

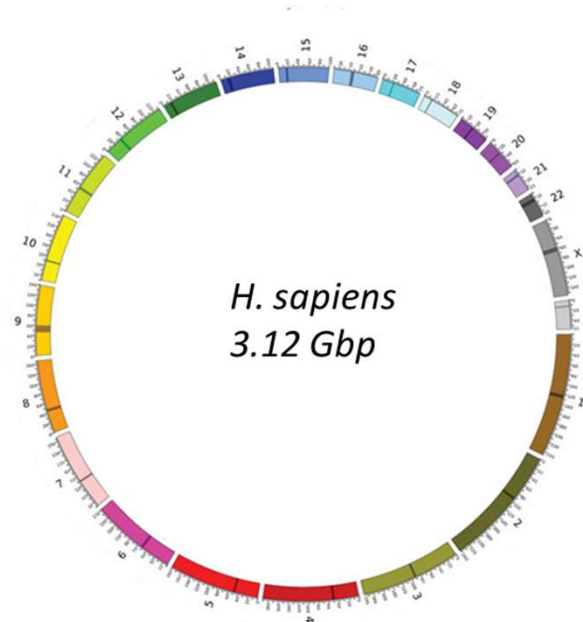


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An epigenetic mechanism for mutation rate modulation in the fungal wheat pathogen *Zymoseptoria tritici*



Fundamental Evolutionary Theory



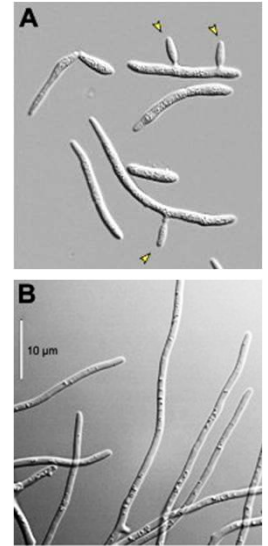
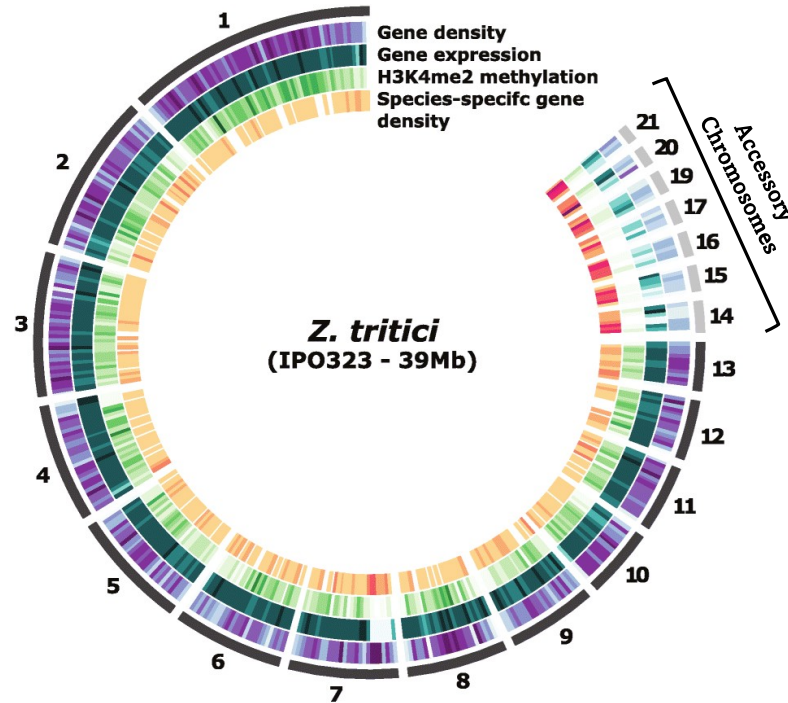
A fundamental tenet of evolutionary biology is that mutations are random events.

