A scheme to induce and selectively maintain specific N+1 disomes

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INTRODUCTION
We wish to create a controlled system in the yeast Saccharomyces cerevisiae to study aneuploidy. Aneuploidy is the condition of having abnormal numbers of chromosomes that can arise through a non-disjunction event during cell division. In continuous cultures of yeast in both industry and the lab, aneuploidy is a condition thought to arise when it provides some sort of growth advantage (1). Our aim is to develop a method by which strains of N+1 aneuploid yeast for each of the sixteen yeast chromosomes can be made and studied. Our scheme uses two genetic tools:

CONDITIONAL CENTROMERE. This centromere (GAL-CEN) can be temporarily disabled when cells are grown in galactose (2).

DUPLICATION MARKER. This marker is a set of genes that can exist in two, mutually exclusive states. Only when it has duplicated can it exist in both states simultaneously (ie, ref. 3).

INDUCTION-SELECTION SCHEME. Haploid cells will contain both the conditional centromere and the duplication marker in one target chromosome.

EXPERIMENTAL DESIGN AND RESULTS

Strain construction I: conditional centromere replaced CEN locus in target chromosome (III, IV, and VI)

- In glucose or raffinose: centromere functional
- In galactose: non-disjunction

Transcription at the GAL1 promoter promotes kinetochore assembly and microtubule attachment at CEN3. Non-disjunction of the chromosome one gene parent N+1 aneuploid daughter cells after one round of cell division; invisible N-1 daughters should also form. In glucose, the promoter is repressed, microtubules attach to CEN3 and accurate cell cycle division continues.

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- Strains were constructed to contain a conditional centromere and duplication marker in chromosome III, IV, or VI.
- Centromere replacement caused no growth defect.
- 2N-1 aneuploids missing chromosome IV slowly grow, exhibiting an abnormal bud neck morphology, and revert frequently.
- Microarrays indicate that His+ Ura+ colonies selected after galactose induction were N+1 for chromosome III.

DISCUSSION

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LITERATURE CITED


AKNOWLEDGEMENTS

- M.J. Mundstock College Research Program for Life Sciences
- Robert and Claire McDonald Award
- Kelly Bokos, for the use of the microarray scanner.
- Lark Sheffer and Gordon Segar, for the use of the microarray scanner.
- David Botella, for donating the DNA to print the arrays for his position.