

# Effects on Gene Expression of Spontaneous Aneuploidy in Yeast Mutation Accumulation Lines

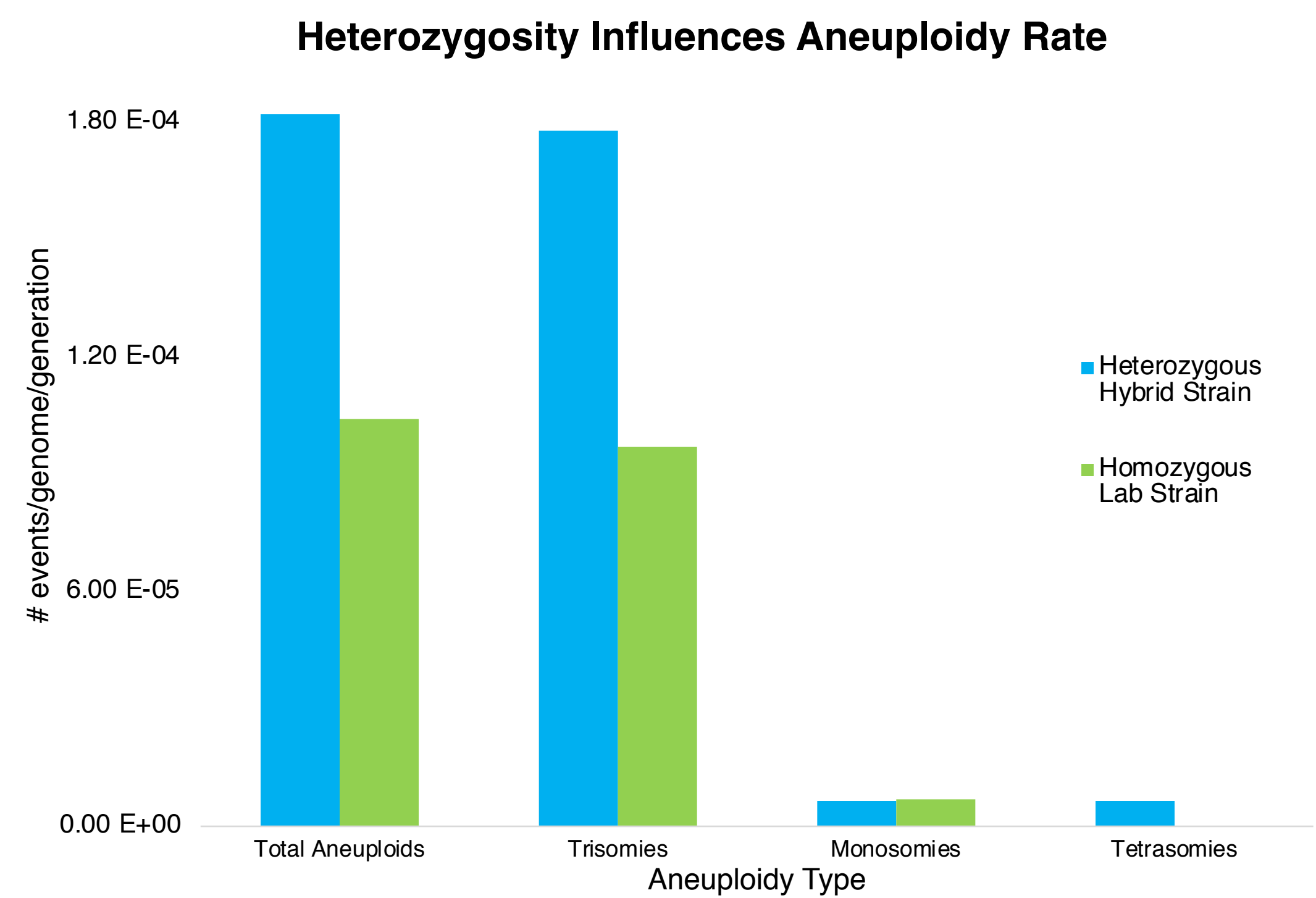
