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The Real Story on Gay Genes

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Homing in on the science of homosexuality—and sexuality itself

by Michael Abrams

Some conservatives argue that homosexuality is a personal choice or the result of environmental influences. Some gay rights activists insist that homosexuality is genetic, hoping that proof from that domain will lead to greater acceptance. Still others, backing the same cause, discourage any investigation into the biological origins of sexual orientation, fearful that positive results will lead to attempts to rid the world of potential homosexuals. A handful of scientists, though, are just curious. For them, the discovery of how an individual becomes gay is likely to shed light on how sexuality-related genes build brains, how people of any persuasion are attracted to each other, and perhaps even how homosexuality evolved.

“Who cares about gay men or lesbian women?” asks geneticist Sven Bocklandt of the David Geffen School of Medicine at UCLA. “Sexual selection defines evolution and creation—such a major player in determining society—and we have no idea how it works. This is much larger than the gay gene; it’s about all sexual reproduction.”


Sven Bocklandt of UCLA's medical school studies the DNA of gay and straight male twins.

Image courtesy of Sven Bocklandt

Bocklandt was once a mere science journalist. It was while producing a documentary for Belgian TV that he first met geneticist Dean Hamer. Hamer had just published a study that claimed not only to have finally proved that male homosexuality was at least partially genetic but also to have pinpointed the stretch of chromosome where one of the genes involved resided. Hamer and his colleagues conducted extensive interviews with 76 pairs of gay brothers and their family members and found that homosexuality seemed to be inherited through the maternal line. This led him to compare the X chromosomes—which can be inherited only from the mother—in those same brothers. There he discovered a shared genetic marker, a patch of DNA called Xq28. Interviews with the subjects also revealed them to be either gay or straight. (In this respect, men are entirely different from women. Studies have shown that women respond to all types of sexual depictions—not only heterosexual and homosexual images but even those of chimpanzees having sex.)

The interview with Hamer fascinated Bocklandt. Not long after, he quit his job and moved to Washington, D.C., to work with Hamer. There he did research on the X chromosome, with hopes of someday finding the gay gene or genes themselves.

Fourteen years later, neither Bocklandt nor any other researcher has pinpointed the precise base pairs that might turn a man gay. Part of this is due to the politics of funding for sex research. For a long period NIH grant proposals that included words like “gay,” “condom,” or even “sexuality” were turned down, much to the ire of researchers like Hamer. Shortly after he published his gay brothers study, Hamer completed a similarly designed family study looking into a genetic cause for a certain kind of anxiety. Since then there have been more than 400 independent studies looking into those genes. There have been no such studies for the gay gene.

It is not clear if Hamer and his team found the locus of the genetic code that causes men to memorize lines from *A Star Is Born*. Although a follow-up study by the team replicated their findings, a study by George Rice, a neuroscientist at the University of Western Ontario, refuted Hamer's findings completely. In addition, two other researchers told me they don't consider Hamer's study valid. Yet Hamer contends that his results suggest there is a link to Xq28 and that the Rice study was biased because one of the coauthors told Hamer that he didn't believe a gay gene could exist. Hamer also says that, if read correctly, the two other studies confirm his findings. "They didn't even look at the entire X chromosome," says Hamer. "They gave up immediately." For laymen, science journalists, and researchers alike, the question remains unresolved.

Whether or not a gay gene, a set of gay genes, or some other biological mechanism is ever found, one thing is clear: The environment a child grows up in has nothing to do with what makes most gay men gay. Two of the most convincing studies have proved conclusively that sexual orientation in men has a genetic cause.

William Reiner, a psychiatrist at the University of Oklahoma Health Sciences Center, explored the question of environmental influences on sexuality with a group that had been surgically shifted from boys to girls. These boys had been born with certain genital deformities; because it is easier to fashion a vagina than a penis, the boys were surgically made into girls at birth. In many cases they were raised as girls, kept in the dark about the surgery, and thought themselves female long into adulthood. Invariably, Reiner found that the faux females ended up being attracted to women. If societal nudging was what made men gay, at least one of these boys should have grown up to be attracted to men. There is no documented case of that happening.