Zymoseptoria tritici

Important observations

In *Z. tritici*

1. Accessory chromosomes have a higher mutation rate

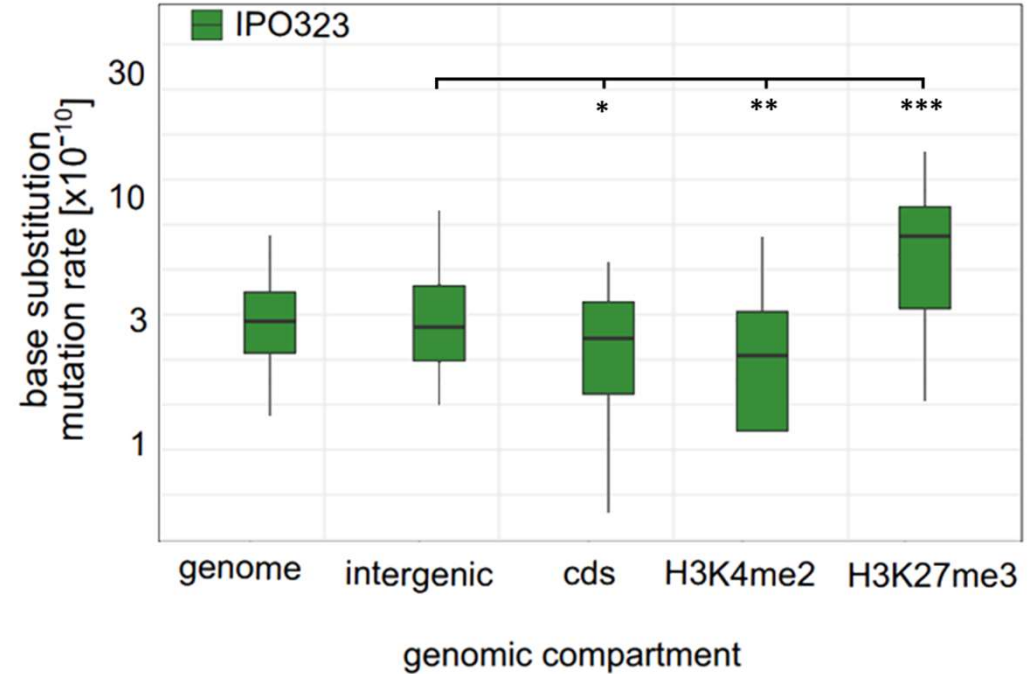


H3K27Me3 & mutation rate

Important observations

In *Z. tritici*

1. Accessory chromosomes have a higher mutation rate
2. The histone mark H3K27Me3 is associated with regions showing increased mutation rate



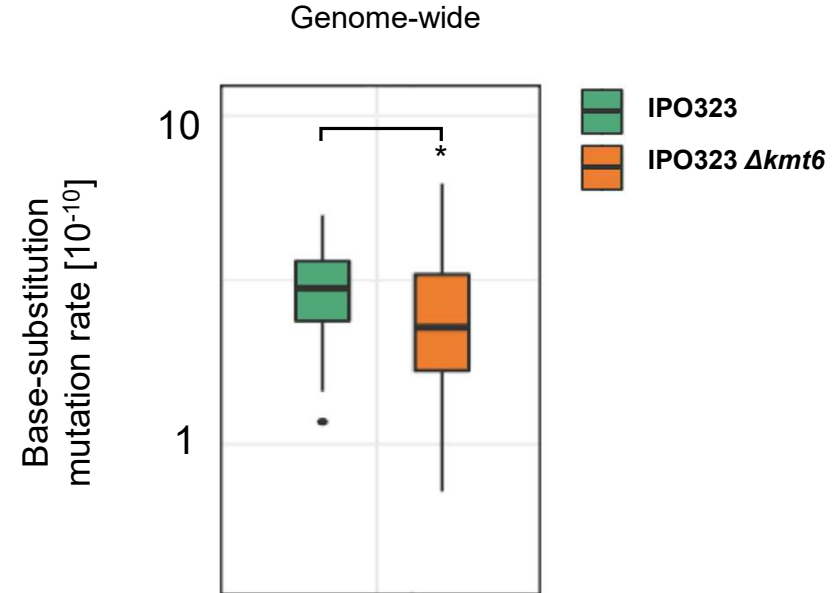
H3K27Me3 & mutation rate



Important observations

In *Z. tritici*

1. Accessory chromosomes have a higher mutation rate
2. The histone mark H3K27Me3 is associated with regions showing increased mutation rate
3. Removal of H3K27Me3 decreases the mutation rate