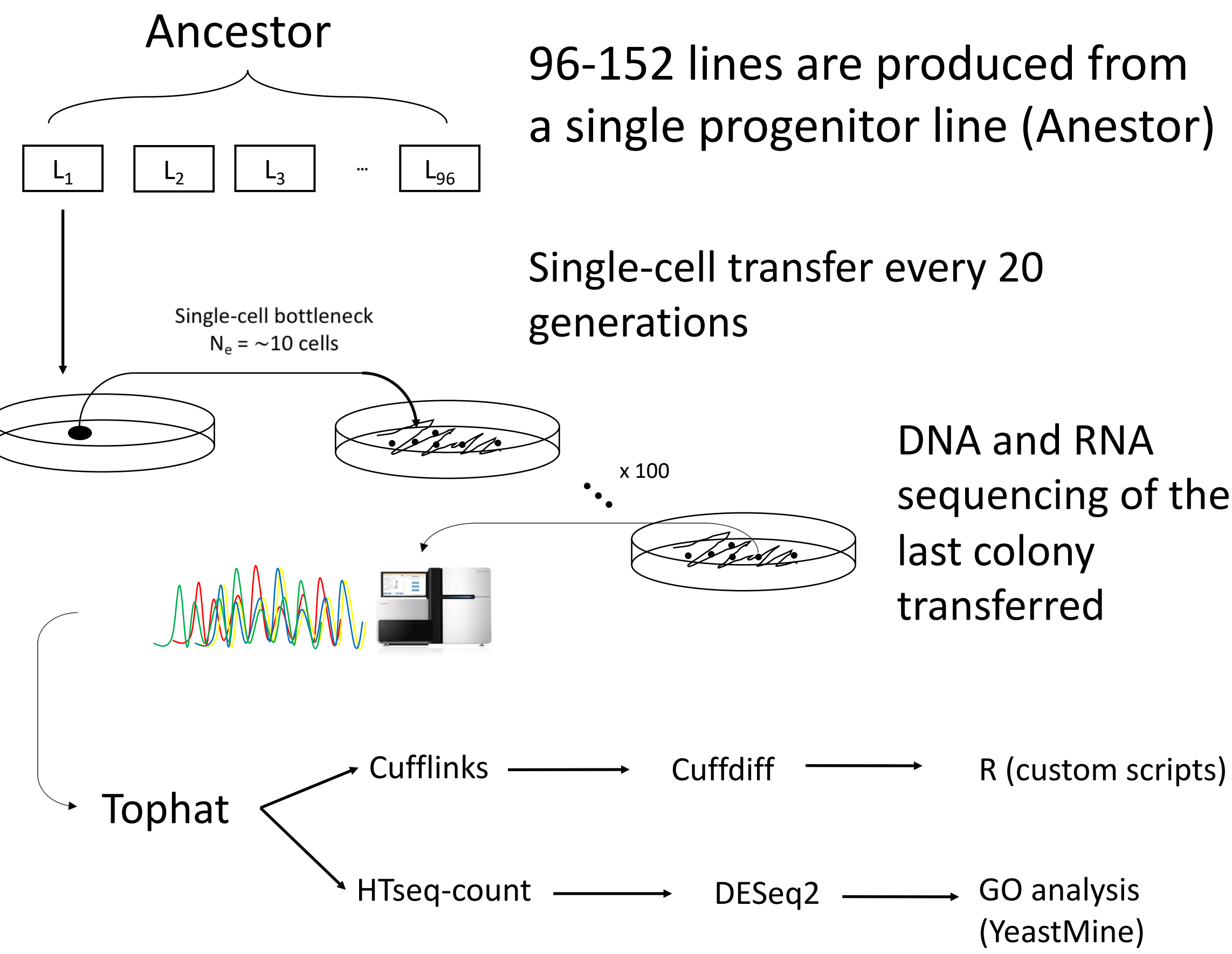
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## Motivation

