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Cellular and Molecular Pathophysiology of Diabetes Mellitus and Discusses Potential Treatments

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Abstract: This paper aims to Cellular and molecular pathophysiology of Diabetes Mellitus and discusses potential treatments where. A cross-sectional study in Iraq was conducted with the objective of elucidating the cellular mechanisms underlying the pathogenesis of diabetes mellitus and the therapeutic modalities employed in its treatment. The study involved 84 patients, 44 males and 40 females, aged 20-40, and collected primary information such as height, weight, body mass index, family history, and laboratory biochemical parameters. The study adhered to the World Health Organization (WHO) guidelines and employed glycosylated hemoglobin (HbA1c) to diagnose diabetes, with the study period spanning from February 1st, 2023, to March 1st, 2023. A primary healthcare center in Iraqi hospitals provided diabetes care to patients. The pathology of this illness involves a gradual breakdown in the functional capacity of the cells located within the pancreas that produce insulin whenever there is high sugar levels. The death of these cells due to high sugar conditions is quite familiar among many forms of diabetics; understanding how this happens will go a long way into creating new and helpful treatment ways that can be used to avoid injuries arising from them on one end or make them reconstitute to those who have ended up losing several of these due to diabetes mellitus (DM) phase Furthermore, environmental toxins, including organic pesticides and heavy metals, have been shown to disrupt glucose homeostasis by affecting the expression of the insulin glucosidase gene where Molecular changes influencing glycaemia extent and cellular function are affected by modifiable lifestyle factors, including body mass, physical activity and diet. These factors may, therefore, be considered as potential therapeutic targets for the treatment of type 2 diabetes, where Diabetes has become one of the biggest health problems on a global scale because much of the mortality and morbidity is caused by a multifactorial disease in addition to genetic predisposition, such as sedentary lifestyles, where high glucose concentrations over long periods of time lead to metabolic changes. A task that leads to general changes in the body that accompany long-term aging in other organs to get rid of certain complications such as retinopathy and diabetic neuropathy. And in the same way, diabetics suffer from an increase in the promotion of atherosclerosis, activation of peripheral arteries and cerebral vessels, and all elements, which creates a deleterious effect on the quality of life of the person suffering from it. In addition, obesity and insulin resistance, when combined with genetic and environmental factors, result in a complex disease condition with numerous contributing factors, including oxidative stress, mitochondrial dysfunction, and inflammation.

Keywords: HbA1c, Insulin resistance, Cellular, Obesity, Diabetes Mellitus, Genetic, Treatment, Glycaemia, IGF-1, BMI, Pathophysiology, Molecular, β cells, Glucose, DHEA.

INTRODUCTION

Diabetes is a significant global public health concern. The prevalence and incidence of diabetes have increased steadily over the past twenty years [Banday, M. *et al*., 2020]. The World Health Organization estimated the number of those infected in 1980 at 910 million, and this figure rose to 244 million in 2014. Diabetes is a group of metabolic disorders characterized by elevated blood sugar levels due to complete or relative insufficiency in insulin secretion, as well as disorders in the metabolism of carbohydrates, fats, and proteins [Galicia-Garcia, U. *et al*., 2020]. The manifestations of diabetes vary from one individual to another and are determined by a healthy diet. At the global level, the impact of diabetes is estimated to affect approximately 190 million people of all ages [Kyrou, I. *et al*., 2020]. Those with this disease are considered to be among the most prominent causes of weakness and death worldwide. Furthermore, diabetes can lead to microvascular complications and organ dysfunction, which can affect the eyes (retinopathy), the kidneys (nephropathy), myocardial infarction, and the nervous system. (Neuropathy) [Bailey, C. J. *et al*., 2019; Li, G. *et al*., 2020]