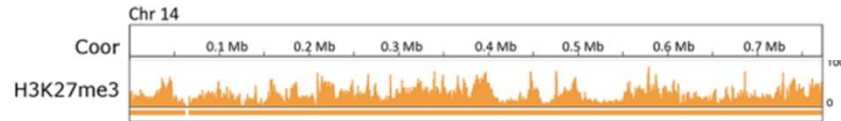
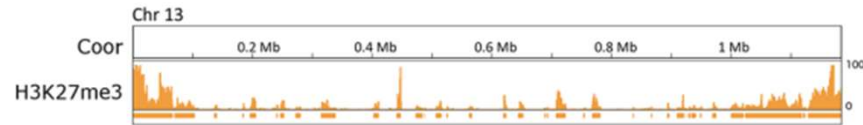


H3K27Me3 & accessory chromosomes

Important observations

In *Z. tritici*

1. Accessory chromosomes have a higher mutation rate
2. The histone mark H3K27Me3 is associated with regions showing increased mutation rate
3. Removal of H3K27Me3 decreases the mutation rate
4. H3K27Me3 is enriched in accessory chromosomes



What does this suggest?



Important observations

In *Z. tritici*

1. Accessory chromosomes have a higher mutation rate
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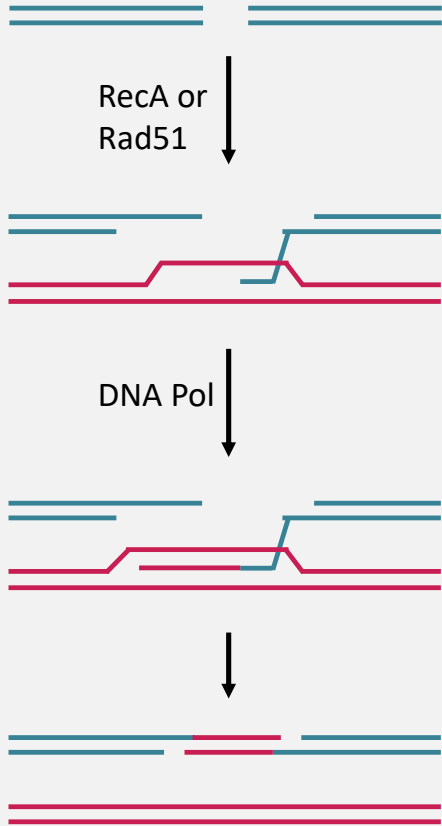
An epigenetic mechanism controlling the mutation rate in *Z. tritici*!

How can we investigate?

DSB repair pathways

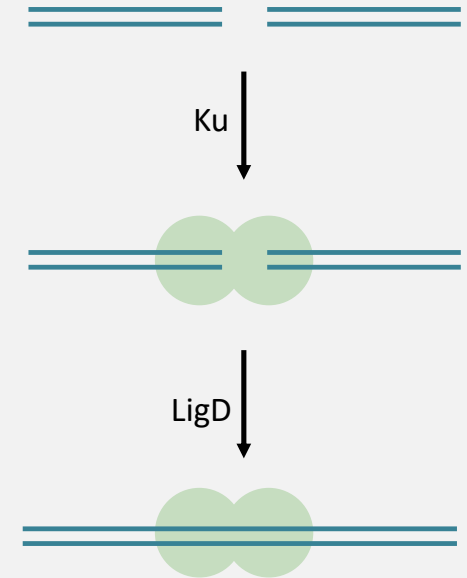


Homologous recombination



Chromatin has been shown to influence the choice of DNA repair pathway which can give different mutational signatures

