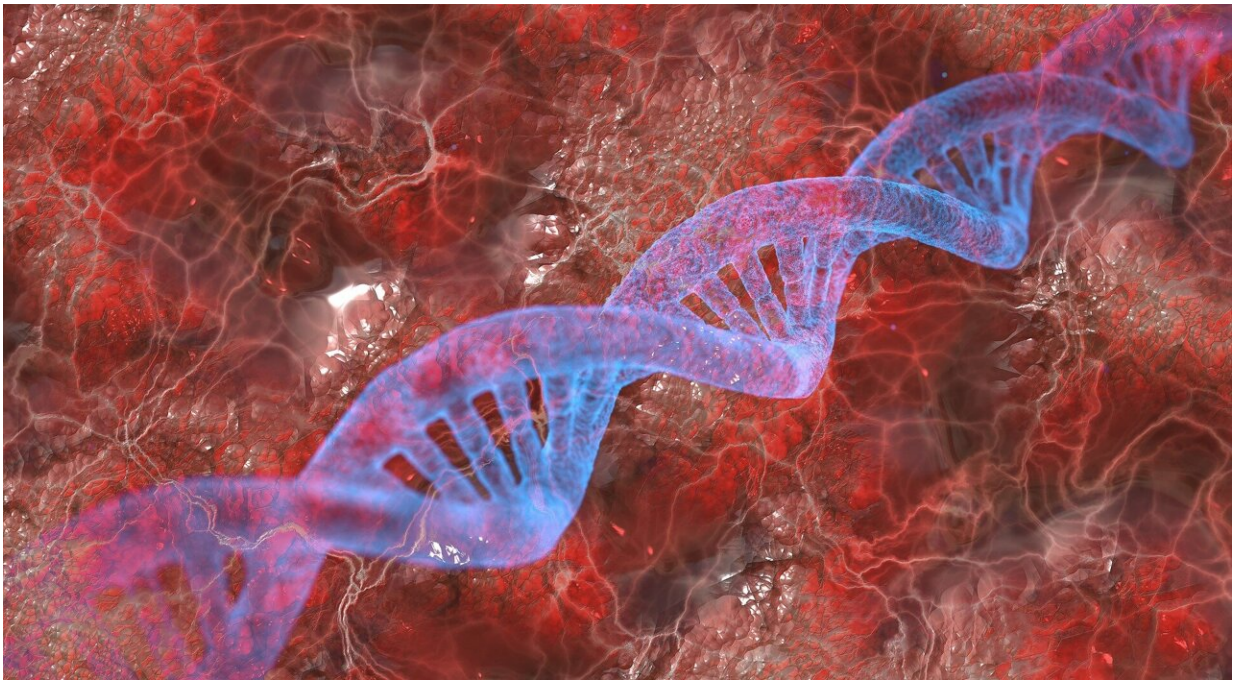
Study links sequence variants to DNA methylation and diseases

July 24 2024



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A new study by scientists at deCODE Genetics shows that sequence variants drive the correlation between DNA methylation and gene expression. The same variants are linked to various diseases and other human traits.

The research is published in the journal *Nature Genetics* under the title

"The correlation between CpG methylation and gene expression is driven by sequence variants."

Nanopore sequencing is a new technology developed by ONT (Oxford Nanopore Technology), that enables us to analyze DNA sequences in real-time. With this technology, DNA molecules are drawn through tiny protein pores, and real-time measurements of electric current indicate which nucleotides in the DNA have passed through the pores. This allows the sequence of nucleotides in the DNA to be read, while also making it possible to detect chemical modifications of the nucleotides from these same measurements.

One such modification is called DNA methylation, thought to be important in determining which genes are used at any given time, and commonly referred to as regulation of gene expression by scientists in the field. Nanopore sequencing technology enables direct measurement of DNA methylation, while also yielding longer reads of DNA sequences than pre-existing technologies have been able to achieve.

These advances offer new opportunities by enabling the measurement of DNA methylation of all CpG sites in the human genome and, as this technology can read long DNA sequences, it is possible to determine DNA methylation on chromosomes from both parents, separately.

In the study, the scientists were able to assign CpG methylation, gene expression and alleles of sequence variants to parental chromosomes, allowing them to investigate correlations among the three sets of measurements on a haplotype level.

The study shows that sequence variants affect DNA methylation, and furthermore, some of these variants can be linked to various diseases as well as other human traits. Importantly, the study shows that the correlation between DNA methylation and gene expression can be

attributed to sequence variants, indicating that these variants are the driving factor.

The majority of sequence variants that have been linked to diseases are found in the noncoding genome, on regions of the genome that do not encode for proteins. For this reason, it has been difficult to understand how noncoding sequence variants lead to diseases.

By studying the effects on DNA methylation, the scientists were able to show that many of these variants correspond to sequence variants that had previously been associated with disease, thereby enabling us to better understand how they lead to the progression of diseases.

More information: The correlation between CpG methylation and gene expression is driven by sequence variants, *Nature Genetics* (2024). DOI: 10.1038/s41588-024-01851-2

Provided by deCODE genetics