Nutri-epigenomics and its Application in the Management of Type 2 Diabetes

Dr. Vanitha G Ramesh

Professor, Indian Academy Degree College Autonomous, Bengaluru – 43

DOI: https://doi.org/10.51584/IJRIAS.2026.11090168

Received: 02 October 2026; Accepted: 07 October 2026; Published: 26 October 2026

ABSTRACT

Type 2 diabetes mellitus (T2DM) is a progressive metabolic disorder characterized by insulin resistance, chronic hyperglycemia, and β-cell dysfunction. Although genetic predisposition raises risk, it might not fully explain differences in the disease's onset, severity, and response to therapy. Nutriepigenomics examines how dietary exposures affect epigenetic mechanisms that regulate gene expression, including DNA methylation, histone changes, and non-coding RNAs. Because they affect insulin signaling, inflammation, oxidative stress, lipid metabolism, and glucose homeostasis, these mechanisms are crucial to the etiology and management of type 2 diabetes. The molecular foundations of nutriepigenomics and its relationship to type 2 diabetes are described in this review. A growing body of research indicates that dietary habits and bioactive substances may improve traditional antidiabetic treatment by altering glucose homeostasis-related epigenetic markers. The scientific underpinnings of nutri-epigenomics in type 2 diabetes are discussed, along with its present and future clinical uses in the prevention and treatment of the condition.

Keywords: Nutriepigenomics; Type 2 Diabetes mellitus(T2D); DNA Methylation; Histone modification; precision nutrition; Epigenetic Biomarkers.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is one of the most pressing health problems in the twenty-first century. The disease develops more and more often because of people's inactive lifestyles, urbanization, and the popularity of unhealthy food (1,2). However, there are cases when people consume the same amount of food without changes in caloric intake, but their bodies respond differently to the load. Therefore, it is essential to explore the particular mechanisms that explain how an individual's organism deals with nutrition better than the general principles of thermodynamics.

The multifactorial pathophysiology of T2DM is complex and comprises interactions among genetic susceptibility, environmental factors, and lifestyle. Despite the fact that genome-wide association studies (GWAS) have identified an ample number of susceptibility loci for T2DM, these variants account for only a small proportion of cases and do not explain the observed variability in the manifestation and progression of the disease (3,4).

Epigenetic changes that occur during adulthood have been associated with the pathogenesis of various diseases, including malignancies, cardiovascular disorders, and type 2 diabetes mellitus (T2DM). Diets consisting of high amounts of sucrose and saturated fats have been shown to induce abnormal DNA methylation and histone modifications in genes controlling inflammatory responses, lipid metabolism, and glucose homeostasis (1). Since persistent nutritional shifts can remodel chromatin structure independently of genetic code, nutritional epigenetics represents an area of considerable interest for diabetes prevention and management. The aforementioned capacity highlights the field's potential role in developing personalized dietary interventions and advancing precision nutrition, as it provides a mechanistic link between diet and gene regulation at the molecular level. Thus, epigenetics offers a plausible explanation of the ability of nutrition to modulate gene expression, thereby bridging the gap between traditional biomedical research and individualized healthcare approaches.

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume XI Issue IX September 2026

EPIGENETIC BASIS AND MECHANISMS

The diet has a number of interconnected biochemical pathways that affect epigenetic processes. The first of these is the one-carbon metabolism pathway, which includes folate, vitamin B12, choline, and methionine, all of which participate in the formation of methyl groups and regulation of DNA methylation. Second, diet is linked to the availability of polyphenols, omega-3 fatty acids, and fiber, which influence the activity of epigenetic enzymes and inflammatory pathways. The third pathway is mediated by the microbiota, as the diet can affect its composition and the production of metabolites that have epigenetic effects (Hollister et al., 2014).