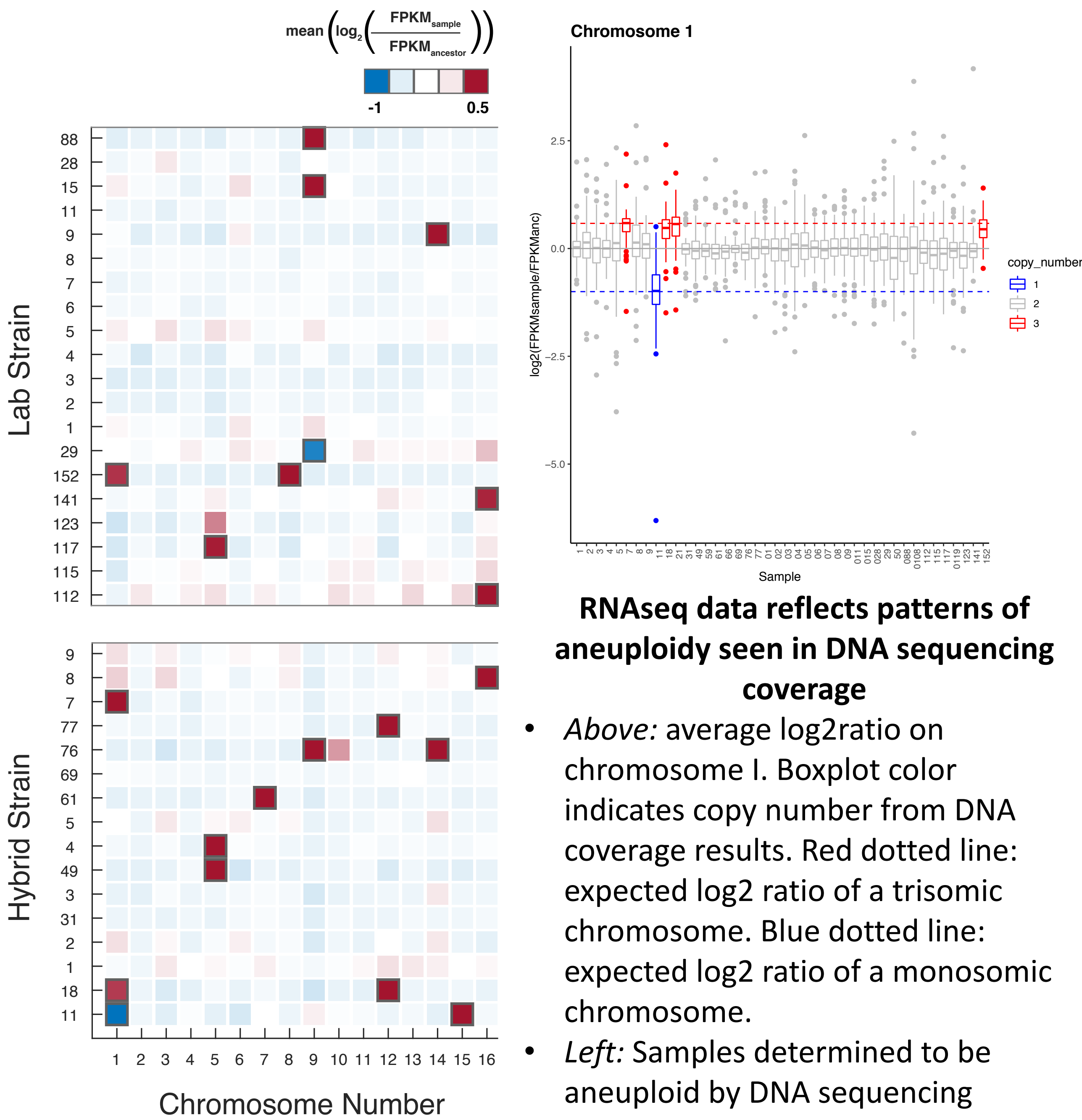
- Studies have claimed that wild yeast show evidence for an intrinsic dosage compensation mechanism at the whole chromosome level (1, 2)
- This finding has been contested, with the criticism that wild yeast cultures are unstable and may have reverted to euploid states (3)
- Other studies have investigated the effect of aneuploidy on gene expression, but generated aneuploid strains artificially, which may not be indicative of natural isolates
- We investigated whether there is an innate dosage compensation response in spontaneously aneuploid yeast that have been put through a 2000-generation mutation accumulation (MA) experiment with a single-cell bottleneck every 20 generations (4).
- MA ensures that there is little to no selection, therefore our samples are free of any selection for or against aneuploidy.

