Diabetes Research

New Methylation Patterns in Type 1 Diabetes Detected

Scientists at Helmholtz Zentrum München have investigated methylation patterns of risk genes for type 1 diabetes. In the 'Journal of Autoimmunity' they report a strong methylation signal in the HLA region, which persists throughout life and leads to correspondingly lower levels of HLA-DR protein. In addition, the authors show that a methylation signal on another gene could potentially serve as a marker of autoimmunity.

Increasingly, the scientific consensus is that not only genes are responsible for the development of diseases, but also what happens around these genes - epigenetics. For example, the attachment of methyl groups to genes, which therefore get read less often, plays an important role in this process. Obviously, this principle also applies to type 1 diabetes, as researchers of the Institute for Diabetes Research (IDF) and the Institute of Computational Biology (ICB) at Helmholtz Zentrum München show in collaboration with researchers from Dresden and the United Kingdom.

For their study, the scientists investigated samples of several prospective type 1 diabetes cohorts. "Generally speaking, it can be said that all 45 of the risk genes we studied for type 1 diabetes showed associations with high methylation rates," explained first author Dr. Alida Kindt. "We were then particularly interested in the methylation of the HLA-DR gene, which is significantly involved in the development of autoimmune diseases."*

The authors found that certain methylations in the HLA-DR region occurred especially in gene variants that indicate an increased risk of type 1 diabetes. "The corresponding pattern was found both in newborns, in toddlers and in adults, and was associated with lower expression of the HLA-DR gene," said Kindt. In addition, the scientists noticed a new methylation signal on the gene for the L-lactate dehydrogenase C chain (LDHC). "This was previously unknown and could potentially be a marker to screen patients for a possible type 1 diabetes risk," said Kindt.

The study was led by Professor Anette-G. Ziegler from the IDF and Ezio Bonifacio, director of the DFG Research Center for Regenerative Therapies (CRTD) at TU Dresden, who comments: "Our research provides new insights into the development of autoimmunity and type 1 diabetes. We had no idea that the genetics underlying type 1 diabetes would be associated with such consistent and profound effects on methylation within the gene. We are particularly interested to see if these effects are at all modifiable by environment and treatment."

Further Information

* The gene HLA-DR (human leukocyte antigen - DR) encodes an MHC class II surface receptor. Its main function is to present to the immune system peptide antigens possibly of foreign origin. This leads to the triggering or suppression of T (helper) cell responses, which eventually lead to the production of antibodies to the antigen.

Background:
Also involved in the research were Jan Krumsiek and Michael Laimighofer from the Institute of Computational Biology (ICB), Jan Knoop, Markus Hippich and Eva-Maria Sedlmeier from the Institute of Diabetes Research (IDF), as well as Tanja Telieps and Rory Wilson from the Institute for Diabetes and Obesity (IDO) and the

Research Unit Molecular Epidemiology (AME). Helmholtz International Fellow John Todd was also involved in the study.

Original Publication:
Kindt, A.S.D. et al. (2017): Allele-specific methylation of type 1 diabetes susceptibility genes. Journal of Autoimmunity, DOI: 10.1016/j.jaut.2017.11.008

The Helmholtz Zentrum München, the German Research Center for Environmental Health, pursues the goal of developing personalized medical approaches for the prevention and therapy of major common diseases such as diabetes and lung diseases. To achieve this, it investigates the interaction of genetics, environmental factors and lifestyle. The Helmholtz Zentrum München is headquartered in Neuherberg in the north of Munich and has about 2,300 staff members. It is a member of the Helmholtz Association, a community of 18 scientific-technical and medical-biological research centers with a total of about 37,000 staff members. www.helmholtz-muenchen.de/en

The Institute of Computational Biology (ICB) develops and applies methods for the model-based description of biological systems, using a data-driven approach by integrating information on multiple scales ranging from single-cell time series to large-scale omics. Given the fast technological advances in molecular biology, the aim is to provide and collaboratively apply innovative tools with experimental groups in order to jointly advance the understanding and treatment of common human diseases. www.helmholtz-muenchen.de/icb

The Institute of Diabetes Research (IDF) focuses on the understanding of the natural history of type 1 diabetes, on the identification of mechanisms and predictive markers of the disease, and the translation of findings into trials to prevent type 1 diabetes in man. In particular, the institute's aim is to develop an immune tolerance using antigen-based therapy. The IDF conducts long-term studies to examine the link between genes, environmental factors and the immune system for the pathogenesis of type 1 diabetes. Findings of the BABYDIAB study, which was established in 1989 as the world's first prospective birth cohort study, identified the first two years of life as being most susceptible for the initiation of type 1 diabetes associated autoimmunity. The Fr1da study is the first population-based approach for the early diagnosis type 1 diabetes associated autoimmunity in childhood. The IDF is part of the Helmholtz Diabetes Center (HDC). www.helmholtz-muenchen.de/en/idf

Scientific Contact:

Prof. Dr. Anette-Gabriele Ziegler
Helmholtz Zentrum München -
German Research Center for Environmental Health
Institute of Diabetes Research
Ingolstädter Landstr. 1
85764 Neuherberg
Tel. +49 89 3187 3405
E-mail