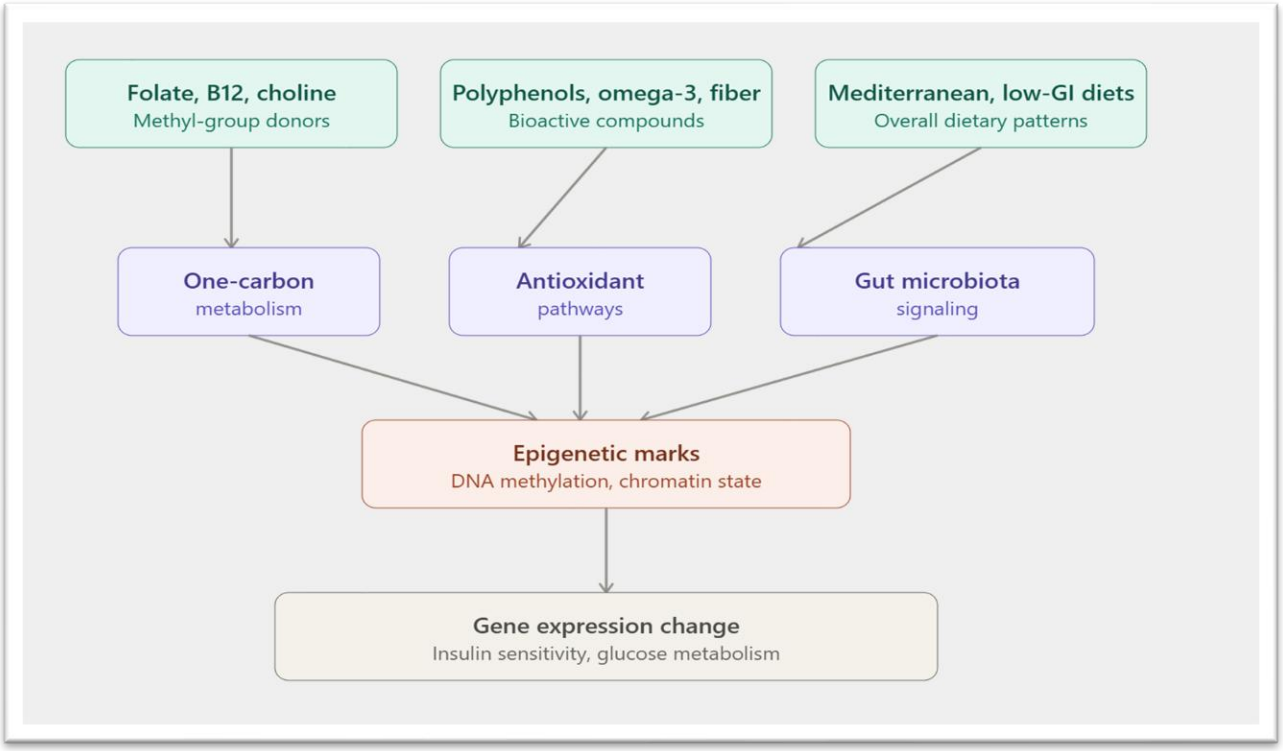


Fig 1: Nutrients and dietary patterns feed into three biological pathways that converge on epigenetic marks, ultimately shifting gene expression relevant to insulin sensitivity and glucose control.

