The H2A.Z histone variant regulates meiotic chromosome dynamics

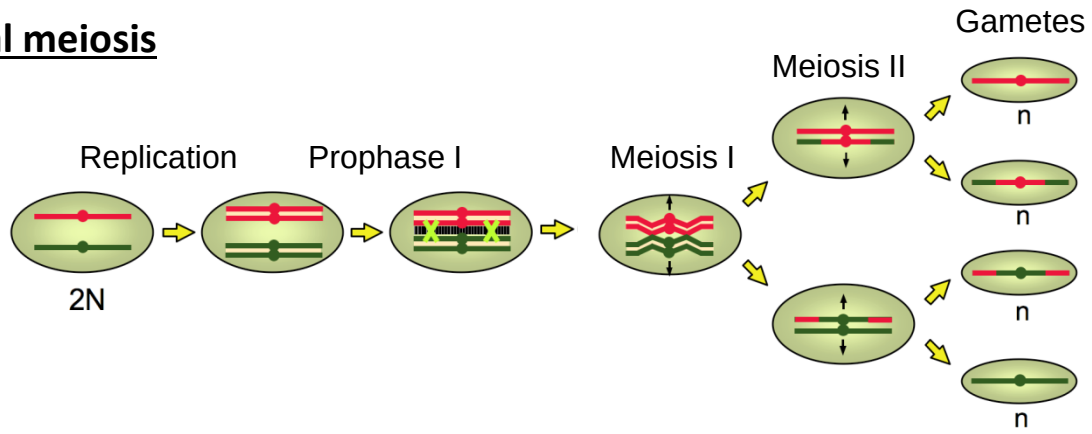
Meiotic chromosome dynamics Group

Pedro San Segundo (Lab P2.2)

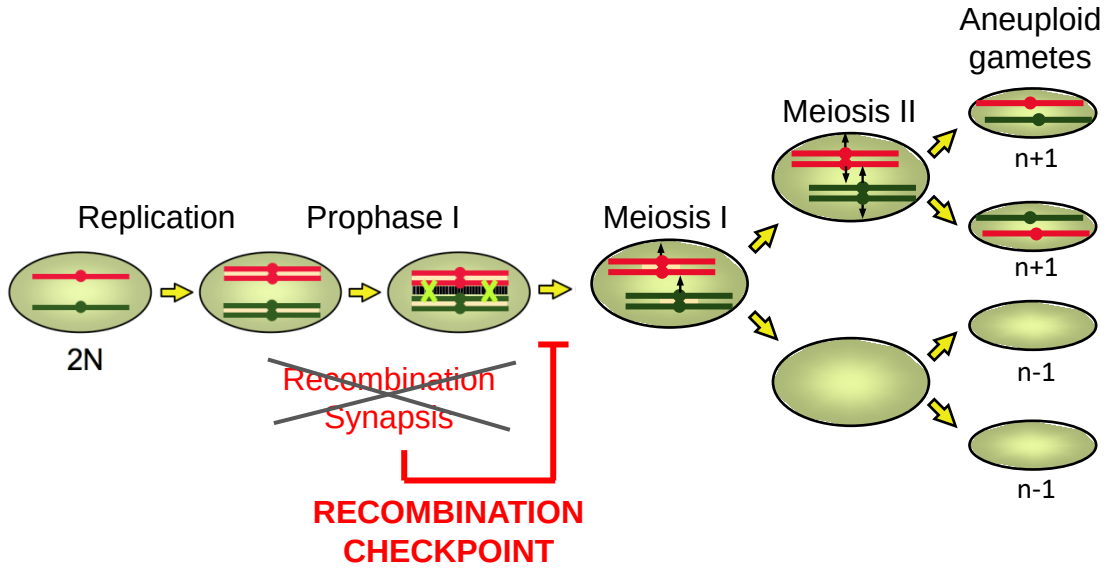
Institute of Functional Biology and Genomics (Salamanca)

Role of H2A.Z in meiosis

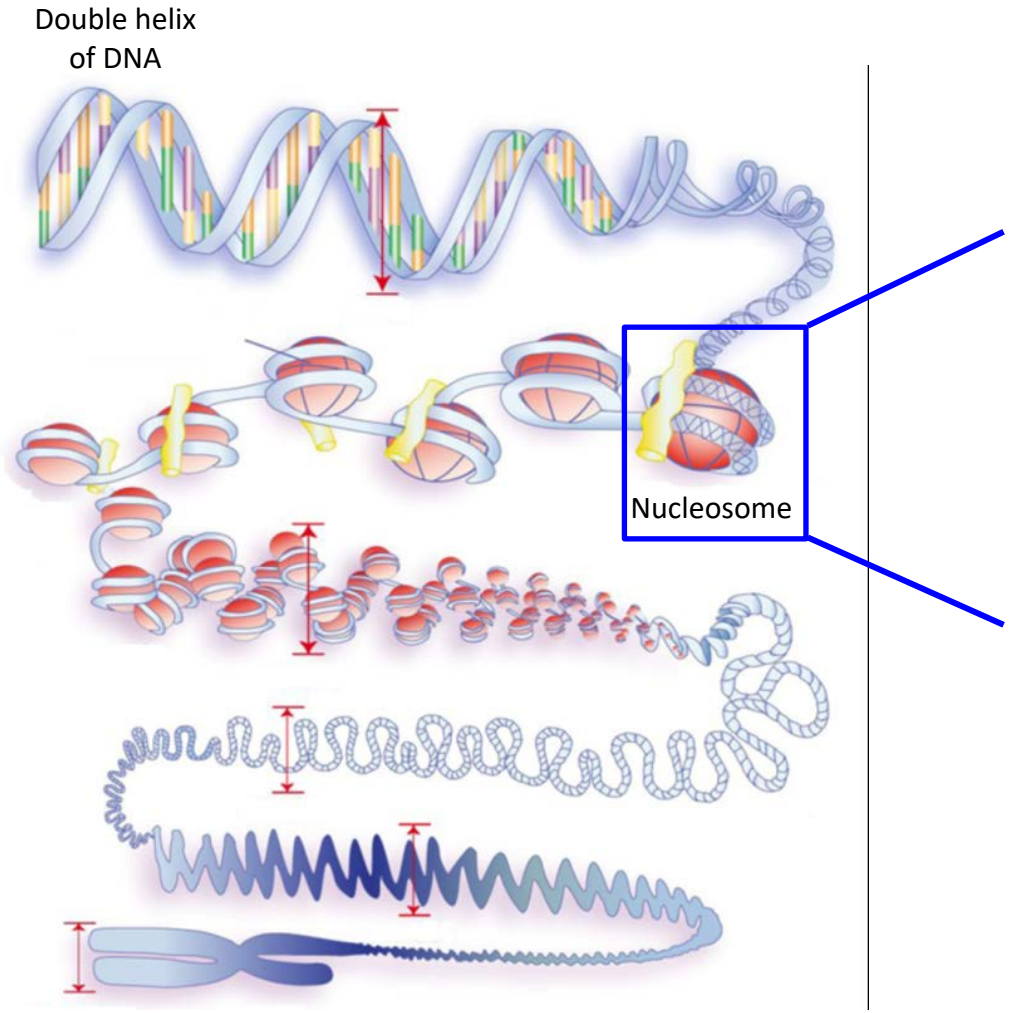
- **Normal meiosis**

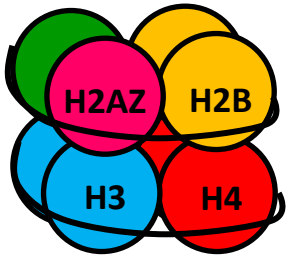


- **Defective meiosis (*zip1* mutant)** → Recombination checkpoint



Chromatin regulation





Histones
+
DNA

Cannonical histones:

H2A, H2B, H3, H4

Variant histones:

CenH3,H3.3,**H2A.Z**, H2A.X, H2Av, H2A-Bbd, MacroH2A

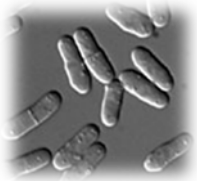
Histone variant H2A.Z is conserved in all eukaryotic organism

