

The link Between DNA Markers on the X Chromosome and Male Sexual Orientation (1993)

In 1993, Dean H. Hamer and colleagues in the US published results from their research that indicated that men with specific genes were more likely to be homosexual than were men without those genes. The study hypothesized that some X chromosomes contain a gene, Xq28, that increases the likelihood of an individual to be homosexual. Prior to those results, researchers had argued that the cause of homosexuality was environmental and that homosexuality could be altered or reversed. Hamer's research suggested a possible genetic cause of homosexuality. The study inspired further research into biological mechanisms of homosexuality.

At the time of the study, Hamer was a researcher at the US National Institutes of Health in Bethesda, Maryland. Hamer had studied human psychological conditions such as addiction and happiness. Stella Hu, Victoria H. L. Magnuson, Nan Hu, and Angela M. L. Pattatucci were Hamer's collaborator at the National Cancer Institute in Bethesda, Maryland, from 1992 to 1995 when Hamer began investigating the genetic causes of homosexuality.

Several other scientists were investigating the cause of homosexuality. In 1991 Simon Levay, at the University of California, San Diego in La Jolla, California, found differences in size for a region of the brain between homosexual and heterosexual men. Scientists had documented size differences between sexes prior to Levay's research, but Levay's results were an early indication of physiological differences between heterosexual and homosexual men. Levay argued that differences in brain sizes between homosexual and heterosexual men could indicate that homosexuality results from genetic factors rather than environmental ones.

Later in 1991 John Michael Bailey, at Northwestern University in Evanston, Illinois, published results about the genetic heritability of homosexuality. Bailey found that both monozygotic and dizygotic twins were more likely to be homosexual than were other related siblings. Since twins share the same DNA, Bailey claimed that the cause of homosexuality was genetical and not environmental. Many people had argued that homosexuality was a result of a diseased or pathological mental state caused by environmental factors. Hamer began investigating the genetics of homosexuality in 1992 after reading Levay and Bailey's reports.

To start the study, Hamer and his team recruited seventy-six homosexual men from the outpatient HIV clinic at the National Institutes of Health Clinical Center, the Whitman-Walker Clinic in Washington, D.C. The team conducted their experiments seven miles away at the National Institutes of Health. The team also recruited a second sample of thirty-eight homosexual brothers, since brothers share much of their DNA, along with their parents or available relatives. Sexual orientation was self-reported and categorized based on the Kinsey scale, a heterosexual-homosexual rating scale that Alfred Kinsey, who worked on human sexuality at Indiana University in Bloomington, Indiana, had developed during the first half of the twentieth century. Hamer and his collaborators noted that although the Kinsey scale rated sexual orientation on a spectrum, the study treated sexual orientation as distinctly two categories, homosexual or heterosexual, to avoid irrelevant or confounding variables in their data. Hamer admitted that while the method of categorizing individuals as either homosexual or heterosexual was overly simplistic, it reliably represented the men in the study.

Based on previous research, Hamer hypothesized that homosexuality was a trait that inherited genetically through the maternal lines. To investigate the maternal inheritance of homosexuality, Hamer and his team analyzed the family tree and DNA of 114 families of homosexual men. Subjects donated blood samples for the DNA analysis and completed questionnaires about personal child-

hood gender identification, childhood and adolescent development, adult sexual behavior, mental health history, and a medical genetic screen.

In their analysis of family trees, the team expected to find a higher percentage of homosexual uncles and cousins on the mother's side of the families. Hamer and his team collected the family histories from the 114 homosexual men recruited. The participants rated the homosexuality of their fathers, sons, brothers, uncles, and male cousins based on the Kinsey rating scale. Researchers then tested the reliability of those ratings by verifying with the relatives of those men the sexual orientations of their family members. The team found higher than average rates of homosexuality in the maternal uncles and cousins of the men studied. The researchers also found a significantly higher rate of homosexuality in maternal relatives compared to paternal relatives, which they cited as evidence that homosexuality may be inherited via the mother's X chromosome. Because their results demonstrated increased rates of homosexuality in maternal uncles and cousins, and because uncles and cousins share inherited DNA with the subjects but were raised in different households, Hamer and his team claimed that this observation favored a genetic cause of homosexuality rather than an environmental one.

To further demonstrate that homosexuality is genetically caused, Hamer and his team then searched for a gene that indicated whether an individual was homosexual. Because males receive their single X chromosomes from their mothers, any genes found on the X chromosome, called X-linked genes, would be passed down from the mother's side of the family. Hamer's team, therefore, investigated genes specific to the X chromosome.

The team prepared DNA samples from the blood donations of all of the participants and their available relatives. The team then analyzed the samples for twenty-two X-linked genetic markers. Genetic markers are sequences within the DNA that can be easily identified. Using DNA linkage, a method used to map the location of genetic markers on a chromosome in relation to each other, Hamer and his team tried to find a common inherited gene to further emphasize the genetic cause for homosexuality.

To find possible genes linked to homosexuality, the team tried to determine if any of the genetic markers were common among the homosexual males. They hypothesized that if they found genetic markers that are within the same region of the X chromosome and are inherited together and commonly among homosexual men, then there were X-linked genes that influenced homosexuality in men. To do so, the researchers used a method called polymerase chain reaction, or PCR. Researchers use PCR to make millions of copies of a particular DNA sequence, in this case the X chromosome markers. The researchers cut DNA samples using enzymes that recognize specific sequences similar to those of the X markers, and then they amplified the DNA using polymerase chain reaction. They then imaged those samples and separated them by size using gel electrophoresis, a method used to visualize and analyze DNA based on their sizes and charges. Each X chromosome marker had a specific associated size and from those specific sizes the researchers could identify exact marker from the gel electrophoresis image of the DNA samples.

The study found several markers clumped within a region of the chromosome labeled as the gene Xq28, a gene at the tip of the X chromosome, as common among homosexual brothers and their homosexual relatives. To see if the gene was inherited, the team used the logarithm of odds scoring method. Scientists use the LOD method to estimate the distances between genes that are close together on the chromosome and are likely inherited together. A LOD score higher than three indicates that the probability that genes are inherited together is a thousand times greater than the probability that genes are not inherited together.

The team found a link of several markers on Xq28 with a LOD score of four, which indicated that because the markers are close to one another, they are likely inherited together. As these markers are found within the gene Xq28, the gene had a high probability of Xq28 gene being inherited along the maternal lineages of homosexual cohorts. Those results, Hamer concluded, are strong evidence that Xq28 contributes to male sexual orientation.

The team published their results in their 1993 article. "A Linkage Between DNA Markers on the X Chromosome and Male Sexual Orientation." Their report received attention from mass media. In 1993, USA Today and Time reported that Hamer and his team demonstrated strong evidence

to support X-linked inheritance of homosexuality and that there existed a genetic component to sexual orientation. The gay community had mixed reviews about the study. Many argued that, while the study could help establish people accept homosexuality as a genetic disposition, others argued that the gay community could be further ostracized if homosexuality became classified as a genetic disease.

In 1995, *Scientific American* published an article about scientific doubts about the genetic influences of homosexuality. A later study duplicated Hamer's study and found no X-linked gene that contributed to male sexual orientation. The researchers of that study agreed with the possibility that homosexuality is genetically inherited, but they found no evidence to justify the claims that Hamer and his team had made that homosexuality was maternally inherited and that the gene Xq28 contributed to homosexuality. After the 1990s, scientists have sometimes questioned that homosexuality is genetically determined and have looked at environmental and behavioral factors instead.

Sources

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