## Methods



Rate of aneuploidy is twice as high in hybrid strain, implying an effect of heterozygosity

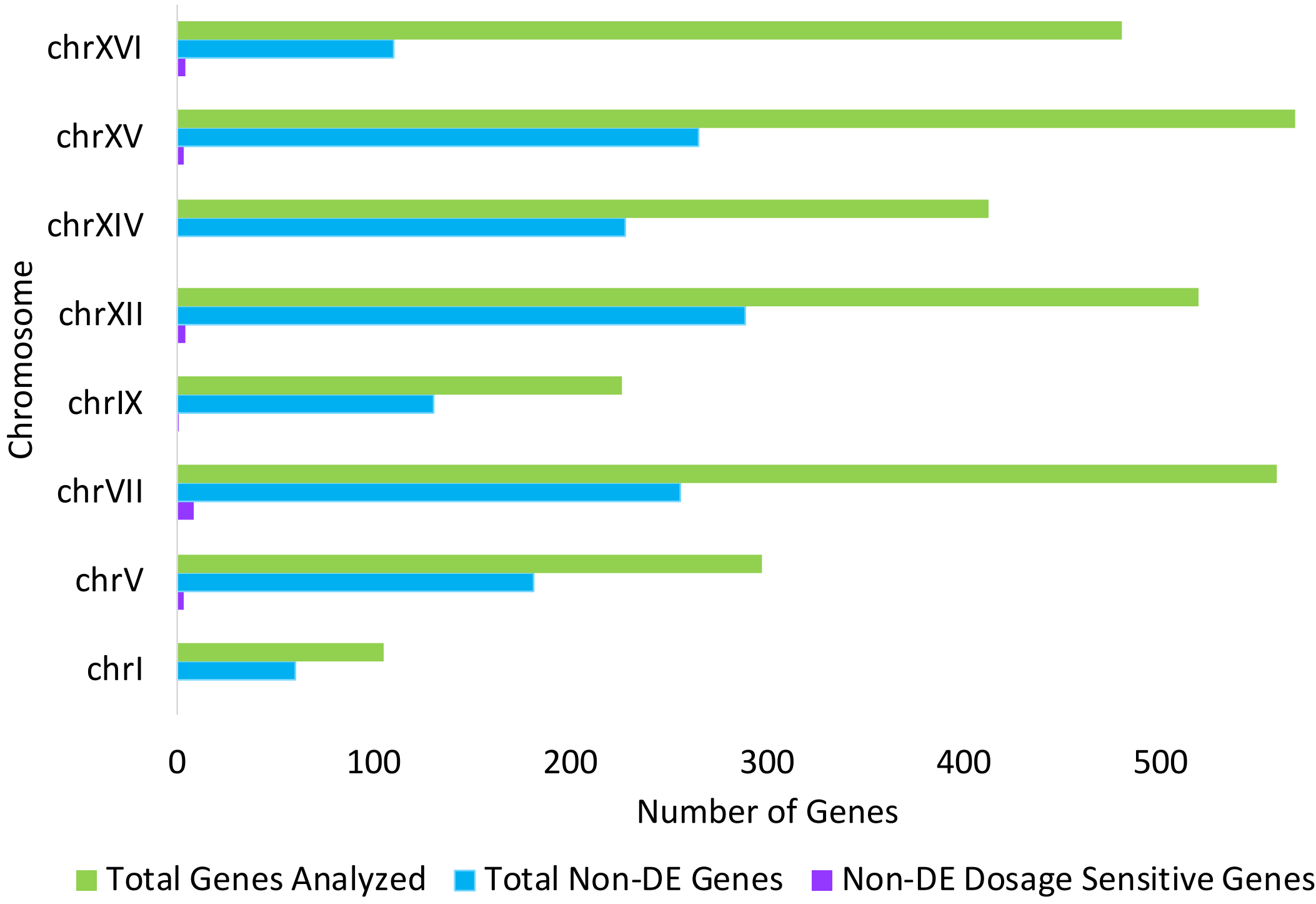
## No evidence for whole-chromosome dosage compensation



### RNAseq data reflects patterns of aneuploidy seen in DNA sequencing coverage

- Above:* average log2ratio on chromosome I. Boxplot color indicates copy number from DNA coverage results. Red dotted line: expected log2 ratio of a trisomic chromosome. Blue dotted line: expected log2 ratio of a monosomic chromosome.
- Left:* Samples determined to be aneuploid by DNA sequencing coverage show differential expression. Black square = aneuploid chromosome

