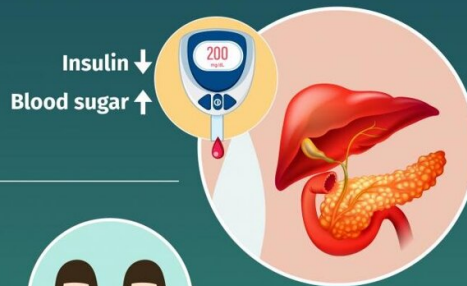


Beyond mere blueprints: Variable gene expression patterns and type 1 diabetes

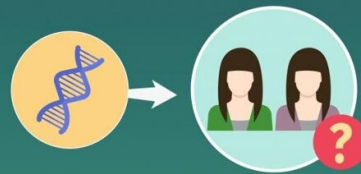
June 18 2021

Epigenetic Factors - The Bridge Between Environmental Insults and Genetic Risk in Type 1 Diabetes

Type 1 diabetes (T1D) is a chronic autoimmune disorder caused by destruction of insulin secreting cells, resulting in hyperglycemia



While genetic factors play a major role in its pathogenesis, they do not explain differential susceptibility to T1D across monozygotic twins with identical genomes

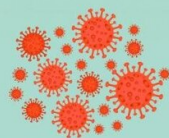


How do environmental and epigenetic factors contribute to the development of T1D?



Review assesses factors affecting autoimmunity in T1D

Environmental influences



Viral infections



Gut microbiota



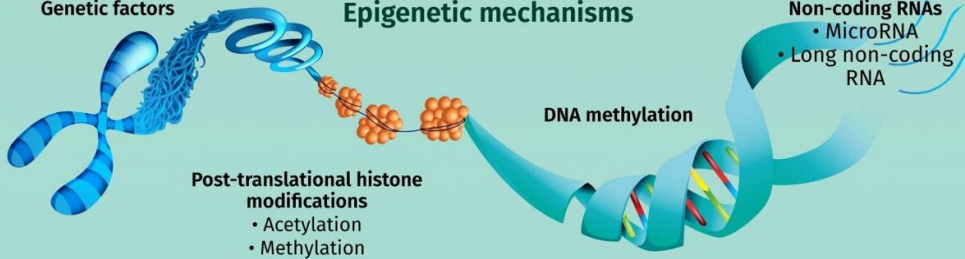
Diet



Stress

Genetic factors

Epigenetic mechanisms



Non-coding RNAs
• MicroRNA
• Long non-coding RNA

DNA methylation

Post-translational histone modifications
• Acetylation
• Methylation

Potential use



Risk assessment



Diagnostic biomarkers



Therapeutic targets

Environmentally induced epigenetic changes involved in T1D, can be potentially useful in devising diagnostic and therapeutic measures



Epigenetic factors -- the bridge between environmental insults and genetic risk in type 1 diabetes. Genetics plays a major role in determining a person's risk of developing type 1 diabetes, but environmental and lifestyle factors are also important. In an article recently published in *Chinese Medical Journal*, a team of researchers explore the interplay of genetic and environmental factors by summarizing the literature on type 1 diabetes and epigenetics--the study of how gene expression patterns can be modified. These findings have important implications in treating type 1 diabetes. Credit: *Chinese Medical Journal*

Type 1 diabetes is a disorder in which the immune system inappropriately targets a class of cells in the pancreas known as β cells that produce the hormone insulin, which plays an important role in regulating bloodstream glucose levels and the metabolism of carbohydrates, lipids, and proteins. The loss of insulin causes a range of health problems for people with type 1 diabetes, and patients become dependent on insulin injections for their survival. Even with insulin therapy, people with type 1 diabetes have shortened lifespans and are at an elevated risk of developing myriad complications.

Previous studies have identified numerous genetic risk factors for type 1 [diabetes](#). One notable finding is the importance of the HLA region, a part of the human genome that contains multiple genes and explains approximately 40–50% of the genetic risk for type 1 diabetes. However, studies of identical twins have identified cases in which one twin develops type 1 diabetes while the other twin does not—which indicates that genetic risk factors cannot fully explain the occurrence of type 1 diabetes. This finding is consistent with the known relevance of certain environmental factors. For example, most studies have found that breastfeeding and vitamin D consumption protect against type 1 diabetes and that cow's milk and the early introduction of gluten increase the risk

of type 1 diabetes. Furthermore, microbes in the human gut play important roles in human health and digestion, and patients with type 1 diabetes often lack diversity in their gut microbiota.

To explain the risk factors for type 1 diabetes more fully, medical researchers have turned to the field of epigenetics, which studies how environmental and lifestyle factors can influence the expression of genes without altering the underlying DNA sequence. In recent years, various research groups have published studies confirming that epigenetic changes related to environmental conditions contribute to the development of type 1 diabetes. [In a review article recently published in *Chinese Medical Journal*](#), a team of researchers from the Huazhong University of Science and Technology led by Drs. Cong-Yi Wang and Fei Xiong set out to summarize how epigenetic factors modulate the risks of type 1 diabetes. They also aimed to discuss the potential of these epigenetic factors to serve as markers for monitoring disease progression and as targets for therapeutics.

One important mechanism of epigenetics is DNA methylation, which refers to the presence of chemical tags called methyl groups on DNA. DNA methylation patterns influence whether and how strongly a gene is expressed, and past studies have identified numerous methylation sites that influence the risk of type 1 diabetes. Some of these methylation sites lie within the previously mentioned HLA regions, which is highly relevant to type 1 diabetes. Other methylation sites affect the INS gene, which is second only to the HLA region in terms of influencing the risk of type 1 diabetes.

Another mechanism of epigenetics is chemical modification of histones, which are proteins around which DNA strands are wound. Several studies have reported abnormal histone modification patterns in patients with type 1 diabetes. These modifications may increase the risk of type 1 diabetes by influencing the expression of genes related to inflammation

and immunity, and the elevated blood glucose levels associated with type 1 diabetes may also cause abnormal histone modification patterns.

Epigenetic effects can also be expressed in the form of noncoding RNAs, which are RNA molecules that have functional roles other than the standard role of providing instructions for protein synthesis.

Noncoding RNAs are a diverse class of genetic molecules, and they can bind DNA, other RNA strands, and proteins. Through their various actions, they can promote or suppress the expression of certain genes. Recent studies have yielded evidence that noncoding RNAs can contribute to type 1 diabetes by influencing the immune system and causing β cell dysfunction.

Dr. Wang says, "Given the relationship between epigenetic changes and type 1 diabetes, various epigenetic changes could serve as markers for [disease progression](#) and treatment effects or even as targets for future therapeutics. For example, noncoding RNAs can be measured noninvasively, while changes in DNA methylation levels and patterns for particular genes could indicate that a genetically predisposed person is developing type 1 diabetes." Furthermore, the researchers cite studies that have yielded evidence that drugs that alter DNA methylation could benefit patients with type 1 diabetes.

Dr. Xiong says, "Based on existing literature, it is clear that environmental insult-induced [epigenetic changes](#) modulate the expression of critical genes relevant to the initiation and progression of autoimmunity and β cell destruction and are therefore implicated in the development of type 1 diabetes." This information will be valuable to [medical researchers](#) who wish to develop new ways to predict the onset of type 1 diabetes, assess the condition's severity and progression, and provide patients with effective treatment options.

More information: Jing Zhang et al, Implication of epigenetic factors

in the pathogenesis of type 1 diabetes, *Chinese Medical Journal* (2021).
[DOI: 10.1097/CM9.0000000000001450](https://doi.org/10.1097/CM9.0000000000001450)

Provided by Chinese Medical Journal

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