Non-homologous End-Joining



This analysis: Hypotheses



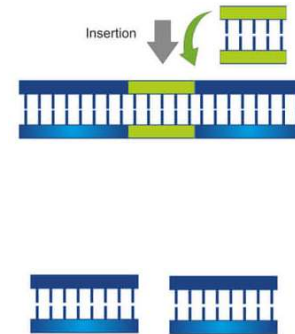
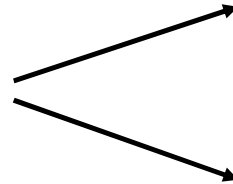
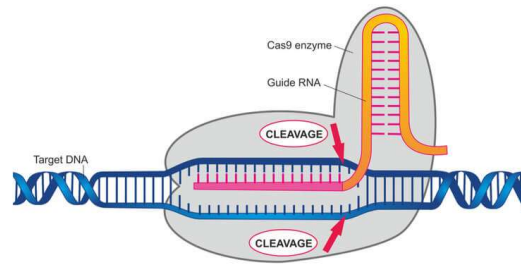
Question

Why do accessory chromosomes of *Z. tritici* have a higher mutation rate than core chromosomes and what is the mechanism?

Hypothesis

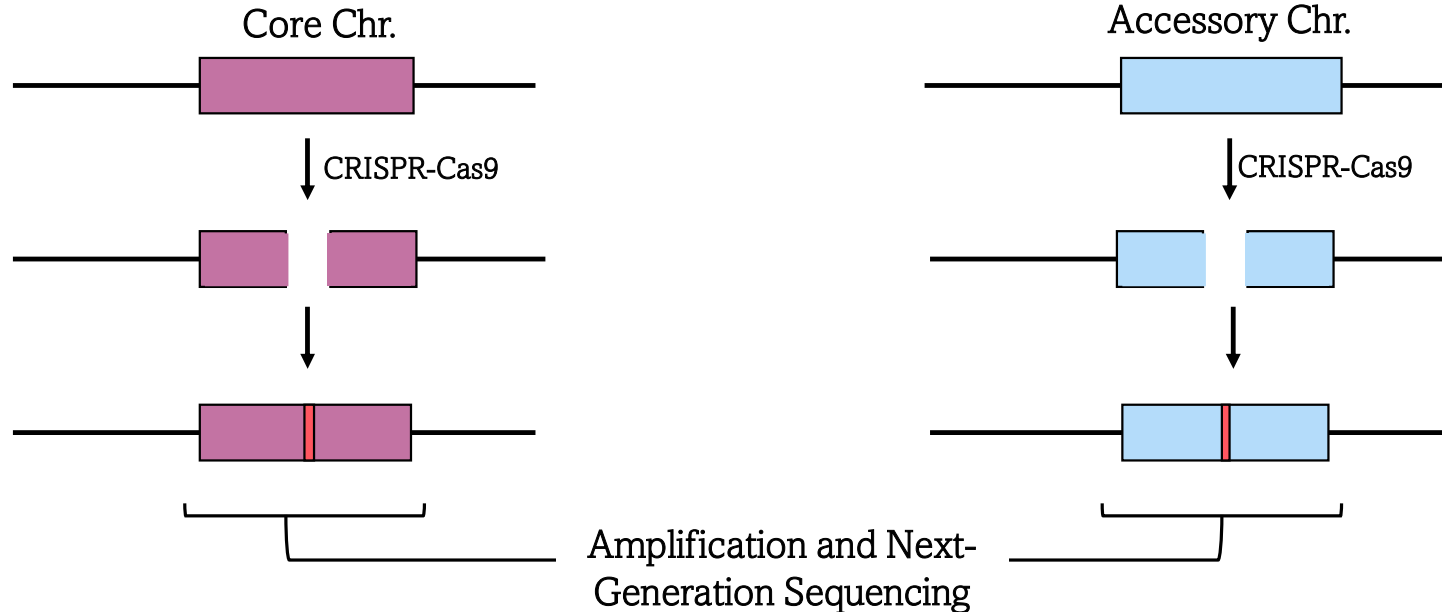
The increased mutation rate of accessory chromosomes of *Z. tritici* is due in part to a chromatin environment which favors error-prone NHEJ over HDR

