*NATURE* | NEWS

# A battle of the sexes is waged in the genes

**Sequencing data point to longstanding conflict between the chromosomes that determine sex.**

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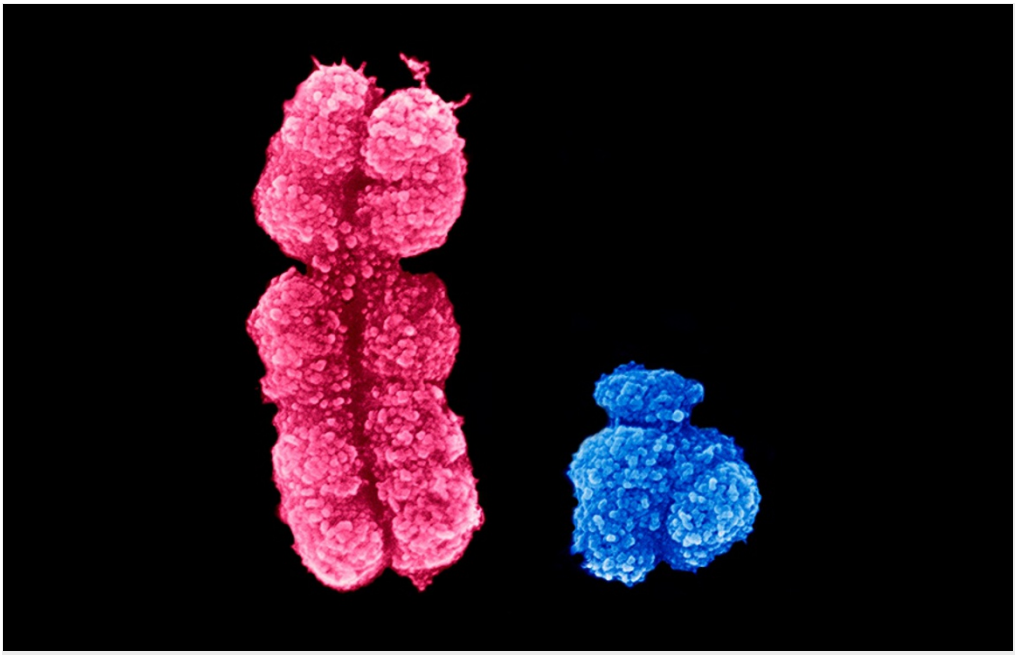
26 June 2015

**SAN JUAN, PUERTO RICO**



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In humans, the Y chromosome (right) is particularly diminutive compared to its counterpart, the X (left).

New DNA sequencing data reinforce the notion that the X and Y chromosomes, which determine biological sex in mammals, are locked in an evolutionary battle for supremacy.

David Page, a biologist who directs the Whitehead Institute in Cambridge, Massachusetts, and his colleagues explored the Y chromosomes carried by males of several species, mapping stretches of mysterious, repetitive DNA in unprecedented detail. These stretches may signal a longstanding clash of the chromosomes.

Page presented the results last week at a meeting of the Society for the Study of Reproduction in San Juan, Puerto Rico. His team's subjects included humans and other primates, a standard laboratory mouse, and a bull named Domino.

"This idea of conflict between the chromosomes has been around for a while," says Tony Gamble, an evolutionary biologist at the University of Minnesota in Minneapolis. But the sequencing data from the bull's Y chromosome suggests that the phenomenon is more widespread than previously thought, he adds.

The mammalian Y chromosome has long been thought of as a sort of genomic wasteland, usually shrinking over the course of evolution and largely bereft of pertinent information. Page's work has helped to change perceptions of the Y chromosome by revealing that it contains remarkable patterns of repeating sequences that appear dozens to hundreds of times[1,2].

But the structure of these sequences and precise measures of how often they repeat have been difficult to determine. Standard sequencing technologies often cannot distinguish between long stretches of genetic code that differ by a single DNA 'letter'.

### Letter by letter

Page and his collaborators avoided this problem by using what he calls 'super-resolution' sequencing (a technique better known as single-haplotype iterative mapping and sequencing, or SHIMS), which can detect such minute variation between lengthy segments of

DNA.

The team sequenced many large, continuous stretches of the Y chromosome and carefully scrutinized the areas that looked as if they overlapped. They found that repeating structures make up about 24% of the accessible DNA in the human Y chromosome, and 44% of that of the bull.

And in the Y chromosome of the mouse, which is much larger than that of a human, repeating structures make up almost 90% of accessible DNA. The intricate patterns, which often contain palindromes — sequence that reads the same in forward and reverse order — carry three families of protein-coding genes. What the genes are doing — and how they got there — remains a mystery, however.

In mammals, the X and Y chromosomes emerged relatively recently from a regular pair of chromosomes before differentiating from one another. They share many of the structures that came from their ancestral source, but these repetitive regions seem to have come from somewhere else.

The repeated genes in the mouse Y chromosome do not resemble anything on the human Y chromosome, but they do have analogues on the mouse X chromosome. And in the mouse, human and bull, the repeated genes on Y and X are expressed in the male germ cells that eventually produce sperm.

**A biological black box**

Taken together, Page argues that this is evidence that the genes are involved in meiotic drive, a somewhat mysterious biological process that subverts the standard rules of heredity. In it, a particular version of a gene — or in this case, an entire chromosome — manages to increase the frequency by which it is transmitted to the next generation.

How that works is unclear. Sperm carry an X or a Y chromosome; genes expressed in the testes, where the cells are produced, may influence which sperm will be more likely to successfully fertilize an egg.

Previous studies lend credence to this idea. A team led by geneticist Paul Burgoyne and collaborators at the MRC National Institute of Medical Research in Mill Hill, UK, found that mice with a partial deletion of the Y chromosome produce offspring with a female-skewed ratio[3]. The researchers subsequently shifted offspring sex ratios in both directions by tinkering with the expression of these multicopy genes.

Of course, mice — in nature and in the lab — usually maintain even sex ratios. Failing to do so could harm species survival. So as these Y-promoting genes made copies of themselves, subsequent mechanisms evolved to suppress their selfish urges. Page's results provide a way to explore that evolutionary history; the data on the bull genome suggest that the mouse X and Y may not be exceptions.

With further high-resolution sequencing data, researchers may find more support for genomic battles of the sexes and possibly uncover other surprises. "There's this rich tapestry of what sexual chromosomes are capable of," says Gamble.

*Nature* | doi:10.1038/nature.2015.17817

## References

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3. Conway, S. J. *et al*. *Mamm. Genome* **5**, 203–210 (1994).