The pathophysiology of diabetes is heterogeneous, resulting in two distinct types. Type 1, or insulin-dependent diabetes, is a chronic disease characterized by the destruction of the beta cells of the islets of Langerhans in the pancreas through an autoimmune process [Otto-Buczkowska, E. *et al*., 2017; Costello, R. A. *et al*., 2023]. This ultimately leads to a deficiency in insulin production by the pancreas. Type 4 non-insulin-dependent diabetes occurs subsequent to a defect in insulin secretion, thereby resulting in insulin resistance [Kalra, S. *et al*., 2018]. (Similar to many other health conditions, such as cancer and neurodegenerative disorders, oxidative stress has been widely linked to the occurrence of diabetes, as evidenced by numerous studies. These studies have demonstrated that oxidative stress is considered an essential element in the development of diabetes and its associated complications. Brownlee proposed that oxidative stress represents a pivotal element in the pathophysiology of diabetes and its complications. This occurs when there is an

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imbalance in the balance of oxidation and reduction within the cell. This result in damage to cell membranes and biomolecules, including this includes DNA, proteins, and lipids [Esser, N. *et al*., 2014; Pradhan, A. D. *et al*., 2001].

The condition of type 2 diabetes is now widely regarded as a disease that affects the population at large [Vandanmagsar, B. *et al*., 2011]. This chronic metabolic disease, which is associated with changes in lifestyle and eating habits, is experiencing a dramatic increase in incidence, affecting more than 530 million people worldwide. (Type 2 diabetes represents the most prevalent form, affecting approximately 90 million individuals worldwide) [Association, A. D, 2019].

A person may be genetically predisposed to diseases that can lead to a diagnosis of diabetes, including obesity, advanced age, a sedentary lifestyle, and eating foods rich in calories [Association, A. D, 2019].

The disease is believed to result from insufficient insulin secretion in the face of an increased demand on the body caused by an increase in insulin resistance in its target tissues, such as the liver, muscles, and fat. This insulin deficiency is primarily a result of the inability of β cells to produce glucose in response to insulin secretion [Shamsuzzaman, A. S. *et al*., 2004].

The Role of Molecular Pathways in the Development of Diabetes

The progression of diabetes at the molecular level is the result of an intricate signalling network. The PI3K/Akt pathway, which plays a central role in insulin-mediated glucose uptake, is a case in point. When there is insulin insensitivity, disruption of this pathway results in abnormal sugar breakdown, which in turn leads to hyperglycaemia in diabetes mellitus [Yoon, K. H. *et al*., 2007].

Additionally, a sequence of molecular reactions results from elevated long-term blood sugar, which in turn leads to worsening cellular failures. When sugars, proteins, lipids, or nucleic acids interact in a way that does not involve an enzyme, the result is the formation of advanced glycation end products (AGEs) [Pories, W. J. *et al*., 1995]. These substances accumulate and prevent cells from functioning normally because they alter their structure at the molecular level, disrupting communication within cells and other routes used in signal transduction [Li, Y. *et al*., 2015].

The pathophysiology of diabetes is dominated by inflammatory pathways. Inflammation is initiated by sustained high glucose levels, leading to varying degrees of beta-cell failure and insulin resistance. A cyclical process exists whereby inflammation leads to further insulin resistance, thereby exacerbating the diabetic condition [Hayden, M. S. *et al*., 2004].

Impact of Cellular Dysfunction on Glucose Homeostasis

One of the key contributors to insulin insensitivity and reduced glucose uptake in the body is cellular stress, which includes oxidative stress, inflammation, and mitochondrial damage. Type 2 diabetes is characterized by metabolic disorders caused by insulin resistance, which is the inability to respond to signals by this hormone. This prevents glucose from entering cells, such as skeletal muscle cells or fat-producing ones. [Chen, F, 2005]

The development of insulin resistance and related diseases is connected to skeletal muscle, liver, fat cells, and pancreatic cells. A number of studies have demonstrated that inadequate glucose uptake, lower Glut4 expression, and faulty insulin signalling result from mitochondrial dysfunction in adipocytes, thereby impacting on blood sugar regulation [IDF Diabetes Atlas, 2021].