H2afz,H2Afv

Mus musculus

H2AvD

Drosophila melanogaster



Pht1

Schizosaccharomyces pombe

HTA4,-8,-9,-11

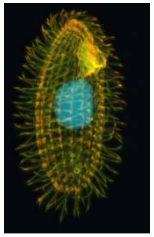
Arabidopsis thaliana

HTZ-1/H2A.Z

Caenorhabditis elegans

H2A.Z

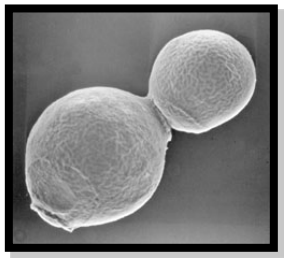
Xenopus leavis



Hv1

Tetrahymena termophila

HTZ1 gen encode H2A.Z histone



HTZ1

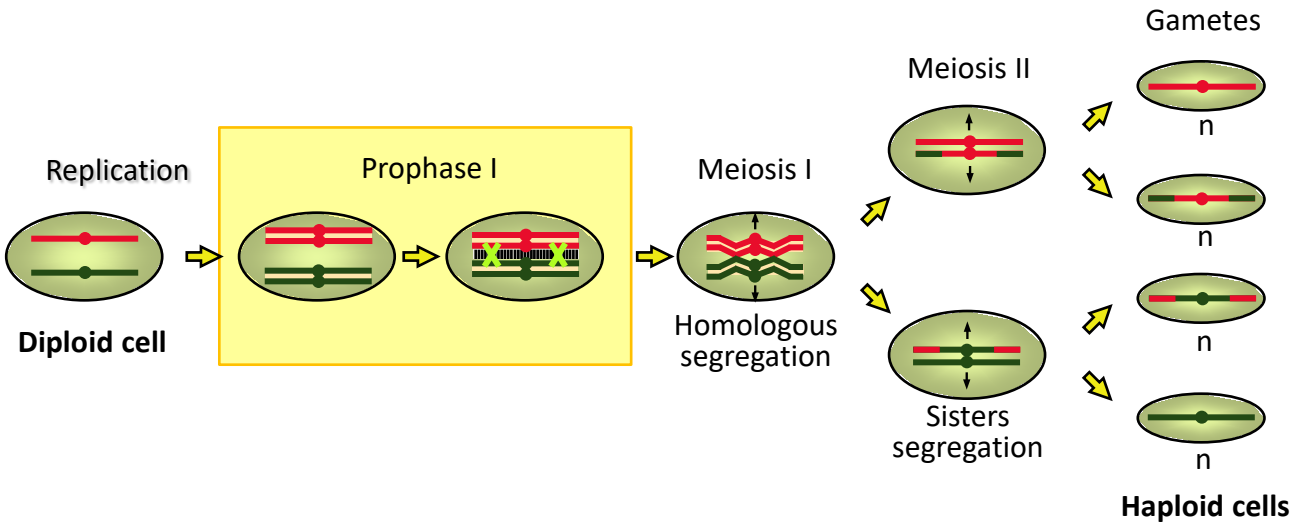
Saccharomyces cerevisiae

90% of homology

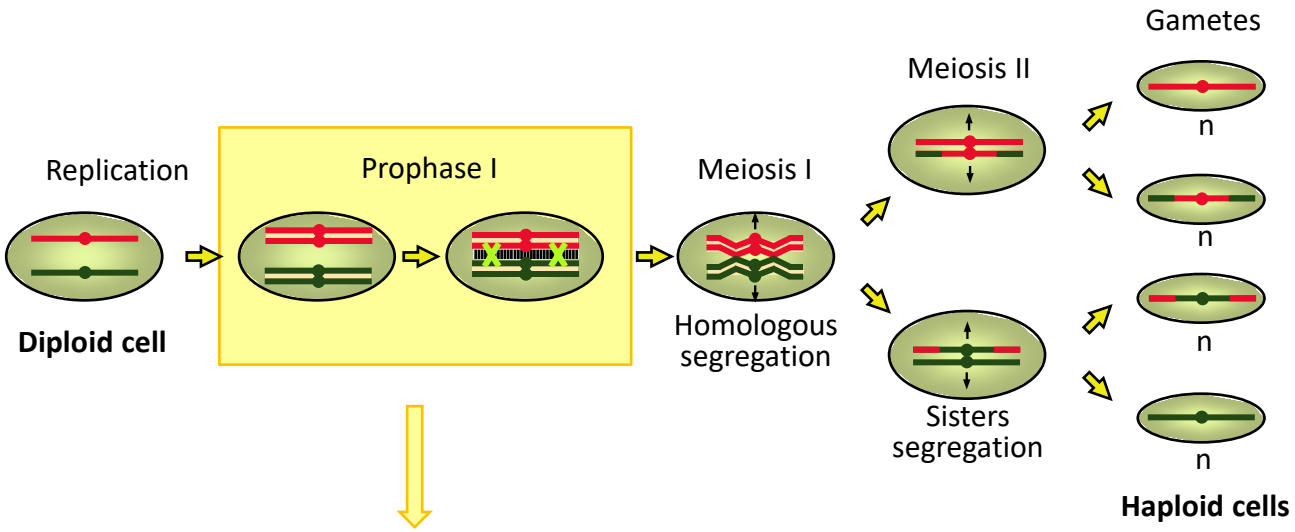
H2AZ,H2AF/Z

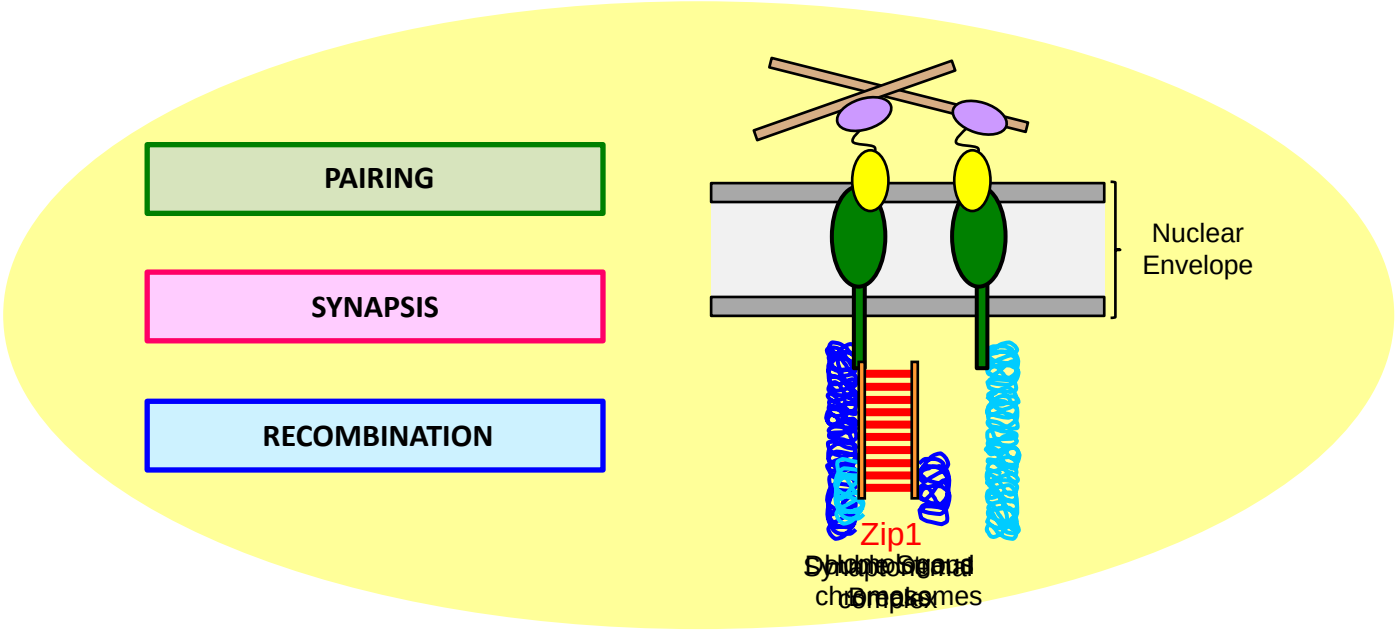
Human

Meiotic prophase

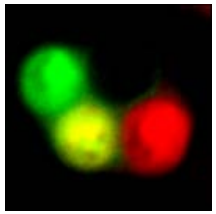


Meiotic prophase



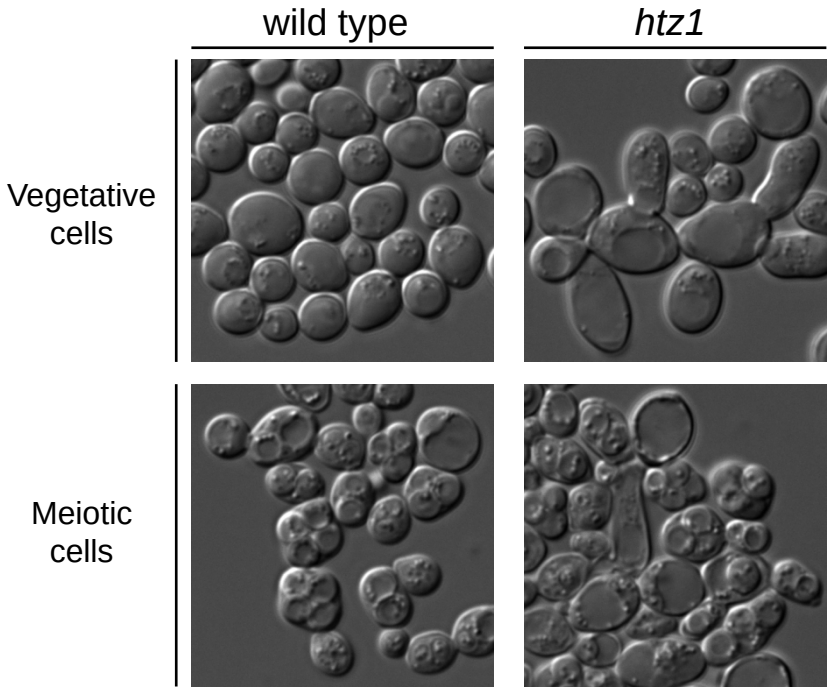


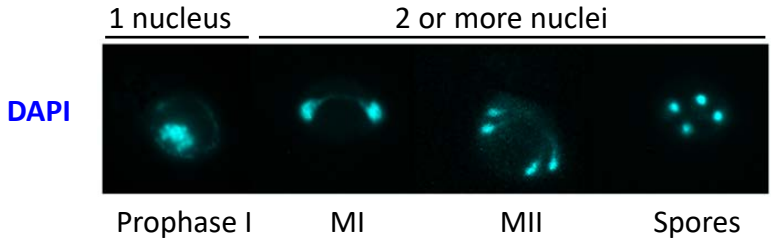
S. cerevisiae

