

By MELISSA HEALY OCT 08, 2015 | 10:53 AM

For men, new research suggests that clues to sexual orientation may lie not just in the genes, but in the spaces between the DNA, where molecular marks instruct genes when to turn on and off and how strongly to express themselves.

On Thursday, UCLA molecular biologist Tuck C. Ngun reported that in studying the genetic material of 47 pairs of identical male twins, he has identified "epigenetic marks" in nine areas of the human genome that are strongly linked to male homosexuality. In individuals, said Ngun, the presence of these distinct molecular marks can predict homosexuality with an accuracy of close to 70%.

That news, presented at the 2015 meeting of the American Society of Human Genetics on Thursday, may leave the genetically uninitiated scratching their heads.

But experts said the results -- as yet unpublished in a peer-reviewed journal -- offer preliminary new evidence that a man's genetic inheritance is only one influence on his sexual orientation. Through the epigenome, the results suggest, some facet of life experience likely also primes a man for same-sex attraction.

Over a person's lifetime, myriad environmental factors -- nutrition, poverty, a mother's love, education, exposure to toxic chemicals -- all help shape the person he will become.

Researchers working in the young science of epigenetics acknowledge they are unsure just how an individual's epigenome is formed. But they increasingly suspect it is forged, in part, by the stresses and demands of external influences. A set of chemical marks that lies between the genes, the epigenome changes the function of genetic material, turning the human body's roughly 20,000 protein-coding genes on or off in response to the needs of the moment.

While genes rarely change over a lifetime, the epigenome is constantly changing. Geneticists suggest that together, the human genome and its epigenome reflect the interaction of nature and nurture -- both our fixed inheritance and our bodies' flexible responses to the world -- in making us who we are.

Ngun's study of twins doesn't reveal how or when a male takes on the epigenomic marks that distinguish him as homosexual. Many researchers believe that a person's eventual sexual preferences are shaped in the uterus, by hormonal shifts during key stages of fetal brain development.

By imprinting themselves on the epigenome, though, environmental influences may powerfully affect how an individual's genes express themselves over the course of his life. Ngun's findings suggest they may interact with genes to nudge sexual orientation in one direction or the other.

"The relative contributions of biology versus culture and experience in shaping sexual orientation in humans continues to be debated," said University of Maryland pharmacology professor Margaret M. McCarthy, who was not involved in the current study. "But regardless of when, or even how, these epigenetic changes occur," she added, the new research "demonstrates a biological basis to partner preference."

To find the epigenomic markers of male homosexuality, Ngun, a postdoctoral researcher at UCLA's Geffen School of Medicine, combed through the genetic material of 47 sets of identical male twins.

Thirty-seven of those twin sets were pairs in which one was homosexual and the other was heterosexual. In 10 of the pairs studied, both twins identified as homosexual.

In identical twins, DNA is shared and overlaps perfectly. But the existence of twin pairs in which one is homosexual and the other is not offers strong evidence that something other than DNA alone influences sexual orientation. Ngun and his colleagues looked for patterns of DNA methylation -- the chemical process by which the epigenome is encoded -- to identify the missing factor in partner preference.

Their analysis generated a dataset far too large for a team of humans to make sense of. So they unleashed a machine learning algorithm on the data to search for regularities that distinguished the epigenomes of homosexual twin-pairs from twins in which only one was homosexual.

In nine compact regions scattered across the genome, they found patterns of epigenomic differences that would allow a prediction far more accurate than a random guess of an individual's sexual orientation, Ngun reported Thursday.

McCarthy and other experts cautioned that the discovery of epigenomic marks suggestive of homosexuality is a far cry from finding the causes of sexual preference.

The distinctive epigenomic marks observed by Ngun and his colleagues could result from some other biological or lifestyle factor common to homosexual men but unrelated to their sexuality, said University of Utah geneticist Christopher Gregg. They could correlate with homosexuality but have nothing to do with it.

"Epigenetic marks are the consequence of complex interactions between the genetics, development and environment of an individual," said University of Cambridge geneticist Eric Miska. "Simple correlations -- if significant -- of epigenetic marks of an individual with anything from favorite football player to disease risk does not imply a causal relationship or understanding."

One longtime researcher in the field of sexual orientation praised Ngun's use of identical twins as a means of teasing apart the various biological factors that influence the trait.

"Our best guess is that there are genes" that affect a man's sexual orientation "because that's what twin studies suggest," said Northwestern University psychologist J. Michael Bailey, who has explored a range of physiological markers that point to homosexuality's origins in the womb. But the existence of identical twin pairs in which only one is homosexual "conclusively suggest that genes don't explain everything," Bailey added.

While Ngun's research needs to be replicated in larger studies of twins, it advances the fitful process of better understanding how — and when — a boy's sexual orientation develops, Bailey said.