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THE ROLE OF OXIDATIVE STRESS AND MITOCHONDRIAL DYSFUNCTION IN TYPE 2 DIABETES MELLITUS

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ABSTRACT

Type 2 diabetes mellitus has become one of the fastest-growing global health crises, affecting millions worldwide. This review explores the intricate relationship between mitochondrial dysfunction and oxidative stress in driving the development and progression of this metabolic disorder. Chronic high blood sugar levels trigger excessive production of reactive oxygen species from dysfunctional mitochondria, creating a destructive cycle that impairs insulin action, damages insulin-producing pancreatic cells, and fuels persistent low-grade inflammation. These interconnected pathological processes ultimately lead to the metabolic breakdown characteristic of type 2 diabetes. The review also examines emerging therapeutic strategies, including mitochondria-targeted antioxidants and lifestyle interventions that show promise in restoring cellular energy balance and breaking this harmful cycle.

KEYWORDS: Type 2 diabetes mellitus; oxidative stress; mitochondrial dysfunction; reactive oxygen species (ROS); insulin resistance; pancreatic β-cell failure; electron transport chain (ETC); glucolipotoxicity; mitochondrial dynamics (fusion/fission); mitophagy; mitochondrial biogenesis; PGC-1α; antioxidant defense systems (SOD, CAT, GPx); NLRP3 inflammasome; chronic low-grade inflammation; stress kinases (JNK, NF-κB); insulin signaling (IRS-1/PI3K/Akt); ER stress; unfolded protein response; mitochondria-targeted antioxidants (MitoQ, SkQ1, MitoTEMPO); AMPK activators; SGLT2 inhibitors; metformin; lifestyle interventions; metabolic syndrome.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) has emerged as one of the most pressing global metabolic epidemics, with its prevalence continuing to rise at an alarming rate worldwide.[1] While insulin resistance and progressive β-cell failure remain the hallmark features of this disorder,[1,2] a growing body of evidence has established that oxidative stress and mitochondrial dysfunction are not merely epiphenomena but rather central pathogenic drivers that propagate and perpetuate the disease.[3,4] Under chronic hyperglycaemic conditions, the mitochondrial electron transport chain becomes a major source of reactive oxygen species (ROS) overproduction, overwhelming endogenous antioxidant defences and creating a state of redox imbalance.[1,2] This excessive ROS burden directly impairs insulin signalling through oxidative modifications of key proteins and activates stress-sensitive inflammatory pathways, while simultaneously compromising mitochondrial bioenergetics, dynamics, and quality control mechanisms.[4,5] Notably, oxidative stress and mitochondrial dysfunction do not simply coexist; rather, they engage in a self-perpetuating vicious cycle wherein mitochondrial ROS production exacerbates mitochondrial damage, which in turn fuels further ROS generation, driving chronic metabolic inflammation and progressive cellular dysfunction.[4] The impact of this pathogenic alliance extends across insulin-sensitive tissues—including skeletal muscle, liver, and adipose tissue—and critically compromises pancreatic β-cell function, ultimately culminating in the metabolic decompensation that characterises overt T2DM.[4,6] This review synthesises current mechanistic understanding of the interdependent roles of oxidative stress and mitochondrial dysfunction in T2DM pathogenesis, examines their contribution to diabetic complications, and explores emerging therapeutic strategies targeting this interconnected pathological axis.

Fundamentals of Mitochondrial Bioenergetics and Redox Homeostasis

Normal Physiology of Oxidative Phosphorylation (OXPHOS) and the Tricarboxylic Acid (TCA) Cycle

Mitochondria are often described as the powerhouses of our cells, and for good reason. They are the primary site where the food we eat is converted into usable energy, a molecule called adenosine triphosphate (ATP). This process is driven by two interconnected pathways: the tricarboxylic acid (TCA) cycle and oxidative phosphorylation (OXPHOS). The TCA cycle, which takes place in the mitochondrial matrix, breaks down nutrients to generate electron carriers. These carriers then feed into the electron transport chain (ETC)—the core of OXPHOS—located on the inner mitochondrial membrane. As electrons pass through

complexes I to IV of this chain, they create a proton gradient that drives ATP synthase (complex V) to produce ATP.[7] This elegant system is the foundation of cellular energy, and its efficiency is paramount for the proper function of every tissue in the body, particularly those with high energy demands like skeletal muscle, the liver, and the pancreas.[7]