The Role of Growth Factors in Vascular Dysfunction

It is encouraging to note that a number of significant findings have been made by recent studies investigating the relationship between vascular problems in diabetic patients and growth factors. Among the growth factors that have been identified as potentially contributing to diabetic vascular disorders, only a few have been confirmed as driving them [Chatterjee, S. *et al*., 2017].

The vitreous of diabetic patients undergoing proliferation consistently exhibit elevated levels of VEGF, a protein that is consistently associated with active proliferation processes in every report [Adeghate, E. *et al*., 2001]. These reports highlight its essential role in the emergence of any proliferative vitreoretinopathy (PVR). To date, no clinical or experimental data support the claim that, without this "main" factor in PVR pathogenesis, plus opposite changes depending on choroidal circulation state or duration of follow-up periods after different interventions, the emergence of PVR would be prevented [Adeghate, E. *et al*.,

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2006]. The experimental data support the claim that, without this "main" factor in PVR pathogenesis, there are opposite changes depending on the choroidal circulation state or duration of follow-up periods after different interventions. It is necessary to evaluate not only angiogenesis characteristics but also VEGF levels (pg/ml) [Alberti, K. G. *et al*., 1998].

Furthermore, an extreme situation is an essential cause of VEGF, showing such that it is known as the greatest incitation for the advancement of proliferative retinopathy in diabetics. We have previously discussed the blockage of VEGF receptors by some drugs, thus preventing them from binding with Ank-grp in the retina. It would be beneficial to ascertain whether another drug which acts against vegfr expression might be able to stop diabetes Mellitus proliferative ailment [Sung, Y. Y. *et al*., 2005].

In the initial stages of diabetic nephropathy, TGF-P has been demonstrated to be elevated in patients with proteinuria or albuminuria. Additionally, TGF-P has been observed to stimulate mesangial cells obtained from tissue in culture for collagen type IV and fibronectin. Secondly, hyperglycaemia has been shown to result in an abundance of fibronectin and collagen production, which can be blocked by TGF-P antibodies. This suggests that this protein may contribute to the thickening of basement membranes observed in diabetes-related kidney disease [Wing, R. R. *et al*., 2011].

MATERIAL AND METHOD

This is a study. A cross-sectional study was conducted in Iraq to know the cellular mechanisms involved in diabetic patients and to learn about the treatment management method. In this study, 84 patients were collected and distributed into 44 male patients and 40 female with the average age ranged between 20-40 years.

In this study, primary information was collected, consisting of height, weight, body mass index, and family history, in addition to biochemical parameters that were extracted in the laboratory.

The care of patients with diabetes was provided by a primary health care centre of Iraqi hospitals during the period from 1 February 2023 to 1 March 2023. All records were studied. The study protocol was approved by the Iraqi ethical code (Declaration of Helsinki 1977). The criteria used to diagnose diabetes included fasting (venous) blood sugar levels exceeding 6.1mmol/l (110mg/dl). The method employed was in accordance with WHO guidelines to define the type of diabetes, which was primarily determined through glycosylate hemoglobin (HbAlc). The acceptable limit range was 3.6-5.3%, while the coefficient of variation was 51.4%. Throughout the entirety of the research period, all samples were subjected to analysis at a centralized facility utilizing a uniform methodology. The table below illustrates the examinations, tests, and classifications of the results.

