# Y Male Sex Chromosomes Degenerate

May 18, 2015

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In many animals, sex is determined by the presence of sex chromosomes. In humans, males have an X and a Y whereas females have two X chromosomes. Despite significant differences that are apparent under the microscope, both the X and Y evolved from non-sex chromosomes (autosomes; chromosomes 1-22 in humans). However, it remains unclear how the Y became dissimilar from the X. For instance, the Y can no longer appreciably swap genetic material with the X, a property that evolved over the last 180 million years and is known as recombination suppression. This property is thought to be important for the Y chromosome to retain its sex-determining genes. But many questions remain unanswered regarding the sequence of events that led to recombination suppression, DNA sequence degeneration (the Y is much smaller than the X), and mechanisms that restore gene dosage balance (genes on the X have one copy in males and two in females).

The threespine stickleback fish has emerged as a powerful model to study vertebrate sex chromosome evolution due to the ability to raise it in the laboratory together with the fact that it has a XY chromosome system that has evolved relatively recently, 13-16 million years ago. A new Fred Hutch study from Dr. Catherine Peichel's Laboratory (Human Biology and Basic Sciences Divisions), led by post-doctoral fellow Dr. Michael White and published in *Molecular Biology and Evolution*, used high-throughput sequencing of DNA and RNA of both female and male fish to infer sequence evolution and dosage compensation. "The threespine stickleback has been an important model in the study of sex chromosome evolution. In this study we provide the first detailed sequence-based characterization of molecular evolution across the X and Y chromosomes of the threespine stickleback", said Dr. White.

Previous work in the Peichel lab (Ross and Peichel, 2008) provided cytogenetic evidence that the Y chromosome structurally diverged from the X through 3 inversions and a large deletion (6Mb). The new report reanalyzed these regions with higher resolution and separated the inversions into a more recent evolutionary group while the deletion represented an older group. Strikingly, some genes within the deletion were maintained on the Y, and these were found to be under purifying selection, a form of natural selection that preserves gene function. Since DNA sequence divergence occurs at different rates on the X and Y chromosomes, the authors compared the sex chromosomes from threespine sticklebacks to the sex chromosomes of the ninespine stickleback, a related species,

because the latter independently evolved a XY chromosome system from a different autosomal ancestor. This comparison revealed an elevated rate of evolution of the X chromosome, particularly for genes that did not have a functional counterpart on the Y. To test whether dosage compensation evolved in threespine sticklebacks, the investigators used RNA sequencing to monitor expression levels of X-linked genes with corresponding genes in the ninespine sticklebacks. This analysis uncovered that within the older region, genes with a single copy in males exhibited decreased expression, arguing against a global dosage compensation mechanism. In support of this, genes with two copies in males had X-biased expression caused by reduced expression of the Y-linked copy. Finally, the authors found that Y-linked genes that were retained under purifying selection were enriched for genes predicted to have a role in intracellular transport.

"Although much progress has been made understanding the evolution of heteromorphic sex chromosomes, it remains unclear whether dosage compensation evolves in males in response to gene loss on the Y chromosome. Recent evidence suggests dosage imbalances in the heterogametic sex are only resolved at the most haploinsufficient genes but this has not been widely studied. Our results strengthen these conclusions. In the oldest region of the threespine stickleback Y chromosome, we found a handful of genes that were still expressed from the Y chromosome. These genes were under strong purifying selection and were enriched for dosage sensitive functions. These patterns have only been recently shown in the well-studied mammalian XY sex chromosome system. Our results provide additional evidence in a vertebrate system that global dosage compensation may not be a common route to restore gene expression imbalance in the heterogametic sex," summarized Dr. White.

White MA, Kitano J, Peichel CL. 2015. Purifying selection maintains dosage-sensitive genes during degeneration of the threespine stickleback Y chromosome. *Mol Biol Evol*. msv078, Epub ahead of print.

See also:

Ross, JA, Peichel CL. 2008. Molecular cytogenetic evidence of rearrangements on the Y chromosome of the threespine stickleback fish. *Genetics,* 179: 2173-2182.

*Image provided by Dr. Michael White.*

Threespine stickleback males possess a young XY sex chromosome system at the early stages of differentiation.