C., Flato, U.A.P., Detregiachi, C.R.P., Buchaim, D.V., Buchaim, R.L., Tofano, R.J., Mendes, C.G., Tofano, V.A.C., Dos Santos Haber, J.F.: Adipokines, Myokines, and Hepatokines: Crosstalk and Metabolic Repercussions. Int. J. Mol. Sci. 22, 2639 (2021). https://doi.org/10.3390/ijms22052639
21. Gouveri, E., Drakopanagiotakis, F., Panou, T., Papazoglou, D., Steiropoulos, P., Papanas, N.: Continuous Glucose Monitoring Among People with and without Diabetes Mellitus and Sleep Apnoea. Diabetes Ther. 16, 1533–1555 (2025). https://doi.org/10.1007/s13300-025-01756-1

22. Zhu, Z., Zhang, X., Pan, Q., Zhang, L., Chai, J.: In-depth analysis of de novo lipogenesis in non-alcoholic fatty liver disease: Mechanism and pharmacological interventions. Liver Res. 7, 285–295 (2023). https://doi.org/10.1016/j.livres.2023.11.003
23. Abbasi, H., Kouchak, M., Mirveis, Z., Hajipour, F., Khodarahmi, M., Rahbar, N., Handali, S.: What We Need to Know about Liposomes as Drug Nanocarriers: An Updated Review. Adv. Pharm. Bull. 13, 7–23 (2023). https://doi.org/10.34172/apb.2023.009
24. Almadani, I.F., Almadani, M.F., AlSawaftah, N., Abuwatfa, W.H., Husseini, G.A.: Nanocarriers Responsive to Light—A Review. Micro. 4, 827–844 (2024). https://doi.org/10.3390/micro4040051
25. Alum, E.U., Nwuruku, O.A., Ugwu, O.P.-C., Uti, D.E., Alum, B.N., Edwin, N.: Harnessing nature: plant-derived nanocarriers for targeted drug delivery in cancer therapy. Phytomedicine Plus. 5, 100828 (2025). https://doi.org/10.1016/j.phyplu.2025.100828
26. Awad, N.S., Paul, V., AlSawaftah, N.M., ter Haar, G., Allen, T.M., Pitt, W.G., Husseini, G.A.: Ultrasound-Responsive Nanocarriers in Cancer Treatment: A Review. ACS Pharmacol. Transl. Sci. 4, 589–612 (2021). https://doi.org/10.1021/acsptsci.0c00212
27. Cong, X., Zhang, Z., Li, H., Yang, Y.-G., Zhang, Y., Sun, T.: Nanocarriers for targeted drug delivery in the vascular system: focus on endothelium. J. Nanobiotechnology. 22, 620 (2024). https://doi.org/10.1186/s12951-024-02892-9
28. Karnwal, A., Sharma, V., Kumar, G., Jassim, A.Y., Dohroo, A., Sivanesan, I.: Transforming Medicine with Nanobiotechnology: Nanocarriers and Their Biomedical Applications. Pharmaceutics. 16, 1114 (2024). https://doi.org/10.3390/pharmaceutics16091114
29. Austria, E., Bilek, M., Varamini, P., Akhavan, B.: Breaking biological barriers: Engineering polymeric nanoparticles for cancer therapy. Nano Today. 60, 102552 (2025). https://doi.org/10.1016/j.nantod.2024.102552
30. Cavalcante de Freitas, P.G., Rodrigues Arruda, B., Araújo Mendes, M.G., Barroso de Freitas, J.V., da Silva, M.E., Sampaio, T.L., Petrilli, R., Eloy, J.O.: Resveratrol-Loaded Polymeric Nanoparticles: The Effects of D-α-Tocopheryl Polyethylene Glycol 1000 Succinate (TPGS) on Physicochemical and Biological Properties against Breast Cancer In Vitro and In Vivo. Cancers. 15, 2802 (2023). https://doi.org/10.3390/cancers15102802
31. kapoor, D. u, Garg, R., Gaur, M., Prajapati, B.G., Agrawal, G., Bhattacharya, S., Elossaily, G.M.: Polymeric nanoparticles approach and identification and characterization of novel biomarkers for colon cancer. Results Chem. 6, 101167 (2023). https://doi.org/10.1016/j.rechem.2023.101167
