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Review Paper

Exploring Novel Biomarkers for Early Diagnosis, Disease Progression, and Treatment Response in Diabetes

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ABSTRACT

Diabetes (DM) exists as an unending metabolic disorder which presents impaired insulin secretion or action that triggers hyperglycemia. Early identification and complications prediction are limited by the symptomatic techniques that use fasting plasma glucose (FPG) and verbal glucose resistance test (OGTT) and hemoglobin A1C (HBA1C). Advances in atomic science and proteomics and metabolomics and genomics research resulted in developing sensitive and specific modern biomarkers. However, metabolic, incendiary, oxidative push, circulating microRNAs and lipidomics markers make way demonstrative and restorative bits of knowledge. Moreover, counterfeit insights (AI) and machine learning (ML) change biomarkers, prescient modeling, and accuracy pharmaceutical revelations. AI control investigations when combined with multi-omic approaches demonstrate high promise for better diabetes screening success and developing therapeutic strategies.

INTRODUCTION

DM is sometimes a perilous metabolic bustle similar to hyperglycemia and shares due to the deficit in discharge, on lapping^[1]. The need for the recognizable trial of unused biomarkers to monitor early disease determination, infection spreading, and assessment of treatment reaction is needed because of the expanded predominance of diabetes around the globe. The conventional symptomatic markers of diabetes, namely verbal glucose

resistance, glycated shapes of hemoglobin (HBA1C) and calm dying, are instances of standard markers that have restricted early arrange diabetes recognizable proof and look at complications^[2]. Later on, there has been increasingly focus on discovering formerly unused biomarkers that will be capable to forward treatment results and to give more information into malady science. Recent advancement in molecular science, proteomics, metabolomics and genomics have found new biomarkers for diabetes with high

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specificity and sensitivity. New research finds that diabetes development or its complications can be affected by oxidative stress markers, circulation microRNAs, (which stands for miRNAs), proteomics and lipidomics profiles or by inflammation mediators^[3,4]. As an example, the dysfunctional beta cells and insulin resistance have been reported to be related to the oxidative stress biomarkers such as glutathione (GSH) and malondialdehyde (MDA)^[5,6]. Similarly, circulating miRNAs including the miR-375 and MIR had-126 have been associated with vascular problems and pancreatic beta cell function^[7,8,9]. Studies of proteome and fat also show the role of haptoglobin, ceramids and Apoc-III in the development of diabetes and risk of cardiovascular disease^[10,11]. They aid in personalized treatment approaches, allow for better diagnosis at an earlier stage and offer better knowledge on how the treatment is metabolized.

limitation of tradition diagnosis markers

Traditional diabetes markers such as hemoglobin A1C (HBA1C), oral glucose tolerance (OGTT) testing (FPG) also suffers from diabetes and prediction problems during early stages. Diabetes problems are diagnosed through such FPGs, though they are not sensitive enough to detect postprandial hyperglycemia, a third pioneer^[12]. Aside from this, FPG levels are also often influenced by a number of circumstances such as stress, illness, and a modern diet, which in turn have many outcomes^[13]. OGTT is the most commonly employed test to diagnose prediabetes and diabetes because it is a measure of glucose tolerance based on two hours of blood glucose measurement after glucose administration. In other words, this can result in false diagnosis^[14]. In addition, OGTT results are further affected by test diets and training as well as test reproducibility^[15].

HBA1C is another common diagnostic indicator that tries to hunt for long term glycemic control and show the average blood glucose levels in the last two to three months. One of many disadvantages is that one cannot identify sudden changes in glucose mirrors in the blood^[16]. In addition, HBA1c measurement is also affected by the anemia, hemoglobin disease and chronic kidney disease, and these will cause the misdiagnosis of diabetes^[17]. Also reported were ethnic differences in HBA1C values that could affect accuracy of tests in different groups^[18].

