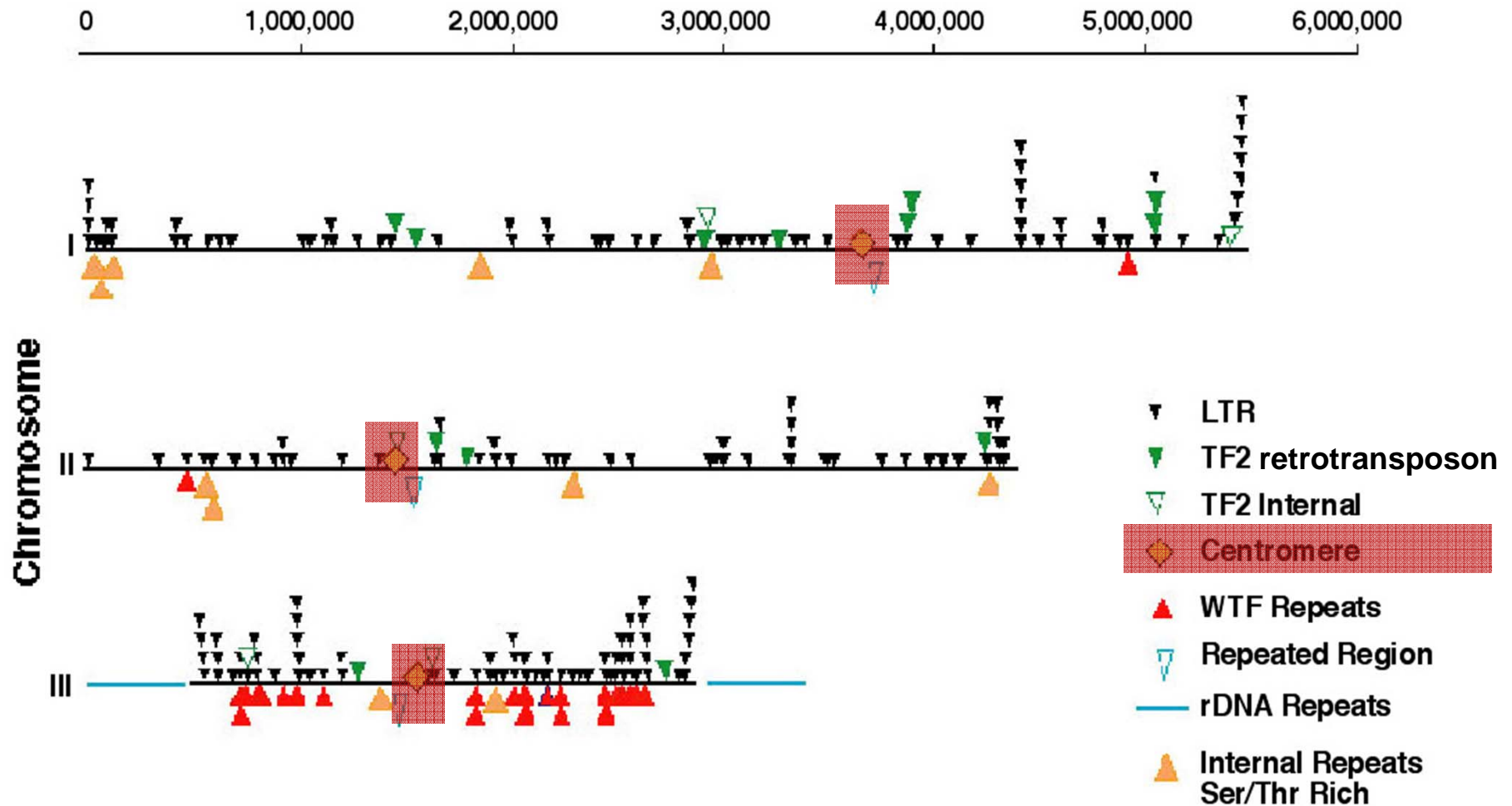


S. pombe genome contains several different classes of repeat elements



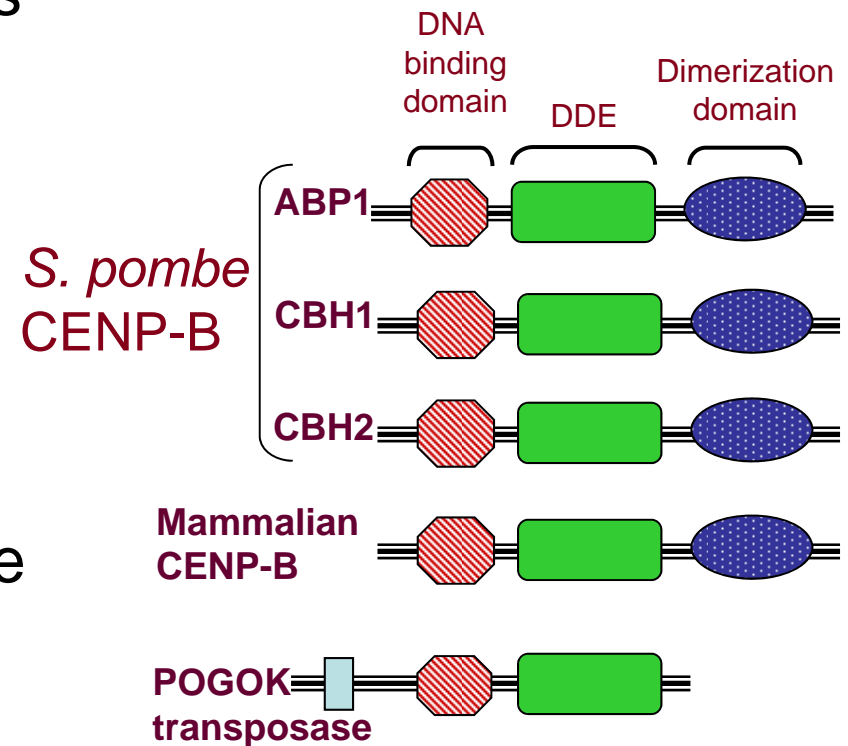
- Transposon-derived proteins
- Heterochromatin

The organization of genome into higher-order structures has important biological implications

