Review

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Adiponectin: A Promising Target for the Treatment of Diabetes and Its Complications

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Review

Adiponectin: A Promising Target for the Treatment of Diabetes and its complications

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Abstract: Diabetes mellitus, a chronic metabolic disorder characterized by hyperglycemia, presents a formidable global health challenge with its associated complications. Adiponectin, an adipocyte-derived hormone, has emerged as a significant player in glucose metabolism and insulin sensitivity. Beyond its metabolic effects, adiponectin exerts anti-inflammatory, anti-oxidative, and vasoprotective properties, making it an appealing therapeutic target for mitigating diabetic complications. The molecular mechanisms by which adiponectin impacts critical pathways implicated in diabetic nephropathy, retinopathy, neuropathy, and cardiovascular problems are thoroughly examined in this study. In addition, we explore possible treatment options for increasing adiponectin levels or improving its downstream signaling. The multifaceted protective roles of adiponectin in diabetic complications suggest its potential as a novel therapeutic avenue. However, further translational studies and clinical trials are warranted to fully harness the therapeutic potential of adiponectin in the management of diabetic complications. This review highlights adiponectin as a promising target for the treatment of diverse diabetic complications and encourages continued research in this pivotal area of diabetes therapeutics.

Introduction: Diabetes mellitus (DM) is one of the most ancient illnesses known to human. Around 3000 years ago, it was first mentioned in an Egyptian text. In recent decades, there has been a significant surge in the global prevalence of diabetes and its associated metabolic complications. The difference between type 1 and type 2 diabetes was established in 1936 [1]. The frequency of type 2 diabetes mellitus (DM), a chronic metabolic condition, has been continuously rising worldwide. According to the World Health Organization, the incidence of obesity worldwide nearly The global diabetic population is steadily rising, currently estimated at 422 million individuals [2]. T2DM is characterized by dysregulation of carbohydrate, lipid, and protein metabolism, which occurs from decreased insulin secretion, insulin resistance, or a combination of the two, usually occurs later in life and is frequently linked to lifestyle factors [3]. Among the three main groups of diabetes, which include Type 1 diabetes mellitus (T1DM) and gestational diabetes, Type 2 diabetes is the most prevalent form [4]. The primary cause of T2DM is a gradual decline in insulin secretion by pancreatic β-cells, typically occurring against a backdrop of pre-existing insulin resistance in skeletal muscle, liver, and adipose tissue [5,6]. According to the World Health Organization (WHO), diabetes stands as a primary contributor to conditions such as blindness, kidney failure, heart attacks, stroke, and lower limb amputations [7]. Diabetes is linked to both microvascular (diabetic retinopathy, neuropathy, and nephropathy) and macrovascular (cardiovascular disease or CVD) complications

[8]. Individuals with diabetes face an elevated risk of CVD, encompassing conditions like coronary heart disease (CHD) [9], hypertension, increased levels of low-density lipoprotein-cholesterol (LDL), and obesity [5,10]

Adiponectin, the most prevalent peptide released by adipocytes plays prominent role in the intricate connection between adiposity, insulin resistance, and inflammation [11]. The levels of adiponectin are inversely correlated with adiposity, that means increase the body fat reduce the adiponectin and reduce the fat accumulation increase the adiponectin level [12]. Adiponectin shows its biological action through several mechanisms such as enhancing insulin sensitivity in the peripheral cells [13–15] anti-inflammatory actions by reducing the production of inflammatory molecules [16], breakdown of fatty acids and inhibits the production of fatty acids in the liver [17], maintain the health and flexibility of blood vessels [18,19] etc. It is also adiponectin also maintain a responsible role for appetite regulation and energy expenditure [20,21].

Till toady there are several treatment options for T2DM. However, treating T2DM is very challenging due to its complex nature and the diversity of factors involved. T2DM is a progressive disease as the production of insulin are reduced day by day irrespective of treatment of diabetes. Insulin resistance is another challenge to treat diabetes. Life style modifications including diet and exercise plays a crucial role for diabetes. However, sustaining these alterations can be arduous. Moreover, chronic conditions like T2DM have significant effects on emotional health.

Recent studies has shown that, A reduction in plasma adiponectin concentration is closely associated with the development of type 2 diabetes mellitus (T2DM) and obesity [22,23]. Both animal and experimental research have demonstrated that adiponectin enhances insulin sensitivity, suggesting it may serve as a preventive measure against the onset of T2DM [24].

In the current review we will discuss recent advancements in studying the pathophysiological functions of adiponectin and its receptors in relation to insulin resistance, type 2 diabetes, and the metabolic syndrome.