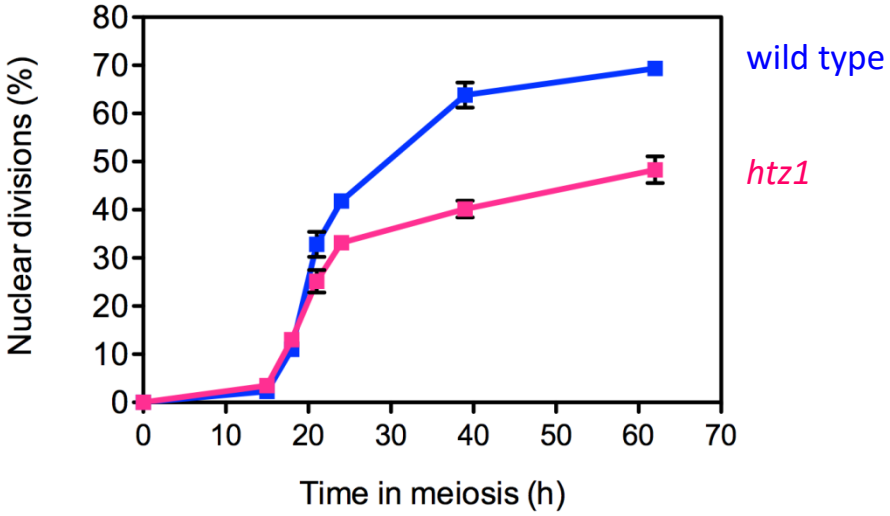


Spores

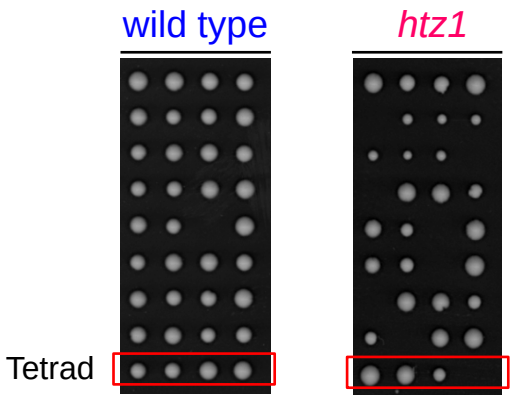
Phenotypes of *htz1* mutant



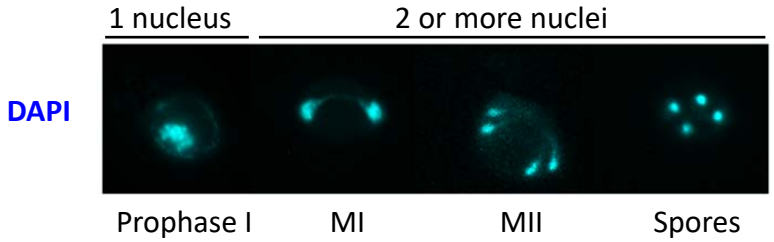


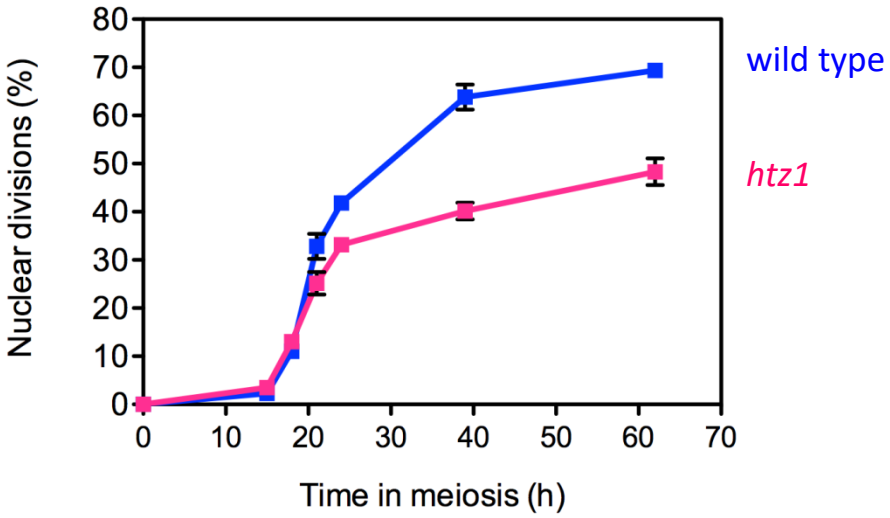


Mutant *htz1* displays a lower efficient in meiotic progression and a reduced viability of spores.



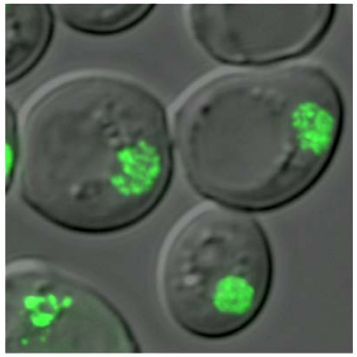
	wild type	*htz1*
Viability of spores	96,07 %	72,84%



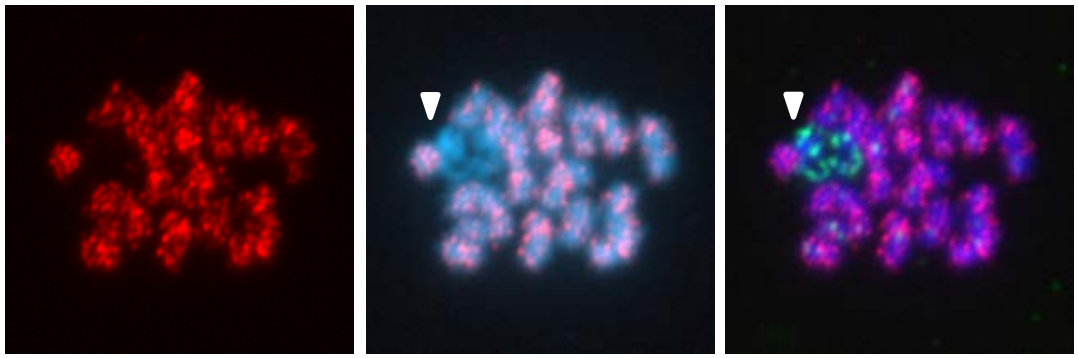


In vegetative cells,
SWR1 complex is necessary to deposit H2A.Z into chromatin

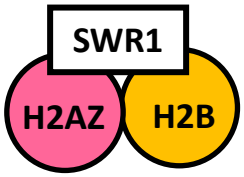
wild type

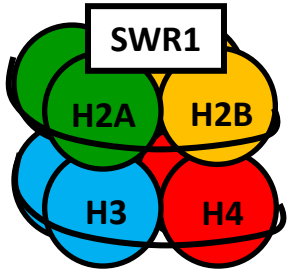


Live meiotic cells

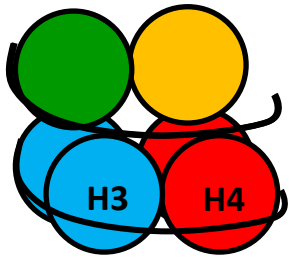


Meiotic chromosome spreads (arrow: rDNA region)