The second study was an examination of twins by psychologist Michael Bailey of Northwestern University. Among identical twins, he found that if one was gay, the other had a 50 percent chance of also being gay. Among fraternal twins, who do not share the same DNA, there was only a 20 percent chance.

At first glance, those results seem to suggest that at least some homosexuality must not be genetic. Identical twins have the same genes, right? How could one turn out gay and the other not gay as often as 50 percent of the time? There are many other traits that are not always the same in identical twins, however, like eye color and fingerprints. The interesting question is, how do any of these major differences arise between two products of the same code?

The solution to that question is exactly what Bocklandt is trying to find. By looking not at DNA but at where DNA is switched off, he hopes to find the true genetic seat of homosexuality. Hamer looked at broad regions of chromosomes using genetic markers, a low-resolution result that tells little more than "something's going on somewhere around here." Bocklandt is hoping to look with a much stronger magnifying glass at the areas Hamer's research highlighted. If he succeeds, it will be a triumph not only for the genetics of homosexuality but also for genetic research in general.

Bocklandt has collected DNA from two groups of 15 pairs of identical twins. In one group, both twins are gay. In the second, one twin is gay, and the other is straight. Identical twins have the same DNA, but the activity of their genes isn't necessarily the same. The reason is something called methylation.

Methylation turns off certain sections of genetic code. So even though we inherit two copies of every gene—one from our mother, one from our father—whether the gene is methylated often determines which of the two genes will be turned on. Methylation is inherited, just as DNA is. But unlike DNA, which has an enzyme that proofreads both the original and the copy to minimize errors, methylation has no built-in checks. It can change from one generation to the next and may be influenced by diet or environment. It's in this mutability that Bocklandt hopes to find the secret, by seeing which flipped genetic switches correlate with homosexuality.

"For each pair we expect to see a whole lot of things that are random—sometimes someone smoked, or medication was used for long periods of time," Bocklandt says. "But basically we compare the gay results with the straight ones and see if any region shows up multiple times for these subjects."

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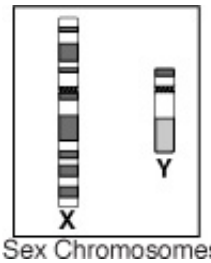
Bocklandt is quick to point out that most likely there is no single "gay gene"—no single switch for sexual orientation. Instead, there are probably a handful of genes that work in ways as yet unexplained. Still, he is confident that the genes involved are few enough that he can find them. Although sexual attraction between humans has its frills—the social dances, the fetishes, the preferred body types—it is still pretty fundamental. "If you're breeding pigs, you can buy a little spray—spray it on a female and it will stand still as if it's having sex," Bocklandt says. "There's nothing like that for humans. Obviously, the behavior is complex—there's phone sex and of course porn—but genetically it's simple. There are limits to what you can code on a genome." He thinks it is likely that perhaps 5 to 15 genes explain sexual orientation in most people.

Ideally, Bocklandt would scan the genome of each individual, looking for a methylation pattern anywhere on any chromosome that shows up repeatedly in the gay member of each twin pair. Unfortunately, at the moment it costs about $10 million a person to map out every base pair of the 46 chromosomes, so Bocklandt is looking only where he suspects to unearth genetic gold. If he finds a pattern, then he will look at the DNA beneath the methylation.



Sex Chromosomes Sex-determining chromosomes

Image courtesy of the National Institute of Health

Actually, the whole genome can be mapped for less than $10 million if you are willing to forfeit the high degree of resolution Bocklandt is after. Alan Sanders, an associate professor of psychiatry at Northwestern, will be looking at the whole genome of about 1,000 gay brothers using the genetic marker technique that Hamer used. A sample that big should eliminate the statistical weaknesses that plagued Hamer. “There are a number of things that go into trying to figure out how much statistical power you have, but the only one that’s in your control is sample size—the bigger the better,” says Sanders. “So that’s what we’re doing.”

For several years Sanders has been collecting DNA from blood or saliva samples from families with two or more gay brothers. In addition to requesting their spit, Sanders’s team asks each individual a set of questions similar to those Hamer used in his study. Then he begins looking at the men’s chromosomal markers to see if the brothers are more similar than what chance would predict. Wherever there is a significant increase in sharing, Sanders plans to look at the genes that can be found near that particular marker. (When two brothers come from the same mother and father, about 50 percent of their genes should be identical.) Not only is the sample size bigger than Hamer’s, but there are now far more genetic markers available, allowing Sanders to zero in on specific genes much faster.

