Sex chromosomes—why the Y genes matter

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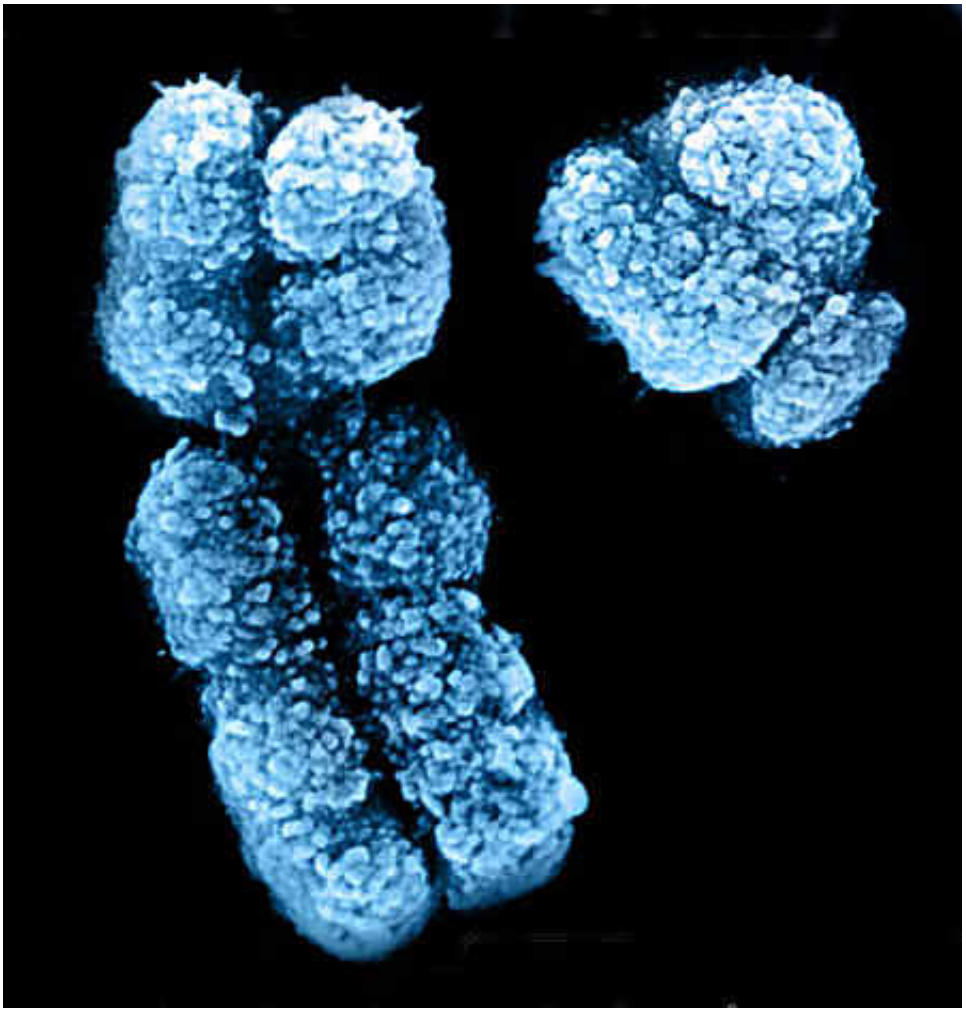

Several genes have been lost from the Y chromosome in humans and other mammals, according to research published in the open access

journal *Genome Biology*. The study shows that essential Y genes are rescued by relocating to other chromosomes, and it identifies a potentially important genetic factor in male infertility.

The Y chromosome is dramatically smaller than the X chromosome and has already lost nearly all of the 640 genes it once shared with the X chromosome.

An extreme example of genes disappearing from the Y chromosome can be found in the Ryukyu spiny rat, which is indigenous to a single island in Japan. In this species, the Y chromosome has disappeared completely, with many Y-linked genes moving to either the X chromosome or non-sex chromosomes (autosomes). Until now, this was thought to be a peculiarity found in one isolated species, but new data suggest that the phenomenon of genes moving from sex chromosomes to autosomes is widespread among mammals, including humans.

Lead author Jennifer Hughes from the Whitehead Institute, USA, said: "Genes that have survived on the Y chromosome are extraordinarily long-lived and likely serve important biological functions. However, there are numerous exceptions where seemingly critical genes have been lost from the Y chromosome in certain mammals. In many cases, these genes were not actually eliminated but have found new homes in the genome.

"Now we've revealed four genes that have been lost from the Y chromosome and rescued by moving to other chromosomes. For the first time, we show that this has occurred in humans, as well as in a diverse range of other mammals. These relocated genes have hung around the genome because they are indispensable for normal development."

The team studied the genomes of humans, apes, rodents, cattle and marsupials, looking for evidence of genes that have relocated from the sex chromosomes to autosomes. By using evolutionary records of species

divergences, they constructed family trees showing how certain genes had moved between chromosomes over time.

The four genes that were identified as having moved from the Y chromosome play key roles in protein synthesis and degradation within mammalian cells. The team found eight separate cases in different species where these genes moved from sex chromosomes to autosomes.

Copies of the EIF2S3 gene are found on the X and Y chromosomes of rodents, and the Y copy is a crucial player in the early steps of sperm production. In humans, this gene was found to be missing from the Y chromosome, but two copies were still present in the genome - one on the X chromosome and one on an autosome.

This suggests that, following the loss of the gene from the human Y chromosome, the X chromosome 'backed up' a copy of its EIF2S3 gene onto an autosome, indicating the importance of this gene. In humans, the autosomal copy of the gene showed increased activity in the testis compared to other tissues, suggesting an essential role in sperm production, and a possible genetic factor in male infertility.

Jennifer Hughes adds: "This research adds new complexities to our understanding of the role of sex chromosomes, genes and sex-specific characteristics, which warrant further investigation."

In order to obtain a broader survey of the impact that jumping-gene rescue of Y gene loss has had on genome evolution, high quality sex chromosome sequences from more species will need to be generated.

More information: Jennifer F Hughes, Helen Skaletsky, Natalia Koutseva, Tatyana Pyntikova and David C Page Sex chromosome-to-autosome transposition events counter Y-chromosome gene loss in mammals *Genome Biology* 2015 DOI: 10.1186/s13059-015-0667-4