Genetic guides to epigenetics

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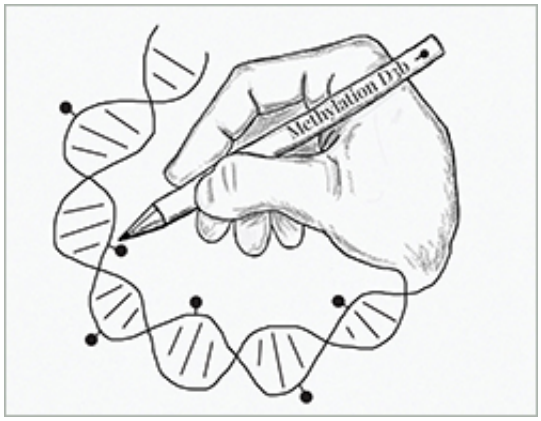

Dirk Schübeler and his group at the Friedrich Miescher Institute for Biomedical Research (FMI) identify determinants that set epigenetic marks along the genome. The new study, published in *Nature*, shows that genetic activity and DNA sequence play a greater role in the regulation of epigenetic marking than previously thought. This questions the popular idea that gene expression can be influenced by external factors via epigenetic marking.

A popular premise of epigenetics is that our experiences can have a lasting influence on the activity of our genes, without altering the DNA sequence. This widely discussed concept proposes that we have the potential to control the epigenetic marking of our genes through our behavior. The appeal of this notion lies in its simplicity: marks placed on our DNA as a result of external factors determine which genes are switched on or off. According to this concept, hunger or stress, a happy childhood, heavy smoking or a healthy diet can influence how genes are regulated. However, convincing evidence for this popular idea is largely lacking.

Researchers at the FMI in Basel have now investigated the mechanisms that underlie the epigenetic marking of the genome. Three enzymes, known as DNA methyltransferases (DNMTs), can tag DNA with methyl groups: in this process, DNMT3A and DNMT3B create new methylation patterns, while DNMT1 ensures that the pattern established is propagated through each cell division.

The team of epigeneticists led by FMI Group Leader and University of Basel Professor Dirk Schübeler, demonstrated how these methylation patterns are established. Lead author Tuncay Baubec comments: "Our studies indicate that the placement of epigenetic modifications follows defined rules. Certain patterns in the DNA sequence together with genetic activity influence where the DNMTs can bind in the genome. This in turn explains the methylation patterns that arise. In this case, one can argue that genes can determine for themselves whether they become methylated or not."

And what about the great potential of epigenetics? Schübeler explains: "The fact that methylation patterns are largely genetically determined does not surprise us. We're glad that we now have a better understanding of the interplay between DNA sequence and methylation. This allows us to recognize where these modifications actually play a role. In addition, methylation patterns are very valuable. For example, in identifying different cell conditions. They are excellent tools for distinguishing different stages of disease, or for monitoring the effectiveness of treatment. But it's time to forget the simple notion that these markings are independent of the underlying DNA sequence."

More information: "Genomic profiling of DNA methyltransferases reveals a role for DNMT3B in genic methylation." *Nature*. 2015 Jan.; DOI: 10.1038/nature14176

"Function and information content of DNA methylation." *Nature* 517, 321–326 (15 January 2015) DOI: 10.1038/nature14192

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