



(REVIEW ARTICLE)



## Regulation of molecular dysfunction with Multi-Omics: A platform of personal care in diabetes syndrome

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### Abstract

The present early screening and analytic tests for diabetes mellitus depend on the changes in the amount of glucose in the blood and autoantibody detection. However, innovative techniques have changed medical research relevance (Diabetes included). For instance, the introduction of genotyping arrays supported large-scale genome-wide relations studies and methods for evaluating international transcripts level, leading to integrated genetics. Additionally, other omics techniques like proteomics and metabolomics are currently being included in biological researchers' daily practices. This short review provides a comprehensive analysis of such omics technologies and concentrates on methods for their incorporation across different omics layers. Unlike a single omics type, multi-omics offers the opportunity to acknowledge the flow of information that triggers the disease. The inclusion of omics as a molecular term means an all-inclusive or international evaluation of various molecules. Most of the multi-omics studies focus on type 2 diabetes. Moreover, medical advancements are also expected to increase the level of anticipation concerning type 2 diabetes. Most data are also being incorporated with treatment responses, thereby offering the needed advancements for precision medicine in type 2 diabetes, which is currently the most prevalent chronic illness experienced in both the developed and developing nations in equal measure.

**Keywords:** Diabetes Mellitus; Metabolic Syndrome; Chronic Care Model; Multi-Omics; Personal Care Management

### 1. Introduction

Diabetes is a complicated metabolic intervention existing in the form of hyperglycemia and triggered by the reduction in insulin production. Type 1 diabetes (T1D) comes as a result of the autoimmune reaction of the T lymphocyte with the enzymes of pancreatic  $\beta$ -cells. Conversely, Type 2 diabetes is caused by multi-organ insulin resistance and is highly associated with older age, numerous genetic factors, and increased body mass index. It is more precise to define diabetes as a continuum of metabolic infections described by the failure of the body to maintain the normal balancing of glucose and multi-organ insulin resistance [1-2, 7]. Type 1 and Type 2 are the most common forms of diabetes. The training in clinical medicine focuses on the importance of evaluating each patient based on the prevailing signs and symptoms and establishing an appropriate management plan. When handling patients who have diabetes, it is evident that they come from different ethnic groups, age brackets, and social backgrounds.

Diabetes is a serious health problem with overwhelming yet avoidable consequences. Different institutions report figures above 10% population of the United States. According to CDC, 10.5% of American citizens had diabetes. National Diabetes Statistics Report (2020) reports that 13% of American citizens had diabetes in 2020 [9]. The figures are expected to increase steadily for the next few years. Moreover, numerous personal and societal prospects for its management have also increased. For instance, one of the key objectives of Healthy People 2020 is to improve the well-

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being of those who have diabetes. Even though new treatment and technology have helped regulate its spread, the associated challenges like self-management are devastating for many individuals. Even with the technological and scientific improvements made toward treating this disease, only a few have been properly controlled. Therefore, it is important to comprehensively recognize how medical phenotypic changes affect response or outcome and recognize molecular signatures (e.g., end products of Omics) that advance the outcome's capability.

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## 2. Relevance and Significance aspects to preventive disease: metabolic syndrome, diabetes

Diabetes mellitus is presently a common chronic illness that affects many people globally at all social and financial development levels. Moreover, even those individuals from the industrialized nations, regardless of the scientific developments and availability of quality healthcare systems like the United States, experience the increasing occurrence of diabetes. Moreover, the chronic care model (CCM) was created to give patients with chronic illnesses different types of self-care and monitoring systems. It provides a method for streamlining the healthcare system through exchanges among different healthcare organizations and communities. The main function of CCM is to gather relevant information important for advancing care in healthcare systems [2]. Apart from being created in America, it synthesizes different modules of disease management programs. The main focus of CCM is to advance the application of existing resources, establish new ones and support a new policy of collaboration between more open-minded and empowered patients. Additionally, it also concentrates on adequate preparation and creating proactive health teams.