Nucleosome without H2A.Z

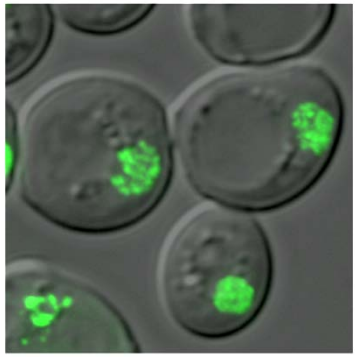


Nucleosome with H2A.Z

In absence of SWR1, H2A.Z displays additional localizations

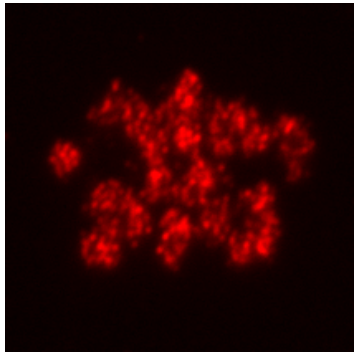
wild type

H2A.Z

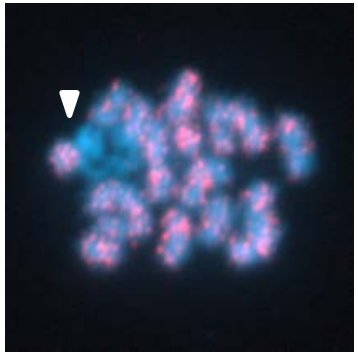


Live meiotic cells

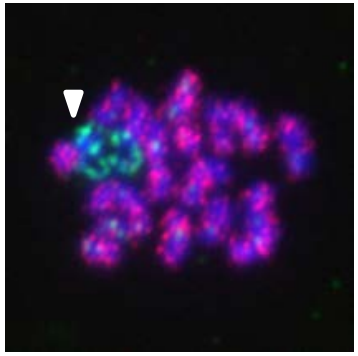
H2A.Z



Chromatin + H2A.Z



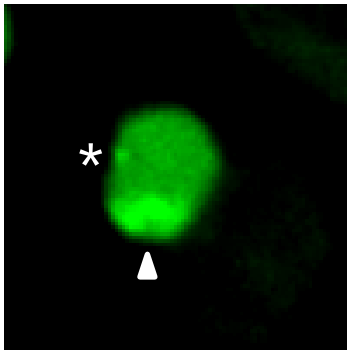
rDNA + H2A.Z



Meiotic chromosome spreads (arrow: rDNA region)

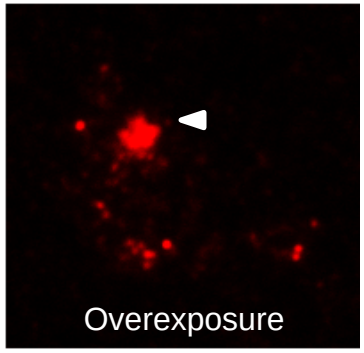
swr1

H2A.Z

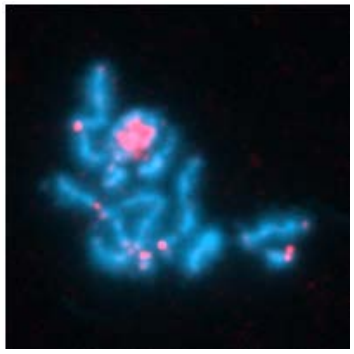


Live meiotic cells

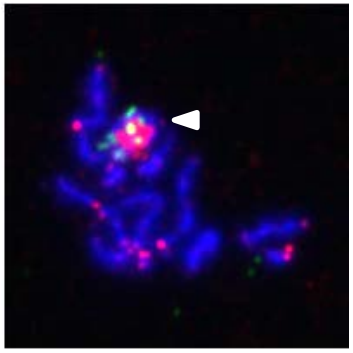
H2A.Z



Chromatin + H2A.Z



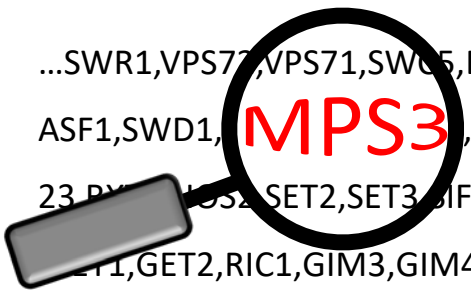
rDNA + H2A.Z



Meiotic chromosome spreads (arrow: rDNA region)

Interaction between H2A.Z and Mps3

H2A.Z



…SWR1,VPS72,VPS71,SWC5,EAF5,EAF7,ISW1,

ASF1,SWD1,[illegible],SAP30,EAF3,PHO

23,RVB2,SET2,SET3,TAF2,SPT3,SPT8,YPT6

,GET1,GET2,RIC1,GIM3,GIM4,GIM5,YKE2,TUB3

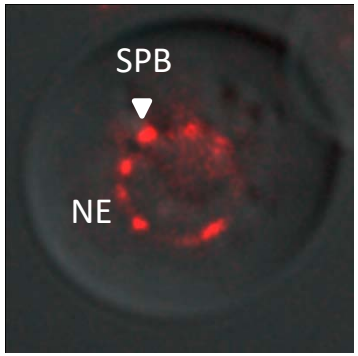
,CIN1,UBP3,UBP6…

(Saccharomyces Genome Database)

Mps3

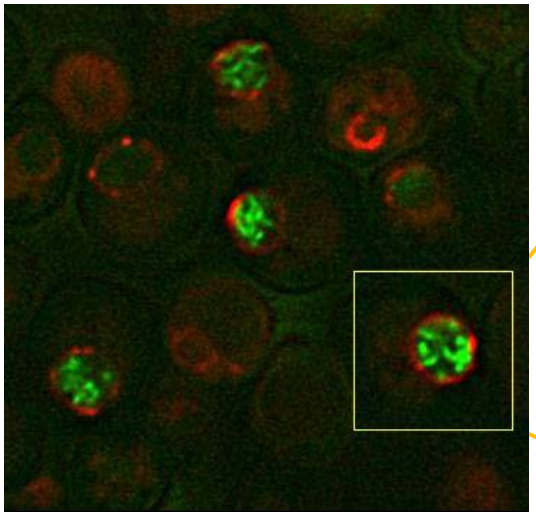
- Spindle Pole Body
- Nuclear envelope

Mps3

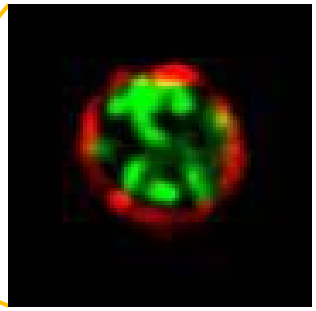


Live cells
(Meiotic prophase)

Mps3 + Zip1



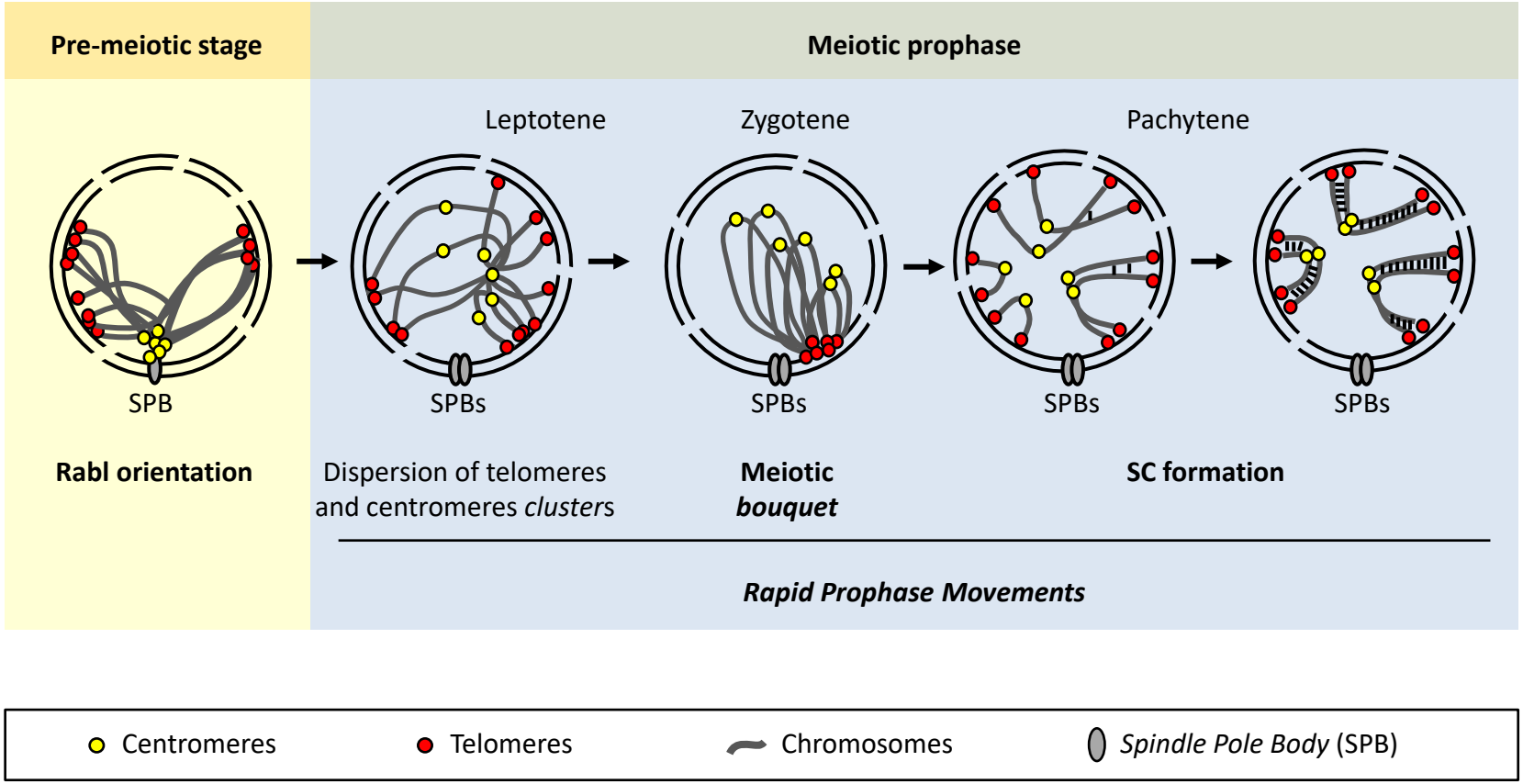
Mps3 + Zip1



Meiotic functions:

- Attachment telomeres to NE
- Meiotic bouquet
- Movement of homologous chromosomes

Dynamics of chromosomes during meiotic prophase



Physical and genetic interaction between H2A.Z and Mps3

(Saccharomyces Genome Database)

H2A.Z

⇩

Mps3

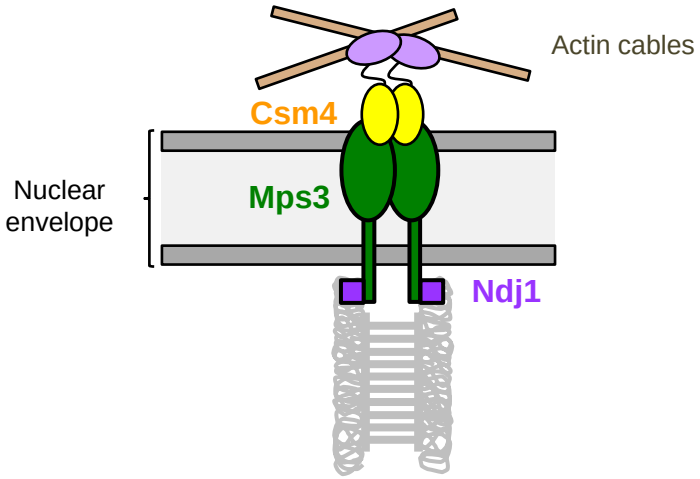
(Uetz et al.,2000)

(Yu et al., 2008)

(Gardner JM et al., 2011)

LINC Complex: KASH-SUN

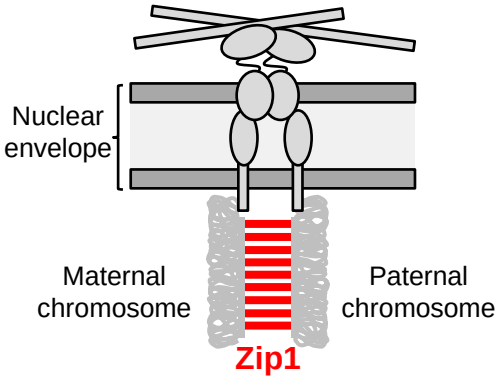
(Linker of Nucleoskeleton and Cytoskeleton)

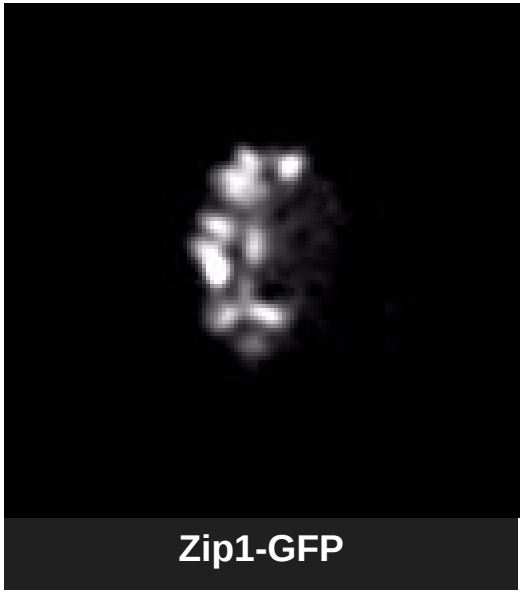


S. cerevisiae

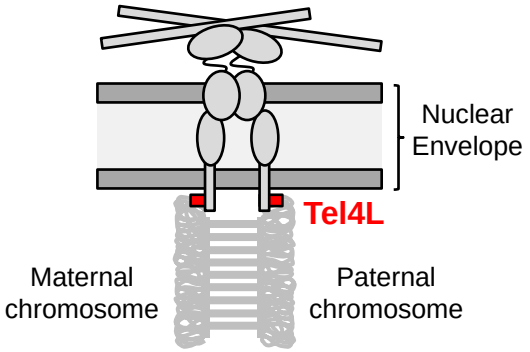
Analysis of chromosome movements

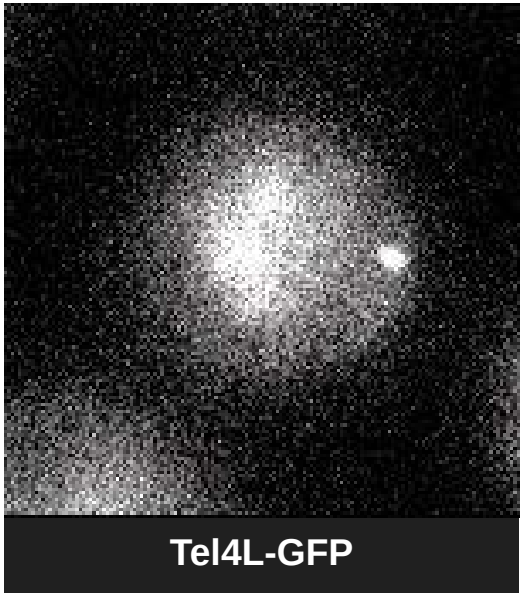
Pair homologous chromosomes movements



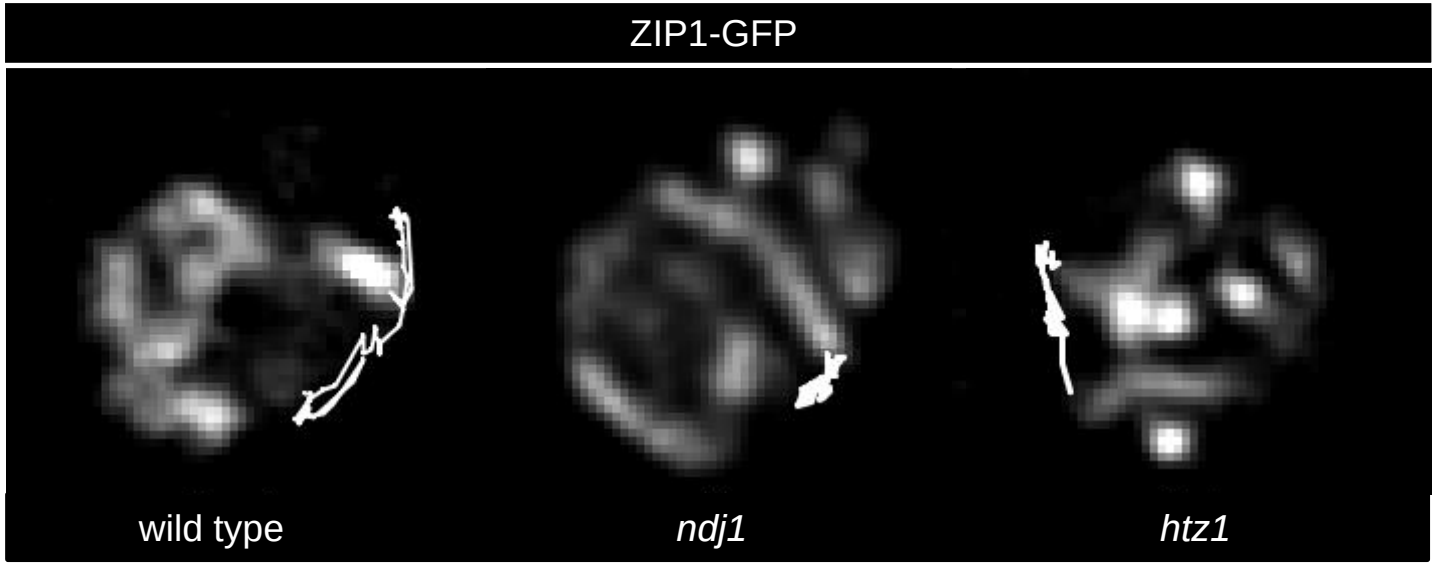


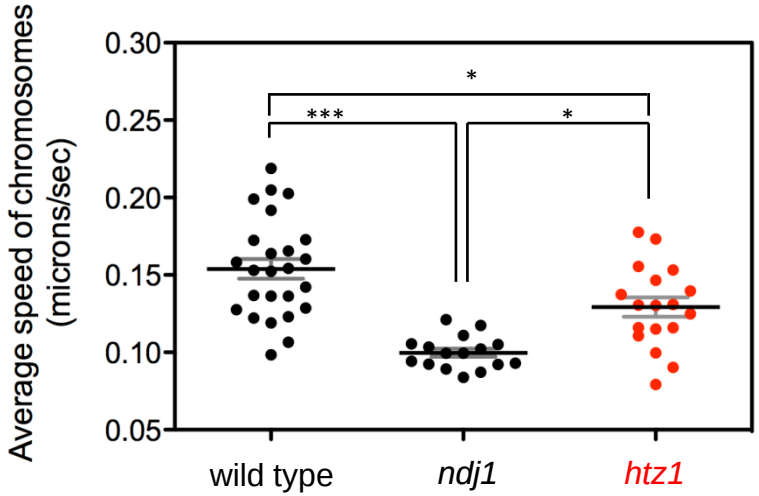
Telomere movement (Tel4L)