## Dosage Sensitive Genes Are a Small Subset of Non-Differentially Expressed Genes

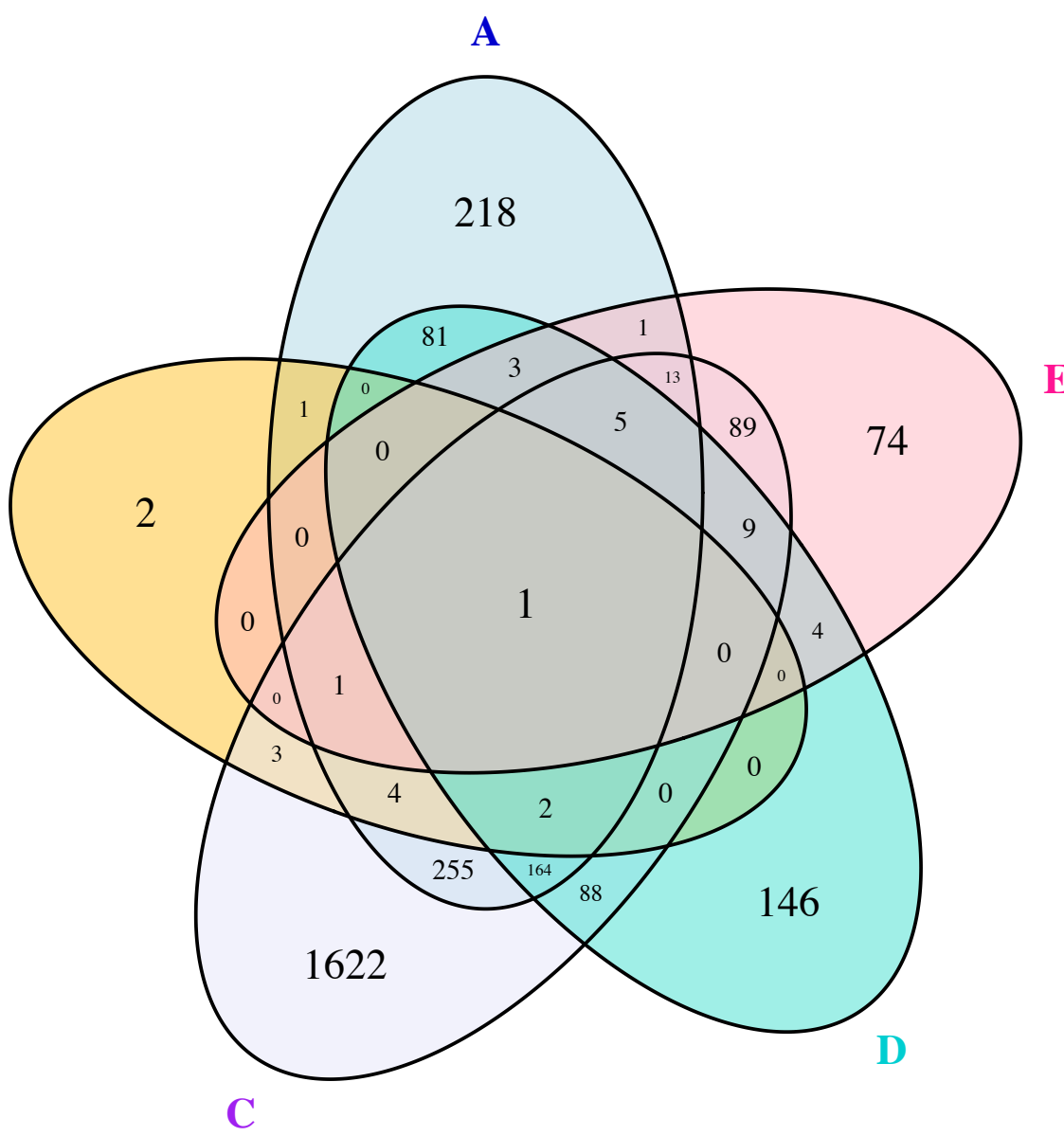


- Dosage sensitive genes found in a previous study are not differentially expressed in this study, adding further evidence that they are dosage-sensitive
- Notably, some of these dosage-sensitive genes are either ribosomal subunits or related to ribosomal biosynthesis. Previous studies have found certain ribosomal genes to regulate their own gene expression, and downregulation of ribosomal genes has been shown to be a characteristic of the environmental stress response in yeast (5,6).

