# Determining genes in Saccharomyces cerevisiae that exhibit a dosage-sensitive consequence for Chromosomal Instability (CIN)

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## A B S T R A C T

The term "chromosomal instability" (CIN) refers to conditions that can alter a cell's chromosomal content during division. In Saccharomyces cerevisiae, we identified genes that affect CIN in a dosage-sensitive manner. CIN is known to have an effect on aneuploidy, but it has recently been shown to have an effect on CIN itself. Gene copy-number variation, or CNV, of dosage-sensitive genes that are present on the chromosome that was lost or gained by the aneuploid cell is one possibility that aneuploidy could influence CIN. Our group created the Improved GFP-based Chromosome Transmission Fidelity (MATA) assay, a novel CIN assay for budding yeast, to test this hypothesis. This high-throughput assay allows us to determine the effects that minor gene copy number changes have on CIN. This assay was used to systematically look for genes that can affect the loss rate of a yeast artificial chromosome (YAC) when its copy number is either increased because of a gene-containing plasmid (Over-Dosage CIN) or decreased because of haploid insufficiency (HI-CIN).

In the Over-Dosage CIN screen as well as the HI-CIN screen, we discovered and validated 139 CIN genes. Previous screenings only revealed 25 known CIN genes out of these 175 genes, leaving 150 unknown CIN genes. The most intriguing finding is that 9 of the 175 CIN gene candidates reduce CIN. This is the first known case of this phenotype, according to our knowledge.

It is common knowledge that CIN and aneuploidy frequently coexist in tumorigenic tissues and can be brought on by the loss or gain of particular genes, which are frequently involved in maintaining genomic integrity. It is currently impossible to predict the effects that individual mutations could have on chromosomal instability, particularly in such a complex and diverse background as cancer cells, as the spectrum of these genes is only partially known. A speedy and dependable approach to quantifying the effects of single copy number variations on CIN is presented here to address this issue.

**Key word:** Tumorigenic tissues, Aneuploidy frequently, Chromosomes, Genetic information, Genes