The Scientist: NewsBlog:
Battle of the X's
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In the course of human history, something wonky happened to the levels of genetic diversity on the X chromosome -- scientists just can't agree on what. Two research teams reported conflicting reports about X chromosome diversity yesterday (Nov. 13) at the *American Society of Human Genetics* meeting in Philadelphia, with differing interpretations about human mating and migration.

Because males only carry one X chromosome, sex-biased evolutionary forces will affect genomic patterns on the X chromosome and on the non-sex chromosomes differently. As such, comparisons of levels of variability between the different chromosomes can be used to test hypotheses about human demographic patterns.

Alon Keinan, an evolutionary geneticist at the Harvard Medical School, and his colleagues compared genetic variation on the X chromosome and on the autosomes using a variety of datasets, including over 100,000 SNPs from the HapMap project, and large swaths of sequence data from individuals originating in West Africa, East Asia and Central Europe. Using either dataset, they found that X chromosomal diversity in non-African populations was significantly lower than would be expected if men and women were equally successful at passing on their genes. This result suggests that the X chromosome underwent a severe genetic bottleneck as humans migrated out of Africa.

Keinan's team tested several selection and demographic models to account for the chromosomal diversity difference, but none of them fit the observed data. The best explanation, they found, was that more men migrated out of Africa and contributed their one X chromosome to the worldwide human gene pool than did women with their pair of X's. "Migration out of Africa occurred mainly via waves of primarily male migration following an initial dispersal," Keinan told *The Scientist*. "Not only is it a viable explanation that explains all the results, but it also makes sense in light of anthropological results." Keinan's results will be published in a future edition of *Nature Genetics*.

Jeffrey Wall, an evolutionary geneticist at the University of California, San Francisco, however, presented his own data showing that X chromosome diversity was, in fact, higher than expected. Wall's team sequenced over 500 kb of noncoding DNA across 61 autosomal and 30 X-linked regions in a panel of 90 people from six geographically diverse populations,

including three from Africa. They found that genetic variation was greater than expected on the X chromosome in all six populations.

Irrespective of the chromosome, overall levels of genetic diversity were also higher in Wall's study than in most previously published reports. Wall thinks that by focusing on non-coding genomic regions that were far from any known genes or functional elements, they turned up patterns of diversity that reflected true demography and were not confounded by any effects of natural selection.

The best explanation for the data, Wall said, can be found in human behavior. Societies were probably polygynous through much of human history, he argued. Thus, some men sired children from many different women, while others left no descendents at all. This skewing of reproductive success manifested itself through greater diversity on the X chromosome. An earlier version of this analysis was also published in September in *PLoS Genetics.*

Why have two such seemingly similar studies come to such different conclusions? Both authors declined to comment on the other's study. Still, Wall thinks we should have an answer once more genome-wide data is available that is unbiased by any sampling effects. "Although we seem to come to different conclusions now, there will be a very definitive answer soon from the 1000 Genomes Project and other sources of data," he said.