Adiponectin: An Overview: Adiponectin, alternatively referred to as AdipoQ, APM1 or ACRP30, is a single-chain adipokine composed of 244 amino acids, possessing a molecular weight of around 26 kilodaltons (kDa) secreted by white adipose tissue. The Adiponectin protein is encoded by the AdipoQ gene located on the chromosome locus 3q27. Adiponectin consists of several distinct structural components. It includes an NH2-terminal hyper-variable region, a collagenous domain consisting of 22 Gly-XY repeats, and a COOH-terminal C1q-like globular domain. When it is secreted into the bloodstream, adiponectin forms three oligomeric complexes, which are a trimer, a hexamer, and a high molecular weight multimer [25]. Adiponectin primarily binds to seven-transmembrane receptors known as AdipoR1 and AdipoR2, to regulate a range of physiological functions including whole-body energy balance, inflammatory responses, insulin sensitivity, and the process of fat metabolism [26]. Unlike traditional G-protein coupled receptors, these receptors possess a cytoplasmic NH2 terminus and an extracellular COOH terminal domain. AdipoR1 is most abundantly expressed in skeletal muscle, whereas AdipoR2 is predominantly expressed in the liver [27]. In humans and mice, AdipoR1 is situated on chromosome 1p36.13-q41, while AdipoR2 is found on chromosome 12p13.31 and 6 F1, respectively. The molecular structure of both forms of the receptor exhibits significant homology, featuring an internal N-terminus and an external C-terminus [28]. AdipoR1 and AdipoR2 are adiponectin receptors that stimulate AMP-activated kinase (AMPK) and PPAR activity, regulating glucose and lipid metabolism. Adiponectin-induced complete AMPK activation requires both Ca2+/CaMKK and AMP/LKB1 [29].

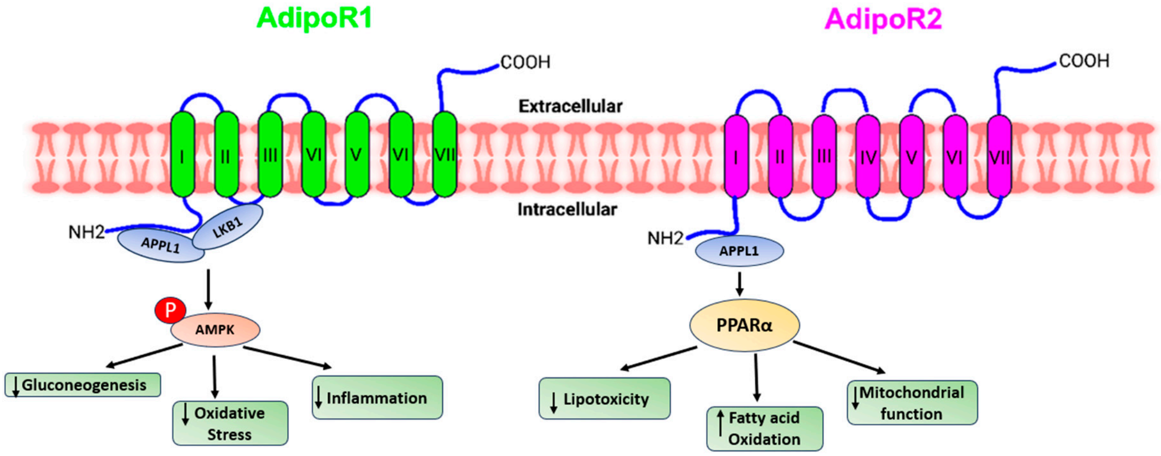

Figure 1. A presentation demonstrating the diverse pathways through which adiponectin receptors exert their functions.

Adiponectin stimulates glucose uptake and fatty acid oxidation in skeletal muscle after binding to AdipoR1, which is mediated by the recruitment of the adaptor protein with the pleckstrin homology domain, phosphotyrosine domain, and leucine zipper domain (APPL). APPL binding to the intracellular domain of AdipoR1 activates Rab5, a small GTPase that enhances GLUT4 membrane translocation and glucose absorption in muscle. APPL also binds to PI3 kinase and Akt, showing that adiponectin can boost insulin signaling as well [30]. The interaction of APPL and AdipoR1 activates AMP-activated protein kinase (AMPK), which inhibits acetyl-CoA carboxylase (ACC) and promotes fatty acid oxidation—adipoR-mediated activation of AMPK leads in higher fatty acid oxidation and decreased obesity. AMPK activation increases glucose absorption and lactate generation in muscle while suppressing gluconeogenesis. Together, the adiponectin signaling pathways underscore the relevance of adiponectin in glucose and lipid metabolism [31].

Adiponectin activates and enhances the production of PPAR ligands via AdipoR2, as well as fatty acid combustion and energy consumption. This is accomplished in part by enhanced expression of the ACO and UCP genes, which include the peroxisome proliferator response element (PPRE) in their promoter regions [32].

Adiponectin Pathway Regulation: Adiponectin regulation is a complicated combination of genetic, hormonal, and environmental factors. The adiponectin regulatory mechanism centers mostly around the expression and release of adiponectin from adipocytes.