RESULTS

Table 1: Socio-demographic Characteristics of study patients in Iraq

Variable	Value
Age (mean±sd)	29.2±4.3
Sex	
Male f (p%)	44 (52.3)
Female f (p%)	40 (47.7)
BMI (mean±sd)	29±2.2
Symptoms f (p%)	
Frequent urination	27 (32.1)
Unexplained weight loss.	19 (17.8)
Blurred vision.	10 (11.9)
Fatigue.	20 (23.8)
Slow healing of cuts and sores	8 (9.5)
Education f (p%)	
PRIMIRY	12 (14.2)
Secondary	23 (27.3)
College	40 (47.6)
High	9 (10.7)

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Outcomes f (p%)	
300-600	25 (29.7)
700-1000	40 (47.6)
>1000	19 (22.6)
Smoking	
Yes f (p%)	20 (23.8)
No f (p%)	64 (76.1)
Marital Status f (p%)	
Single	30 (35.7)
Married	40 (64.2)

Table 2: Evaluation of secondary outcomes in patients with diabetes

Variable	Value
SBP (mmHg)	132 ± 16
DBP (mmHg)	78 ± 9
Pulse pressure (mmHg)	54 ± 13
HR (bpm)	73 ± 7
Diabetes duration (years)	4.5 ± 1.3
HbA1c (%)	7.5 ± 1.1
eGFR (ml/min/1.73m2)	7.4 ± 1.1
BNP (pg/ml) median [IQR]	166 [77–288]

Table 3: Outcomes of patients according to Insulin, Glucose, Potassium pH, Total Calcium

Insulin, n (%)	13–17 mIU/L
Glucose	10.57 ± 0.65
Potassium	4.11 ± 0.37
pH	7.77 ± 0.11
Total Calcium	2.89 ± 1.37

Table 4: Descriptive statistics of a sample of patients with diabetes according to GH, IGF1 DHEA

v	MEAN±SD
GH	1.0783±0.9
IGF1	162.275±74.0772
DHEA	139.502±76.4714

An important correlation that can be made here is with the role that IGF-1 might play in causing insulin resistance, which is one of the major characteristics of type 2 diabetes since the cells become less sensitive toward insulin. It has been found through research that high levels of IGF-1 could result in resistance to this hormone, thereby causing abnormalities when it comes to sugar levels, hence raising chances for diabetes onset.

Table 5: Describe Correlations between IGF_1, insulin with diabetes

Correlations				
			v	Diabetes
Spearman-R	IGF_1	Correlation Coefficient	1.000	0.45
		Sig. (2-tailed)	.	0.023
		N	84	
	insulin	Correlation Coefficient	0.23	1.000
		Sig. (2-tailed)	0.001	.
		N	84	84

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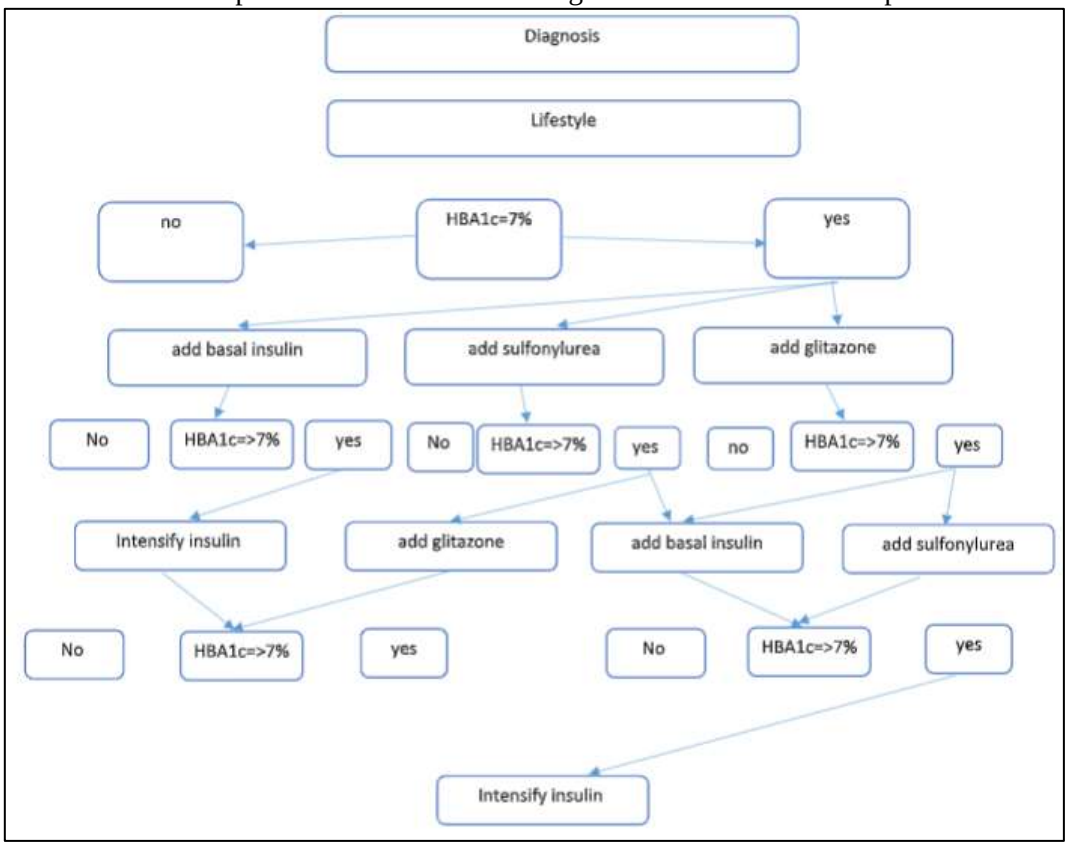
Table 6: Logistic regression criteria to determine the risk factor in this study on patients

