

Highlight on fusing multiple chromosomes in yeast into a single chromosome

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Abstract

Multiple biological mysteries remain in the definition and organization of genetic information into different chromosomes. Up to now, genome architecture at the chromosome level remain enigmatic concerning the reasons why evolution and natural selection arranged genetic information in separate segments in eukaryotic cells as compared to the single chromosome in the prokaryotic world. Specifically, one important unresolved question has been the role of chromosomes in cellular physiology and biochemical processes. By deleting the centromere and telomere regions of different chromosomes in *Saccharomyces cerevisiae* and fusing the different chromosomes into one chromosome, research reported by Shao and coworkers in *Nature* revealed the technical possibility of concatenating all genetic information into one segment. Furthermore, cell viability assays revealed that there was no significant loss of cell viability after the fusing of 16 chromosomes into a single chromosome. This highlighted that centromere and telomere sequences were not critical to overall cellular function, physiology and biochemistry. More importantly, the results highlighted that genetic information and its organisation at the sub-chromosome level play a more important role in defining cellular biochemical processes and physiology such as metabolism and cell division processes. Collectively, the technical feasibility of fusing multiple chromosomes into a single chromosome has been shown in new research that deleted the centromere and telomere regions of different chromosomes for fusing the resulting genetic information into a single chromosome. Little loss of viability and function in cells with a single chromosome and the stability of replicating the chromosome revealed that centromere and telomere sequences may not play critical roles in defining cellular physiology and biochemistry. More importantly, genomic information and its regulation was shown indirectly to have a more direct influence on cell physiology and metabolism than chromosomal architecture.

Keywords: genome architecture, chromosomes, centromere, telomere, cell viability, cellular physiology, fusing chromosomes, cell division, DNA replication, *Saccharomyces cerevisiae*,

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Highlight

Chromosomes serve as physical platforms for the encoding of genetic information expressed in sequence of nucleotides. While the high fidelity encapsulation of genetic information is of high importance, the structure of the chromosome also play critical roles in enabling the reading and writing of new genetic information onto the platform. For example, a highly compacted chromosome structure known as heterochromatin prevents the transcription of genes encapsulated within the structure, while, on the other hand, chromosome in a more open structure known as euchromatin facilitates the reading of genetic information and transcription into mRNA. Hence, chromosomal biology plays important roles in affecting gene expression at multiple levels ranging from the high fidelity encapsulation of genetic information for long-term storage to the periodic need to open the chromosomal structure for transcription and reading of genetic information.

More importantly, the chromosomal structure must also be flexible enough to allow chemical modifications to be made to individual or subset of nucleotides. Known as epigenetic modifications that links environmental influence to gene expression, chromosomes with such place holders contain critical information important to the correct reading and writing of genetic information. For example, regions of the chromosome that are highly methylated are repressed for transcription, while other regions with acetylated groups are in a more open conformation suited for transcription. Thus, epigenetic modifications place a different level of control to gene expression.

But, fundamentally, why does genetic information arrange into specific chromosomes, and why do we have defined number of chromosomes for each species? What determines the number of chromosomes on which genetic information can be encoded?¹ Writing in *Nature*,² Shao and coworkers reported the fusion of 16 yeast chromosomes into a single chromosome with the concomitant maintenance of cell viability. By deleting the centromere and telomere of each chromosome and fusing two chromosomes together, the research team was able to progressively reduce the number of chromosomes in *Saccharomyces cerevisiae*. Viability assays revealed that there was little loss of viability. In addition, cells with single chromosome could undergo the normal cell division process. Specifically, the cells were shown to be viable after the fusing of multiple yeast chromosomes into a single chromosome, which illuminated that arrangement of genetic information could be changed without causing deleterious effects on the cells.

Collectively, organization of genomic information into different chromosomes was thought to play important roles in the maintenance of genome integrity and cell physiology. However, recent research highlighting the possibility of removing the organizational structure of genomic information in different chromosomes revealed that genetic information itself play a more important role in defining the organization, biochemistry and physiology of cells than chromosome

structure. Specifically, the team deleted the centromere and telomere of different chromosomes in yeast and fused the resulting chromosomes into a single chromosome. Viability test of the resulting cells revealed normal cell physiological processes with little loss of viability. Thus, the new results highlighted that centromere and telomere sequence are not critical in defining cellular function besides serving as placeholders for the cell division and DNA replication machinery respectively. Finally, the research highlights that there needs to be a rethink of our understanding of organization of genomic information into different chromosomes in a cell and its implications.

Conflicts of interest

The author declares no conflicts of interest.

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- 2 Shao, Y. *et al.* Creating a functional single-chromosome yeast. *Nature* **560**, 331-335, doi:10.1038/s41586-018-0382-x (2018).