Biomarkers for Early Diagnosis of Diabetes

Metabolic biomarkers

If diabetes is diagnosed early, it can be avoided to maintain treatment conversion. Metabolic biomarkers, such as glycated hemoglobin (HBA1C), insulin resistance markers, and glucose levels, are examples of metabolic biomarkers that are important indications of those who are prone to diabetes. Glucose still remains as a key biomarker for diabetes and it is being determined with diabetic oral glucose resistance (OGTT) testing and sobber plasma glucose (FPG)^[1]. On the other hand, despite the potential limitation on glucose levels reliability on the diagnosis of early metabolism, such results are still remarkable as food consumption, stress, and circadian rhythms^[13,20] cause a significant variation. Additionally, OGTT is prone to a lot of the time and is vulnerable to the error of predicting conflicting results^[15]. HBA1C is another important metabolic biomarker as more reliable and practical alternative to FPG and OGTT, reflecting medium term blood glucose over 2-3 month^[16]. Unlike glucose base testing it does not require fasting and does not reflect temporary fluctuations in level of blood glucose as HBA1C is not affected by them. However, the disadvantages are that diabetic diabetes cannot be classified in patients with

hemoglobinopathy, anemia, or chronic kidney disease [18,24]. As well reports have emerged suggesting there are also ethnic differences in the measurement of HBA1C, which raises concerns over the applicability of much of the work to so many groups [25]. However, HBA1C is often used for diabetes screening even in the presence of these challenges, since there is a strong association with glucose periodontal long-term control of risk of complications [26]. Blood glucose levels and HBA1C became interest early predictors of diabetic's risk from markers of resistance to insulin. One way that glucose tolerance can be assessed given levels of glucose and insulin in the cold is with a homeostasis model AKA using that as a common metric [27]. Increased HOMA-IR measurements correlated with an increased risk of diabetes in the metabolic syndrome and obese patients [28]. Additionally, obokins like leptin and obonectin greatly affect the sensitivity of insulin and glucose to body weight. Spot associated IR is often accompanied by increased leptin levels; but in our case, higher obnectin levels, which should be more resistant to insulin and more prone to type 2 diabetes were found [29]. These new biomarkers were found to provide valuable information on metabolic changes happening before the onset of the disease which can help in improving the current early detection methods. [30]

Inflammatory Biomarkers

The chronic low-grade inflammation makes a significant contribution to insulin resistance, pancreatic beta cell inequity and progression of type 2 diabetes (T2D). Two important, inflammatory biomarkers, were interleukin 6 (IL6) and tumor necrosis factor alpha (TNF\$), were thoroughly explored for their role in metabolic disorders and as initial predictors of diabetes risk. In other words, obesity is associated with the inflammation and the inflammation results in insulin resistance and hypoglycemia dysregulation

which leads to the release of these inflammatory cytokines, and these cytokines are from immune cells, adipose tissue and macrophages. [31]

Tumor Necrosis Factor-Alpha (TNF- α)

Important testing biomarker for diabetes is TNF- $\hat{\pm}$ It does that because it's a major regulator of inflammation and has been shown to actually interfere with insulin signaling [32]. Reducing the phosphorylation of Layered-1 (IRS-1) with Glucose Receptor Blocking results in decreasing muscle and adipose tissue sensitivity to insulin. In addition, the fact that a rise in TNF\$ values is already rising in people with obesity and diabetes mellitus type 2 further supports an involvement in the relationship with long-lasting inflammation and metabolic disorders [33]. TNF-He triggers oxidative damage and NF- $\hat{\text{M}}$ activation along with wearing of pancreatic beta cell death in order to further increase hyperglycemia. [34] Insulin resistance and circulation are both extremely correlated both clinically and epidemiologically. For instance, obese patients with metabolic syndrome have increased TNF concentration and TNF function in incipient diabetes [35,36]. These results are interpretas as a useful biomarker for early identification of diabetes, and insulin sensitivity [37] it may be a potential and potential target for diabetes treatment.