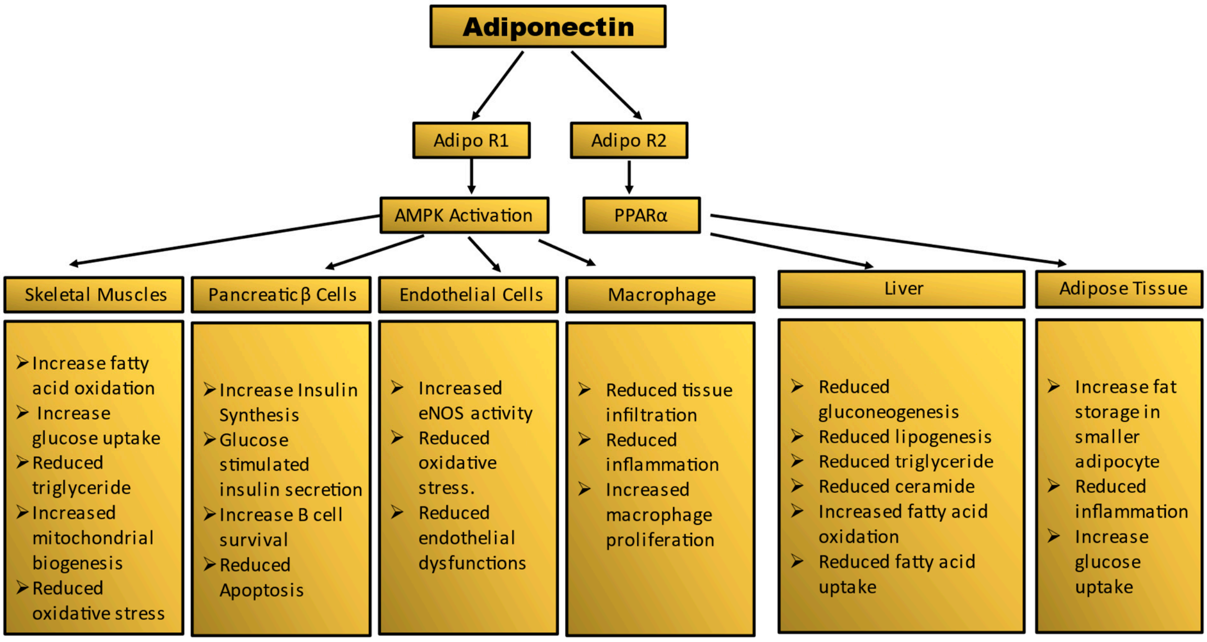

Figure 2. Summary of tissue-specific functions of adiponectin. Mechanism of adiponectin actions in prevention of insulin resistance and diabetes.

Genetic Factors: Adiponectin is mostly generated in white adipose tissue by mature adipocytes. Originally assumed to be expressed solely by adipose tissue, it is now widely documented that adiponectin is generated and released by a variety of cell types, including skeletal and cardiac muscles [33,34]. The normal range of adiponectin in human plasma is 2-20 ug/mL. Adiponectin levels can be influenced by genetic variations in the ADIPOQ gene, which encodes adiponectin. Some genetic polymorphisms are linked to increased or decreased adiponectin production [35].

Insulin Sensitivity*:* Insulin sensitivity is one of most important determinant of adiponectin levels. Higher the insulin sensitivity higher the adiponectin secretion. On the other hand reduced insulin sensitivity in several diseases such as diabetes and obesity the adiponectin level also decreases [36]. A team of researchers from the Karolinska Institutet in Stockholm, Sweden conducted a study involving 942 men. They found a robust correlation between insulin sensitivity and three ADIPOQ variants—namely, rs17300539, rs3774261, and rs6444175. In obese individuals, lower serum adiponectin levels were observed compared to those in normal, healthy individuals [37].

Inflammatory State*:* The levels of Adiponectin in the bloodstream decline following an elevation in proinflammatory cytokines like TNF-α and IL-6, along with endothelial reticulum stress and adipocyte hypertrophy. This phenomenon is associated with conditions linked to expanded adipose tissue, including obesity, Type 2 Diabetes Mellitus (T2DM), cardiovascular disease, and metabolic syndrome [38].

Adipose Tissue Distribution: The adiponectin levels are influenced by the distribution of adipose tissue. Subcutaneous adipose tissue is associated with higher adiponectin levels compared to visceral fat [39].

Diet and Nutritional Factors: Several dietary components such as omega-3 fatty acid, and polyphenols are influenced production of adiponectin [40]. A group of researchers from Universidade de São Paulo, São Paulo, Brazil observed in a double-blind, placebo-controlled, 2-month clinical trial with 80 individuals that, supplementation of ω-3 fatty acid showed an increase in serum adiponectin [41].

Physical Exercise: Regular physical exercise mainly aerobic exercises such as jogging or cycling, as well as resistance training, can increase adiponectin levels. Although exercise enhances the insulin sensitivity, which is linked to adiponectin secretions [42].