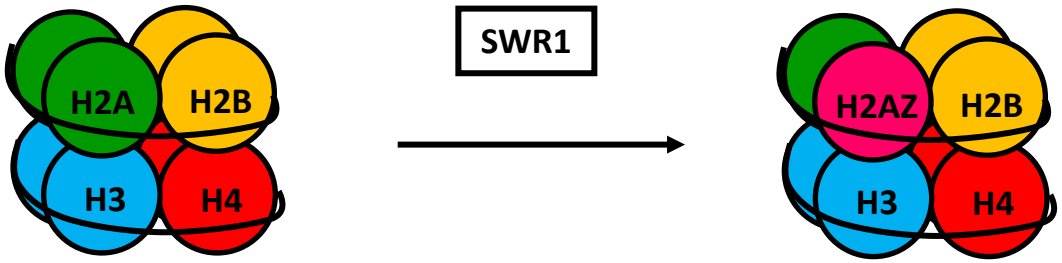


H2A.Z is necessary for rapid prophase chromosome movement





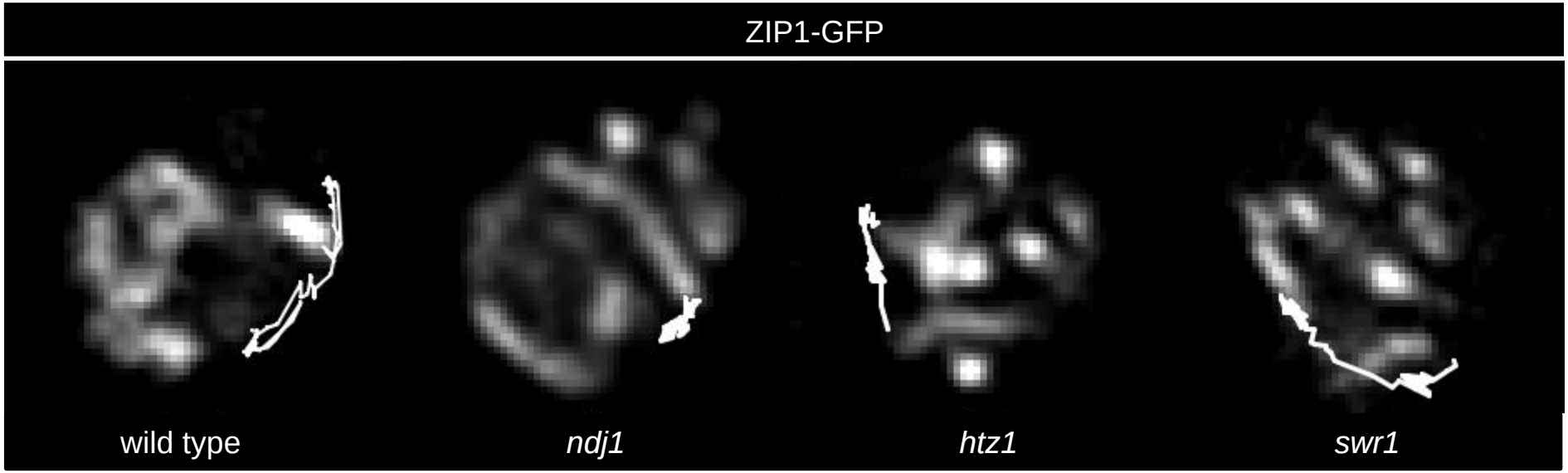
Does *swr1* mutant display defects in chromosome movements?

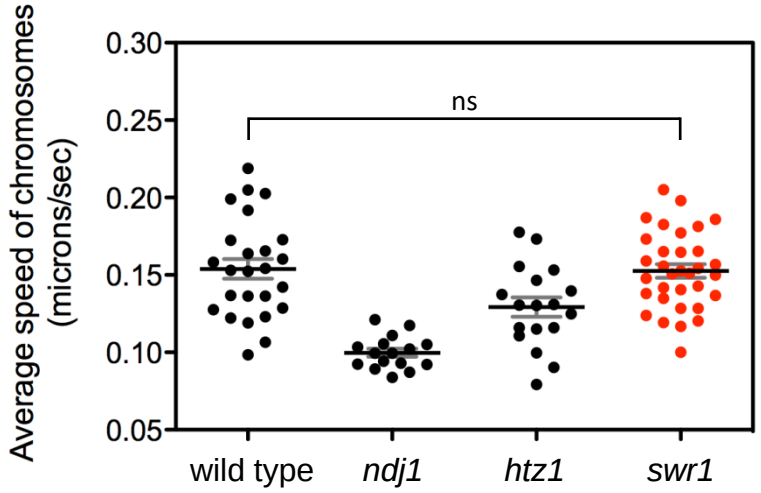


Nucleosome without H2A.Z

Nucleosome with H2A.Z

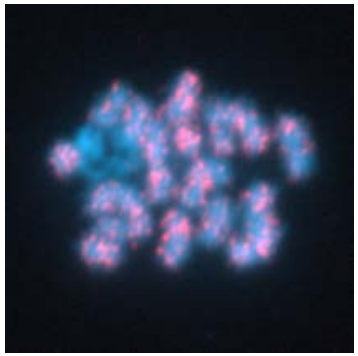
The function of H2A.Z in chromosome movement is independent of its SWR1-dependent chromatin deposition



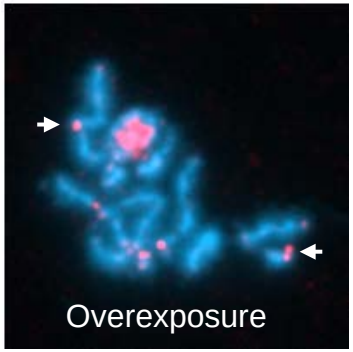


Do H2A.Z and Mps3 colocalize in telomeres, in *swr1* mutant?