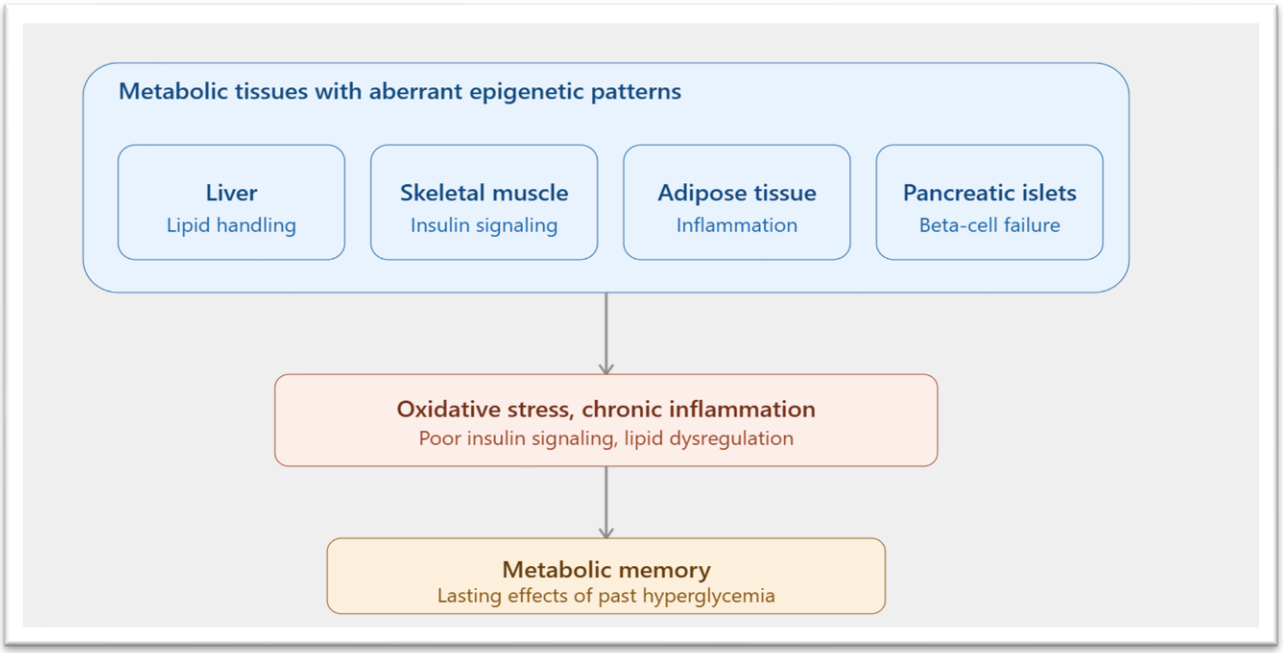


Fig 2: T2DM pathogenesis — how epigenetic dysregulation plays out across specific tissues, and how precision nutrition tries to use that same biology diagnostically.

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume XI Issue IX September 2026

The two diagrams together illustrate the main trajectory of the paper: nutrition influences epigenetic modifications through specific biochemical processes (first diagram), and those modifications become disrupted in crucial metabolic tissues in T2DM, leading to a "metabolic memory" that remains even after glycemic control improves (second diagram). The sections on precision nutrition and its limitations focus more on strategies and evidence gaps rather than on mechanisms, making them more suitable for a written summary than for a diagram — I can create a workflow diagram for the precision nutrition process (biomarker → stratification → intervention) if that would be useful as well.

These nutrient-dependent processes and epigenetic mechanisms can be generally divided into three subtypes: DNA methylation, post-translational histone modifications, and non-coding RNA, including microRNA. Altogether, these processes affect the transcription of genes that are responsible for the proper functioning of insulin and glucose metabolism. According to the researchers' conclusions, diets that are rich in plants, the Mediterranean diet, and low glycemic diets can improve the level of methylation and, therefore, change the expression of genes responsible for metabolic processes. From this, it can be seen that the quality of the entire diet is much more important than the contribution of individual nutrients. Thus, nutrition is presented as a system in which nutrients can act as effectors for the regulation of gene expression.

DIETARY REGULATION: NUTRIENTS AND MECHANISMS

3.1 Methyl-Donor Nutrients and One-Carbon Metabolism

Folic acid, Vitamin B12, choline, betaine and other B-vitamins individually participate in 1C metabolism and impact DNA and histone methylation reactions by affecting the pool of S-adenosylmethionine. The alterations in 1C metabolism and resultant DNA methylation have been linked to development of glucose intolerance. Imbalance in dietary methyl-donor nutrients may lead to decreases in overall DNA methylation or site-specific increases in methylation.

