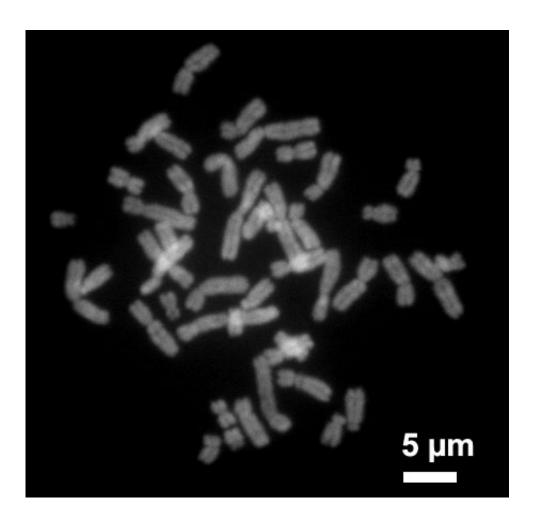


Male Y chromosomes not 'genetic wastelands'

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Human chromosomes during metaphase. Credit: Steffen Dietzel/Wikipedia

When researchers say they have sequenced the human genome, there is a caveat to this statement: a lot of the human genome is sequenced and assembled, but there are regions that are full of repetitive elements, making them difficult to map. One piece that is notoriously difficult to



sequence is the Y chromosome.

Now, researchers from the University of Rochester have found a way to sequence a large portion of the Y chromosome in the fruit fly Drosophila melanogaster—the most that the Y chromosome has been assembled in <u>fruit flies</u>. The research, published in the journal *Genetics*, provides new insights into the processes that shape the Y chromosome, "and adds to the evidence that, far from a genetic wasteland, Y chromosomes are highly dynamic and have mechanisms to acquire and maintain <u>genes</u>," says Amanda Larracuente, an assistant professor of biology at Rochester.

The notorious Y chromosome

Y chromosomes are sex chromosomes in males that are transmitted from father to son; they can be important for male fertility and sex determination in many species. Even though fruit fly and mammalian Y chromosomes have different evolutionary origins, they have parallel genome structures, says Larracuente, who co-authored the paper with her Ph.D. student Ching-Ho Chang. "Drosophila melanogaster is a premier model organism for genetics and genomics, and has perhaps the best genome assembly of any animal. Despite these resources, we know very little about the organization of the Drosophila Y chromosome because most of it is missing from the genome assembly."

That's in part because most Y chromosomes do not undergo standard recombination. Typically, genes from the mother and father are shuffled—or, "cross over"—to produce a genetic combination unique to each offspring. But the Y chromosome does not undergo crossing over, and, as a result, its genes tend to degenerate, while repetitive DNA sequences accumulate.



Sequencing vs. assembling

Each chromosome is made up of DNA. When mapping a genome, traditional sequencing methods chop up strands of DNA and read—or sequence—them, then try to infer the order of those sequences and assemble them back together.

But, "there is a difference between sequencing a genome and assembling a genome," Larracuente says. There are so many repetitive strands on the Y chromosome that the pieces tend to look the same. It is difficult, therefore, to figure out where they come from and how to reassemble the strands—like trying to put together a puzzle when all of the pieces are exactly the same color. "When we try to take those bits of DNA and assemble them to see what the chromosome looks like, we can't fill in some of those gaps. We might have the sequence, but we don't know where it goes."

A different type of recombination

Using sequence data generated by new technology that reads long strands of individual DNA molecules, Chang and Larracuente developed a strategy to assemble a large part of the Y chromosome and other repeat-dense regions. By assembling a large portion of the Y chromosome, they discovered that the Y chromosome has a lot of duplicated sequences, where genes are present in multiple copies. They also discovered that although the Y chromosome does not experience crossing over, it undergoes a different type of recombination called gene conversion. While crossing over involves the shuffle and exchange of genes between two different chromosomes, gene conversion is not reciprocal, Larracuente says. "You don't have two chromosomes that exchange material, you have one chromosome that donates its sequence to the other part of the chromosome" and the sequences become identical.



The Y chromosome has therefore found a way to maintain its genes via a process different from crossing over, Larracuente says. "We usually think of the Y chromosome as a really harsh environment for a gene to survive in, yet these genes manage to get expressed and carry out their functions that are important for male fertility. This rampant gene conversion that we're seeing is one way that we think genes might be able to survive on Y chromosomes."

More information: Ching-Ho Chang et al. Heterochromatin-Enriched Assemblies Reveal the Sequence and Organization of the Drosophila melanogaster Y Chromosome, *Genetics* (2018). DOI: 10.1534/genetics.118.301765

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