Variable	CS (OI)	P Value
Sex	1.2 (0.5-1.4)	0.55
Insulin	2.4 (1.54-4.2)	<0.001
IGF-1	2.87 (1.8-4.8)	0.023
Glucose	3.1 (2.2-5.5)	<0.001
Age	0.9 (0.5-1.11)	0.91
DHEA	1.88 (1.31-2.55)	0.03
BMI	1.91 (1.1-3.1)	<0.001
HbA1c		

Table 7: Management of type 2 diabetes in Iraq

1	Acarbose (Precose)	Delay complex carbohydrate absorption	0.5–0.8	25–100 mg tid w/meals
2	Miglitol (Glyset)	absorption		25–100 mg tid w/meals
3	Metformin (Glucophage)	increase peripheral glucose uptake	1–2	IR: 1000–2550 mg/d divided bid or tid ER: 500–2000 mg/d
4	Sitagliptin (Januvia)	Slow inactivation of incretin hormones	0.5–0.8	25–100 mg/d
5	Nateglinide (Starlix)	Stimulate insulin secretion from the pancreas	1–1.5	0.5–4 mg tid to qid
6	Chlorpropamide (Diabinese)	Stimulate insulin secretion from the pancreas	1–2	100–750 mg/d
7	Glimepiride (Amaryl)	1–8 mg/d	1–2	1–8 mg/d
8	Glipizide (Glucotrol)	1–8 mg/d	1–2	IR: 2.5–40 mg/d

Table 8: Treatment options for diabetics according to the ADA and the European Association



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DISCUSSION

Diabetes mellitus is a complex and intriguing issue that involves researching the abnormal levels of blood sugar in the human organism. Diabetes mellitus is a metabolic disorder that is characterized by a deficiency in insulin production or the inability of the human body to utilize the insulin hormone effectively [Wing, R. R. *et al*., 2011; Look AHEAD Research Group, 2010].

Further research has demonstrated that chronic inflammation and oxidative stress impede the action of insulin in the body, thereby leading to insulin resistance [DeFronzo, R. A. *et al*., 2015].