Services designed based on CCM realize improved outcomes like inclusiveness and resolution. Therefore, the inclusion of CCM at all stages of healthcare must be authenticated for viability in health systems globally. Prevention and timely intervention linked to incorporated management can be a comprehensive and systemic solution to the challenging and complicated problem of ensuring people access quality care for chronic illnesses like diabetes [2]. The application of isolated modules of CCM is not enough to improve the clinical results. Nonetheless, additional benefits can be realized through interventions incorporating various elements of CCM. Some of the recognized elements that positively impact operational and medical results related to disease management include self-management, decision backing, organization of healthcare, and medical information system, among others.

These components lead to improved healthcare delivery structures that support various methods for decision support, connect healthcare systems to the available resources, provide all-inclusive self-management backup systems for patients and monitor patient-focused medical information systems. Even though there is enough proof showing that CCM is extensively used in handling different diseases like diabetes and asthma, few studies assess how CCM has been used in diabetes care [13]. The inclusion of different components in one intervention can play an important role in improving CCM adoption. Moreover, changing the roles of medical practitioners and registered nurses to treat diabetes more effectively is a strong strategy that generates clinical benefits. Modernized care can also sustain advanced training programs that assist patients in self-manage diabetes [16]. Prospected system-level CCM advancements should establish well-defined access points for healthcare workers to intervene with patients who are likely to suffer from diabetes.

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## 3. Evidence-Based validation: The Value of Multi-Omics

Concerning the pathophysiology of diabetes, a malfunctioning of the results cycles between insulin production and discharge leads to the irregularly increased amount of glucose in the blood. When it comes to the malfunctioning of  $\beta$ -cell, the rate of insulin discharge is reduced, thereby reducing the body's capacity to retain and balance physiological glucose levels. Nonetheless, insulin resistance leads to increased glucose secretion in the liver and reduced intake in the muscle. The  $\beta$ -cell malfunction is always more serious than insulin resistance regardless of whether both processes occur on time in the pathogenesis and lead to the development of diabetes [4]. When both  $\beta$ -cell malfunction and insulin resistance occur, hyperglycemia intensifies, thereby resulting in the progression of Type 2 Diabetes Mellitus. Meals containing huge amounts of calories have more fats and carbohydrates that increase the amount of glucose in the blood and supply low levels of lipoproteins, chylomicrons, and their residues that contain high concentrations of triglycerides. This activates a reaction of the oxygen species concentrations, which eventually results in an abnormal creation of inflammatory molecules.

Considering that inflammation is a known igniter of oxidation stress, an antiproliferative interaction occurs between the two processes after eating with resulting amplification of dangerous postprandial impacts. According to Sha and his colleagues (2020), the constant and indicated rise in steady-state levels of reactive oxygen species adds magnificently to the pathogenesis of Type 2 diabetes and insulin resistance [12]. It implies that a pro-oxidant surrounding leads to a mitochondrial malfunction, endoplasmic reticulum stress, and superoxide production ( $O_2^-$ ). Therefore, these trigger

different pathways aiding the pathogenesis of diabetes problems [4]. Using the pathways, increased intracellular leads to the stimulation of many pro-inflammatory pathways, thereby causing continuous epigenetic changes, which causes a constant expression of proinflammatory genes even after the glucose concentration in the blood becomes normal. Moreover, an increase in the amount of blood of free fatty acids also causes a mitochondrial malfunction through different mechanisms, including the inclusion of free fatty acids into the mitochondrial membranes, thereby supporting electron leakage.

Reduced involvement in physical activities and increased inactive behaviors create a connection between obesity and type 2 diabetes and are related to increased signs of chronic systemic inflammation. This leads to the discharge of proinflammatory molecules to the bloodstream using particular tissues like the group of 11 cytokines. The pro-inflammatory cytokines are responsible for autoimmune response to  $\beta$ -cells in the body, hindering  $\beta$ -cell function and supporting apoptosis. Inflammatory resolution is likely to stop the development of type 2 diabetes. Research indicates that the removal of the macromolecular NLRP3 inflammasome that generates pro-inflammatory cytokines leads to improved insulin sensitivity [11]. Deliberate loss in weight is still the main treatment to improve insulin sensitivity and, in certain situations, prevent type 2 diabetes in people with obesity. Continuous exercise and participation in more physical activities generate anti-inflammatory cytokines like soluble TNF receptors that are competitors with inflammatory cytokines. People who actively participate in physical activities also have lower inflammatory cytokines and leptin, a molecule linked with C-reactive protein [1]. Moreover, extensive physical exercise can improve type 2 diabetes-inducing oxidative stress by triggering the production of antioxidants like glutathione, thereby resulting in a lasting decrease in free radical levels.