Hormonal Regulation: Leptin, another hormone secreted by adipose tissue, can influence adiponectin levels by opposing effects on metabolic regulation [43]. Insulin can stimulate adiponectin production and secretion. With improved insulin sensitivity, as seen with weight loss and exercise, can lead to increased adiponectin levels [44].

Adiponectin Receptors: Adiponectin shows its effects after binding to specific receptors, AdipoR1 and AdipoR2. Various tissues, including skeletal muscle, liver, and the cardiovascular system shows expression of these receptors which can influence the secretion of adiponectin [45].

Aging: As individuals age, there is a decrease in the activity of brown adipose tissue, a decline in sex hormone levels, and an expansion of abdominal adipose tissue. This is accompanied by a shift of lipids from the subcutaneous fat compartment to the visceral fat compartment. This ultimately results in reduced the production of adiponectin [46].

Therapeutic Interventions: Certain medications and lifestyle interventions can influence adiponectin levels. Anti diabetic drug such as thiazolidinediones (TZDs), metformin can increase adiponectin levels [47,48].

Adiponectin and Diabetes: In 1995, a group of researchers from Whitehead Institute for Biomedical Research, Cambridge, Massachusetts first discovered adiponectin [12]. This was a significant discovery because at the time, adipose tissue was primarily viewed as a passive energy storage site. Following studies, it was shown that adiponectin plays an important role in modulating insulin sensitivity. Higher levels of adiponectin have been linked to better insulin sensitivity, whereas lower levels have been linked to insulin resistance [49]. Several studies has shown a significant correlation between adiponectin levels and diabetes.

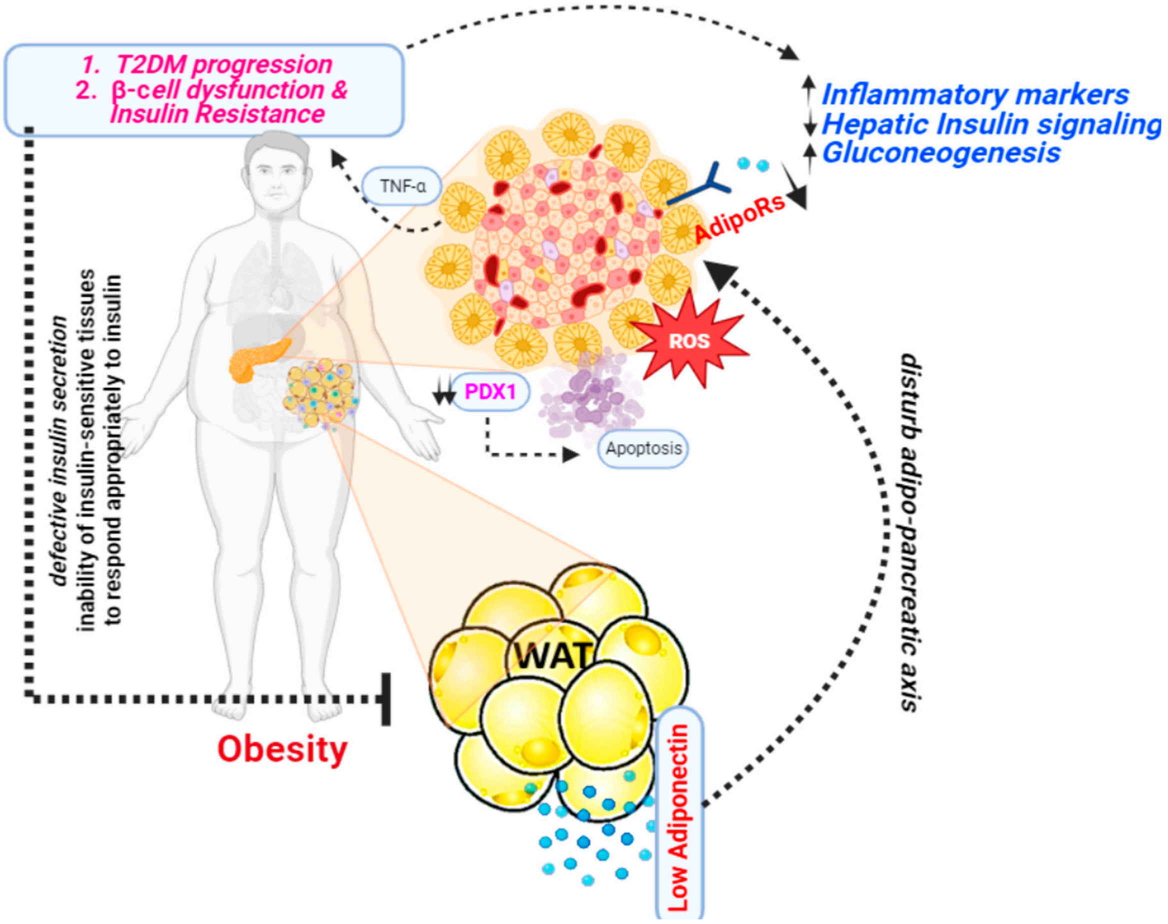

Figure 3. A presentation illustrating the mechanism through which adiponectin functions as an antidiabetic agent.

