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The Configuration Robustness of a Functional Genome is Revealed by Single-Chromosome Fission Yeast Models

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Abstract

The physical units that house genetic information are called chromosomes. Chromosome counts in eukarya differ amongst organisms; for example, the male ant Myrmecia pilosula has one chromosome, whereas the fern Ophioglossum reticulatum has hundreds Chromosome number reduction by fusion happened during the evolution of apes to humans, as evidenced by the strong resemblance between human chromosome 2 and two ancestral ape chromosomes 2A and 2B. It is unknown if changes in chromosomal counts over time in a particular species encourage speciation and offer adaptive advantages. Various chromosomes In an interphase nucleus, chromosomal territories (CTs) often occupy distinct areas.It is recognised that chromosomal architecture and spatial structure regulate gene expression and define cellular processes [1-15]. The tolerance for chromosome configuration changes, both organic and synthetic, varies. Thai Fea's muntjacs (Muntiacus feae) exhibit 2n = 12, 13 (female), or 14 (female and male) .The karyotypes of the Indian muntjac (M. muntjak vaginalis) and Chinese muntjac (M. reevesi), two closely related species, are noticeably different.

Introduction

The artificially created Saccharomyces cerevisiae single- and two-chromosome budding yeast strains showed significant alterations in global chromosomal architecture, but little change in gene expression profiles and no obvious deficiencies in different phenotypes.On the other hand, splitting native chromosomes in Saccharomyces cerevisiae to increase chromosomal counts from 16 to 21 or 30 likewise appears to be phenotypically inert .Unknown is whether eukaryotic genomes exhibit great tolerance to chromosomal arrangement alterations on a regular basis. To investigate through experiment the consequences of extreme We employed the model organism Schizosaccharomyces pombe, which normally has three chromosomes, to study chromosome configuration change in an organism other than S. cerevisiae .Schizosaccharomyces pombe has chromosomes 1, 2, and 3 that are and 3.5 Mb, respectively, making up its approximately 13.8 Mb genome .Even though Saccharomyces cerevisiae and Schizosaccharomyces pombe are both unicellular fungi, their evolutionary distance from one another is great.In Additionally, they exhibit several variations at the chromatin and cellular levels (such as centromere structure, epigenetic control of chromatin, cell morphology, and pattern of cell division.In this study, we created viable strains by fusing three natural chromosomes into one in various configurations. The functional genome of Schizosaccharomyces pombe can sustain drastic alterations in both chromosome numbers and genome organisation, according to our additional characterizations of the single-chromosome strains.

Subjective Heading

One centromere and two telomeres are typical components of eukaryotic chromosomes. The complex construction of kinetochores, which are in charge of microtubule attachment and accurate chromosome separation during cell division, takes place at the centromere, a designated chromosomal region and Musacchio. The chromosome end structures known as telomeres are crucial for maintaining the stability of the genome (Bianchi and Shore, 2008; We performed chromosome fusion together with the removal of non-unique regions at the ends of chromosomes, including the telomeric sequences and a portion of the subtelomeric sequences, using the site-specific HO endonuclease and the Cre-loxP system. Procedures are shown schematically in Figures S1A and S1B. (also see the details in STAR Methods). Two different strains of two chromosomes were obtained: Chr3-2 and Chr1-3. The names of the fused chromosomes and the order of their fusion were used to identify these strains (the right end of the first chromosome was fused with the left end of the second chromosome). Pulsed-field gel electrophoresis (PFGE) examination of the Chr3-2 and Chr1-3 strains verified the presence of chromosome fusions.

Discussion

To create single-chromosome strains, we next carried out another round of chromosomal fusion. On natural Chr3, there are two rDNA arrays at each end. Both rDNA arrays in the Chr3ci-2 and Chr1-3ci strains had one of them already removed. In order to prevent mortality brought on by full rDNA loss, we preserved the last remaining rDNA-harboring end of Chr3 and created the chromosome fusions Chr3ci-2-1 (fusing the left end of chromosome 1 with the right end of chromosome 2) and Chr2-1-3ci (fusion between chromosome 2 right end and chromosome 1 left end). The previously unfused chromosome's centromere was removed concurrently with the chromosomal fusion. (Figures S1A–S1B–S2D–S2E) (also see the details in STAR Methods). Chr3ci-2-1c and Chr2c-1-3ci, respectively (abbreviated as 3ci-2-1c and 2c-1-3ci in the figures), were the names given to the two resulting strains. We further removed cen3 from these