Understanding the cellular and molecular processes that underlie diabetes mellitus is critical for the development of effective treatments and interventions. These investigations are ongoing, and new facts about the disease are being uncovered that may have implications for better controlling or preventing it at some point in the future. It is, therefore, essential to understand the cellular and molecular processes involved in LeTNT type 1 in order to develop effective treatments and interventions. Research in this field continues to advance our knowledge of the disease and offers hope for improved management. [DeFronzo, R. A. *et al*., 2009]

In physiological conditions, glucose is the primary metabolic fuel for the brain. In return, other organs oxidize fatty acids in addition to glucose [Bordbar, A. *et al*., 2011]. Given the exceptional dependence of the brain on glucose and the inability of the brain to synthesize glucose or store it in the form of glycogen for more than a few minutes, it is clear that the brain requires a continuous supply of glucose from the circulation [Väremo, L. *et al*., 2015]. Furthermore, glucose plays a pivotal role in the biosynthesis of numerous compounds integral to the composition of cell membranes and glycosylated proteins. Given the immediate life value of maintaining plasma glucose concentration, it is not surprising that the physiological mechanisms that prevent hypoglycaemia or correct it quickly are sophisticated and precise [Wilson, D. F. *et al*., 2017].

Glucose levels are maintained within narrow limits, and this depends on the rates at which glucose enters the circulation and is removed from tissues. The primary organs responsible for regulating blood glucose levels are the liver, which produces glucose, and the kidneys, which remove glucose from the body. These mechanisms are so effective that hypoglycaemia is an uncommon clinical event, except for hypoglycaemia following treatment with insulin or sulfonylureas [Pedersen, M. G. *et al*., 2019].

Type 2 diabetes is characterised by three pathophysiological disorders: defective insulin secretion, peripheral insulin resistance, excessive liver glucose production, and obesity, which is particularly prevalent in individuals with type 2 diabetes [Abdul-Ghani, M. A. *et al*., 2010].

Adipocytes secrete a number of vital products, including leptin, tumour necrosis factor-alpha, free fatty acids, and adiponectin. These products modify insulin secretion, action, and body weight and may contribute to insulin resistance.

In the initial stages of the disease, glucose tolerance remains unimpaired despite insulin resistance. This is because pancreatic beta cells compensate for this by increasing insulin production. When resistance and a state of compensated hyperinsulinism persist, beta cells in some individuals become unable to maintain a state of hyperinsulinism, resulting in impaired glucose tolerance (IGT). This is characterized by an elevation in glucose levels following a meal. Further decline in insulin secretion and increase in glucose production by the liver result in the development of overt diabetes mellitus, characterised by hyperglycaemia during fasting [Welsh, K. J. *et al*., 2016].

A defining feature of type 2 diabetes is a diminished capacity of insulin to exert its effects on target tissues, particularly the liver and muscle. This is the consequence of a complex interaction between genetic predisposition and obesity. Conversely, insulin resistance is a relative phenomenon, as supraphysiological levels of circulating insulin return plasma glucose to normal [Welsh, K. J. *et al*., 2016].

Insulin resistance impairs the utilization of glucose in insulin-sensitive tissues and increases glucose production by the liver, both of which contribute to hyperglycemia. The primary factor responsible for elevated fasting plasma glucose levels is increased glucose production by the liver, while decreased peripheral glucose utilization leads to hyperglycemia.

CONCLUSION

Loss of processes in the bloodstream of the heart due to type 1 or 2 diabetes requires a

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comprehensive studio to account for fibroblast pathology and therapeutic white cells that allow the disease to develop in cultures. Carrying out an advanced procedure for further work or receiving windows in front of the operation in the morning allows for solving the above problem from the previous year. It is possible to move to the implementation of school curricula or existing precursors at home with different β schools to monitor the children's past with the help of the indicator.