Interleukin-6 (IL-6)

Another inflammatory cytokine involved in metabolism regulation is IL-6: it has two parts. Insulin resistance and risk of diabetes are related to chronic research, but it has particular advantages, as with the stimulation of glucose metabolism during training [38]. The course of action also benefits [39,40] as another marker of systemic inflammation, and improved insulin signaling in peripheral organs, and liver glucose production. Further, there is positive correlation



between increased IL-6 mirrors reported by diabetic patients, and type 2 diabetes incidence in prospective cohort studies [41]. Also, IL-6 most likely initiated the activity of the activator of Janus kinase/signal converter and transcriptional signaling pathway activator (JAK/STAT), which has been shown to well promote systemic inflammation and insulin resistance [42]. Nevertheless, the part of IL-6 in diabetes is diverse, as there have been proved by the research that training in IL-6 generations can benefit glucose metabolism, particularly in training. [43]

Biomarkers for Monitoring Disease Progression

Oxidative Stress Markers

Oxidative stress is important in diabetic disease in a progression following the course of diabetic disease with insulin resistance and beta cell dysfunction and diabetic complications. Determining biomarkers of oxidative stress allows for development of disease progression and treatment. Malondialdehyde (MDA) is used as a measure of the main oxidative stress biomarker due to oxidative damage when diabetes occurs. Superoxide squumutase is also known as a reduced activity of the enzyme in the diabetic state. Thus, this is the spontaneously generated enzyme of superoxides radicals with more oxidative stress [44,45]. Moreover, growth of insulin resistance is correlated with lowering of glutathione levels (GSH), a major antioxidant against reactive oxygen species. [46]

Circulating microRNAs

In particular, small, non-encoded RNAs referred to as circulating microRNAs (miRNAs) play a role in gene expression and are correlated with the development and complications of diabetes is known to control the pancreatic insulin secretion and beta cell function [47]. miR-126 is a supposed

disease marker, associated with the endothelial cell function and the complications involved in diabetes [48]. Additionally, miR-21 was correlated with inflammation and the development of diabetic nephropathy. [49] The development of proteomy and lipidomer diabetes can be investigated in greater detail via proteomic and fatty agent approaches. APOC-III, one of the important biomarkers, is known to be able to grow up with diabetic dyslipidemia and is correlated to the cardiovascular risk of disease [50]. Another category of sphingolipids is exacerbating problem related to diabetes through inducing better insulin resistance and metabolic disorders [51]. In addition, it was connected to haptoglobin, a glycoprotein that participates in inflammation and oxidative stress and that is associated with disease surveillance. [52]

Biomarkers for Treatment Response in Diabetes

There is a need to develop biomarkers to evaluate effects of the diabetes therapy to better manage glucose and also determine indications for this treatment to decrease complications. The three major biomarkers for treatment are the glucose change markers, pharmacological marker markers for personalized treatment, and antidiabetic drug response biomarkers.

Glycemic variability markers assess

The blood glucose variation index also takes into account the mesoglycemia (HBA1C) in addition to the variability of blood glucose levels that cause complications of diabetes. Implicit CGM based metrics such as time within the region (TIR), moderate intensity distal blood glucose (MAGE), and coefficient of change in glucose (CV%) can actually provide data of actual glucose variation [53]. A major predictor for adapting therapies that stabilize glucose levels, including GLP-1 receptor



and SGLT2 inhibitor, is large glucose variability and inducing oxidative stress and cardiovascular risk.^[54]

Pharmacogenomic markers for personalized therapy

Pharmacogenomic markers have the potential to be based on genetic differences to be used in pharmacologically based individualized treatment in expectations in particular, since everyone responds differently to antidiabetic drugs. For example, variations in SLC22A1 (fabric carrier family 22 member 1) affected metformin absorption^[55,56] during TCF7L2-polymorphism. KCNJ11 and CYP2C9 Gente tests may help to offer personalized treatments, enhance treatment outcomes, and decrease risk of undesirable adverse drug reactions^[57,58]. Pharmacogenomics used to treat diabetes allows precision medicine (same as optimization of drug response in all patients.^[59]

Response biomarkers for anti-diabetic drugs

Measureable indications of the effectiveness of the drug in the individual patient are given by biomarkers, ie antidiabetic drugs. An example is that increased levels of SOBER-C peptide with better glycemic control is due and can be used to predict responses to GLP-1 receptor agonist^[60]. With regards to improving weight loss and insulin sensitivity in patients treated with GLP-1 receptor agonists, fibroblast growth factor 21 was considered as a biomarker^[61]. In addition, metformin can be monitored with the effects on their concentrations of lactic acid and AMPK activation, reflected in mitochondrial function and drug resistance^[62].