By setting up a stand at Gay Pride parades and approaching “gay friendly” groups like PFLAG (Parents, Families and Friends of Lesbians and Gays), Sanders has found more than 4,000 gay men with a brother who are interested in participating. He has already started mapping the first 500 and estimates that by mid-2008 the world will know where—if anywhere—to find the gay gene.

“We definitely should be able to put to rest one way or another whether the Xq28 finding is replicable,” says Sanders. “We should be able to address that to anyone’s satisfaction.”

The question of whether there is a gay gene—and if so, where it resides—is hardly the only question about sexual orientation that remains unanswered. If either Bocklandt or Sanders is lucky enough to spot the genes responsible for homosexuality, there will most likely be more questions raised than answered. “Frankly, the biggest problem of the genetic possibilities is the evolutionary problem,” says Michael Bailey, the researcher who found that women get turned on by anything, who is now working with Sanders. “And I don’t think that Dean [Hamer] has taken that problem seriously enough.” Men who like men are obviously less likely to procreate. Even if social pressures through the ages led some gay men to have some children, the significantly lower rate of reproduction would eventually lead to the disappearance of the gene (as Hamer does note in his book, *The Science of Desire: The Search for the Gay Gene and the Biology of Behavior*).

Possible explanations abound, but an ingenious one was recently put to the test. Perhaps, the theory goes, some genes, when found in men, make them more likely to be gay and when found in women make them more likely to have children. (“Fecund” is the word the researchers use.) The increased number of grandchildren that a parent might have through such a superfertile daughter would offset whatever loss of genetic posterity comes from having a gay son.

How such a gene might work is anyone’s guess. Perhaps the gene simply increases attraction to men, so a male with the gene comes out liking men, and a female with the gene comes out really liking men. Whatever the mechanism, it turns out that an Italian study found that women with gay family members have more children than women with all straight relatives. Andrea Camperio-Ciani, a professor of ethology and evolutionary psychology at the University of Padua, interviewed 98 gay men and 100 straight men and found that the mothers of gay men had an average of 2.7 children, while the mothers of straight men averaged 2.3.

That study has been criticized in some circles for the same old reason: The sample size was not big enough. But the man with the generous sample size hopes to answer that question too. “We’ll look at the offspring of female relatives of gay men—especially of sisters. How many do they have compared to the relatives of straight men?” asks Sanders. “We’re also trying to replicate that.”

Another way to pass on the seemingly nonreproducing gay gene would be for a nonreproducing gay man to have an extra interest

in seeing that the offspring of his siblings survive. Biologist E. O. Wilson first put forward this idea of kin selection as an explanation for homosexuality in 1978, but for some time now it has been considered an unlikely scenario.

Michael Bailey conducted a study in 2001 to find out if gay uncles treat their nephews and nieces any better than straight uncles treat theirs. They did not. Thinking that Bailey did not control for the income level of the uncles surveyed—richer uncles tend to be more generous—Qazi Rahman, a professor of psychobiology at the University of East London, tried to replicate the study in England. In addition to looking at how they spent their money, Rahman tried to see if gay men had some kind of extra psychological generosity by asking questions like, “Assuming you had a million pounds, would you buy gifts for your family?” Again, Rahman found no difference between straight and gay men. He admits that looking at “presents and stuff” might seem a crude measure for an adaptation that was selected for thousands of years ago, but he sees no other way that such an impulse would manifest itself today.

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But 21st-century Western society, and the homosexuals therein, could be something of an anomaly in human history, according to Paul Vasey, an associate professor of psychology at the University of Lethbridge in Alberta. “Do I think the social contexts are less representative of our evolutionary past? I’d say yes,” Vasey says. “The kind of gay men and lesbian women we are familiar with in Western culture express their homosexuality as egalitarian—they’re not differentiated as far as gender.” In other times and other places, one partner typically adopts a masculine role, while the other adopts the feminine. Another problem with kinship selection studies that look only in England and, in particular, the United States, is that kinship ties for homosexuals might not be as strong as they would be elsewhere. “The United States is profoundly homophobic,” says Vasey, “so you can’t be directing altruism at your family members if they’ve kicked you out and you’ve moved to the other side of the country.”

