Sexual Evolution: From X to Y

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http://www.hhmi.org/biointeractive/gender/index.html

It's not much to look at. Under a microscope, the Y chromosome is a tiny rod only one-third the size of all the other human chromosomes, including its partner, the X. But for a puny scrap of genetic material, the Y chromosome packs a real biological wallop. It sets in motion the development of everything needed to make a male—directing the production of not just the proper external equipment but also the internal accessory organs and a trillion or so sperm.

But the Y chromosome, as important as it is for sex determination, didn't always exist. In fact, both the X and the Y derive from what was once a perfectly normal pair of chromosomes that had nothing to do with sex. Recall that reptiles come in two sexes, even though they do not have sex chromosomes. So the X and Y were born sometime after mammals and reptiles diverged, about 300 million years ago. In a sense, turning a pair of autosomes (the term used to describe all non-sex chromosomes) into the X and Y has been a remarkable 300 million year experiment—one that is still ongoing.

What did these ancestral chromosomes look like? The answer lies in the genes that are common to both the X and Y. Although the Y houses a handful of genes that make a male, about half the genes that reside on this chromosome are also found on the X. They encode proteins that take care of general housekeeping and cellular maintenance tasks, needs shared by both sexes. At first researchers handled these shared genes as oddities. Now these genes are recognized as living fossils, representatives of the genes that were present on the pair of identical chromosomes from which X and Y sprang.

Somewhere along the way, though, the X and Y parted company—each to follow its own evolutionary path. The Y most likely came to be when it somehow acquired SRY, or a gene that performed a similar role in sex determination. Then, at some point, X and Y lost the ability to recombine—a process in which chromosomes pair off and swap bits of genetic information. Such swapping is necessary for maintaining chromosomal integrity. In females, the two Xs can still partner with one another and exchange DNA. But with no proper partner, the Y began to unravel, losing many of its genes. Such genetic decay would explain why the Y chromosome has only 30 or so genes while the X supports thousands.

But the Y chromosome is more than a rotting X. It also harbors genes that are male specific. Some of these genes, it appears, used to be located on various autosomes; they relocated to their home on the Y some 30 to 50 million years ago. This genetic migration may represent an opportunistic move—perhaps the Y provided a safe haven for genes that benefit males but are inconsequential or even somehow harmful to females. Sequestering such genes to chromosomal regions that are present only in males may have helped keep harmony within the species.

Many species, from the fruit fly to the mouse, carry genes essential for male fertility on their Y chromosomes. In humans, the genes involved in sperm production have also made their

way to the Y. This evolutionary trend has clinical ramifications: Deletions on the Y chromosome can cause infertility, a problem that affects about 3 percent of men.
Thanks to the mapping and sequencing of the Y chromosome, researchers are now unraveling the mechanism by which these deletions may occur. In some cases, it appears that recombination can take place between sets of matching sequences present on the Y chromosome. So a single Y chromosome might fold over, line up these similar patches of genetic sequence, and then accidentally delete everything that lies in between—including genes that are important for sperm production and development.

Because infertile males cannot pass these defects along to their offspring, such deletions represent new mutations—changes that occur very early in a male embryo or even in the single sperm that donated its Y on fertilization. But there have been rapid advances in reproductive technologies. Now infertile males who produce at least a small amount of sperm can become biological fathers by a procedure called ICSI—intracytoplasmic sperm injection. Doctors can obtain isolated sperm cells from these otherwise infertile individuals and then inject them directly into a female oocyte to achieve fertilization.

Unfortunately, any sons conceived by this method will also possess the defective Y chromosome, making them infertile as well—unless they opt to undergo a similar procedure when they decide to raise a family. This raises the eerie possibility that someday entire lineages may reproduce only with the aid of a laboratory technician. In time, society will need to grapple with the long-term consequences of such interventions. Until then, scientists will continue to study the sex chromosomes—particularly the Y, which despite its small stature continues to make important contributions to our understanding of sex, chromosomal evolution, and human biology.

Key Concepts

- The X and Y sex chromosomes did not always exist. They evolved some 300 million years ago from a pair of identical autosomes—chromosomes that have nothing to do with sex.
- Today the sex chromosomes look quite different. The Y is one-third the size of the X and contains only 30 or so genes, as opposed to the thousands present on the X.
- Half the genes that reside on the Y chromosome also have a counterpart on the X. These common genes can be considered living fossils; they provide a snapshot of the ancestral autosomes from which these sex chromosomes derived.
- The X and Y chromosomes most likely parted company, evolutionarily speaking, when they lost the ability to recombine—a process in which chromosomes pair off and swap bits of genetic information. Such swapping is necessary for maintaining chromosomal integrity.
- Without a recombination partner, the Y chromosome decayed, losing many of its resident genes. With every passing generation, this tiny chromosome continues to evolve.
- X inactivation evolved to compensate for the fact that most of the genes on the X chromosome are present in a double dose in females. This process shuts down one copy of these genes in all the cells of the female, so that she does not end up producing unnecessary—or indeed toxic—amounts of the proteins they encode.
- The Y chromosome harbors many genes that control male development and fertility. These male-specific genes appear to have relocated to their home on the Y some 30 to 50 million years ago.

- Because genes that control the development of sperm are located on the Y, deletions on that chromosome can cause infertility.
- Mapping and sequencing of the Y chromosome have revealed a mechanism whereby such mutations may occur. It seems possible that a single Y chromosome might fold over, lining up patches of matching sequence, and accidentally delete all the information in between—including genes relevant to sperm production.
- Males that are infertile cannot pass these defects along to their offspring by the conventional means. Thus, these deletions represent new mutations that occur very early during embryonic development or in the single sperm cell that donated its Y during fertilization.
- Rapid advances in reproductive technologies allow some infertile males to become biological fathers. Using techniques such as ICSI (intracytoplasmic sperm injection), doctors can insert individual sperm cells obtained from these otherwise infertile men directly into an egg. Any sons produced by such a procedure, however, will inherit their father's defective Y chromosome and will themselves be infertile.
- Studies of the X and Y chromosomes will continue to bolster our understanding of sex, chromosomal evolution, and human biology.