Future Perspectives and Emerging Trends

As these multi-amic technology, precision medicine, and artificial intelligence (AI) and

machine learning (ML) are accelerating their development in the diabetes biomarker research, and these will be the approach on the signage of the era^[63]. These techniques can change diabetes management by enabling a greater depth of insight into how to tailor care, which treatment will work optimally, the disease pathophysiology.^[64]

AI and machine learning in biomarker discovery

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Multi-omics approach in diabetes research

In understanding of pathogenesis diabetes, a multiomics strategy for diabetes research approaches from genetics, transcriptomics, proteomics, lipidomics and metabolomics is necessary. The multiomics analysis helps to discover the molecular networks that are interconnected which influence diabetes development and response to diabetes treatment versus single biomarker analysis. For instance, transcriptome studies revealed that gene expression changes in pancreatic beta cells exposed to glucose stress; whereas, metabolic analysis showed particular lipid species linked with insulin resistance^[66]. Mass spectrometry in combination with progression of high slew rate sequencing are employed to identify of multi-Aamics signals that enable identification of diabetes types and prediction of drug efficacy.

Potential for precision medicine in diabetes management

Accurate medical diabetes therapy is to change treatment according to the genetic makeup, metabolic process profile and environmental condition of each individual. Previous studies have



already determined in pharmacological genomics how genetic variation affects individuals' response to antidiabetic drugs such as cloth and metformin sulfonyl. Future research will attempt to integrate a number of OMICS data records into AI based predictive models to design individual treatments. For instance, predictive algorithms, disease history based on patient's biomarker profile, and lifestyle factors can adopt personalized glyceic targets and medication regimes [67]. It enables the classification of the patients in specific subgroups in a precision medicine way. This is because, there is clinical research information and BIAB available, the treatment increases and side effects are lower.

CONCLUSION

Diabetes This is a worldwide health issue and requires progressed observation, recognition, and treatment steps. Despite the fact that frequently utilized, conventional symptomatic markers, for example, HBA1C, OGTT, and Calm plasma glucose are less exact, reproducible, and touchy to non-type glyceic variable. Through progress in biomarkers for atomic, metabolic, fiery, and oxidative stretch, treatment campaigns have been appraised and illness and early discovery are checked. Glucose, hemoglobin An affront resistance markers (TNF-INSÂ±, IL-6), oxidative harm markers as well as circulating microRNAs are biomarkers that describe the complex pathophysiology of diabetes and its complications. Additionally, identifiable proof of markers and the prediction of infection through artificial intelligence (AI) and machine learning (ML) has completely disrupted the problem of discerning the high-risk patients and the improvement of methods to be able to enhance the treatment programs. Thanks to the combination of multiamic advances such as transcriptomics, proteomics, lipidomics, metabolomics and genomes, advances have been made to understand diabetes heterogeneity. It

allows for distinguishing proof of unused treatment targets and subtypes of infections. These propels aid the ability to arrange treatment for diabetes based on an individual's hereditary, physiological, and way of life qualities, or accuracy medication, for short. AI underpins information, multiomics, and custom-made treatment investigation. End of the utilize is to anticipate malady courses, make strides the adequacy of medications, and give better diagnostic rebellious of diabetes. Through coordination of these advancements into clinical care, people in the healthcare occupations can be more effectively produced and more patient centered diabetes care that ultimately reduces the burden of diabetes complications and increases the life expectancy of millions of people worldwide.

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CONFLICT OF INTEREST

The authors claim no conflict of interest

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