

# The Recovery of Dma1,2Δ *S. cerevisiae* on phleomycin

Katie Forester

Faculty Advisor: Brian Strahl, Department of Biochemistry and Biophysics

## Abstract

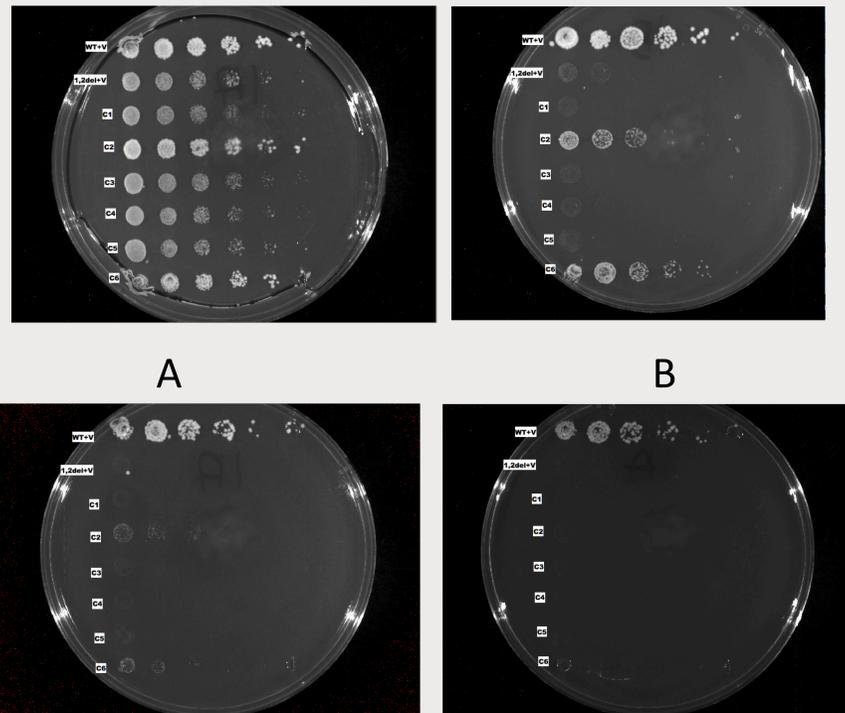
Proteins Dma 1 and 2 in budding yeast *Saccharomyces cerevisiae* play an important role in DNA damage repair. In particular, we have examined the modification that occurs on histone H3, acetylation of K56, and analyzed how it influences gene expression in Dma 1 and 2 deficient strains of *S. cerevisiae*. We show that the lack of Dma 1 and 2 causes the downregulation of H3K56ac. Additionally, we show that the lack of Dma 1 and 2 has toxic phenotypic effects when plated on a drug assay with phleomycin. Finally, we look at the ability of suppressor colonies of the Dma proteins to survive on various levels of phleomycin.

## Background

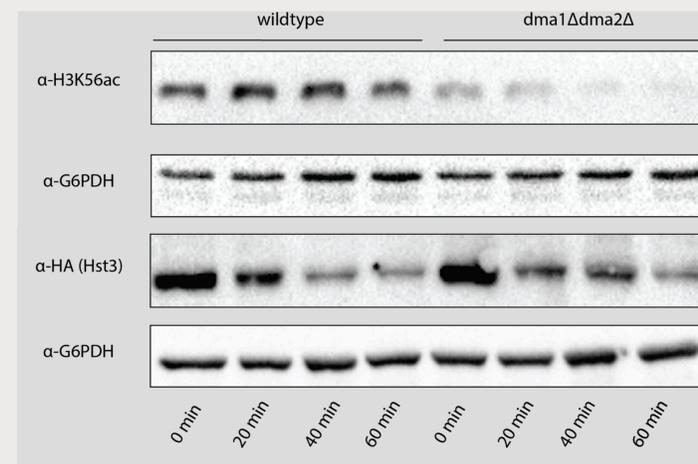
In eukaryotic cells, genetic information is packaged into chromatin. In order to create the DNA-protein complex that is known as chromatin, a series of proteins known as histones work to form nucleosomes. Each nucleosome consists of 147 bp of DNA wound around a histone protein complex consisting of two copies of each of the following core histone proteins: H3, H4, H2A, and H2B<sup>1</sup>. Levels of acetylation, methylation, phosphorylation, and ubiquitination can characterize histones. These post-translational histone modifications can be linked to differences in gene expression by the recruitment of histone modifiers or by chromatin restructuring in its entirety.

In the *S. cerevisiae* strain BY4741, proteins Dma1 and 2 play a critical role in DNA damage repair. The acetylation of histone H3 lysine 56 (H3K56Ac) is a core domain modification of histones<sup>2</sup>. H3K56Ac has been identified as important to genomic stability and DNA damage response in yeast<sup>1</sup>. Therefore, by studying the levels of H3K56Ac in a Dma1,2Δ strain, alongside the response of this strain on varying levels of phleomycin drug plates, the role of Dma 1 and 2 in *S. cerevisiae* can be better understood.

## Results



Images A-D show the ability of Dma 1,2Δ suppressor colonies to recover on varying levels of phleomycin drug plates. From top to bottom, the colonies read WT, Dma 1,2Δ, and suppressor colonies 1-6. Image A-D has the following levels of phleomycin present: +0 μL, +5 μL, +10 μL, +15 μL.



The image above shows decreased levels of H3K56ac in the double mutant strain.

## Conclusion

Based on Images A-D, it can be determined that suppressor colonies 2 and 6 are rescued on phleomycin in a Dma1,2Δ strain of budding yeast. As seen in Image B, while the Dma1,2Δ and suppressor colonies 1, 3, 4, and 5 are sick, suppressor colonies 2 and 6 are behaving similarly to the phenotype. Additionally, Image E shows that H3K56ac levels decrease in the mutant strain, while H3 remain approximately the same. H3 levels likely don't change due to its presence almost everywhere in *S. cerevisiae*. This suggests that Dma 1 and 2 help to regulate H3K56ac levels in budding yeast.

## Future Directions

In order to further determine the role of Dma 1 and 2 proteins in budding yeast, it is important to look at how suppressor colonies 2 and 6 were able to be rescued on phleomycin drug plates. There are two possible genes that will be further tested using western blotting: Htz1 and RRP6. RRP6 is an exosome complex endonuclease involved in RNA processing that is present in suppressor colony 6. Since it has been determined that H3K56 acetylation levels are lower in the double mutant strain, relating this downregulation with the functionality of Htz1 or RRP6 could lead to understanding how these colonies were recovered.

## Resources

1. Yuan J, Pu M, Zhang Z, Zhenkun L. Histone H3-K56 acetylation is important for genomic stability in mammals. *Cell Cycle*. 2009; 8(11): 1747-1753.
2. Xu F, Zhang K, Grunstein M. Acetylation in histone H3 globular domain regulates gene expression in yeast. *Cell*. 2005;121:375-385.