Gut microbiota comprises numerous microbial species that affect an individual's physiology and takes part in various biological processes. For instance, they can control the immune system and metabolism [10]. Additionally, Gut resident microorganisms generate numerous metabolites that play an important role in physiology in healthy people. Production of a metabolite can be affected by other developments like age, nutrition, and lifestyle, resulting in metabolic interferences that can culminate in disease. Extensive knowledge of gut microbiota has demonstrated its substantial responsibility in developing diabetes [11]. Moreover, recent research shows that changes in dysbiosis can cause type 2 diabetes mellitus. Meals with high-fat content can trigger the manufacture of up to threefold lipopolysaccharide, thereby reducing inflammation and insulin resistance. The production of short-chain fatty acids can be affected by intestinal dysbiosis, thereby supporting gut barrier integrity and insulin production. The manufacture of other metabolites like amino acids can be affected by dysbiosis, thereby enhancing glucose homeostasis, and preventing type 2 diabetes development.

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#### 4. The Molecular based approach utilizes the Preventive and Prediction Tool

Pathogenesis and treatment of type 2 diabetes are complicated and multifactorial and require genetic, proteomic, and epigenetic approaches. The dominant mechanism of the metabolic illnesses overlaps and interrelates, though their individual features are not the same. It is important to categorize the main mechanisms taking place in these disorders to adopt a targeted and efficient treatment. However, this still comes with challenges, especially in the present treatment plans and the objective of precision medicine [5]. The idea of precision medicine was introduced in 2008 and proposed that medical practitioners and nurses should perform a diagnosis depending on molecular identification instead of work experience. Moreover, precision medicine was additionally suggested by the National Institute of Health to recommend individualized medical treatments designed for particular features of every patient. Apart from the outdated phenotypes, precision medicine can describe a patient's situation using genetic, proteomic, and epigenomic data obtained from different omics approaches [6]. Considering that the strength of single-omics information is limited, merging multi-omics information can always give room for a more detailed summary of personal characteristics.

Recent studies categorized different types of metabolic illnesses into three molecularly and medically different groups depending on metabolomics, proteomics, peptidomics, and medical data using a multi-omics-based structure to discover intra-disease diverseness and inter-disease resemblances. Additionally, the outcome can be used as a point of reference when it comes to assessing data of multi-omics studies and precision medicine. Precision medicine will likely improve treatment acceptability and efficiency in people with metabolic illnesses. Nonetheless, before it becomes a daily activity, more is needed in multi-omics profiling assessments [1]. Analysis of a multi-omics stage is important for an all-inclusive assessment of metabolic illnesses, necessary for projections, diagnosis, and treatment. Speedily developing innovations have provided similar opportunities to evaluate and include personal omics data, thereby playing an important role in obtaining biological differences to improve particular clinical treatment. When it comes to incorporating multi-omics, genomics has all the genetic data [15]. Additionally, proteins are always the final initiators to finish biotic activities and the elements of different biological decrees. Metabolomics is an indication of the present biological activities or procedures, while epigenetics and transcriptomics opine that these alterations are generated.

Therefore, understanding at multi-omics phases is important for an all-inclusive assessment of metabolic illness, which is necessary for envisaging, diagnosis and treatment.

Type 2 diabetes has been the emphasis of multi-omics research and genetics, and metabolomics and medical influences are anticipated to advance future type 2 diabetes forecasting. Apart from using multi-omics for type 2 diabetes, recent research has also integrated many data sources with treatment responses, providing the necessary opportunity for the upcoming precision medicine in type 2 diabetes and other metabolic illnesses. Moreover, clinical control of type 2 diabetes mainly concentrates on controlling plasma glucose levels and giving room for the risk of diabetes complications. Substantial inconsistencies are experienced when it comes to responding to even similar interventions [3]. Therefore, a precise understanding of the prevalent causes of different pharmacological reactions is essential when it comes to catalyzing the advancement and adoption of the most precise intervention plans dependent on the patients' exceptions characteristics. This is the establishment of incorporated multi-omics information that supports the adoption of precision medicine for type 2 diabetes. For instance, many studies have incorporated information gathered by genomics, metabolomics, and proteomics assessments in a combined structure to create individualized dietary interventions for type 2 diabetes.

