Genomes of identical twins reveal epigenetic changes that may play role in lupus

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Identical twins look the same and are nearly genetically identical, but environmental factors and the resulting cellular changes could cause disease in one sibling and not the other. In a study published online in *Genome Research*, scientists have studied twins discordant for the autoimmune disease lupus, mapping DNA modifications across the genome and shedding light on epigenetic changes that may play a role in the disease.

Because the genetic makeup of monozygotic twins (commonly known as identical twins) is nearly identical, phenotypic traits and heritable diseases are often concordant, manifesting in both siblings. However, some phenotypes and diseases such as autoimmune disease can arise in only one sibling, suggesting other factors such as environment likely play a role in determining phenotypic differences.

Epigenetic modifications, cellular changes that can influence expression of genes, are now widely recognized to influence phenotype and frequently occur in disease. Furthermore, environmental factors such as diet and chemical exposure can change the epigenetic status of genes. Recent research has identified epigenetic modifications at several aberrantly regulated genes in autoimmune diseases such as systemic lupus erythematosus (SLE), and other studies have suggested that epigenetic differences are associated with phenotypic discordance between identical twins.

In this work, researchers from Spain and the United States performed

the first genome-wide high-throughput analysis of a specific epigenetic modification, DNA methylation, in the context of autoimmune disease. Taking advantage of the identical genetic background in monozygotic twins, the group directly compared DNA methylation in healthy twins and twins discordant for autoimmune diseases, including SLE, looking for changes that could be related to pathogenesis in one sibling and not the other.

In the case of SLE, the group found widespread changes in DNA methylation status at a significant number of genes. Dr. Esteban Ballestar, senior author of the study, noted that this is the largest number of genes exhibiting DNA methylation changes observed in an autoimmune disease to date, and includes genes previously implicated in SLE pathogenesis. Importantly, Ballestar's team found that a significant number of the novel differentially methylated genes are related to multiple immune system functions and are potentially linked to SLE.

"Our study suggests that the effect of the environment or differences in lifestyle may leave a molecular mark in key genes for immune function that contributes to the differential onset of the disease in twins," Ballestar said. Most studies of DNA methylation and human disease have been in the context of cancer research, Ballestar noted, and he hopes that this work will attract more researchers to also investigate DNA methylation alterations in autoimmune disease and other disorders for the development of therapies.

More information: Changes in the pattern of DNA methylation associate with twin discordance in systemic lupus erythematosus. Genome Res, doi:10.1101/gr.100289.109

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