

Researchers use new technique to shed light on inherited diseases

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Hehuang Xie and two students at a laboratory bench look at samples.

In 1957, Conrad Waddington published a landmark essay collection that explained a concept he called "the epigenetic landscape."

It described how a cell moves through the process of cellular differentiation, becoming a blood or kidney or heart cell, much like a marble rolling down a mountain. At the time, why or how the cell differentiated and whether it could return to its former undifferentiated

state was poorly understood, although the knowledge could be crucial to solve health problems such as cancer or hereditary diseases.

Hehuang Xie, an associate professor at the Virginia Bioinformatics Institute at Virginia Tech, believes that the answer may be in biochemical process called DNA methylation, as described in a recent paper in *Genome Research*.

Xie tracked potentially important [patterns](#) that may shed light on how cancer and other diseases passed along in families using a novel technique to study methylation across the entire genome.

Researchers have begun to understand that epigenetics play a great role in how traits are expressed and how the developmental history of a cell is passed down.

Epigenetic changes do not occur at the level of DNA sequences but instead alter chromatin—the blocks of protein and DNA that build the chromosomes and direct gene expression in complex organisms. Chromatin changes may be present through generations and could provide clues about inheritance of cancers and other diseases.

DNA methylation, in which a methyl group is added to DNA, is one way in which the expression of genes may be altered.

DNA methylation patterns are heritable, and thus may be a way of tracing how cancers begin since the methylation pattern helps cells differentiate into specific tissues. But the inheritance of methylation patterns has been up until now very hard to track across generations.

Xie is the first to study methylation patterns across the entire genome using a technique called hairpin bisulfite sequencing.

Previously, the technique has only been used to look at specific sequences in a genome to establish whether methylation patterns have been passed from mother to daughter cells. Now, for the first time, Xie has been able to look at entire genomes using next-generation sequencing techniques to monitor DNA methylation inheritance.

"In this study, we integrated hairpin bisulfite sequencing data with various '-omics' data to scrutinize the inheritance of DNA methylation patterns that are difficult to track," Xie said. "We made a number of interesting observations. For instance, accurate methylation inheritance is highly dependent on the binding of specific trans-factors to local sequences. In addition, the genome-wide hairpin bisulfite sequencing technique we developed provides several advantages over traditional strategies for DNA methylation studies and does not add to the cost of sequencing."

The research should lead to greater understanding about certain cancers and environmental factors contributing to them, as well as other influences on the genome that are generally harder to quantify.

More information: The complete study is available online: genome.cshlp.org/content/24/8/1296.full

Provided by Virginia Tech

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