This analysis: creating DSBs



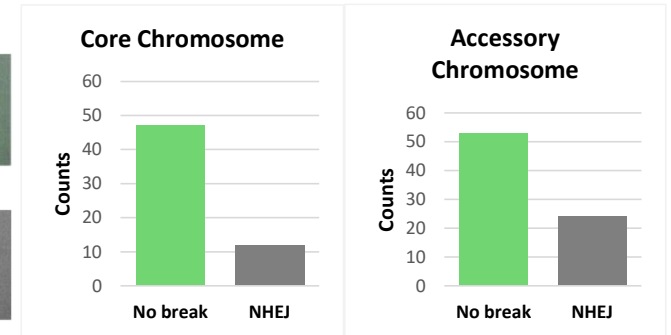
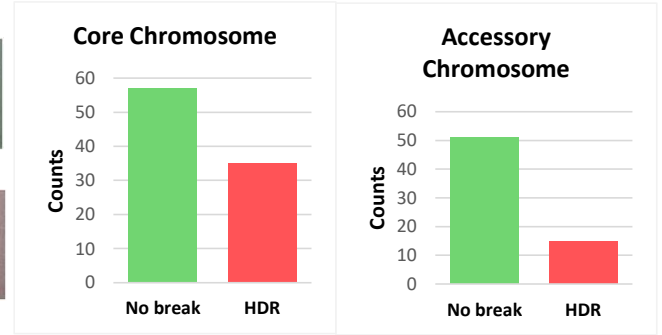
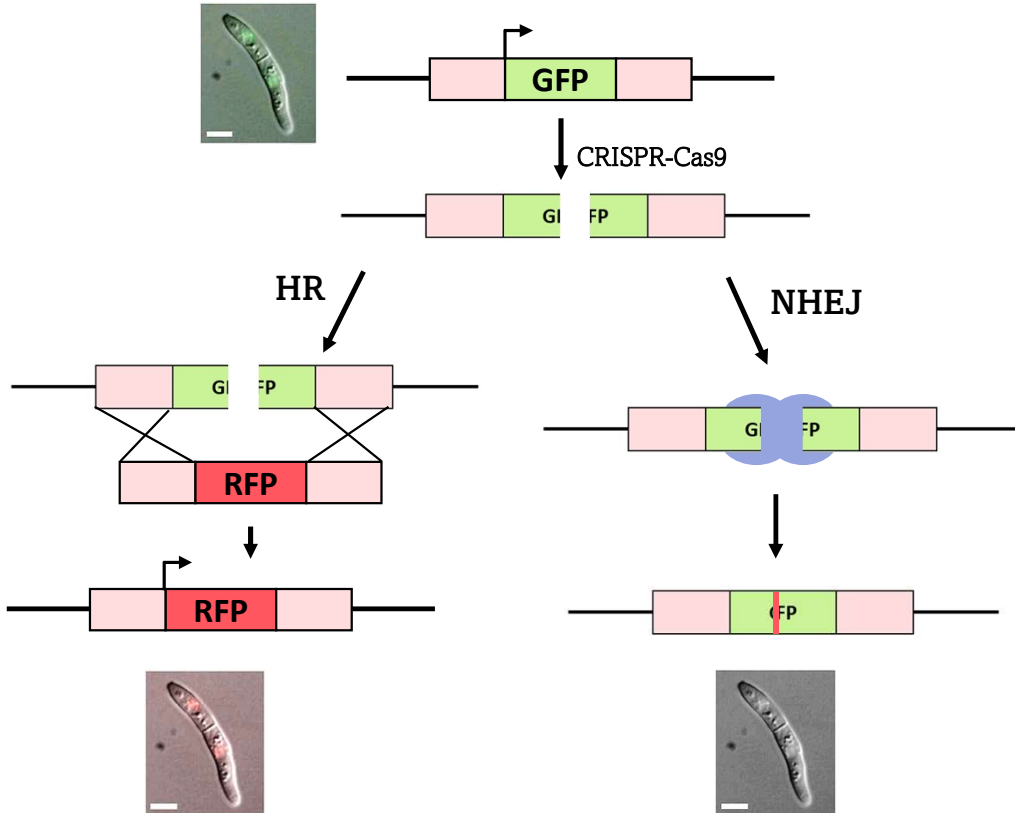
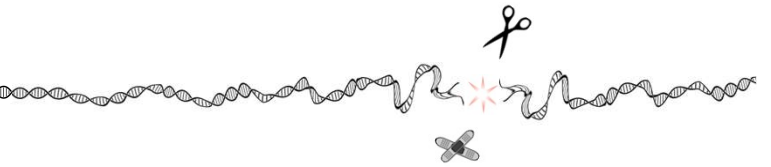
Analysis 1: Mutations from DSBs

