

The Role of DNA Methylation in Diabetes Pathogenesis

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Background

DNA methylation is a crucial biological mechanism involving the addition of methyl groups to the DNA molecule. This process can alter the function of a DNA segment without modifying its sequence. Particularly when it occurs in a gene promoter, DNA methylation usually serves to suppress gene transcription. In humans, this mechanism is vital for proper development and plays a significant role in various fundamental processes such as genomic imprinting, X-chromosome inactivation, the repression of transposable elements, aging, and carcinogenesis. Currently, research efforts are expanding to explore the implications of DNA methylation in diabetes, aiming to uncover novel insights that could lead to better understanding and management of this condition.

Research Question and Objectives

This project aims to explore the relationship between DNA methylation patterns and diabetes, focusing on how these epigenetic modifications influence the disease's development and progression.

The specific objectives are to:

- Identify DNA methylation changes in key regulatory genes involved in glucose metabolism and insulin signaling pathways in diabetic versus non-diabetic individuals.
- Assess the potential of identified methylation markers for predicting diabetes onset and progression.

[This study](#) highlights the profound impact of diabetes on cardiac cell gene expression with over 3200 genes differentially regulated, contrasting with the stability of DNA methylation patterns, underscoring the complexity of diabetes-induced cardiac alterations and the key role of fibroblast-monocyte interactions.

[This article](#) describes DNA methylation, a stable epigenetic mechanism crucial for regulating gene expression and cell identity, is influenced by metabolic changes, impacting the development of diseases like type 2 diabetes (T2D). Recent genome-wide studies have significantly enhanced our understanding of T2D's molecular basis, positioning DNA methylation as both a potential cause and consequence of T2D. This makes it a promising biomarker for developing T2D therapeutic strategies.

Data and Remarks

The data we found describes methylation sites in sick and healthy patients, along with age, gender, disease type and tissue.

The files are in csv format and contain ~75Gb of data (over 8,000 healthy control patients and ~60 patients with type 2 diabetes).

[Dataset source](#)

Notes:

1. This dataset contains ~740 samples of Alzheimer's disease patients (which might be better for training) but it seems like there are less papers looking into this relation and weaker correlation to methylation compared to diabetes.
2. The data can also be used to predict patients' age.

Hypothesis

In the end, we expect to identify specific DNA methylation patterns that are significantly associated with diabetes. The research process's crucial points are rigorous data collection and analysis to ensure accuracy, and thorough validation of findings to confirm their relevance to diabetes.

However, several factors could challenge the success of this research. Sample variability, such as differences in lifestyle, genetic background, and disease stage among participants, could obscure genuine methylation differences related to diabetes.

Computational Model, Algorithm, and Statistical Tests

To predict diabetes from DNA methylation we will try to use the methods learned in the course (such as HMM) or other regression models.

Steps to be Taken

Our first step will be cleaning and analyzing our dataset. Next we will plot and investigate the methylation levels in diabetic and non-diabetic patients. For training, we will try the methods learned in the course (such as HMM) and some classic algorithms such as logistic regression and gradient based methods.

Citations

- Relevant databases for accessing methylation and genetic data (GEO, EGA, 1000 Genomes Project).
- Recent publications on DNA methylation and diabetes from PubMed or similar resources.
- [Sequence data and association statistics from 12,940 type 2 diabetes cases and controls - PMC](#)

The study explored how changes in DNA methylation are involved in the development and progression of T2D.

- [The role of DNA methylation in the pathogenesis of type 2 diabetes mellitus | Clinical Epigenetics](#)

This article reviews the role of DNA methylation in the development and pathogenesis of type 2 diabetes. It discusses several genes involved in insulin production and type 2 diabetes pathogenesis, examining how their methylation status affects gene expression and contributes to the disease.

- [Epigenome-wide meta-analysis identifies DNA methylation biomarkers associated with diabetic kidney disease | Nature Communications](#)

The article presents an analysis that identifies DNA methylation biomarkers associated with diabetic kidney disease (DKD).