Insulin resistance and adiponectin: Insulin resistance has a hereditary component that is not fully understood and is frequently passed down through generations. Furthermore, obesity has a significant hereditary component that inevitably worsens insulin resistance. As a result, obesity and insulin resistance are often present for many years before additional alterations such as high blood pressure, dyslipidemia, T2DM, and cardiovascular disease develop [19,50]The discovery that, in both mice and humans, a loss of adipose tissue results in higher levels of circulating triglycerides and fatty acids and insulin resistance serves as more evidence of the critical role that adipose tissue plays in regulating whole-body metabolism by sequestering fat [51–53]. Additionally, the appropriate release of adipokines like leptin and adiponectin, which improve insulin sensitivity, depends on the amount of adipose tissue. Lipodystrophies affect adipokine secretion in humans and mice.

The first study to show that adiponectin actively influences insulin sensitivity was reported in 2001. A C-terminal globular adiponectin fragment can lower plasma glucose levels by boosting fatty acid oxidation in muscle [14,54,55]. Globular adiponectin appears to function in conjunction with AMP-activated protein kinase (AMPK) (and later by inhibiting acetyl-CoA carboxylase) and PPAR-(peroxisome proliferator-activated receptor alpha) to create its metabolic action in the muscles. Ceramidase silencing can inhibit AMPK phosphorylation in C2C12 myotubes, indicating a function for sphingolipid metabolism with adiponectin signaling in this tissue. Adiponectin binding increases glucose uptake (through GLUT4 translocation) and non-oxidative glycolysis while decreasing intramyocellular triacylglycerol concentration and boosting fatty acid oxidation. Furthermore, adiponectin influences the quantity of mitochondria and the kind of oxidative fibers [54].Adiponectin's actions on skeletal muscles are diminished in disease situations. Obese and insulin-resistant rats had poorer binding of globular and full-length adiponectin, which may be attributed to a lower density of adiponectin receptors. Human investigations, on the other hand, have not shown changed levels of Adipor1/Adipor2 RNAm related with insulin resistance states [56].

Apoptosis and Adiponectin: Liu et al reported that, by stimulating the AdipoR1/AMP-activated protein kinase (AMPK) signal pathway, adiponectin decreased early apoptotic cells and prevented the mitochondrial apoptosis process. Furthermore, PPAR linked to the ATF2 promoter area and suppressed ATF2 transcription. ATF2 transcriptional suppression was associated with adiponectin's ability to prevent apoptosis in adipocytes [57]. Zuo et al. reported Adiponectin suppresses inflammation and reduces apoptosis caused by excessive hyperglycemia by inhibiting the TLR4/NF-B signaling pathway [58]. The apoptotic-inducing influence of adiponectin is primarily facilitated by AdipoRs, which trigger the activation of caspase family members (caspase 3, 8, 9)[59,60].

Treatment of beta-cell line INS-1 cells with cytokine combination (IL-1b/IFN-c) or palmitic acid strongly promoted apoptosis, which could be greatly suppressed by gAPN via caspase-3 inhibition without altering NF-jB [61]. Lin et al. reported Adiponectin cotreatment partially reversed high glucose-induced INS-1 cell death, malfunction, and decrease in insulin gene expression, which was mediated at least in part by transiently activating the AMPK signaling system [59]. Adiponectin has also been identified to modulate several additional molecular pathways involved in apoptosis. This contains the Bcl-2 family of proteins, which are critical in managing the balance of pro-apoptotic (cell death-promoting) and anti-apoptotic (cell death-inhibiting) signals inside the cell. Adiponectin has the ability to modulate the expression and activity of the Bcl-2, Bax, and Bak proteins [62].

Adiponectin may also have an effect on the tumor suppressor protein p53, which is important in starting apoptosis in response to cellular stress or injury. The action of adiponectin on p53 may contribute to its proapoptotic effects [63,64]Adiponectin has also been demonstrated to influence the iNOS/ROS/RNS pathways. All chemicals involved in cellular signaling and stress responses are iNOS (inducible nitric oxide synthase), ROS (reactive oxygen species), and RNS (reactive nitrogen species). The regulation of these pathways by adiponectin may contribute to its proapoptotic effects [65].

β-cell function and Adiponectin: There have been a number of research looking at the direct impact of adiponectin on insulin secretion in β-cells. A group of researchers from University of Tokyo reported that, Adiponectin enhances insulin release from isolated mouse islets by promoting the exocytosis of insulin granules, with no discernible impact on ATP production, KATP channels, membrane potential, calcium influx, or activation of AMPK [66]. An additional investigation demonstrated that adiponectin safeguards β-cells from apoptosis induced by prolonged serum deprivation and glucotoxicity. These outcomes are facilitated by the activation of both MEKextracellular signal-regulated kinase (ERK) 1/2 and PI3K-Akt pathways [67]. James E P et al. reported that globular adiponectin induces a notable enhancement in cell viability, dependent on ERK1/2 signaling, along with a substantial rise in Pdx-1 expression in rat β-cell lines [68]. Adenosine monophosphate–activated protein kinase (AMPK) is triggered by adiponectin, leading to the direct phosphorylation and subsequent inhibition of acetyl-CoA carboxylase activity in β-cells [69].

