

# The secret of DNA methylation

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Methylation refers to a chemical modification of DNA and this modification can occur in millions of positions in the DNA sequence. Until now, scientists believed that this epigenetic phenomenon actively reduced the expression of certain genes. Today, a team of researchers from the University of Geneva (UNIGE), Switzerland, led by Emmanouil Dermitzakis, Louis-Jeantet Professor at the Faculty of Medicine, reveals that this is not always the case and that DNA methylation may play both a passive and active role in gene regulation. The mechanistic relationships between DNA sequence variability and gene expression therefore prove to be more complex and variable than originally assumed.

This discovery, published in the journal *eLife*, highlights the potential risks associated with over-interpreting a correlation rather than a causal link between two variables, especially when it comes to assessing disease [predisposition](#).

The [genome](#) contains many genetic variations responsible for the diversity of living beings and their predisposition to developing certain diseases. Because of these variations, genes may be expressed differently from one individual to another. The same gene may likewise be expressed differently in different cells of a single person. These differences among individuals or cells may be mediated by genetic and/or epigenetic effects. Epigenetics is the chemical modification of DNA and its associated proteins, which may serve as a way for our cells to remember past exposures to [environmental challenges](#) or mediate genetic effects. It, therefore, offers a new way to study the role of the

environment on the expression of our genes.

## Causality vs. correlation

One epigenetic phenomenon, which the team from UNIGE has investigated, is [DNA methylation](#). Until now, scientists believed that DNA methylation actively reduced the expression of certain [genes](#). After having conducted a large-scale study performed on cells from the umbilical cords of 204 [newborns](#), the researchers from UNIGE demonstrate that DNA methylation may play both a passive and active role in [gene regulation](#). Indeed, in some cases, contrary to what was expected, DNA methylation has no impact on gene expression. The mechanistic relationships between DNA variability and gene expression prove to be more complex and variable than previously assumed. It was therefore essential to determine whether a causal link exists between methylation and gene expression, rather than relying on a simple correlation.

"The results of this study shed light on the great complexity of factors that contribute to the physiological differences between people and allow us to better understand how genetic diseases develop," explains Maria Gutierrez-Arcelus, first author of this article and member of the Swiss National Centre of Competence in Research Frontiers in Genetics.

This study highlights the prime importance of determining the causal relationship between biological variables in order to be able to draw reliable conclusions. Correlations are useful when we want to make the assessment of the status of a patient. But it is only with causal relationships that we can make decisions on the relevant medical interventions and expect a predictable and reliable outcome. "Correlation simply allows you to state the facts about someone's health. Causality is the way to actually intervene. It is the difference between stating that a door is locked and having the key to open it", says Emmanouil

Dermitzakis, professor at the University of Geneva Medical School.

The researchers predict that the approach described in their study will pave the way to further develop the modelling of biomedical parameters and large-scale datasets in order to improve biological knowledge and patient outcome.

Provided by University of Geneva

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