Chromatin + H2A.Z

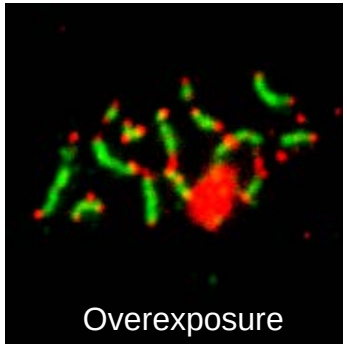


wild type

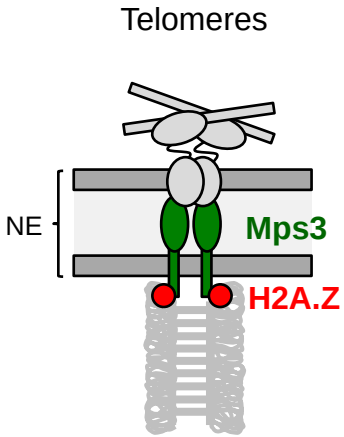


swr1

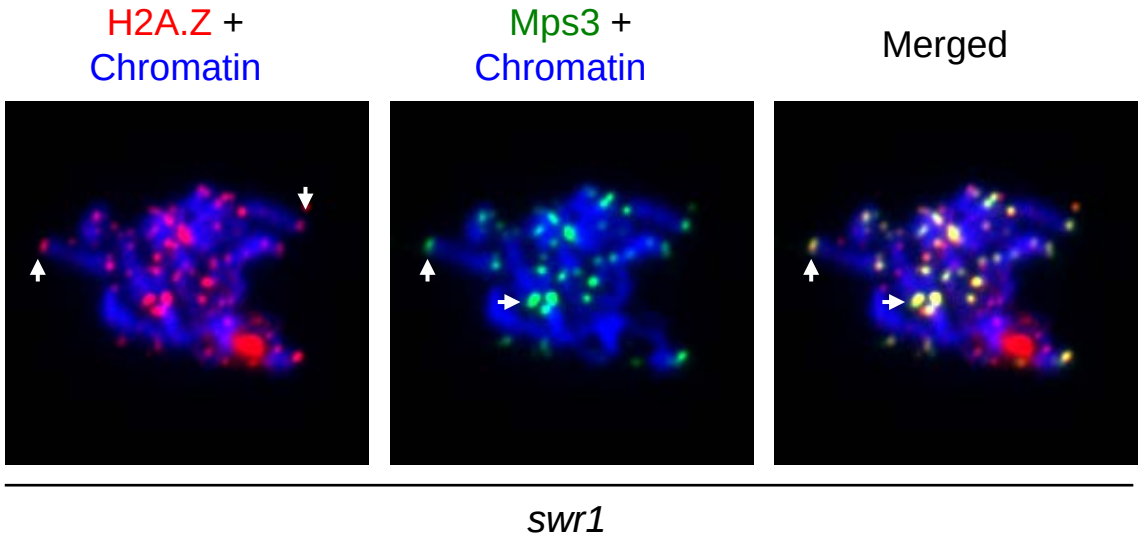
Zip1 + H2A.Z

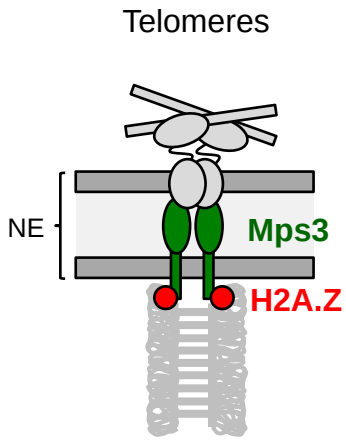


swr1

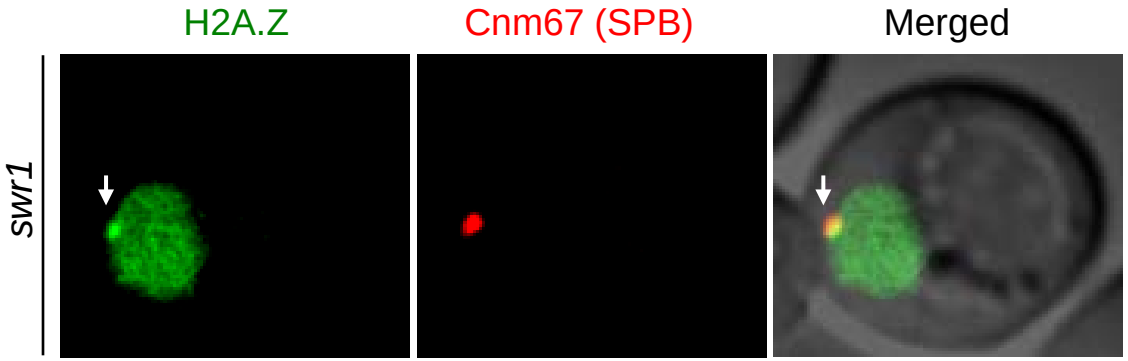


In *swr1* mutant, H2A.Z colocalize with Mps3 in telomeres

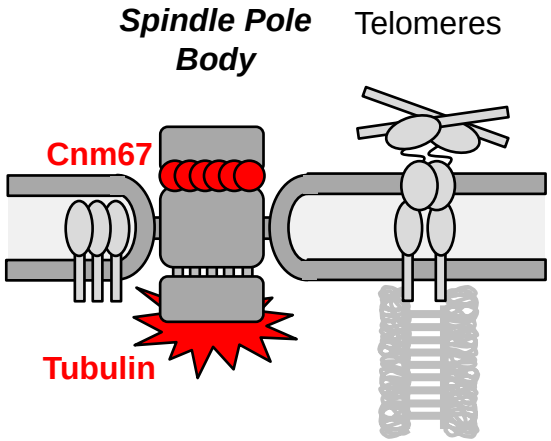


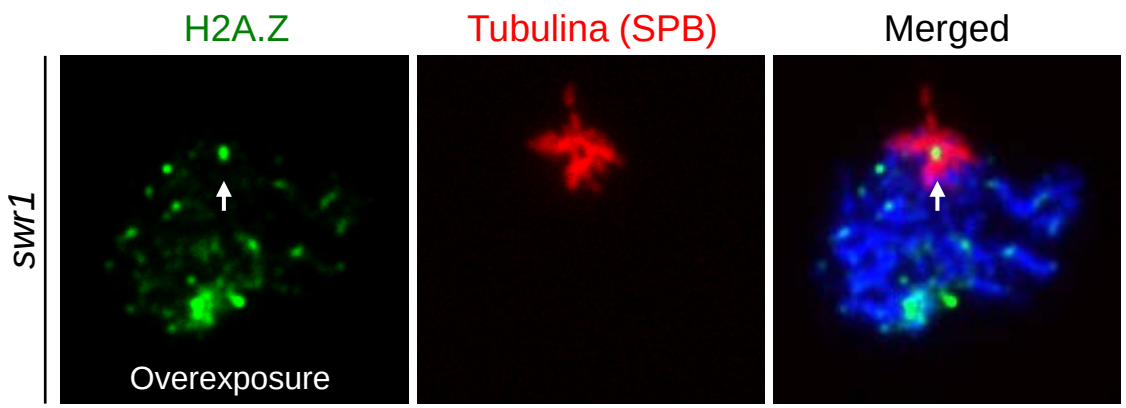


In absence of Swr1, H2A.Z is localize in Spindle Pole Body

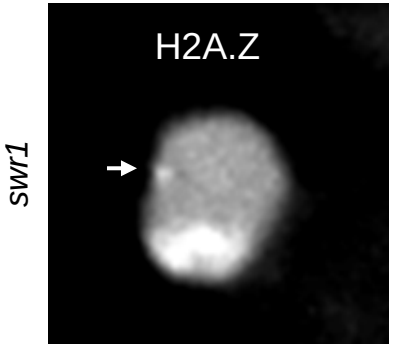


Live meiotic cells



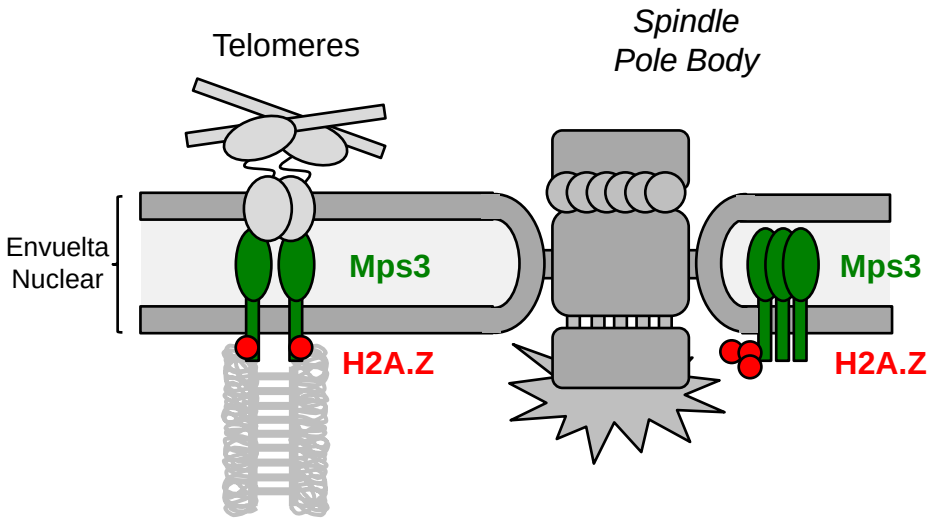


Pachytene chromosome spreads

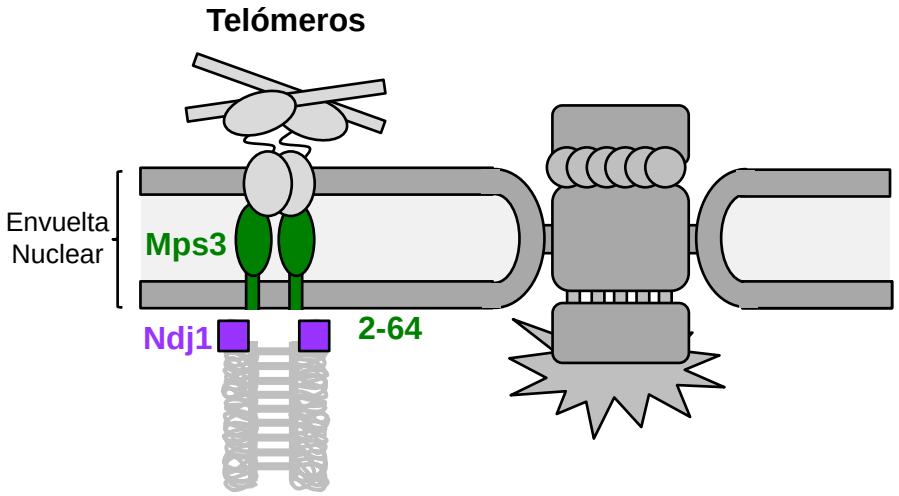


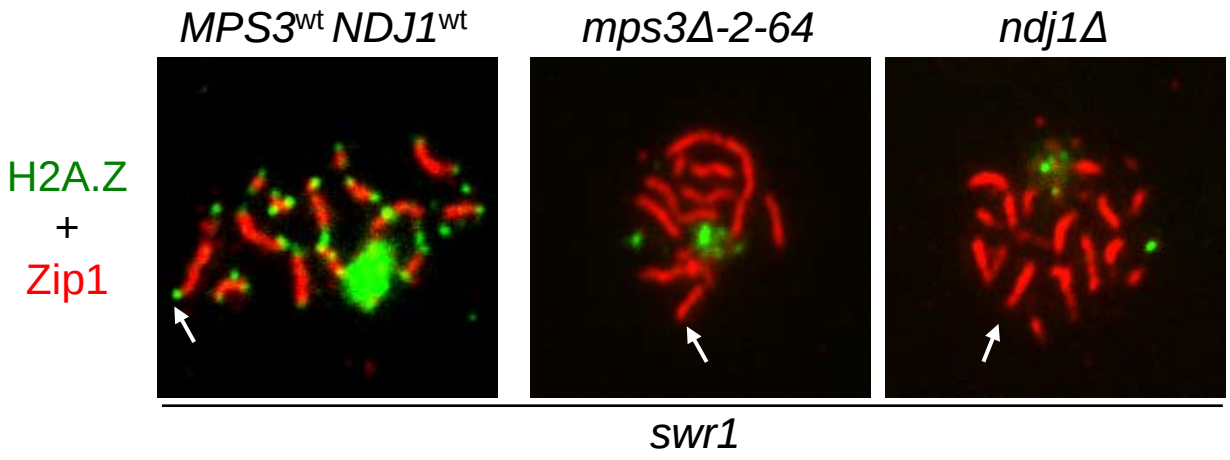
Live meiotic cell

In *swr1* mutant, H2A.Z is localize in telomeres and Spindle Pole Body similar to Mps3