Adiponectin knockout mice exhibit compromised glucose tolerance, even in the presence of normal or lower-than-normal insulin levels [70]. Transgenic ob/ob mice expressing the globular domain of adiponectin demonstrate heightened insulin sensitivity and elevated insulin secretion in comparison to nontransgenic mice[32,71,72] In vivo experiments conducted in C57BL/6 mice reveal that intravenous administration of adiponectin leads to an augmentation in insulin secretion[66] .

An observational study involving Asian children found that adiponectin levels exhibit an inverse relationship with body weight, body mass index, and proinsulin levels in both boys and girls. Moreover, in girls, there is an inverse association between adiponectin levels and insulin concentration as well as the homeostasis model assessment of insulin resistance (HOMA-IR) [73]. Studies have demonstrated a positive correlation between adiponectin levels and insulin sensitivity. Conversely, there is an inverse correlation between adiponectin levels and fasting proinsulin concentration, as well as the proinsulin-to-insulin ratio, which serves as a marker of β-cell failure [74]. Furthermore, it has been suggested that the decrease in adiponectin levels is longitudinally linked with a reduced ability of β-cells to compensate for insulin resistance in women with a history of gestational diabetes [75]. In overweight Hispanic adolescents, a cross-sectional study affirmed that both leptin and adiponectin are individually linked to insulin sensitivity, while they do not exhibit an association with insulin secretion [76].

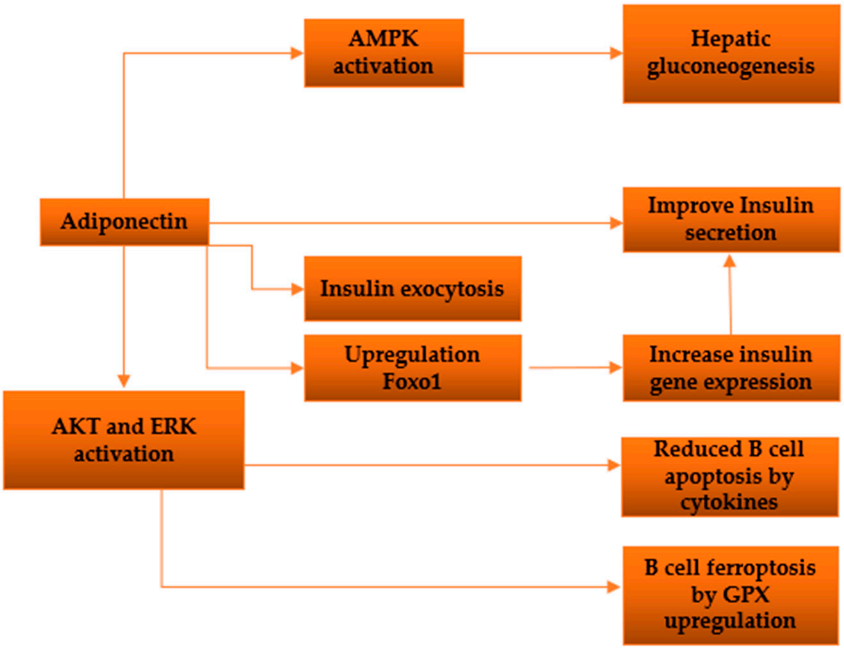

Figure 4. Diagram depicting the investigated pathways illustrating the impacts of adiponectin on pancreatic β-cells.

Oxidative stress and adiponectin: The production of reactive oxygen species (ROS) leads to oxidative stress, causing a range of cellular and molecular alterations, including dysfunction in mitochondria, which disrupts normal physiological processes in the body [77–80].While oxidative pathways are crucial in mitochondrial-mediated processes, the exact molecular mechanisms responsible are still unclear. The compromised mitochondrial function is evident in insulin resistance across different cell types. Furthermore, ongoing research is unraveling the roles of the master antioxidant pathway involving nuclear factor erythroid 2-related factor 2 (Nrf2), Kelch-like ECHassociated protein 1 (Keap1), and antioxidant response elements (ARE) in elucidating various molecular pathways associated with diabetes.