Vasey has therefore been studying a group of Samoans called fa’afafine, whom he describes as more of a third sex than homosexual as commonly construed. These men, who grow up to dress and act like women and are extremely integrated into their society, would be offended to find themselves described as homosexual. They don’t have sex with each other, and because their appearance isn’t masculine, they don’t consider themselves men who sleep with other men. In an initial study, Vasey found that the fa’afafine do exhibit heightened avuncular tendencies with their nieces and nephews. “They babysit, they teach them about the culture, they give them money,” he says. To make sure that these traits do not merely reflect a more general fondness for all children, Vasey will soon head back to Samoa to refine and, with luck, replicate the study.

To put the kibosh on the idea that the evolution of a gay gene presents an unsolvable conundrum, Sergey Gavrilets, a theoretical evolutionary biologist at the University of Tennessee, developed a mathematical model of how a set of what he calls “sexually antagonistic” genes might evolve. “Sexuality can be explained as one example of sexual conflict—there may be genes that are beneficial for one sex but detrimental for the other,” he says. He didn’t put kin selection into the equation. (“I don’t think it works, because if you have zero children and compensate for the loss by helping someone else, that help would have to be extremely efficient.”) But he did include Camperio-Ciani’s results and also assumed that gay genes would be passed down on the mother’s side, on the X chromosome, as indicated by Hamer.

The model shows that over centuries an effect you might call the homophobe’s paradox has been at work on the human genome: The more intolerant the society, the more likely it is to maintain gay genes. If a society’s conventions keep homosexuals in the closet, then they will be more likely to conform, get married, and have children. This is especially true if gay genes are also responsible for making women more fecund. Imagine, for instance, that for every extra child that such a gay gene–carrying woman has, a gay man can have one fewer and the balance necessary for the survival of the gene is still maintained. The more children he has, thanks to what his contemporaries demand of him, the less evolutionary pressure there is for his female counterpart to have more. “As a society becomes more intolerant, there’s more pressure to have offspring,” says Gavrilets. “The real [evolutionary] cost of being homosexual isn’t too big if you’re forced to have kids.” On the other hand, the more tolerant the society, the more gay men can be free to be who they are, so the more likely they will be childless—and the more difficult it will be for any female in the family to make up for the loss.

“Bullshit,” says Bocklandt. “A mathematical model is a nice exercise, a mental masturbation about how these things could work, but it makes better sense to do that once we know a bit more. One of the problems that none of the mathematical models take into account is that we have no idea what it meant to be gay 10,000 years ago. We have some idea what it meant 200 years ago but not 10,000.”

It is also becoming increasingly clear that gay genes are not the only biological factor that influences homosexuality. Some homosexual men appear to have their sexuality oriented not by their DNA but by the environment they experienced in the womb. Ray Blanchard, a psychiatric researcher at the University of Toronto, found in 1996 that men with older brothers were more likely to be gay than those without. His study showed that for every older brother a man has, his odds of being gay go up by 33 percent. If the likelihood that a couple’s first son will be gay is 2 percent (a reasonable guess), Blanchard says, the probability that the 5th son will be gay is only 6 percent. But if some poor woman has 14 sons, the 15th would have a 50 percent chance of being gay.

> The more intolerant the society, the more likely it is to maintain gay genes. The real evolutionary cost of being homosexual isn't too big if you're forced to have kids.

Blanchard's discovery has been replicated more than 20 times. Most recently, in 2006, psychologist Tony Bogaert of Brock University in Ontario quashed the possibility that the older-brother effect results from boys having been teased, beaten, or otherwise affected by their older brothers. Bogaert collected data from gay and heterosexual men who grew up in nonbiological families—in most cases, either adopted or raised in "blended" families. "This allowed me to really pit biological versus nonbiological explanations against each other," Bogaert says. The statistics came back the same as they had in previous studies. "It's not the brother you lived with; it's the environment within the same womb—sharing the same mom."

