The Role of the MHC in Mate Selection

Excerpted from: Love with the Proper Stranger, by Meredith F. Small
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What draws people of the opposite sex together? Biologists have a general answer – we are members of a sexually reproducing species and need to join up with someone of the opposite sex to mate, conceive offspring, and pass our genes on to the next generation. But what scientists cannot yet fully explain is why people are attracted to particular members of the opposite sex. Why that man and not another; why that woman and not her friend?

Recent research combining genetics and behavior suggests there may be a hidden agenda at work. It looks as if we may avoid prospective mates who are too similar to us in the genes that drive the immune system. And data that may explain some of the basics of human attraction and mating are coming from a very special group of people – the Hutterites, a closed religious sect in which people marry young, stay married for life, and value fidelity.

In a nation that is commonly likened to an ethnic melting pot, the Hutterite communities have remained remarkably homogeneous. Every Hutterite can trace his or her ancestry to the 400 or so members of the Anabaptist sect who migrated from Europe to the United States in the 1870s to escape religious persecution. The founders settled on three communal farms in South Dakota. Today, the Hutterites, more than 35,000 strong, are spread across the northern United States, as well as western Canada, in 350 colonies.

From a population geneticist's point of view, the Hutterites are ideal research subjects. The 400 original settlers themselves were closely related. They are believed to have descended from about 90 individuals. Written genealogies go back nearly 16 generations. The rules of Hutterite culture, which include within-group marriage as well as lifelong fidelity, prevent the usual shenanigans responsible for the exchange of genes across geographic, ethnic, racial and religious borders. As a result, the Hutterites are relatively inbred. In addition, they are highly fertile (with an average family size of nine) and do not practice birth control, allowing a geneticist to get a picture of how genes are passed along under "natural" conditions.

In the late 1950s, biologist Arthur Steinberg, and his colleagues at Case Western Reserve University, began visiting the Hutterites for an extensive project that included measuring people, checking their health (administering EKGs, for example, and testing cholesterol levels), drawing blood for genetic studies, and, most important for analysis, recording genealogies. They visited most of the colonies and developed a priceless bank of information about the population. In the 1970s, these data were handed down to Alice Martin of Northwestern University Medical School, who in turn passed them on to Carole Ober, a geneticist with anthropological training now working in the Department of Human Genetics at the University of Chicago. In 1982, Ober began a long-term project on one of the original lineages, focusing on 31 of the 44 colonies in South Dakota.

Ober's main interest is a genetic system found in all vertebrates; the major histocompatibility complex, or MHC (known in humans as human leukocyte antigen system, or HLA), and its effect on fertility and mating. ... Ober found that fetal loss increased significantly when Hutterite parents shared all the genes of the HLA system, or just genes in the HLA-B region. Ober is quick to say that, at this stage in the research, we cannot declare with certainty that the HLA genes themselves – and not some other genes found in the same region on the chromosome – interfere with fertility, but since pregnancy is essentially an intrusion by foreign tissue, HLA is probably involved. If natural selection is operating so strongly during reproduction, organisms should be "designed" to avoid the fetal wastage that comes with shared HLA genes. But how?

In the late 1970s, Kunio Yamazaki and colleagues observed that inbred laboratory mice were more likely to mate with mice having dissimilar MHC genes. Working with mice in a more natural setting (outdoor pens that gave the animals considerably more freedom to move about and interact), Wayne Potts, now at the University of Utah, confirmed Yamazaki's findings. The first generation of offspring in his mouse colony produced far fewer pups carrying matching MHC regions than might be expected if the parents were mating at random.

In some of his experiments, Yamazaki, now at the Monell Chemical Senses Center in Philadelphia, placed newborn male mice with foster mothers of a different MHC strain. He noted that when the time came for these males to choose mates, they avoided females whose MHC genes were similar to their foster mothers', even when that meant winding up in the position of mating with a female whose MHC genes were similar to their own. In other words, exposure during development, rather than some innate MHC mate-choice program, appears to be at work.

These startling results suggested that animals might somehow be able to detect prospective mates whose MHC genes are more or less similar to their own, and then to choose mates accordingly. They may have evolved such an ability because of MHC's importance in the immune system, or simply because MHC sensibility is a way to distinguish relatives from non-relatives, thus avoiding inbreeding. To find out, scientists have shifted their studies of mate choice from the more traditional variables of outward appearance, to the realm of genetics.

Inspired by the mouse studies, Ober launched a project on mate choice in the Hutterites in 1992. Hutterites go about finding mates as most people do – by socializing. After graduating from high school, young adults travel with their parents to other colonies. ... These social gatherings are opportunities for young people to interact and are the way that most Hutterites meet their spouses. Most marry in their early twenties, after a year of courtship. The same colonies tend to exchange visits over and over, resulting in a history of marriages between particular colonies, and even particular families. In fact, 20 percent of Ober's sample were "double" marriages, with two or more siblings from one family married to siblings from another.

After genetically typing 411 couples, Ober discovered that, in this inbred popoulation, where there is a much higher likelihood of falling in love with someone carrying a similar haplotype, spouses shared fewer HLA genes than expected. Ober traced HLA inheritance further and found that when a husband and wife did have a matching strand, the set of genes in question most often came from the paternal side, for both the wife and the husband. In other words, men and women appear to have avoided finding a mate with HLA genes that resembled their mother's. It did not seem to matter if their partner had genes like their father's. As in mice, people may somehow imprint on their mother's HLA and then be drawn to someone with genes different from hers.

But how do people, or mice for that matter, know who is who in the first place? Research on mice, rats, and even humans has implicated smell as a possible cue for distinguishing MHC/HLA genes. Mice and rats, researchers have shown, can easily distinguish the urine and body odor of fellow creatures caged in the same way, fed the same food, and bred to be genetically identical in all but their MHC genes. Remarkably, research has also shown that humans can smell the difference in body odor, urine, and feces among mice of various MHC types.

A controversial finding, published in 1995, suggests that the sense of smell also plays a role in human mate choice. Claus Wedekind, and colleagues at the University of Bern, presented women with T-shirts imbued with the body scent of men with various HLA haplotypes. The women (who were not taking birth control pills and were in the middle of their menstrual cycle, and thus at their most fertile) preferred the T-shirts of men with HLA haplotypes unlike their own. The women also tagged these T-shirts as smelling like their current partners, suggesting that odor has something to do with their real-world mate choices. (Interesting, women who were taking the pill – which simulates pregnancy – preferred T-shirts of men with HLAs like their own.)

Rachel Herz and Elizabeth Cahill, also at Monell Chemical Senses Center, would not be surprised to find that women attempt to sniff out a genetically proper mate. Surveying both sexes about which senses are important, they found that "for females, how someone smells is the single most important variable" in choosing a lover. If odor does provide information about the immune system, it makes evolutionary sense for women to pay attention to smell. They have much to lose if they mate with an inappropriate male and give birth to a baby with a reduced ability to fight off disease.

But unlike mice, humans – as primates – rely mostly on vision, not smell, to navigate through life. Perhaps other sensory cues – embedded in facial features or body shape, for example – alert us to the hidden genes in potential partners. However, if those cues are there, Ober and other researchers have yet to discover them.

During our ancient hunter-gatherer days, when humans lived in small bands separated by great distances, finding a mate with a different set of HLA genes and producing children with immunologic advantages may have been critical to survival. At this point in human history, with our restless, globe-trotting populations and relatively unlimited number of possible mates, we are unlikely, even across a crowded room, to spy someone with the same HLA haplotype. But even if we did, as the Hutterites have demonstrated, our genes would probably compel us to look the other way.