Physiological Generation and Enzymatic Scavenging of Reactive Oxygen Species (ROS)

While the ETC is incredibly efficient, it is not perfect. A small percentage of electrons inevitably "leak" from the chain, particularly from complexes I and III, and react with oxygen prematurely. This reaction generates reactive oxygen species (ROS), primarily the superoxide anion ($O_2^{\bullet -}$).[7,8] In a healthy state, this is a controlled and even beneficial process. At low to moderate levels, ROS act as vital signaling molecules, playing important roles in cellular processes like proliferation and defense responses.[9,10] However, problems arise when this delicate balance is tipped. An overproduction of ROS, for example due to nutrient excess in diabetes, overwhelms the system and shifts ROS from a beneficial signal to a damaging molecule that can harm proteins, lipids, and DNA.[10] This state is known as oxidative stress and is a critical driver of cellular dysfunction.[8]

Intrinsic Antioxidant Defense Systems

To prevent this kind of damage, our cells are equipped with a sophisticated and powerful defense network: the antioxidant system. This system acts as a multi-layered shield to keep ROS in check. The very first line of defense is a team of specialized enzymes that work together to neutralize ROS almost instantly.[8,10]

- **Superoxide Dismutase (SOD):** This is the first responder. It rapidly converts the highly reactive superoxide anion ($O_2^{\bullet -}$) into less harmful hydrogen peroxide (H_2O_2).
- **Catalase (CAT) and Glutathione Peroxidase (GPx):** These enzymes are responsible for the next step. They safely break down the hydrogen peroxide produced by SOD into water and oxygen, neutralizing the threat completely.[8.10]

The coordinated action of these enzymes is crucial for maintaining a healthy redox balance. When this system is compromised, as is often the case in metabolic diseases like type 2 diabetes, the cell becomes vulnerable to the damaging effects of oxidative stress.[8]

The Vicious Cycle: Hyperglycemia-Induced Oxidative Stress and Mitochondrial Impairment

Overactivation of Upstream Pathways (Polyol Flux, Hexosamine, AGEs, and PKC Activation)

Sustained high blood glucose levels trigger major metabolic alterations inside cells, driving excessive production of reactive oxygen species (ROS).[14] Under these hyperglycemic conditions, cells direct surplus glucose into alternative pathways that amplify oxidative stress rather than clearing it efficiently.[12]

The primary pathways contributing to this cellular stress include:

- **The Polyol Pathway:** Excess glucose is converted into sorbitol by aldose reductase, which consumes vital NADPH in the process.[14] Because NADPH is required to regenerate reduced glutathione—a crucial intracellular antioxidant—its depletion leaves the cell heavily exposed to oxidative damage.[13]
- **Advanced Glycation End-Products (AGEs):** Intracellular intermediates non-enzymatically react with amino groups on proteins and lipids, forming AGEs that disrupt normal cellular architecture and stimulate toxic signaling cascades via their specific receptors (RAGE).[16]
- **The Hexosamine Pathway:** A fraction of excess fructose-6-phosphate is shunted away from glycolysis into this pathway, altering gene expression and transcription factors through abnormal protein O-GlcNAcylation.
- **Protein Kinase C (PKC) Activation:** Increased diacylglycerol (DAG) levels driven by glycolysis intermediates hyperactivate pathological PKC isoforms, impairing vascular function and worsening cellular damage.[14]

Electron Transport Chain (ETC) Complexes I and III Dysfunction and Proton Leak

The root driver behind these damaging metabolic pathways is mitochondrial dysfunction, specifically the overproduction of superoxide within the electron transport chain (ETC).[14] When cells experience a constant overload of electron donors derived from glucose and fatty acids, the mitochondrial proton gradient becomes abnormally high.

This electrochemical surplus stalls electron transfer at Complex I and Complex III within the inner mitochondrial membrane. Trapped electrons leak directly onto molecular oxygen, turning it into superoxide radicals (O^{-}_{2}).[16] This surge in superoxide further inhibits critical downstream enzymes like glyceraldehyde-3-phosphate dehydrogenase (GAPDH), worsening

upstream metabolite accumulation and establishing a destructive feedback loop.[14] Additionally, chronic proton leaks uncouple oxidative phosphorylation, wasting energy and dropping overall ATP synthesis efficiency while accelerating local oxidative damage.