The older-brother effect accounts for about 15 to 30 percent of gay men, Blanchard estimates. How sharing a biological mother could induce homosexuality in men remains pure guesswork, however. Bogaert and Blanchard hypothesize that with each male child the mother develops an immunity to certain male-specific proteins, like molecules relating to the Y chromosome. Perhaps her body sees them as foreign and mounts an immune attack, which might alter certain structures of the male brain.

Whatever the cause of homosexuality, be it genetic, hormonal, or even sociological, the result is a change somewhere in the brain. Simon LeVay, once a neurobiologist at the Salk Institute, thought he found that part of the brain in 1991. Comparing the gray matter in the cadavers of gay and straight men, he found that an area in the anterior hypothalamus known as INAH-3 was smaller in gay men, about the size it is in women. A study by William Byne of the Mount Sinai School of Medicine in New York City turned up similar results.

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Michael Baum, a biologist at Boston University, got a more detailed look by studying ferrets, whose biology is well understood. He has shown that the anterior hypothalamuses of gay and straight ferrets—as well as of male and female ferrets—are also of different sizes. The structural distinctions have clear behavioral consequences. Ferrets find their mates primarily by odor. Using a "reporter gene," Baum proved that a receptor in the anterior hypothalamus responds differently to the same odor depending on the sex of the ferret. Creating a lesion in that part of the brain can make a male ferret approach other males. Baum also finds that administering the right steroids early in life can reverse the animals' sex response: Female ferrets dosed with testosterone early in life act masculine.

Odor does not affect us as much as it does ferrets, but that is not to say that odor doesn't influence our sexual response. Ivanka Savic Berglund, a neuroscientist at the Karolinska Institute in Stockholm, put gay men, straight men, and women in a PET scanner (not all at the same time) and watched how their anterior hypothalamus lit up when presented with an odor similar to one found in men's sweat and one similar to a scent found in women's urine. The gay men's brains responded the way the women's brains did. "I was so pleased when I saw the paper—it kind of made my day," says Baum. "But I think it would have been great if she had used real sweat."

So is brain development the final frontier for seeking the source of homosexuality? "At first blush you might think, 'Well, gosh, maybe gay men didn't get enough testosterone early in life," says Marc Breedlove, a neuroscience professor at Michigan State University. "But as we find markers that should tell us about prenatal testosterone, they haven't shown a consistent pattern." Such studies are puzzling for Breedlove, who has spent much of his career proving that for animals things really are that simple. Castrated male rats given ovarian steroids as adults go straight for other male rats, while others given testosterone still flirt with females (however futile their propositions). "We can cause animals to be as masculine or feminine as we want by manipulating their exposure to testosterone," he says. "If I take a female rat pup and I give her just one dose of testosterone, in a few hours that testosterone is gone, and yet for the rest of her life she's masculine."

Lab rats are easier to manipulate than people, however. "I love my rats," says Breedlove, "but they're not very complicated." Apparently, humans are unlike the rest of the animal kingdom. Still, low testosterone or high testosterone could up the chance that a boy would grow up to be gay. No experiment has yet ruled that out.

If researchers do prove that testosterone can alter human sexual orientation—gay gene or no gay gene—the possibility of preventing homosexuality will become a reality. Even a hint of that option is enough to provoke an outcry among activists. Recently word got out that Charles Roselli, a physiologist at Oregon Health and Science University, was trying to find out how hormones affect the brains of gay sheep. PETA roped tennis star and lesbian activist Martina Navratilova into writing a letter to the university, calling the research homophobic and cruel. She accused the researchers of trying to find a "prenatal treatment for various sexual conditions."

What drives the sex researchers (some of whom are openly gay) is most often pure curiosity. They just want to know. "People whose motivations are political don't comprehend that anyone could be interested in why," says Ray Blanchard. And that why isn't just a why for homosexuality but a why for sexuality, period.

"I can't focus enough on how these are not gay genes—these are straight genes," Bocklandt says. "If you want to find a gene that makes you see colors, you compare the genes of people who see colors with the genes of people who are color-blind. They're not genes for color blindness. What we're talking about here is the most basic thing, the most basic question. Why does a crocodile recognize the opposite sex and want to f**k?"