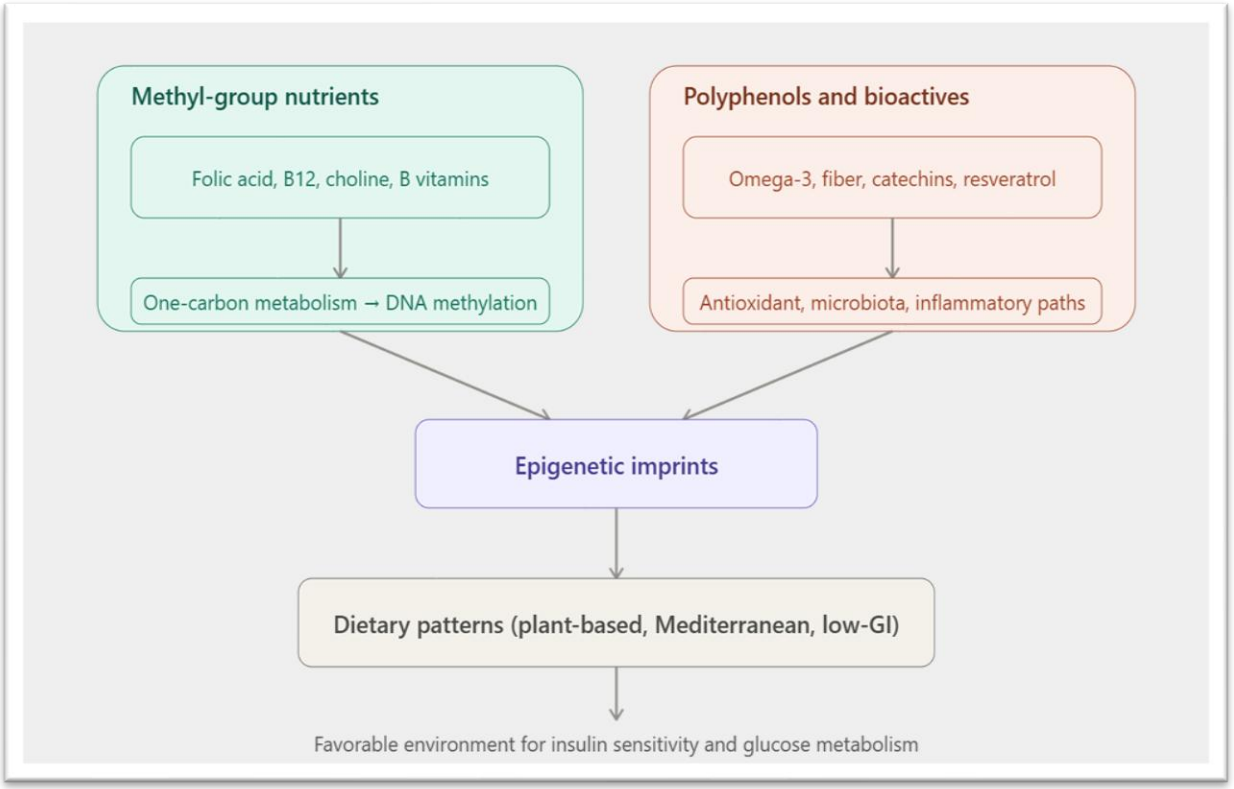


Fig 3: This one divides the two nutrient categories from that paragraph into separate tracks: polyphenols and bioactives feeding antioxidant/microbiota/inflammatory pathways on the right, and methyl-donor nutrients feeding one-carbon metabolism on the left. Both converge on epigenetic imprints, followed by dietary patterns, and ultimately the beneficial metabolic outcome the passage refers to.

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume XI Issue IX September 2026

3.2 Bioactive Compounds, Antioxidant Pathways, and Microbiota

Polyphenols (e.g., catechins, resveratrol), omega-3 fatty acids, fiber, and specific micronutrients may impact oxidative stress and the gut microbiome, as well as inflammatory pathways. These bioactive molecules can affect the expression or function of DNA methyltransferases, histone deacetylases, and microRNA processing machineries. Overall, these effects are frequently linked to a decreased pro-inflammatory DNA methylation profile and improved insulin-signaling gene network.

It follows that an optimized nutritional pattern can promote a healthy epigenetic environment that supports glucose homeostasis and insulin sensitivity. The combined endocrine and epigenetic impact of nutrition on the development of T2DM serves as the mechanistic basis for dietary interventions.

T2DM PATHOGENESIS AND EPIGENETIC DYSREGULATION

Aberrant epigenetic regulation contributes to several key pathophysiological mechanisms of type 2 diabetes. Changes in DNA methylation, histone acetylation/methylation, and non-coding RNA profile are reported in liver, skeletal muscle, adipose tissue, and pancreatic islets with oxidative stress, chronic low-grade inflammation, lipid dysregulation, insulin resistance, and β-cell dysfunction as downstream consequences.

One of the most clinically relevant phenomena is metabolic memory, which involves post-hyperglycemic damage that persists even after restoration of glucose levels. The key role in the development of metabolic memory is played by epigenetic processes. Thus, both genetic and environmental factors contribute to the formation of disease depending on individual characteristics.