Various research groups have incorporated information on dietary intake, physical exercise, and sleep through the application of the appointed algorithm, indicating that nutritional measures entrenched in this process are more essential than the old-fashioned dietary guidance concerning the control of postprandial blood glucose. Moreover, a genome-wide association study has incorporated an exclusively described metabolomics profiling with the objective of giving biological data concerning how genetic changes impact metabolism and how the metabolic changes in plasma can assist in recognizing essential genes within genomics areas linked with type 2 diabetes [7,14]. Moreover, extensive study methods that can recognize highly complicated configurations in huge datasets have been important in disease prognostic prototypes and biological mechanisms anticipation. It is open that a multi-optics method offers opposing data for the prediction and medical treatment of type 2 diabetes. In the coming years, comprehensive training methods can also be used in multi-omics research on type 2 diabetes.

The key theoretical advances in acknowledging type 1 diabetes include the implementation of the immune model and the inclusion of the metabolic disease perception to incorporate other metabolic interferences apart from that of glucose. The immune paradigm also establishes that the immune system can safeguard the  $\beta$  cells by triggering checkpoints that stop the immune attack, similar to what occurs to cancer cells that avoid immune recognition and clearance [8]. Additionally, this occurrence is called the anti-inflammatory reaction and immune control. Consequently, it is extensively understood that the treatment of type 1 diabetes should focus on reducing the proinflammatory reaction and pre-immune control.

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## 5. Discussion

Due to the overall burden of metabolic ailments, many studies are trying to establish the most suitable treatment, indicating the importance of supporting precision medicine. Even though surrounding factors like age and sex substantially impact polygenic illnesses like type 2 diabetes, genetics is considered the basis of phenotypes. Moreover, the close direction of precision medicine depends on the amalgamation of multi-omics techniques and conforming evaluations. Apart from understanding how to incorporate and evaluate the data from multi-omics techniques being the main information gap, it is also the key problem experienced in precision medicine when it comes to recognizing and adopting this multi-omics information concerning clinical practice. The response to the question will entirely rely on the connections between the clinical features and the general biology of disease. Moreover, it is important to describe etiological subsections of these illnesses depending on the physiological characteristics described by multi-omics techniques and then assess the subgroup characteristics with the medical features depending on the laboratory factors and imaging data from calculated magnetic resonance imaging. Additionally, machine learning can be essential in studying these interactions. Precision medicine is likely to experience these problems, and the way scientists handle these problems establishes the prospected direction of precision medicine.

### *Perspectives and Limitation*

Drug discovery through the application of omics technique can be essential through non-invasive information collection to demonstrate disease advancement to accomplish direct and adaptable phenotype modeling of the disease. Moreover, it could indicate the molecular source and biomarkers of illnesses. These techniques can also be important when it comes to recognizing at-risk persons, epidemiology, and integrating cures as individualized medicine. Additional information concerning the biological pathways using the multi-omics information can disclose the association between an illness and surrounding factors. Therefore, that might result in earlier and more precise diagnoses using biomarkers

of illnesses together with developed pharmacological and advanced mediations for particular groups of patients. Type 3 diabetes has been launched new paradigms to prevent earlier against two main disorders with some essential collective mechanisms, for example, insulin resistance, hyperlipidemia, mitochondria dysfunction, and endothelial dysfunction which reflects the potential risk of chronic disorders like Cardiovascular and neurodegenerative disease that can also maximize these benefits of multi-omics methods focusing on their described common pathways.

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## 6. Conclusion

The advent of Molecular sensitivity, systemic assessment, and technology, for example, the advancement of next-generation sequencing and mass-spectrometry technology plans give extensive research concerning the entire cellular system. Moreover, effectively making use of multi-omics data needs appropriate data blending of different omics layers and efficient bioinformatics plans, and standardized procedures. Additionally, a huge amount of data and insufficient associated research for highlighting tools and assessment used in multi-omics methods, and a lack of well-defined standards for data cleaning are other problems connected with multi-omics technologies. Moreover, the limitation of such pathways assessment is that the applied methods, by design, fail to include the connection of these pathways that forms the whole system. Even though global connection networks substantially cover these intersections, assessment of these networks is exclusively problematic considering their substantial size.