Purpose: verify differential mutation rate between core and accessory chromosomes can occur a result of DSBs



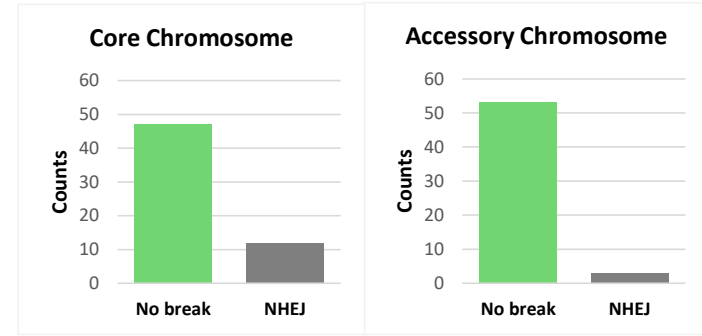
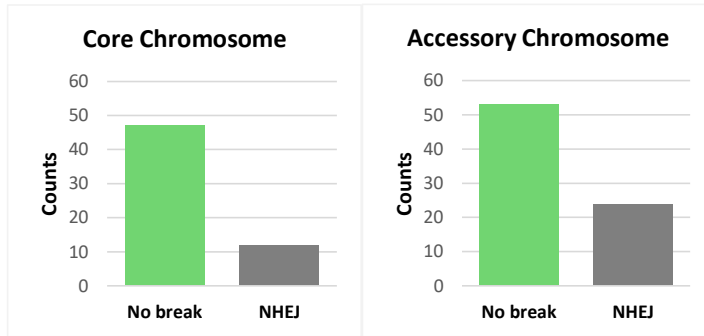
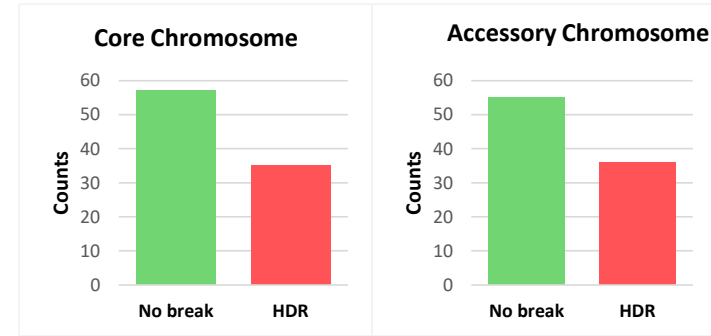
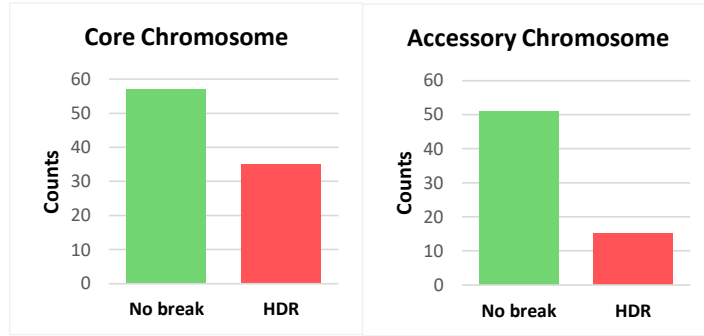
Analysis 2 – Repair pathway