Kadowaki and colleagues' findings revealed that oxidative stress was elevated in mice lacking AdipoR1 and AdipoR2, offering compelling evidence that the adiponectin-AdipoR pathway plays a pivotal role in reducing oxidative stress [29]. In a mouse model of kidney disease, the absence of adiponectin resulted in heightened albuminuria and elevated expression of genes associated with oxidative stress [81]. In experiments conducted on cultured murine pre-adipocytes (3T3-L1), it has been observed that oxidative stress leads to a reduction in the secretion of adiponectin [82]. In 2006, Chen et al. conducted experiments using cultured pre-adipocytes (3T3-L1) and discovered that ROS decreased the expression of adiponectin mRNA. In a separate study, 3T3-L1 pre-adipocytes were subjected to oxidative stress by introducing H2O2 or glucose oxidase into the incubation medium [83]. In 2015, Pan et al. discovered that H2O2 decreased adiponectin production by 3T3-L1 adipocytes by a factor of 2, and led to a threefold increase in the synthesis of TNF-α and IL-6. The oxidative stress induced by the addition of H2O2 to the incubation medium of 3T3-L1 pre-adipocytes resulted in elevated mRNA levels of leptin, IL-6, and MCP-1 (monocyte chemoattractant protein 1), along with increased secretion of these proteins by adipocytes. Notably, there was an almost threefold increase in the secretion of IL-6 [84,85].

In 2003, Talior and colleagues reported that a high-fat diet and hydrogen peroxide (H2O2) both induce the activation of protein kinase Cδ (PKC-δ). They conducted experiments with 3T3-L1 adipocytes and found that H2O2 also triggers the activation of several kinases, including Akt (an anti-apoptotic kinase), JAKs (Janus kinases), and ERK1/2 (extracellular signal-regulated kinase) [86].

Anti-inflammatory functions of adiponectin: Numerous metabolic strains that contribute to insulin resistance and T2DM also trigger the activation of inflammation- and stress-related enzymes, namely IκB kinase-β (IKKβ) and JUN N-terminal kinase (JNK). This implies that these kinases likely play pivotal roles in the development of these disorders [87]. Specifically, IKKβ initiates the activation of the transcription factor nuclear factor-κB (NF-κB), and obesity leads to heightened expression of NF-κB-regulated genes, such as pro-inflammatory cytokines, in both the liver and adipose tissue [88]. These cytokines, encompassing TNF, IL-6, and IL-1β, can potentially induce insulin resistance in the originating tissues like the liver and adipose tissue [89]. Furthermore, they may be disseminated through the circulation, exerting their influence on more remote locations such as vessel walls, skeletal and cardiac muscle, the kidneys, and circulating leukocytes [90]. The involvement of IL-6 signaling in insulin resistance has sparked controversy, displaying occasional paradoxical effects [91]. Elevated levels of circulating IL-6 and CRP, which is stimulated by IL-6 in the liver, are observed in obesity and serve as predictive markers for Type 2 Diabetes in predisposed individuals [92]. While hepatic and adipose tissue production of IL-6 is believed to contribute to insulin resistance, its generation in skeletal muscle, particularly during intense exercise, is considered advantageous [93]. The examination of mice with specific deletion of the IL-6 receptor in hepatocytes has further fueled the debate, as these mice appear to be shielded from both local and systemic insulin resistance [94].

A number of experimental studies with genetic loss-of-function manipulations indicate that ablation of adiponectin contributes to diet-induced insulin resistance, increased vascular remodeling in response to injury, and severe cardiac damage under ischemic conditions [95]. A sequence of in vitro experiments has shown that adiponectin has the capacity to impede the production and influence of TNFα, which is a pivotal proinflammatory cytokine. This effect has been observed in different types of cells, including cardiac and vascular cells [96]. Devaraj et al. provided evidence that adiponectin can inhibit the production of CRP induced by high glucose levels. This inhibition occurs through adiponectin's capacity to suppress the activation of nuclear factor-κ B (NF-κB). These findings align with earlier research that demonstrated adiponectin's ability to mitigate TNF-α-induced NF-κB activation in endothelial cells. This, in turn, leads to decreased expression of cell adhesion molecules and interleukin (IL)-8 [97].