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## Compliance with ethical standards

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### *Disclosure of conflict of interest*

The authors declare no conflicts of interest.

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## References

- [1] Alcazar O, Hernandez LF, Nakayasu ES, Nicora CD, Ansong C, Muehlbauer MJ, Bain JR, Myer CJ, Bhattacharya SK, Buchwald P, Abdulreda MH. Parallel multi-omics in high-risk subjects for the identification of integrated biomarker signatures of type 1 diabetes. *Biomolecules*. 2021; 11(3): 383.
- [2] Baptista DR, Wiens A, Pontarolo R, Regis L, Reis WCT, Correr CJ. The chronic care model for type 2 diabetes: a systematic review. *Diabetology & metabolic syndrome*. 2016; 8(1): 1-7.
- [3] Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, Ostolaza H, Martín C. Pathophysiology of type 2 diabetes mellitus. *International journal of molecular sciences*. 2020; 21(17): 6275.
- [4] Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, Ostolaza H, Martín C. Pathophysiology of type 2 diabetes mellitus. *International journal of molecular sciences*. 2020; 21(17): 6275.
- [5] Hu C, Jia W. Multi-omics profiling: the way toward precision medicine in metabolic diseases. *Journal of Molecular Cell Biology*. 2021; 13(8): 576-593.
- [6] Khan MS, Azmir J. Multi-omics for Biomedical Applications. *J Appl Bioanal*. 2020; 6(3): 97-101.
- [7] Kussmann M, Kaput J. Translational genomics. *Appl Transl Genomics*. 2014; 3(3):43-47.
- [8] Liu C, Sun YV. Anticipation of Precision Diabetes and Promise of Integrative Multi-Omics. *Endocrinology and Metabolism Clinics*. 2021; 50(3): 559-574.
- [9] National Diabetes Statistics Report. Center for disease control and prevention. 2020. <https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf>
- [10] Odenkirk MT, Stratton KG, Gritsenko MA, Bramer LM, Webb-Robertson BJM, Bloodsworth KJ, Weitz KK, Lipton AK, Monroe ME, Ash JR, Fouches D. Unveiling molecular signatures of preeclampsia and gestational diabetes mellitus with multi-omics and innovative cheminformatics visualization tools. *Molecular omics*. 2020; 16(6): 521-532.

- [11] Ozougwu JC, Obimba KC, Belonwu CD, Unakalamba CB. The pathogenesis and pathophysiology of type 1 and type 2 diabetes mellitus. *J Physiol Pathophysiol*. 2013; 4(4): 46-57.
- [12] Sha Q, Lyu J, Zhao M, Li H, Guo M, Sun Q. Multi-Omics analysis of diabetic nephropathy reveals potential new mechanisms and drug targets. *Frontiers in genetics*. 2020; 11: 1605.
- [13] Stellefson M, Dipnarine K, Stopka C. The chronic care model and diabetes management in US primary care settings: A systematic review. *Preventing chronic disease*. 2013; 10. <http://dx.doi.org/10.5888/pcd10.120180>.
- [14] Tayanloo-Beik A, Parhizkar Roudsari P, Rezaei Tavirani M, Biglar M, Tabatabaei-Malazy O, Arjmand B, Larijani B. Diabetes and Heart Failure: Multi-Omics Approaches. *Frontiers in Physiology*. 2021; 1198.
- [15] Wang G, Sander M. A multi-omics roadmap of  $\beta$ -cell failure in type 2 diabetes mellitus. *Nature Reviews Endocrinology*. 2021; 17(11): 641-642.
- [16] Wigger L, Barovic M, Brunner AD, Marzetta F, Schöniger E, Mehl F, Kipke N, Friedland D, Burdet F, Kessler C, Lesche M. Multi-omics profiling of living human pancreatic islet donors reveals heterogeneous beta cell trajectories towards type 2 diabetes. *Nature Metabolism*. 2021; 3(7): 1017-1031.