32. Singh, R., Srinivas, S.P., Kumawat, M., Daima, H.K.: Ligand-based surface engineering of nanomaterials: Trends, challenges, and biomedical perspectives. OpenNano. 15, 100194 (2024). https://doi.org/10.1016/j.onano.2023.100194
33. Hsu, C.-Y., Liao, C.-C., Lin, Z.-C., Alalaiwe, A., Hwang, E., Lin, T.-W., Fang, J.-Y.: Facile adipocyte uptake and liver/adipose tissue delivery of conjugated linoleic acid-loaded tocol nanocarriers for a synergistic anti-adipogenesis effect. J. Nanobiotechnology. 22, 50 (2024). https://doi.org/10.1186/s12951-024-02316-8
34. Wang, S., Zhang, J., Zhou, H., Lu, Y.C., Jin, X., Luo, L., You, J.: The role of protein corona on nanodrugs for organ-targeting and its prospects of application. J. Controlled Release. 360, 15–43 (2023). https://doi.org/10.1016/j.jconrel.2023.06.014
35. Tsitouridou, A., Parhizkar, M., Wu, C.-Y., Chen, T., Tsaoulidis, D.: CFD approaches in microfluidics for the development of polymeric, lipid-based and inorganic nanoparticles for drug delivery. Chem. Eng. J. Adv. 24, 100853 (2025). https://doi.org/10.1016/j.ceja.2025.100853
36. Ashrafizadeh, M., Delfi, M., Zarrabi, A., Bigham, A., Sharifi, E., Rabiee, N., Paiva-Santos, A.C., Kumar, A.P., Tan, S.C., Hushmandi, K., Ren, J., Zare, E.N., Makvandi, P.: Stimuli-responsive liposomal nanoformulations in cancer therapy: Pre-clinical & clinical approaches. J. Controlled Release. 351, 50–80 (2022). https://doi.org/10.1016/j.jconrel.2022.08.001
37. Du, J., Lane, L.A., Nie, S.: Stimuli-Responsive Nanoparticles for Targeting the Tumor Microenvironment. J. Control. Release Off. J. Control. Release Soc. 219, 205–214 (2015). https://doi.org/10.1016/j.jconrel.2015.08.050
38. 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
39. Teixeira do Nascimento, A., Stoddart, P.R., Goris, T., Kael, M., Manasseh, R., Alt, K., Tashkandi, J., Kim, B.C., Moulton, S.E.: Stimuli-Responsive Materials for Biomedical Applications. Adv. Mater. 37, e07559 (2025). https://doi.org/10.1002/adma.202507559
40. Wang, T., Liu, Y., Wu, Q., Lou, B., Liu, Z.: DNA nanostructures for stimuli-responsive drug delivery. Smart Mater. Med. 3, 66–84 (2022). https://doi.org/10.1016/j.smaim.2021.12.003
41. Yang, J., des Rieux, A., Malfanti, A.: Stimuli-Responsive Nanomedicines for the Treatment of Non-cancer Related Inflammatory Diseases. ACS Nano. 19, 15189–15219 (2025). https://doi.org/10.1021/acsnano.5c00700

42. Xie, X., Zhang, M., Luo, H.: Regulation of metabolism by circadian rhythms: Support from time-restricted eating, intestinal microbiota & omics analysis. Life Sci. 351, 122814 (2024). https://doi.org/10.1016/j.lfs.2024.122814
43. Smokovski, I., Steinle, N., Behnke, A., Bhaskar, S.M.M., Grech, G., Richter, K., Niklewski, G., Birkenbihl, C., Parini, P., Andrews, R.J., Bauchner, H., Golubnitschaja, O.: Digital biomarkers: 3PM approach revolutionizing chronic disease management — EPMA 2024 position. EPMA J. 15, 149–162 (2024). https://doi.org/10.1007/s13167-024-00364-6