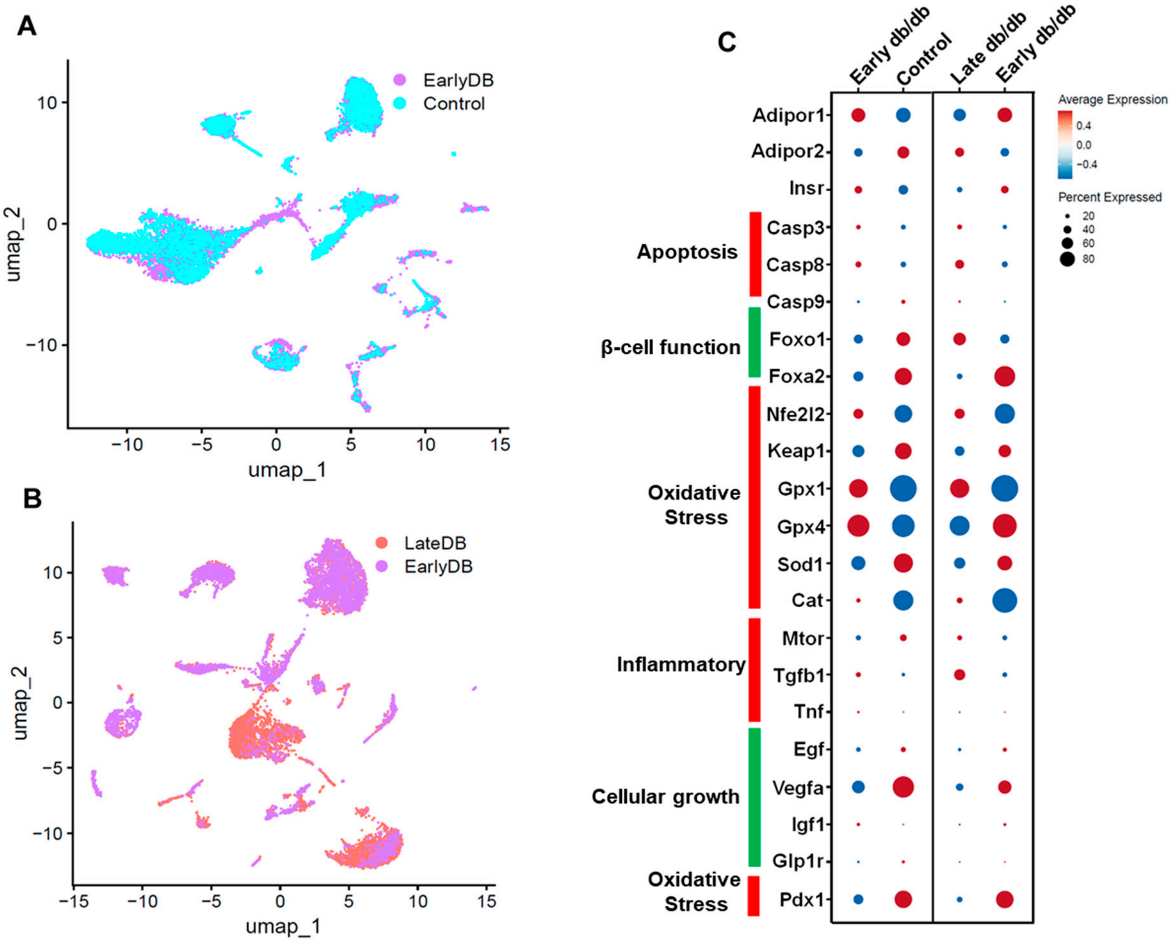

Figure 5. Single-cell UMAP Visualization depicting the cellular landscape comparison of Early db/db vs Control (A), Late db/db vs Early db/db (B) of pancreatic islet cells. The differential expression of critical genes in Adiponectin signaling, Apoptosis, β-cell function, Oxidative stress, Inflammation and Cellular growth (C).

Single cell data from db/db mice pancreatic islet cells: We retrieved single-cell data of pancreatic islet cells from GEO (https://www.ncbi.nlm.nih.gov/geo/) using the accession number GSE165267. Data was analyzed using the software, Seurat v4.1.1 implemented in R v4.2.1. In our observations, we noted a decrease in adiponectin receptor levels compared to the control group, coinciding with the progression of diabetes in the pancreatic islet cells of diabetic model mice. This reduction in adiponectin receptor was associated with an upregulation of apoptosis-related genes, specifically casp3 and casp9, and a downregulation of antioxidant genes such as gpx4, gpx1, and sod1. Additionally, there was an upregulation of inflammatory genes including Mtor, Tgfb1, and tnf. These findings align with our earlier hypotheses and support the proposed pathway involving the role of adiponectin [98–100]

Future Directions and Challenges: A multimodal strategy is required for future developments in adiponectin-based diabetic therapy. Adiponectin receptor agonists are being developed by researchers in order to imitate the positive effects of adiponectin on insulin sensitivity and glucose metabolism. Gene treatments have the potential to increase adiponectin expression or activity in diabetics. The goal of pharmaceutical treatments is to find molecules that can increase adiponectin production from adipose tissue. Understanding how food and exercise affect adiponectin levels is also an important area of research. Combinatorial techniques, personalized medicine approaches, biomarker research, and rigorous clinical trials are all critical components in enhancing the promise of adiponectin-based therapeutics for improving metabolic health in diabetic patients. It is critical to understand that any new therapies will need to go through extensive testing and regulatory processes before they can be used in clinical trials. It is best to check contemporary scientific literature or healthcare practitioners with current understanding in the subject for the most up-to-date information.

Conclusion: In conclusion, the significance of adiponectin in diabetes management cannot be overstated. Its pivotal role in regulating glucose metabolism and insulin sensitivity highlights its potential as a promising therapeutic target. As research in this sector advances, tapping the full potential of adiponectin may lead to novel and successful diabetic therapies. Further research, including clinical trials and in-depth molecular investigations, will be critical in achieving the full therapeutic potential of this unique hormone. With ongoing effort and scientific study, the road to improving diabetes management with adiponectin-based therapy holds enormous potential.

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Conflicts of Interest: The authors declare no conflict of interest.

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