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two strains, producing Chr3c-2-1c and Chr2c-1-3c (abbreviated 3c-2-1c and 2c-1-3c in the figures), two more single-chromosome strains. Overall, we were able to produce four single-chromosome fission yeast strains with either two centromeres (one active and one quiescent) or just one centromere, and two alternative chromosome orders. By using PCR to amplify the junctions of chromosomal fusion and centromere deletion and sequencing the PCR results, we confirmed that the creation of single-chromosome strains was effective (Figure S3A). One enormous chromosome was present in each of the four strains, according to PFGE analyses (Figure 1B). Additionally, the sizes of the DNA fragments produced by NotI or SgsI digestion agreed with the calculations (Figures S3B and S3C). ChIP-qPCR analysis revealed that the central domain (cnt) of cen2 in Chr3ci-2-1c included Cnp1 but not H3K9me2, which is a sign of active pericentric heterochromatin. The 3ci-2 strain's inactivated cen3 remained silent after inactivation, however, as evidenced by the presence of H3K9me2 in the cnt of cen3 but not Cnp1. the bottom and middle panels of Figure 1C show the second cycle of chromosomal fusion).Additionally, we used southern blotting to evaluate the telomeres in the chromosome fusion strains and discovered that, as predicted, telomere signals gradually reduced after chromosome fusions that were also accompanied by a decrease in telomere counts.

Despite making up only about 10% of the genes in single-chromosome strains, DEGs were numerous and numbered in the hundreds. We questioned if cellular phenotypes and fitness were impacted by these transcriptional alterations. The size and shape of single-chromosome cells were identical to WT cells (Figure 4A). When single-chromosome cells were cultivated in the nutrient-rich Yeast Extract Supplemented (YES) medium at 30°C, their growth rates were comparable to or slightly lower than those of WT cells (Figures 4B, S10A, and S10B). Using live- Using cell imaging to examine mitotic spindles, researchers discovered that the dynamics and length of mitotic spindles in single-chromosome strains and the wild type were comparable.When single-chromosome strains are repeatedly streaked on YES plates 20 times at a 3 day interval, no obvious changes in colony growth are seen. This suggests that single-chromosome strains can maintain their ability to self-renew for many generations.

Conclusion

The single-chromosome strains demonstrated comparable sensitivity to camptothecin (CPT), a topoisomerase I inhibitor, but appeared to be slightly more susceptible to hydroxyurea (HU), a ribonucleotide reductase inhibitor, and methyl methanesulfonate (MMS), a DNA damaging agent, than the WT. Interestingly, compared to the WT, single-chromosome strains and two-chromosome strains (Chr3ci-2 and Chr1-3ci) were less responsive to the drugs thiabendazole and carbendazim (Figures 4D, S10E, and S10F). Considering that TBZ and CBZ We hypothesised that because there are fewer centromeres in the chromosome fusion strains, there may be less requirement for microtubules during cell division. These findings suggest that Schizosaccharomyces pombe may withstand dramatic changes in chromosomal number and structure.

Wild-type and single-chromosome fission yeast strains' genomic DNA was isolated, and g-TUBE was used to shear it into fragments of about 15 kb (Covaris). The SMRTbell Express Template Prep kit 2.0 was used to create the SMRTbell library (Pacific Biosciences). In a nutshell, 15 g of the sheared DNA were put through the first enzymatic reaction to remove single-stranded overhangs, and then they were given a treatment with repair enzymes to fix any damage that might have been done to the DNA backbone next to DNA. The double-stranded pieces' ends were polished for damage repair before being terminated with an A-overhang. At 20°C for 900 minutes, ligation with T-overhang SMRTbell adapters was carried out. The SMRTbell library was ligated, then exonuclease was used to digest it, and then 1 AMPure PB beads were used to purify it. The FEMTO Pulse automated pulsed-field capillary electrophoresis device was used to evaluate the size distribution and concentration of the library**.**

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Conflict of Interest

The authors declare that they are no conflict of interest.

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