Mitochondrial DNA (mtDNA) Vulnerability, Mutational Accumulation, and Impaired Repair Mechanisms

Unlike nuclear DNA, mitochondrial DNA (mtDNA) lacks protective histone packaging and sits directly adjacent to the inner membrane where ROS are continuously generated.[15] This proximity makes the circular mitochondrial genome exceptionally vulnerable to oxidative modifications, notably the formation of 8-hydroxy-2'-deoxyguanosine (8-OHdG).

Although mitochondria possess basic repair mechanisms, such as base excision repair (BER), chronic hyperglycemic stress overwhelms these pathways. Over time, unrepaired oxidative lesions lead to somatic mutations within mtDNA, structural deletions, and a progressive drop in copy numbers in vulnerable tissues.[11] Because mtDNA encodes essential core subunits of the respiratory chain complexes, these accumulated mutations result in structurally malformed ETC proteins, worsening electron leakage, increasing free radical output, and locking the cell into a permanent state of mitochondrial failure.[15]

Mitochondrial Dysfunction as a Driving Force in Insulin Resistance (IR)

Pathological Interplay in Insulin-Sensitive Tissues (Skeletal Muscle, Hepatic, and Adipose Tissues)

Insulin resistance (IR) is fundamentally tied to how effectively individual tissues handle energy substrates like glucose and fatty acids. In a healthy state, skeletal muscle accounts for the vast majority of insulin-stimulated glucose disposal, relying heavily on proper mitochondrial oxidative phosphorylation (OXPHOS) to burn circulating fuel.[18] However, in individuals with early metabolic decline, skeletal muscle mitochondria show a reduced oxidative capacity and smaller structural size, leading to an intracellular backlog of lipids and unburned metabolites.

Similarly, in the liver, impaired mitochondrial beta-oxidation contributes to non-alcoholic fatty liver disease (NAFLD) and heightens hepatic glucose production, ignoring normal insulin-driven suppression signals. Adipose tissue undergoes a parallel breakdown: hypertrophied fat cells become hypoxic, triggering local inflammation and dysregulated

lipolysis that floods the bloodstream with free fatty acids (FFAs), compounding systemic metabolic distress.[23]

Lipid Intermediates (Diacylglycerols and Ceramides) and Substrate Overload

When energy intake chronically surpasses mitochondrial oxidative capacity—often termed substrate overload—excess lipids cannot be safely burned off inside the mitochondria. Instead, they accumulate within non-adipose insulin-sensitive cells in the form of ectopic fat. Crucially, it is not the stored triglycerides that cause harm, but rather bioactive lipid intermediates such as diacylglycerols (DAGs) and ceramides.[31]

Elevated intracellular DAGs aberrantly activate novel protein kinase C (PKC) isoforms (such as PKC theta in muscle and PKC epsilon in the liver). Once activated, these kinases phosphorylate key regulatory sites on insulin receptor substrates, effectively throwing a wrench into the normal cellular machinery required to clear glucose from the blood.[28] Concurrently, accumulated ceramides disrupt membrane fluidity and lipid microdomains, suppressing downstream protein recruitment and sealing the tissue's resistance to insulin.

ROS-Mediated Interference of Downstream Insulin Signaling Cascades (IRS-1, PI3K/Akt Pathway)

Mitochondrial reactive oxygen species (ROS) act as direct chemical disruptors of the canonical insulin signaling pathway. Under normal physiological conditions, the binding of insulin to its cell-surface receptor triggers auto-phosphorylation, which subsequently recruits and phosphorylates insulin receptor substrate-1 (IRS-1) on tyrosine residues. This sparks a downstream cascade activating phosphatidylinositol 3-kinase (PI3K) and Protein Kinase B (Akt/PKB), ultimately driving the translocation of glucose transporter type 4 (GLUT4) vesicles to the cell membrane.[32]

Excess mitochondrial superoxide production alters this delicate sequence by promoting atypical serine and threonine phosphorylation of IRS-1 instead of tyrosine. This shift neutralizes IRS-1 function, preventing the downstream activation of PI3K and Akt. Without functional Akt signaling, cells fail to pull glucose inward, resulting in sustained hyperglycemia and locked metabolic resistance.[21]