REFERENCES

1. Banday, M., Sameer, A. & Nissar, S. "Pathophysiology of diabetes: an overview." *Avicenna J Med*, 10.4 (2020): 174-188.
2. Galicia-Garcia, U., Benito-Vicente, A., Jebari, S., Larrea-Sebal, A., Siddiqi, H., Uribe, K. B., *et al*. "Pathophysiology of type 2 diabetes mellitus." *Int J Mol Sci*, 21.17 (2020): 6275.
3. Kyrou, I., Tsigos, C., Mavrogianni, C., Cardon, G., Van Stappen, V., Latomme, J., *et al*. "Sociodemographic and lifestyle-related risk factors for identifying vulnerable groups for type 2 diabetes: a narrative review with emphasis on data from Europe." *BMC Endocr Disord*, 20.S1 (2020): 134.
4. Bailey, C. J. & Day, C. "Treatment of type 2 diabetes: future approaches." *Br Med Bull*, 126.1 (2019): 123-137.
5. Li, G., Wei, T., Ni, W., Zhang, A., Zhang, J., Xing, Y., *et al*. "Incidence and risk factors of gestational diabetes mellitus: a prospective cohort study in Qingdao, China." *Front Endocrinol*, 11 (2020): 636.
6. Otto-Buczkowska, E. & Jainta, N. "Pharmacological treatment in diabetes mellitus type 1-insulin and what else?" *Int J Endocrinol Metab*, 16.1 (2017): e13008.
7. Costello, R. A., Nicolas, S. & Shivkumar, A. "Sulfonylureas." *In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing*; 2023.
8. Kalra, S., Bahendeka, S., Sahay, R., Ghosh, S. Md F., Orabi, A., Ramaiya, K., *et al*. "Consensus recommendations on sulfonylurea and sulfonylurea combinations in the management of type 2 diabetes mellitus − international task force." *Indian J Endocrinol Metab*, 22.1 (2018): 132-157.
9. Ojo, *et al*. Medicine in Novel Technology and Devices 19 (2023) 1002478.
10. Esser, N., Legrand-Poels, S., Piette, J., Scheen, A. J. & Paquot, N. "Inflammation as a link between obesity, metabolic syndrome, and type 2 diabetes." *Diabetes Res Clin Pract*, 105 (2014): 141-150.
11. Pradhan, A. D., Manson, J. E., Rifai, N., Buring, J. E. & Ridker, P. M. "C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus." *JAMA*, 286 (2001): 327-334.
12. Vandanmagsar, B., Youm, Y. H., Ravussin, A., Galgani, J. E., Stadler, K., Mynatt, R. L., Ravussin, E., Stephens, J. M. & Dixit, V. D. "The NLRP3 inflammasome instigates obesity-induced inflammation and insulin resistance." *Nat Med*, 17 (2011): 179-188.
13. Association, A. D. "Prevention or Delay of Type 2 Diabetes: Standards of Medical Care in Diabetes-2019." *Diabetes Care*, 42 (2019): S29-S33.
14. Shamsuzzaman, A. S., Winnicki, M., Wolk, R., Svatikova, A., Phillips, B. G., Davison, D. E., Berger, P. B. & Somers, V. K. "Independent association between plasma leptin and C-reactive protein in healthy humans." *Circulation*, 109 (2004): 2181-2185.
15. Yoon, K. H., Lee, J. H., Kim, J. W., Cho, J. H., Choi, Y. H., *et al*. "Epidemic obesity and type 2 diabetes in Asia." *Lancet*, 368 (2006): 1681-1688.
16. Pories, W. J., Swanson, M. S., MacDonald, K. G., Long, S. B., Morris, P. G., *et al*. "Who would have thought it? An operation proves to be the most effective therapy for adult-onset diabetes mellitus." *Ann Surg*, 222 (1995): 339-350.
17. Li, Y., Ley, S. H., Tobias, D. K., Chiuve, S. E., VanderWeele, T. J., *et al*. "Birth weight and later life adherence to unhealthy lifestyles in predicting type 2 diabetes: prospective cohort study." *BMJ*, 351 (2015): h3672.
18. Hayden, M. S. & Ghosh, S. "Signaling to NF-kappaB." *Genes Dev*, 18 (2004): 2195-2224.
19. Chen, F. "Is NF-kappaB a culprit in type 2 diabetes?" *Biochem Biophys Res Commun*, 332 (2005): 1-3.
20. IDF Diabetes Atlas. "International Diabetes Federation Diabetes Atlas, 10th ed." *International Diabetes Federation: Brussels, Belgium*, (2021).
21. Chatterjee, S., Khunti, K. & Davies, M. J. "Type 2 diabetes." *Lancet*, 389 (2017): 2239-2251.
22. Adeghate, E. "Diabetes mellitus-multifactorial in aetiology and global in prevalence." *Arch Physiol Biochem*, 109 (2001): 197-199.
23. Adeghate, E., Schattner, P. & Dunn, E. "An Update on the Etiology and Epidemiology of