Purpose: compare repair pathway frequencies between core and accessory chromosomes



Quantification by flow-cytometry cell counting

Analysis 3 – Global H3K27Me removal



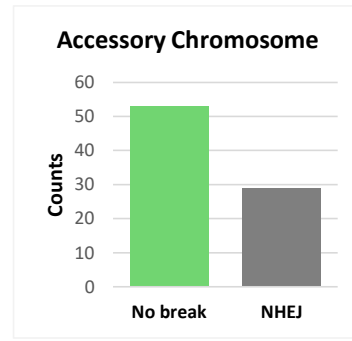
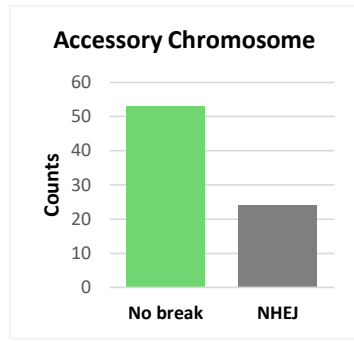
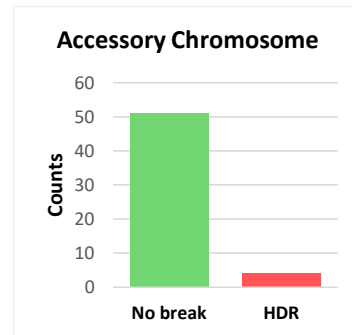
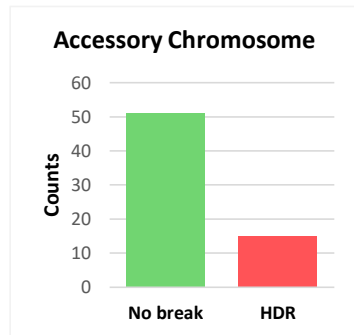
WT

H3K27Me3 removal ($\Delta kmt6$)

Analysis 4 – Adaptory mutation rate

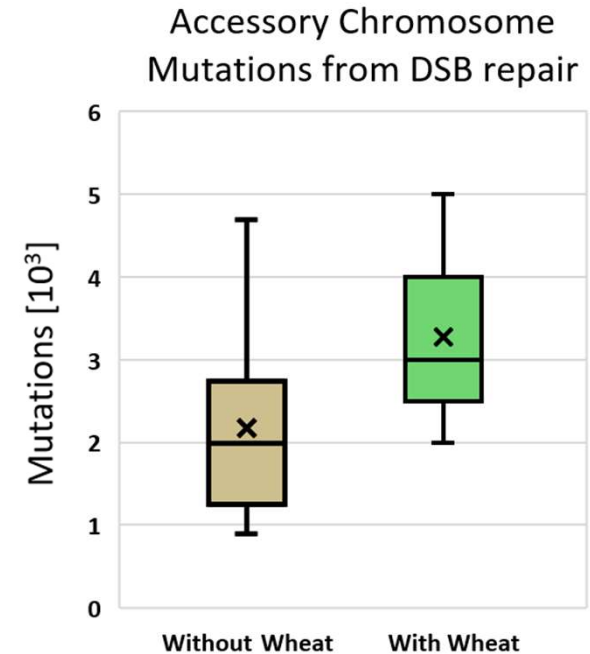


Put *Z. tritici* in wheat and see if the mutation rate changes at these loci



Without Wheat

With Wheat



Cas9-mediated breaks + sequencing



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Thank You for Your Attention