Pancreatic beta-Cell Failure and Glucolipotoxicity

Intrinsic Vulnerability of β-Cells to Oxidative Stress Due to Low Antioxidant Reserves

While peripheral tissues develop insulin resistance, blood glucose levels initially remain stable because pancreatic beta-cells step up insulin production. However, beta-cells possess a unique structural vulnerability: they express exceptionally low levels of intrinsic antioxidant defense enzymes—such as catalase, glutathione peroxidase, and superoxide dismutase—compared to other metabolic organs.[24]

Consequently, when beta-cells are chronically exposed to high circulating levels of both glucose and free fatty acids (a state known as glucolipotoxicity), they cannot efficiently neutralize the resulting tidal wave of mitochondrial ROS.[20] This natural antioxidant deficit leaves beta-cell proteins, lipids, and DNA exposed to rapid oxidative destruction, setting the stage for secretory failure and cell death.

Mitochondrial ATP-Sensitive Potassium ATP Channel Disruption and Impaired Insulin Secretion

Glucose-stimulated insulin secretion (GSIS) relies entirely on pristine mitochondrial bioenergetics. Under normal conditions, glucose entering the beta-cell is metabolized via glycolysis and the TCA cycle, causing a spike in the intracellular ATP-to-ADP ratio. This energy surge closes ATP-sensitive potassium K_{ATP} channels on the plasma membrane, depolarizing the cell, opening voltage-gated calcium channels, and triggering the exocytosis of insulin-containing granules.[29]

In the presence of chronic oxidative stress and mitochondrial damage, ATP production drops significantly, preventing proper K_{ATP} channel closure. Furthermore, mitochondrial structural decay impairs the metabolic signaling loops that amplify insulin release. As a result, even when blood glucose is high, the beta-cell fails to mount an appropriate insulin secretory response, marking the transition from prediabetes to overt clinical T2DM.[26]

Endoplasmic Reticulum (ER) Stress, Unfolded Protein Response (UPR), and Apoptotic Pathways

The demand to synthesize massive quantities of insulin places an intense burden on the beta-cell endoplasmic reticulum (ER). Mitochondrial dysfunction and oxidative stress compromise

this delicate organelle, causing unfolded or misfolded proteins to accumulate inside the ER lumen—a condition known as ER stress.[17]

To cope, the cell activates an adaptive defense network called the Unfolded Protein Response (UPR). However, if mitochondrial impairment and high glucose levels persist, the UPR shifts from being protective to destructive. Prolonged signaling via stress sensors like PERK, IRE 1 alpha, and ATF6 triggers downstream apoptotic executioners, leading to programmed cell death (apoptosis) and a dramatic net reduction in functional beta-cell mass.[20]

Crosstalk Between Mitochondrial Dysfunction and Chronic Low-Grade Inflammation

Activation of Stress Kinases (JNK, p38 MAPK, and NF- kappa B) by Mitochondrial ROS

Type 2 diabetes is widely recognized as a chronic, low-grade inflammatory condition where systemic metabolic pathways intertwine with immune signaling. Mitochondrial ROS serve as primary signaling messengers that trigger inflammatory pathways within insulin-target cells.[19]

When mitochondrial electron leakage spikes, excess free radicals directly activate key serine/threonine stress kinases, including c-Jun N-terminal kinase (JNK), p38 mitogen-activated protein kinase (p38 MAPK), and the inhibitor of nuclear factor kappa B kinase (IKK) complex.[22] The activation of IKK leads to the degradation of I kappa B and the subsequent nuclear translocation of Nuclear Factor kappa B (NF- kappa B), a master transcription factor that drives the widespread expression of pro-inflammatory genes and worsens cellular insulin resistance.

Inflammasome Activation (NLRP3) and Pro-inflammatory Cytokine Secretion (TNF-alpha, IL-1beta, IL-6)

Beyond classical stress kinases, mitochondrial dysfunction directly triggers innate immune sensors, most notably the NOD-like receptor family pyrin domain-containing 3 (NLRP3) inflammasome (Schroder & Tschopp, 2010). Damaged, ROS-leaking mitochondria release mitochondrial DNA (mtDNA) and cardiolipin into the cytoplasm, which act as potent danger signals (DAMPs) that assemble and activate the NLRP3 inflammasome complex.[33]