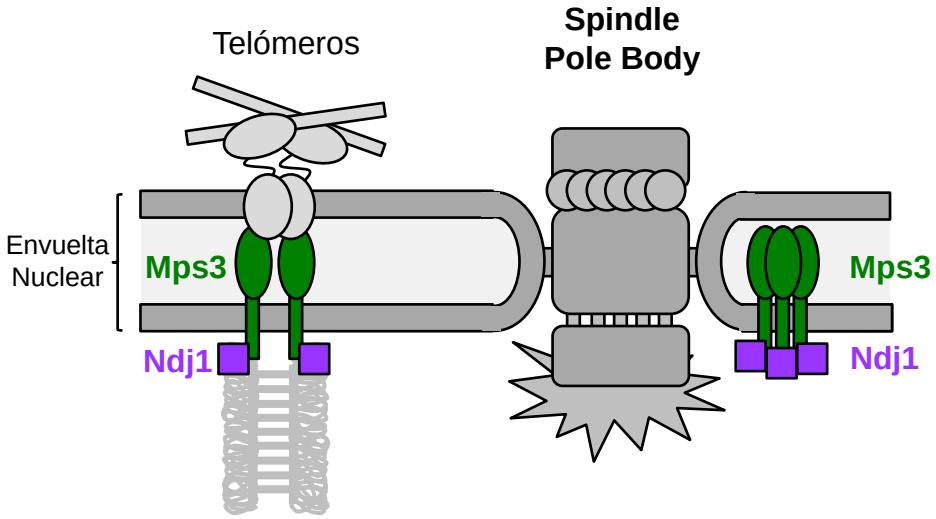


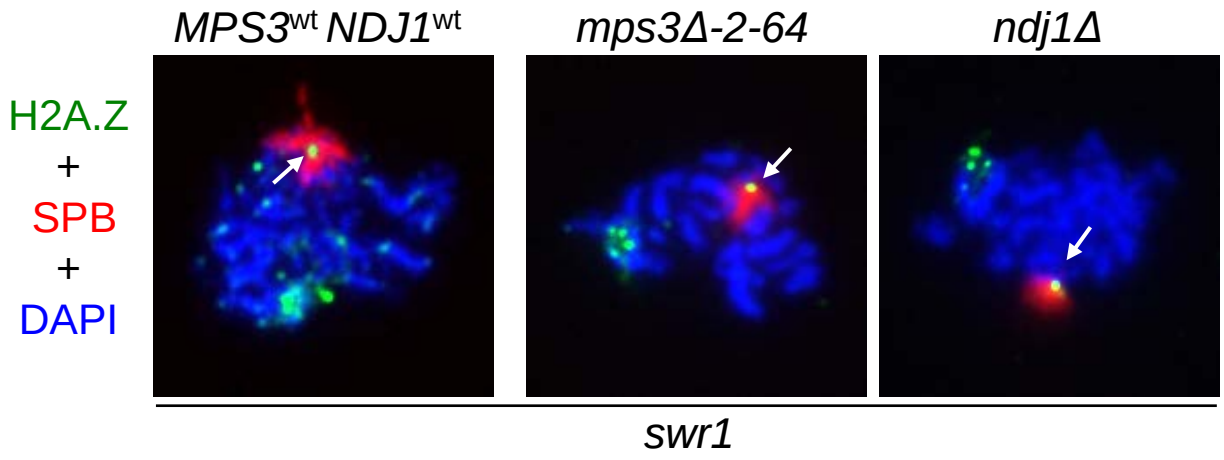
Telomeric localization of H2A.Z depends on the N-terminal region of Mps3 and Ndj1





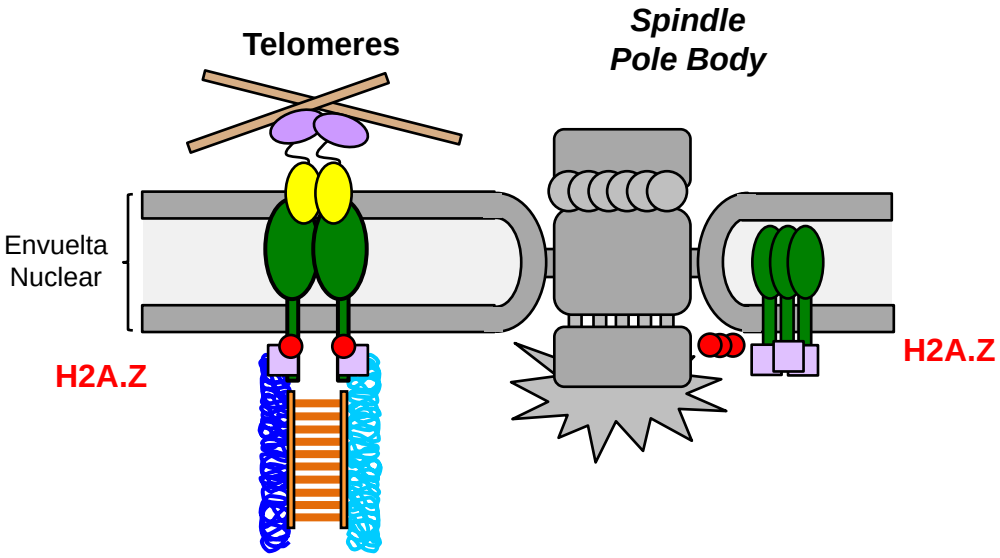
In absence of the N-terminal region of Mps3 or Ndj1, localization of H2A.Z is maintained in SPB





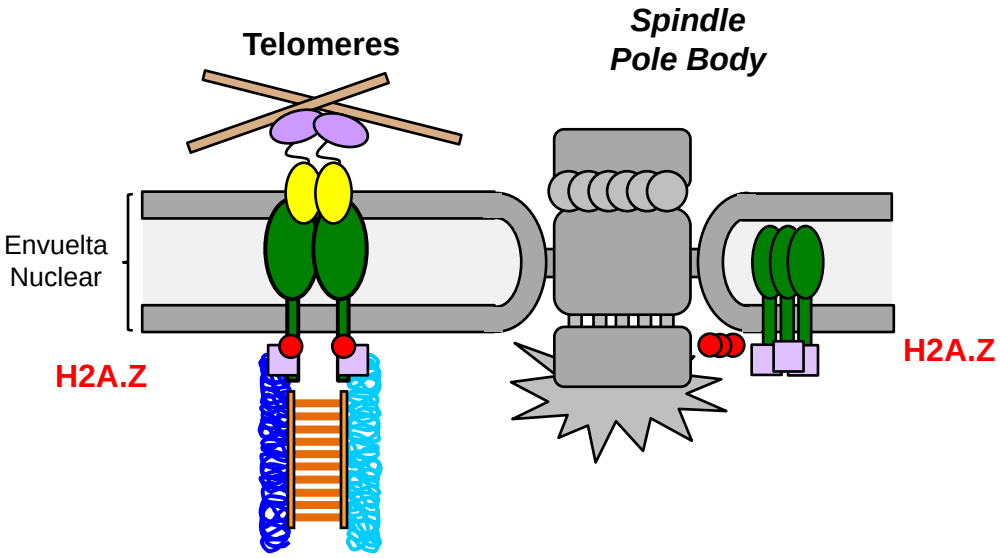
Conclusions

- Acurate meiotic progression and viability of spores
- H2A.Z is necessary for chromosome movements during meiotic prophase
- In *swr1* mutant, H2A.Z is localized in telomeres and SPB



Model

- Acurate meiotic progression and viability of spores
- H2A.Z is necessary for chromosome movements
- In *swr1* mutant, H2A.Z is localized in telomeres and SPB



Openned-questions:

- How H2A.Z regulates chromosome movements during meiotic prophase?
- Does exist a relationship between localization of H2A.Z in telomeres and SPB?
- What is role of H2A.Z in SPB? Other proteins implicate

Thanks
for your attention!