Genetics& Society
Garriga lecture notes 3/11/09

Sex and behavior; Using Y to study history

Human gender identity and sexual orientation
Much less is known about how sexual behavior is regulated in humans than in the animals that we discussed. Besides being an interesting question, another reason for determining how we develop our gender identity and sexual orientation is to help parents with children that are intersexual, having genitalia that have both male and female characteristics. Should those children be allowed to decide if any intervention is attempted when they become older? Or should parents try to shape the outcome by raising the child as a boy or girl and use surgery and hormone treatments to reinforce the chosen path. In the past many psychologists believed that children were plastic when it came to gender identity and sexual orientation. They believed that the social environment could shape the sexual identity of the child and biology had little to do with whether a child identified with being a girl or boy.

The prevailing views on gender identity and sexual orientation have changed, and current thinking emphasizes biology with genes and hormones shaping the sexual behavior of humans. We will consider two areas where biology is thought to be important: brain structure and genetics.

Brain Structure: Regions of the hypothalamus, a part of the brain that connects the pituitary gland to other brain regions, are sexually dimorphic. Groups of neurons known as nuclei in the hypothalamus are different in size in men and women. One region known as INAH3 for interstitual nucleus of the anterior hypothalamus 3 is larger in men than in women. (In rats some of the regions of the brain that are larger in males are known to shrink in size in newborn females because the cells die in the absence of androgens. Why the INAH3 is larger in men is not known.) In 1991, Simon LeVay published a paper showing that while heterosexual men have a larger INAH3, homosexual men have a smaller INAH3, comparable to the size in women. One interesting interpretation of this finding is that this region controls sexual orientation. It is also possible that this region is smaller because these men are homosexuals.

Genetics: Genetics studies of humans often begin with twin studies. Identical twins are genetically identical. So if there is a genetic component to a particular trait, then identical twins should share that trait more often two people that are identical twins. Siblings and relatives should also share the trait more often than unrelated individuals. Twin studies show that when one identical twin is homosexual, the other twin is much more likely to be gay. When a man or women is gay, there is also an increased frequency that that individual's siblings will be gay compared to the general population. One interesting observation is that these effects are sex specific. Being a lesbian does not affect the likelihood of your brothers being gay, and being gay does not affect the likelihood of your sisters being lesbian. The interpretation is that the genes involved in homosexuality are sex specific.

In 1993, Dean Hamer published a genetic study that suggested a gene on the X chromosome affected the likelihood that a man would be gay. Studying the families of gay men, Hamer found that brothers, maternal male cousins and maternal uncles had an increased probability of being gay. What these men can share that are not shared by paternal cousins and uncles are an X chromosomes. (You should look at the pedigree in the slides and understand why this is true.) This observation suggests that as allele or alleles on the X chromosome can influence the likelihood that men will become gay. Studying brothers of where two brothers are gay, Hamer looked at DNA polymorphisms at various positions along the X chromosomes to see if they were associated in the two gay brothers. If an allele of a gene influences the likelihood that a man will be gay, a polymorphism linked to that allele will be represented more often in brothers that are gay. A polymorphism the region of the X chromosome known as Xq28. Random brothers have the same polymorphism 50% of the time and different polymorphisms 50% of the time, the expected result. But gay brothers have the same polymorphism about 80% of the time, consistent with a gene in this region influencing whether a man is gay. This is a interesting result, but other investigators have not been able to repeat the finding.

The conclusion from these studies is genes are likely to influence a person's sexual orientation, but the number and identity of the genes are unknown. Maybe not surprising, the genetics of sexual orientation is probably complex.

Using Y to study history

We began our sojourn into the role that genetics has recently played in the study of human history. The next couple of lectures will focus on two chromosomes that have been instrumental in studying human migrations and evolution, the Y chromosome and the mitochondrial chromosome. We will start with the Y chromosome and focus on a bit of American history that involved Thomas Jefferson.

Advantages of using the Y: Unlike autosomes or the X chromosome, crossing over does not scramble the relationship between alleles on the X chromosome. When determining paternity, the DNA of the child, mother and putative father are compared. Let's say that we amplify a specific position on chromosome 1 by PCR and find that the child has two sized PCR products of 100 and 120 base pairs and that the mother has two sized products of 100 and 110. We can conclude that the child inherited this part of chromosome 1 represented by the 100 base pair product from her mother and the other, the 120 base pair product, from her father. If the man accused of being the father doesn't have a 120 base pair product in this assay, then he is not the father. If he does, he could be the father. The more regions of the chromosomes tested that show that the accused man could be the father, the more likely that he is the father. When many chromosome positions are tested and match, we can be almost certain that the man is the father. This works great when we have the DNA from the two parents and the child. This does not work over generations because we do not have the DNA from all of the people involved. One advantage of the Y chromosome is that it is passed down from father to son, so we know that any PCR products amplified from part of my Y chromosome, for example, would be the same as those of my father Maurice Garriga, my paternal grandfather Francisco Garriga, my

paternal great grandfather Unknown-to-me Garriga, etc's. That, of course, is only true if there were no non-Garrigas lurking around my ancestral womenfolk. Ignoring this worrisome qualification, I also know that my father's brother, Carlos Garriga, and his son, Frank Garriga, would have the same PCR product as me. What is even more useful is this is true for all parts of our Y chromosome. Crossing over, which reshuffles alleles at each meiosis, does not affect the Y chromosome because the sequences on the Y are not shared with the X chromosome (other than at the ends). In males, the X and Y pair in meiosis 1, but crossing over only occurs at the ends in the pseudoautosomal region. So in my case, my Y chromosome was inherited like my last name—that was the point of all those Garrigas. All of my ancestors with the name Garriga have the same Y chromosome. All of those male ancestors with different last names had a different Y chromosome. We will talk bout how this was used to ask whether the children of Sally Hemings, a slave at Monticello, could have been fathered by the third president of the United States, Thomas Jefferson.