44. Boudaba, N., Marion, A., Huet, C., Pierre, R., Viollet, B., Foretz, M.: AMPK Re-Activation Suppresses Hepatic Steatosis but its Downregulation Does Not Promote Fatty Liver Development. EBioMedicine. 28, 194–209 (2018). https://doi.org/10.1016/j.ebiom.2018.01.008
45. Wu, K.K.-L., Cheung, S.W.-M., Cheng, K.K.-Y.: NLRP3 Inflammasome Activation in Adipose Tissues and Its Implications on Metabolic Diseases. Int. J. Mol. Sci. 21, 4184 (2020). https://doi.org/10.3390/ijms21114184
46. Naeem, S., Zhang, J., Zhang, Y., Wang, Y.: Nucleic acid therapeutics: Past, present, and future. Mol. Ther. Nucleic Acids. 36, 102440 (2024). https://doi.org/10.1016/j.omtn.2024.102440
47. Abdelsayed, M.: AI-Driven Polypharmacology in Small-Molecule Drug Discovery. Int. J. Mol. Sci. 26, 6996 (2025). https://doi.org/10.3390/ijms26146996
48. Battaglia, M., Ahmed, S., Anderson, M.S., Atkinson, M.A., Becker, D., Bingley, P.J., Bosi, E., Brusko, T.M., DiMeglio, L.A., Evans-Molina, C., Gitelman, S.E., Greenbaum, C.J., Gottlieb, P.A., Herold, K.C., Hessner, M.J., Knip, M., Jacobsen, L., Krischer, J.P., Long, S.A., Lundgren, M., McKinney, E.F., Morgan, N.G., Oram, R.A., Pastinen, T., Peters, M.C., Petrelli, A., Qian, X., Redondo, M.J., Roep, B.O., Schatz, D., Skibinski, D., Peakman, M.: Introducing the Endotype Concept to Address the Challenge of Disease Heterogeneity in Type 1 Diabetes. Diabetes Care. 43, 5–12 (2020). https://doi.org/10.2337/dc19-0880
49. Lyu, Y., Yang, X., Yang, L., Dai, J., Qin, H., Zhou, Y., Huang, Y., Wang, Y., Wu, D., Shuai, Q., Li, Q., Xin, X., Yin, L.: Lipid nanoparticle-mediated hepatocyte delivery of siRNA and silibinin in metabolic dysfunction-associated steatotic liver disease. J. Control. Release Off. J. Control. Release Soc. 373, 385–398 (2024). https://doi.org/10.1016/j.jconrel.2024.07.011
50. Kim, M., Jeong, M., Hur, S., Cho, Y., Park, J., Jung, H., Seo, Y., Woo, H.A., Nam, K.T., Lee, K., Lee, H.: Engineered ionizable lipid nanoparticles for targeted delivery of RNA therapeutics into different types of cells in the liver. Sci. Adv. 7, eabf4398 (2021). https://doi.org/10.1126/sciadv.abf4398
51. Mehrdadi, S.: Lipid-Based Nanoparticles as Oral Drug Delivery Systems: Overcoming Poor Gastrointestinal Absorption and Enhancing Bioavailability of Peptide and Protein Therapeutics. Adv. Pharm. Bull. 14, 48–66 (2024). https://doi.org/10.34172/apb.2024.016
52. Emma, M.R., Giannitrapani, L., Cabibi, D., Porcasi, R., Pantuso, G., Augello, G., Giglio, R.V., Re, N.L., Capitano, A.R., Montalto, G., Soresi, M., Cervello, M.: Hepatic and circulating levels of PCSK9 in morbidly obese patients: Relation with severity of liver steatosis. Biochim. Biophys. Acta Mol. Cell Biol. Lipids. 1865, 158792 (2020). https://doi.org/10.1016/j.bbalip.2020.158792
53. Yonet-Tanyeri, N., Parker, R.S., Falo, L.D., Little, S.R.: Investigation of the Impact of Manufacturing Methods on Protein-Based Long-Acting Injectable Formulations: A Comparative Assessment for Microfluidics vs. Conventional Methods. Pharmaceutics. 16, 1264 (2024). https://doi.org/10.3390/pharmaceutics16101264

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