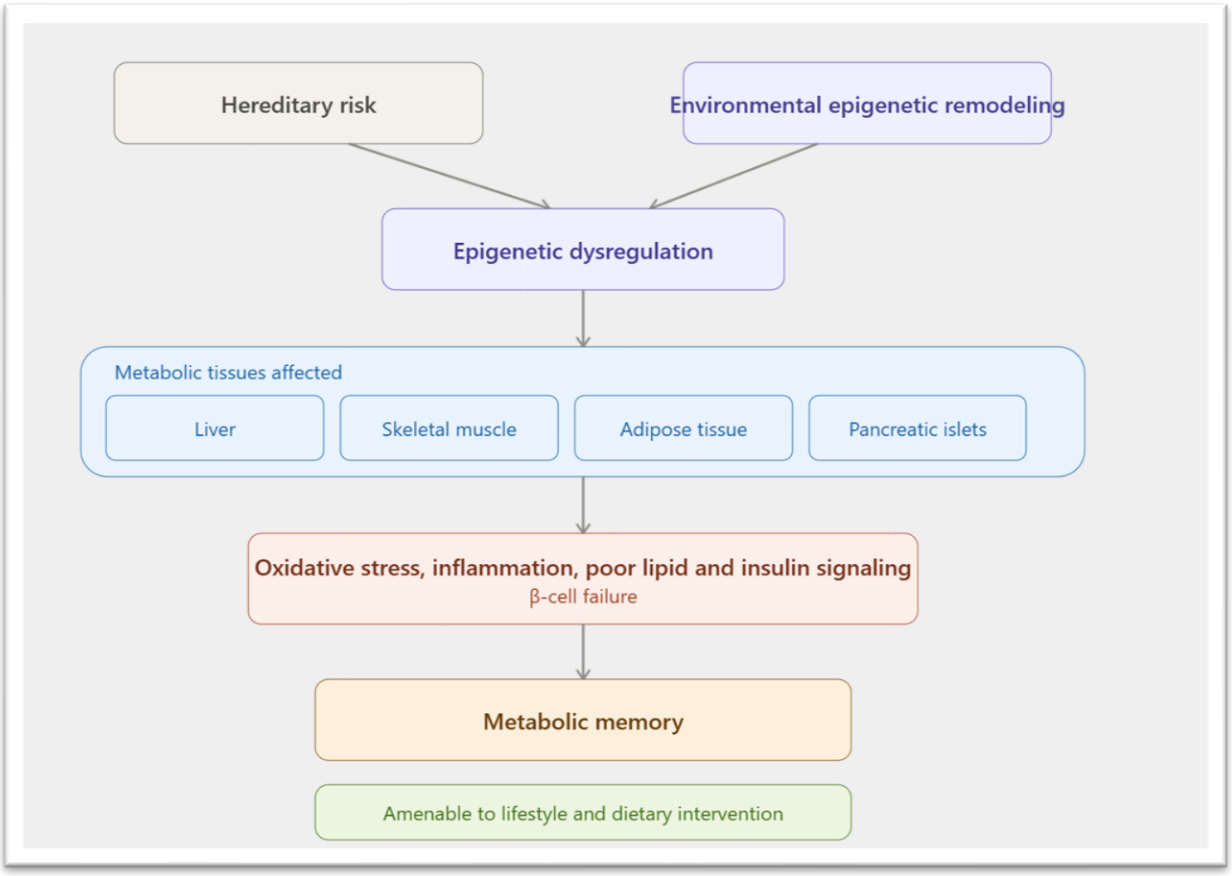


Fig 4: Dietary treatment is presented as a molecular-level intervention rather than merely calorie-based since methylation in these tissues reacts to exercise and diet composition.

Importantly, the methylation patterns in metabolic tissues are sensitive to lifestyle factors, such as physical activity and diet. This suggests that epigenetic modifications are amenable to interventions and that the approach

ISSN No. 2454-6194 | DOI: 10.51584/IJRIAS |Volume XI Issue IX September 2026

of dietary therapy may act on mechanisms that go beyond the control of caloric and macronutrient intake by regulating genes.

PRECISION NUTRITION APPLICATIONS

Precision nutrition is one of the most promising applications of nutriepigenomics. Instead of giving a general recommendation for all people, this section of nutrition uses molecular information to target.

