

Identification of novel pathways or early biomarkers that are predictive of metabolic changes or insulin resistance associated with disease development.

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Introduction

Diabetes affects more than 463 million people worldwide, according to the International Diabetes Federation, with type 2 diabetes (T2D) accounting for around 90% of all diabetes cases in 2019. T2D caused about 4.2 million deaths in 2019 and is also a trigger for other non-communicable diseases, putting significant strain on national health systems. T2D is linked to a slew of serious comorbidities, including cardiovascular disease (the most common of which are ischemic heart disease, myocardial infarction, peripheral arterial disease, heart failure, and stable angina), kidney disease, and liver disease (including nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), liver failure, cirrhosis, and hepatocellular carcinoma), as well as an increased risk of non-Hodgkin lymphoma, etc.). Early intervention in the development of type 2 diabetes can reduce the outcomes of such comorbidities. There has been a lot of work and money put into finding biomarkers that can detect T2D early and help with preventative interventions in recent decades [1].

Hyperglycemia is one of the most common clinical signs of diabetes mellitus. As a result, the most common screening procedure is to check blood glucose levels using a glycated haemoglobin test. When glucose levels are high, however, the illness is already present. Biomarkers that can be used to define the development from a subclinical to a clinical stage have been identified thanks to significant research investments, and several biomarkers have been described as having potential predictive value to distinguish between progressors and non-progressors [2].

Prediabetes is the key threshold. Prediabetes is an asymptomatic disease of the normoglycemia–hyperglycemia transitional state, in which plasma glucose levels are higher than usual but not high enough to be diagnosed as diabetes. Prediabetics have impaired fasting glucose (IFG), impaired glucose tolerance (IGT), or both, as well as a higher chance of developing type 2 diabetes. Microvascular issues (such as retinopathy, nephropathy, and neuropathy—all common consequences in the hyperglycemic group) have already been linked to metabolic changes. The question of whether prediabetes warrants clinical detection and intervention is currently being contested among worldwide professional organisations, and there is no consensus on overall criteria.

The relevance of tackling prediabetes is essential, however, because lifestyle changes in prediabetic patients can reduce the chance of developing diabetes by 40 to 70%. The biggest issue with prediabetes is that it might result in overdiagnosis and, as a result, overtreatment. Anti-diabetic medications such as biguanides or thiazolidinediones, as well as GLP-1 analogues and -glucosidase inhibitors, are among the pharmacological options for prediabetes. In addition to medication, bariatric surgery (such as gastric bypass or sleeve gastrectomy) has been explored in prediabetic patients with promising outcomes, including the return of IGT to normal levels in 98 percent of cases [3].

Several metabolic abnormalities have already developed in the prediabetic stage, occurring before clinical symptoms. Early intervention can be facilitated by identifying these imbalances using suitable and precise biomarkers. In the United States, one out of every three people has prediabetes, and 11% will acquire diabetes [8]. Prediabetes is on the rise around the world, with estimates that by 2030, the number of persons with the disease would have risen to more than 470 million. Each year, 5–10% of people will develop diabetes and diabetic comorbidities like hypertension [4].

Novel biomarkers may be able to help with diabetic progression risk classification. A evaluation of new and developing biomarkers that can be used as targets to enhance clinical outcomes of disease progression through early intervention was conducted in this work. To find the most relevant biomarkers, researchers looked at review literature on the issue. The most often cited biomarkers across research were further reviewed and debated among the acquired data. The primary goal of our review was to assess each biomarker's research stage and molecular route in order to emphasise their value in clinical implementation.

Type 2 diabetes has a complex aetiology, making accurate screening, diagnosis, and prognosis difficult for doctors. The rapidly growing field of metabolomics, which employs analytical techniques such as mass spectrometry and nuclear magnetic resonance to identify biomarkers of diabetes and the insulin-resistant state that precedes overt pathology, has emerged as a promising approach for identifying biomarkers of diabetes and the insulin-resistant state that precedes overt pathology. Initial findings from metabolomic research have

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pointed to amino acids and lipid metabolism as potential biomarkers for insulin resistance and identifying those at risk of developing diabetes. These biomarkers will aid in the advancement of diabetes research and management. Several indicators discovered in particular could be utilised to detect diabetes risk early. Changes in certain biomarkers can also indicate whether or not therapy therapies for type 2 diabetes and the metabolic syndrome are beneficial. Indeed, branched-chain aminoacids hold a lot of potential as a type 2 diabetes risk biomarker, enabling for early dietary and exercise interventions to treat or possibly prevent the illness [5].

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