

Identical twins can share more than identical genes

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An international group of researchers has discovered a new phenomenon that occurs in identical twins: independent of their identical genes, they share an additional level of molecular similarity that influences their biological characteristics. The researchers propose a mechanism to explain the extra level of similarity and show that it is associated with risk of cancer in adulthood. The results appear in the journal *Genome Biology*.

"The characteristics of an individual depend not only on [genes](#) inherited from the parents but also on epigenetics, which refers to molecular mechanisms that determine which genes will be turned on or off in different cell types. If we view one's DNA as the computer hardware, epigenetics is the software that determines what the computer can do," said senior author Dr. Robert A. Waterland, associate professor of pediatrics - nutrition at the USDA/ARS Children's Nutrition Research Center and Texas Children's Hospital and of molecular and human genetics at Baylor College of Medicine.

Epigenetics works by adding or removing chemical tags to genes to mark which ones should be used in different cell types. One of the better studied tags, known to play an important role in development and [cancer](#), is the methyl chemical group. Here, in a large group of identical and fraternal twin pairs, Waterland and his colleagues studied a group of genes called metastable epialleles. Previous work indicated that methyl tags are randomly added to metastable epialleles during early embryonic development and maintained throughout life.

"We expected that the patterns of methyl tags added to metastable epialleles would be equally random in identical twins and fraternal twins," Waterland said. "Instead, we found that the methylation patterns matched almost perfectly in identical twins, a degree of similarity that could not be explained by the twins sharing the same DNA. We call this phenomenon 'epigenetic supersimilarity.'"

Identical twins are formed when the very early embryo - essentially a ball of cells - splits into two parts, and each continues to develop into a separate human being. The authors proposed and tested a simple model to explain epigenetic supersimilarity.

"If, in this group of genes, the epigenetic markers are established before the embryo splits into two, then the markers will be the same in both twins," Waterland said. "In essence, both twins inherit an intimate molecular memory of their shared developmental legacy as a single individual. On the other hand, genes at which epigenetic markers are set after the embryo splits can have greater epigenetic differences between the two twins."

Cancer connection

Epigenetic supersimilarity seems to occur in a relatively small group of genes, but, as the researchers discovered, many of these are associated with cancer. To test whether these epigenetic markers might affect risk of cancer, the scientists in Houston teamed up with cancer epidemiologists running the Cancer Council Victoria's Melbourne Collaborative Cohort Study in Melbourne, Australia. Back in the 1990s, this large study was set up to assess different risk factors for cancer.

"By analyzing peripheral blood DNA samples from healthy adults in our study, we have been able to show that methylation at epigenetically supersimilar genes is associated with risk of subsequently developing several types of cancer, including lung, prostate and colorectal cancer," said Dr. Roger Milne, associate professor and head of Cancer Epidemiology at Cancer Council Victoria, and an author on the study.

This study shows that, at the epigenetic level, identical twins are more similar to each other than previously recognized.

"Our findings should prompt a re-evaluation of previous genetic studies on twins," Waterland said. "For decades, researchers have studied genetically [identical twins](#) to estimate what proportion of disease risk is determined by one's genes. To the extent that epigenetic supersimilarity affects risk of disease, as our results indicate, genetic risk estimates based on twin studies have been inflated."

More information: Timothy E. Van Baak et al, Epigenetic supersimilarity of monozygotic twin pairs, *Genome Biology* (2018). [DOI: 10.1186/s13059-017-1374-0](#)

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