Epigenetic classifiers; specifically DNA methylation signatures and circulating microRNA; are currently explored for three therapeutic areas: patient stratification; prediction of risk of T2DM; and assessment of drug targets. Such biomarkers can be particularly useful in prediabetes and early disease where the lifestyle intervention still can make a difference and bring benefits for patients in the long-term.

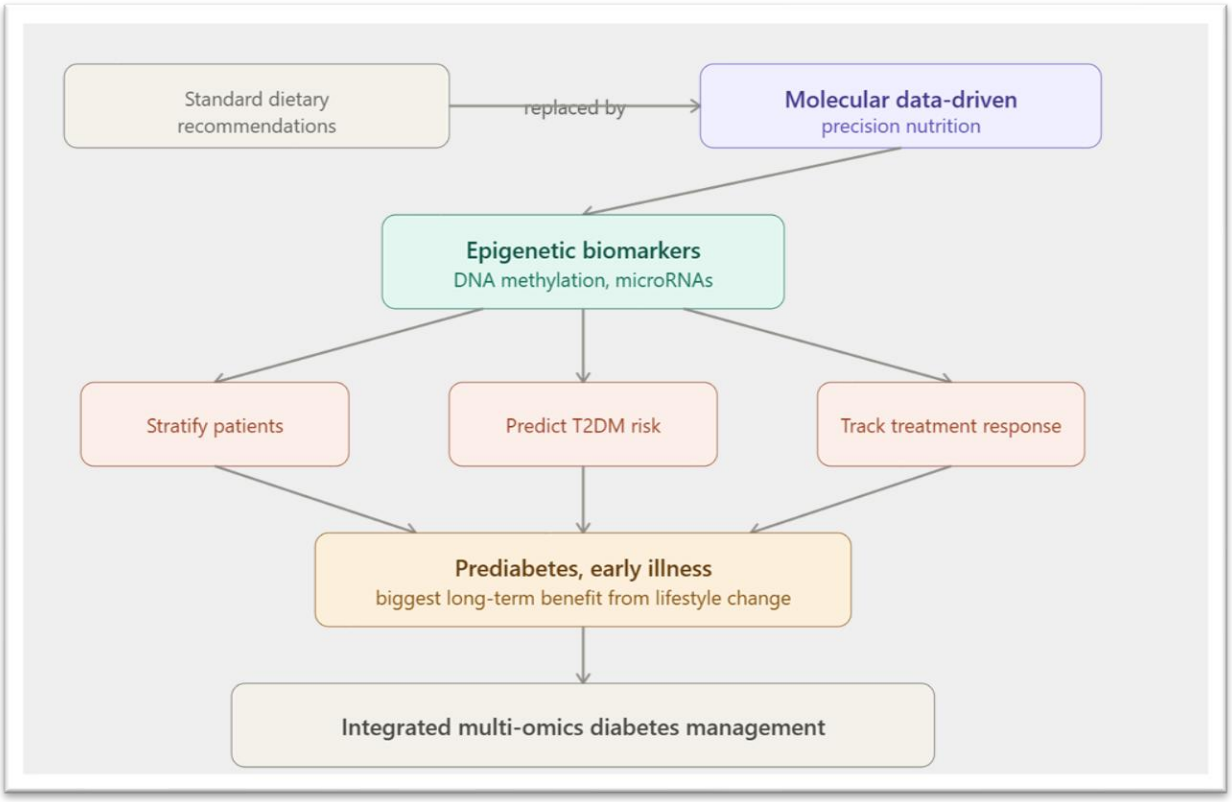


Fig 5: It begins by contrasting the standard-recommendation approach with the molecular-data approach that precision nutrition replaces. Next, it explicitly divides the two biomarkers (microRNAs and DNA methylation) into the three different clinical uses listed in the paragraph: response tracking, risk prediction, and stratification. Finally, it funnels through the prediabetes/early-illness emphasis to the final goal of integrated multi-omics management.

The field is moving towards integrating nutritional, genetic, epigenetic, and metabolic information. The combination of these data types will improve the accuracy of risk prediction models and help identify optimal dietary interventions for patients at risk or with T2D to re-establish healthy epigenetic function.