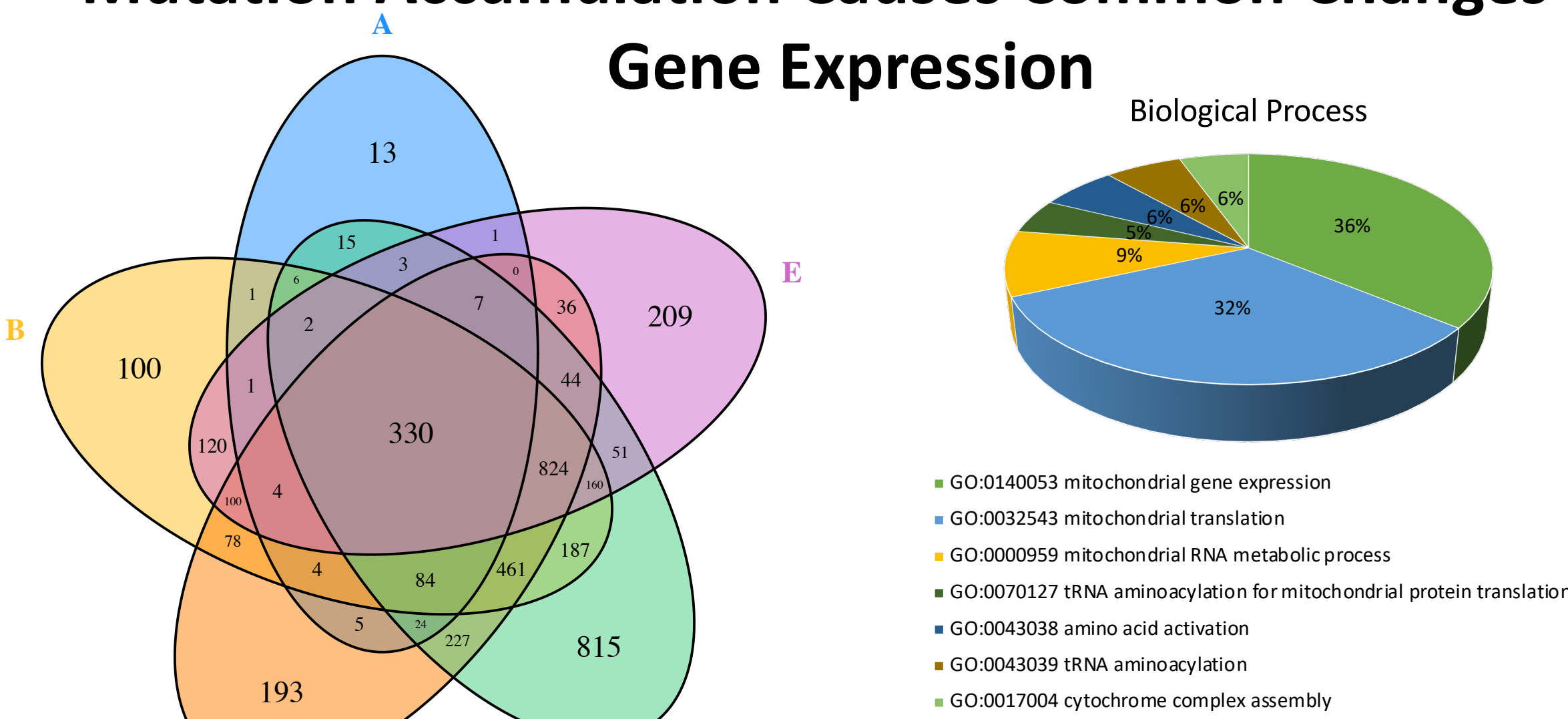
## Aneuploids share differential expressed genes located on euploid chromosomes

Venn diagram showing overlap of differentially expressed genes on euploid chromosomes shared between aneuploid samples

A: Trisomy Chr V  
B: Trisomy Chr I  
C: Trisomy Chr I, XII  
D: Trisomy Chr VII  
E: Trisomy Chr XII



## Mutation Accumulation Causes Common Changes in Gene Expression



*Left:* Venn diagram depicting overlap of differentially expressed genes in five different euploid lines (heterozygous hybrid strain). *Right:* GO enrichment of the 330 shared genes.

- 330 genes were found to be commonly differentially expressed in every euploid line.
- Most GO terms found were related to mitochondrial gene expression or translation.

## Conclusion

- The rate of aneuploidy is affected by level the of heterozygosity
- Whole-chromosome average gene expression correlates nearly perfectly with the expected ratio of an aneuploid chromosome
- Dosage sensitive genes were found to be not significantly differentially-expressed on aneuploid chromosomes
- Our findings conclude that there is no whole-chromosome dosage compensation in spontaneously-aneuploid yeast, but there is some compensation or attenuation of genes that are highly dosage-sensitive.

## References

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## Acknowledgements

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