Once activated, caspase-1 processes precursor proteins into active pro-inflammatory cytokines, specifically interleukin-1 beta (IL-1 beta) and interleukin-18 (IL-18). Along with

tumor necrosis factor-alpha (TNF-alpha) and interleukin-6 (IL-6) secreted via NF- kappa B pathways, these cytokines establish a toxic paracrine and endocrine loop that damages neighboring tissues, impairs insulin receptor signaling, and suppresses systemic metabolic function.[19]

Macrophage Polarization and Tissue-Specific Systemic Inflammation

The localized release of mitochondrial-derived cytokines and lipids reshapes the immune landscape within metabolic tissues, particularly driving macrophage polarization (Olefsky & Glass, 2010). In healthy metabolic tissues, anti-inflammatory M2 macrophages predominate, maintaining tissue repair and homeostasis. However, exposure to extracellular ROS, free fatty acids, and local cell debris triggers a phenotypic shift toward pro-inflammatory M1 macrophages.[25]

These M1 macrophages infiltrate skeletal muscle, liver, and expanding white adipose tissue, forming crown-like structures around stressed adipocytes. They sustain a constant local inflammatory environment that reinforces mitochondrial dysfunction in neighboring parenchymal cells, sealing a self-perpetuating, systemic cycle where metabolic disease and chronic inflammation feed directly into one another.[27]

Mitochondrial Dynamics, Quality Control, and Autophagic Failure

Imbalance in Mitochondrial Dynamics: Fusion (Mitofusins, OPA1) vs. Fission (Drp1, Fis1)

Mitochondria are highly dynamic organelles that constantly shift their architecture through balanced cycles of fusion and fission to adapt to shifting cellular energy demands. In healthy cells, fusion—regulated by outer membrane proteins Mitofusin 1 and 2 (Mfn1, Mfn2) and inner membrane optic atrophy 1 (OPA1)—allows mitochondria to mix contents, repair minor defects, and optimize oxidative phosphorylation.[41] Conversely, fission—governed by cytosolic dynamin-related protein 1 (Drp1) and mitochondrial fission 1 protein (Fis1)—segments the network to isolate severely damaged segments for destruction.

Under the chronic metabolic stress of type 2 diabetes, this delicate equilibrium is severely disrupted. Elevated glucose and lipid levels hyperactivate Drp1, driving excessive mitochondrial fragmentation while downregulating the expression of fusion proteins Mfn2 and OPA1.[36] This unmitigated shift toward fission produces a dense population of small,

swollen, and inefficient mitochondria that struggle to meet cellular energy requirements and leak massive amounts of reactive oxygen species (ROS).

Impaired Mitophagy and Accumulation of Senescent, Damaged Mitochondria

To maintain intracellular quality control, cells rely on mitophagy—a specialized form of autophagy that selectively clears out dysfunctional, ROS-leaking mitochondria via the PINK1/Parkin signaling pathway.[43] When a mitochondrion loses its membrane potential, the kinase PINK1 accumulates on its outer membrane and recruits the ubiquitin ligase Parkin, tagging the organelle for lysosomal degradation.

In insulin-resistant tissues, however, this vital clearance mechanism is blunted. Nutrient overload and chronic low-grade inflammation impair autophagic flux, preventing the successful degradation of damaged organelles.[39] As a result, senescent and structurally compromised mitochondria accumulate within skeletal muscle, liver, and beta-cells. This backlog acts as a permanent internal source of oxidative stress, deepening the metabolic pathology and locking the tissue in a state of chronic cellular injury.

Transcriptional Downregulation of Biogenesis Regulators (PGC-1 alpha, NRF-1/2, TFAM)

Beyond clearing old mitochondria, cells must continuously synthesize fresh, functional organelles to sustain metabolic health—a process known as mitochondrial biogenesis. Peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1 alpha) acts as the master transcriptional coactivator driving this entire network. When active, PGC-1alpha partners with nuclear respiratory factors 1 and 2 (NRF-1/2) to stimulate mitochondrial transcription factor A (TFAM), which directly controls the replication and transcription of mitochondrial DNA.[44]

In the context of T2DM, chronic exposure to inflammatory cytokines and excessive lipid intermediates suppresses the expression and activity of PGC-1alpha. This transcriptional shutdown halts fresh mitochondrial production.[34] Combined with impaired mitophagy and excessive fission, this lack of biogenesis results in a severe net deficit of functional respiratory machinery, culminating in the metabolic exhaustion characteristic of advanced insulin resistance.