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Diabetes Mellitus." *Ann N Y Acad Sci*, 1084 (2006): 1-29.
24. Alberti, K. G. & Zimmet, P. Z. "Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus provisional report of a WHO consultation." *Diabete Med*, 15 (1998): 539-553.
25. Sung, Y. Y., Lee, Y. S., Jung, W. H., Kim, H. Y., Cheon, H. G., Yang, S. D. & Rhee, S. D. "Glucose intolerance in young TallyHo mice is induced by leptin-mediated inhibition of insulin secretion." *Biochemical and Biophysical Research Communications* 338.4 (2005): 1779-1787.
26. Wing, R. R., Lang, W., Wadden, T. A., Safford, M., Knowler, W. C., Bertoni, A. G., Hill, J. O., Brancati, F. L., Peters, A., Wagenknecht, L. & Look, A. R. G. "Benefits of modest weight loss in improving cardiovascular risk factors in overweight and obese individuals with type 2 diabetes." *Care*, 34 (2011): 1481-1486.
27. Look AHEAD Research Group. "Long-term effects of a lifestyle intervention on weight and cardiovascular risk factors in individuals with type 2 diabetes mellitus: four-year results of the Look AHEAD trial." *Arch Intern Med*, 170 (2010): 1566-1575.
28. DeFronzo, R. A., Ferrannini, E., Groop, L., Henry, R. R., Herman, W. H., Holst, J. J., Hu, F. B., Kahn, C. R., Raz, I. & Shulman, G. I. "Type 2 diabetes mellitus." *Nat Re Dis Primers*, 1 (2015): 15019.
29. DeFronzo, R. A. "From the triumvirate to the ominous octet: a new paradigm for the treatment of type 2 diabetes mellitus." *Diabetes*, 58.4 (2009): 773–795.
30. Bordbar, A., Feist, A. M., Usaite-Black, R., Woodcock, J., Palsson, B. O. & Famili, I. "A multi-tissue type genome-scale metabolic network for analysis of whole-body systems physiology." *BMC Syst Biol*, 5.1 (2011): 180.
31. Väremo, L., Scheele, C., Broholm, C., Mardinoglu, A., Kampf, C., Asplund, A., Nookaew, I., Uhlén, M., Pedersen, B. K. & Nielsen, J. "Proteome-and transcriptome-driven reconstruction of the human myocyte metabolic network and its use for identification of markers for diabetes." *Cell Rep*, 11.6 (2015): 921–933.
32. Wilson, D. F., Cember, A. T. J. & Matschinsky, F. M. "The thermodynamic basis of glucose-stimulated insulin release: a model of the core mechanism." *Physiol Rep*, 5.12 (2017).
33. Pedersen, M. G., Tagliavini, A. & Henquin, J.-C. "Calcium signaling and secretory granule pool dynamics underlie biphasic insulin secretion and its amplification by glucose: experiments and modeling." *Am J Physiol-Endocrinol Metab*, 316.3 (2019): E475-E486.
34. Abdul-Ghani, M. A. & DeFronzo, R. A. "Pathogenesis of Insulin Resistance in Skeletal Muscle." In: Benian, G. M. (Ed.), *J Biomed Biotechnol*. 2010 (2010):476279.
35. Welsh, K. J., Kirkman, M. S. & Sacks, D. B. "Role of Glycated Proteins in the Diagnosis and Management of Diabetes: Research Gaps and Future Directions." *Diabetes Care*, 39.8 (2016): 1299-1306.

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