LIMITATIONS AND CHALLENGES

The main limitation of nutriepigenomics is that, despite its great potential, it has so far encountered numerous challenges for implementation. Firstly, the results of experiments are promising, although there is still insufficient research to prove causality. Secondly, individual variability, long-term processes, and the influence of other factors on gene expression make genetic counseling difficult.

A large proportion of the existing studies were cross-sectional, tissue-specific, or conducted on a small scale, making replication difficult and limiting causal inferences. Analytical pipelines, epigenomic platforms, and sample-collection protocols need standardization. Larger-scale investigations in humans are needed to identify which epigenetic changes associated with T2DM are predictive, reversible, and therapeutically relevant. The future of the research will rely on clinical validation and a more comprehensive view of the epigenetic regulation of the disease.

CONCLUSION

Nutri-epigenomics provides a physiologically plausible mechanism by which nutrition may influence the risk and progression of T2DM. There is growing evidence that changes in DNA methylation, histone modifications, and non-coding RNA are involved in the development and progression of diabetes. This field may be a valuable tool for prevention and treatment of T2DM.

In addition to the conventional method of controlling blood sugar levels, nutritional intervention may help to modulate gene expression involved in insulin sensitivity, inflammatory processes, and β-cell survival. While the idea has been tested in clinical practice limited to a few cases, further research is needed to fully understand the mechanism and individualize the dietary recommendations for people with type 2 diabetes.

REFERENCES

1. Jazieh C, Arabi TZ, Asim Z, et al. Unraveling the epigenetic fabric of type 2 diabetes mellitus: Pathogenic mechanisms and therapeutic implications. *Front Endocrinol (Lausanne).* 2024;15:1295967. doi:10.3389/fendo.2024.1295967.
2. Geng X, Li Z, Yang Y. Emerging role of epitranscriptomics in diabetes mellitus and its complications. *Front Endocrinol (Lausanne).* 2022;13:907060. doi:10.3389/fendo.2022.907060.
3. Ling C, Rönn T. Epigenetics in human obesity and type 2 diabetes. *Cell Metab.* 2019;29(5):1028-1044. doi:10.1016/j.cmet.2019.03.009.
4. Dhawan S, Natarajan R. Epigenetics and type 2 diabetes risk. *Curr Diab Rep.* 2019;19(8):47. doi:10.1007/s11892-019-1168-2.
5. Martinez JA, Milagro FI, Claycombe KJ, Schalinske KL. Nutritional epigenomics: On the importance of dietary patterns and specific nutrients in shaping epigenetic outcomes. *Adv Nutr.* 2014;5(4):436-445. doi:10.3945/an.113.005850.
6. Zhao Y, Barrere-Cain RE, Yang X. Nutritional systems biology of type 2 diabetes. *Genes Nutr.* 2015;10:31. doi:10.1007/s12263-015-0481-3.
7. Rumui D, Dama A, Gorica E, Halim VS, Setiawan AF, Tjia XC, et al. Precision nutrition in type 2 diabetes prevention through molecular nutrigenomic and epigenetic modulation of insulin signaling and glucose metabolism. *Int J Mol Sci.* 2026;27(4):1631. doi:10.3390/ijms27041631.
8. Li CCY, Young PE, Maloney CA, Eaton SA. Nutrition and its role in epigenetic inheritance of obesity and diabetes across generations. *Semin Cell Dev Biol.* 2020;97:86-95. doi:10.1016/j.semcdb.2019.09.012.
9. Corella D, Ordovás JM. Nutrigenetics and nutrigenomics: Insights into diabetes. *Nutrients.* 2014;6(12):5338-5369. doi:10.3390/nu6125338.
10. Cheng et al. Type-2 diabetes epigenetic biomarkers: Present status and future directions for global and Indigenous health. *Front Mol Biosci.* 2025. doi:10.3389/fmolb.2025.1502640.
11. Novel micro-ribonucleic acid biomarkers for early detection of type 2 diabetes mellitus and associated complications: A literature review. *PubMed Central (PMC).* Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11765584/
12. The potential use of DNA methylation biomarkers to identify risk and progression of type 2 diabetes. *PubMed Central (PMC).* Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4378313/
13. Genotype-based precision nutrition strategies for the prediction and clinical management of type 2 diabetes mellitus. *PubMed Central (PMC).* Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC10921165/.