Therapeutic Interventions and Future Perspectives

Mitochondria-Targeted Antioxidants (MitoQ, SkQ1, MitoTEMPO)

Traditional broad-spectrum antioxidants have largely fallen short in clinical trials for diabetic complications because they cannot cross the lipid bilayers of the inner mitochondrial membrane in sufficient concentrations to neutralize free radicals at their primary site of production.[40] To overcome this, researchers developed mitochondria-targeted antioxidants by chemically attaching a lipophilic triphenylphosphonium (TPP) cation to active antioxidant cores, allowing them to accumulate hundreds of fold inside the mitochondrial matrix driven by the negative membrane potential.

Compounds such as MitoQ, SkQ1, and MitoTEMPO have shown remarkable preclinical efficacy in neutralizing local ROS, preventing mtDNA mutations, and preserving oxidative phosphorylation in insulin-sensitive tissues.[35] By cutting off oxidative stress at its source, these targeted agents protect beta-cell function, improve vascular health, and mitigate the progression of diabetic tissue damage.

Pharmacological Modulators of Mitochondrial Biogenesis and Function (AMPK Activators, SGLT2 Inhibitors, Metformin)

Beyond direct antioxidants, modern pharmacological strategies focus on restoring cellular energy sensors and stimulating healthy mitochondrial renewal. Metformin, the first-line medication for T2DM, acts primarily by mildly inhibiting mitochondrial complex I, which transiently lowers ATP production and activates AMP-activated protein kinase (AMPK).[45] Activated AMPK subsequently phosphorylates and turns on PGC-1alpha, boosting mitochondrial biogenesis and fatty acid oxidation.

Similarly, newer classes of diabetes medications, such as sodium-glucose cotransporter-2 (SGLT2) inhibitors, have demonstrated significant cardiorenal and metabolic benefits that extend beyond mere glucose lowering. These agents help normalize cellular bioenergetics, reduce cytosolic sodium and calcium overload, and promote a shift toward efficient myocardial and renal ketone metabolism, protecting mitochondrial structure from glucotoxic strain.[42]

Lifestyle Modifications (Caloric Restriction and Structured Exercise Training)

Despite major pharmacological advancements, lifestyle interventions remain the most powerful and natural tools for reversing mitochondrial decline in metabolic disease. Both

caloric restriction and structured aerobic or resistance exercise training robustly activate AMPK and SIRT1 pathways, which in turn upregulate PGC-1alpha expression and trigger comprehensive mitochondrial biogenesis.[37]

Regular physical activity clears ectopic lipid accumulation, shifts macrophage polarization toward an anti-inflammatory profile, and restores structural balance to mitochondrial dynamics by enhancing fusion capacity. This restores oxidative capacity in skeletal muscle and significantly improves whole-body insulin sensitivity.

Emerging Diagnostic and Translational Challenges

While targeting mitochondrial dysfunction holds immense therapeutic promise, translating these discoveries into routine clinical practice presents notable hurdles. Key challenges include the lack of standardized, non-invasive biomarkers to accurately quantify tissue-specific mitochondrial health in living patients—current metrics often rely on circulating cell-free mtDNA or systemic oxidative stress markers that lack cellular specificity.[38] Furthermore, designing delivery systems that can safely and specifically target metabolic tissues without disrupting normal physiological redox signaling remains an active area of pharmacological investigation.

Conclusion and Future Directions

Type 2 diabetes mellitus is no longer viewed merely as a simple disorder of systemic glucose imbalance, but rather as a complex systemic pathology driven by profound mitochondrial failure and sustained oxidative stress. The vicious cycle linking hyperglycemia, lipid oversupply, excessive ROS generation, and impaired quality control creates a self-perpetuating feedback loop that degrades insulin signaling, destroys pancreatic beta-cell mass, and fuels chronic low-grade inflammation.

Future research must focus on translating promising bench-side innovations—such as mitochondria-targeted antioxidants, selective mitophagy activators, and personalized metabolic modulators—into safe, effective clinical therapies. By directly repairing the compromised mitochondrial network and restoring cellular redox balance, clinicians will be better equipped to halt or even reverse the debilitating long-term complications of type 2 diabetes.

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