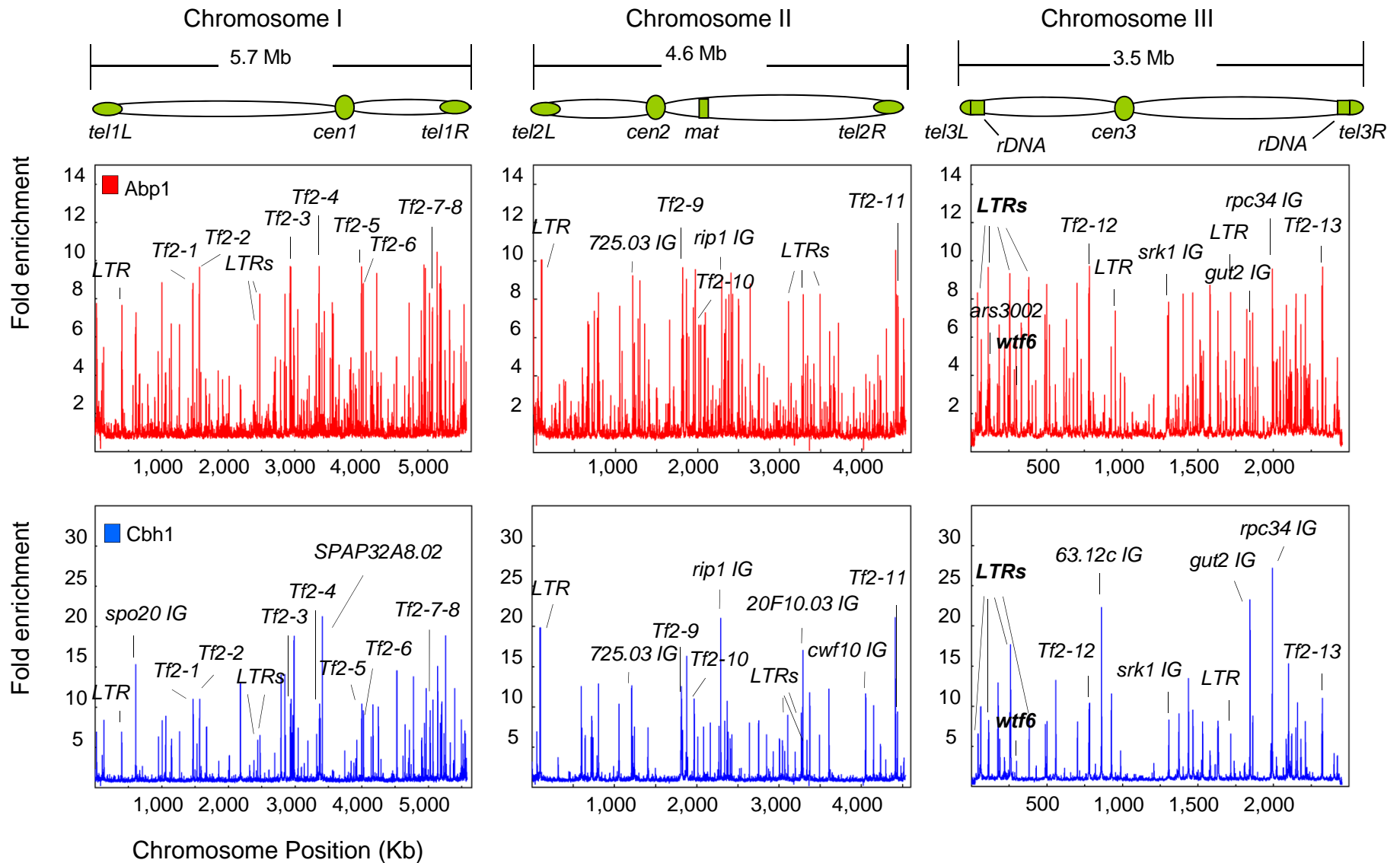
- Stable maintenance of gene expression patterns during development
- Maintenance of genomic integrity and prohibition of inter- or intrachromosomal recombination in repetitive DNA sequences
- Lineage-specific control of long-range chromatin interactions
- Proper segregation of chromosomes
- Cancer and other human diseases

Host genome surveillance for retrotransposons and repeats by transposon-derived proteins

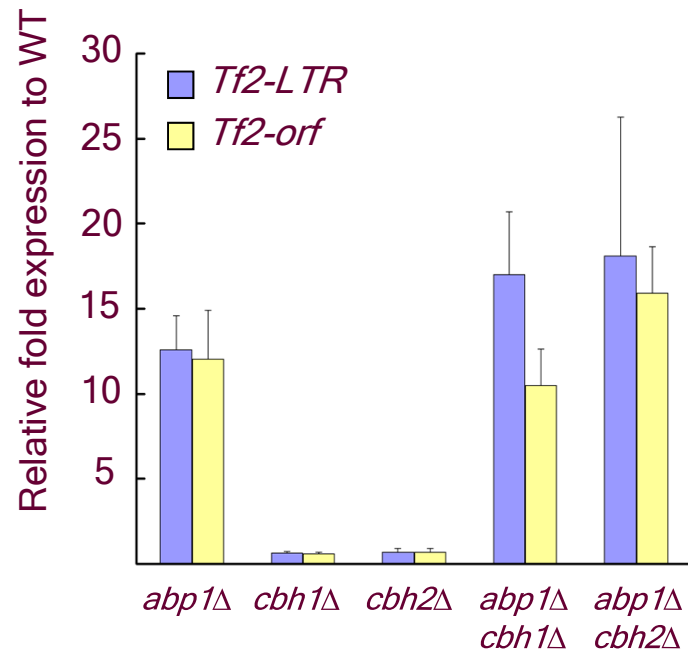
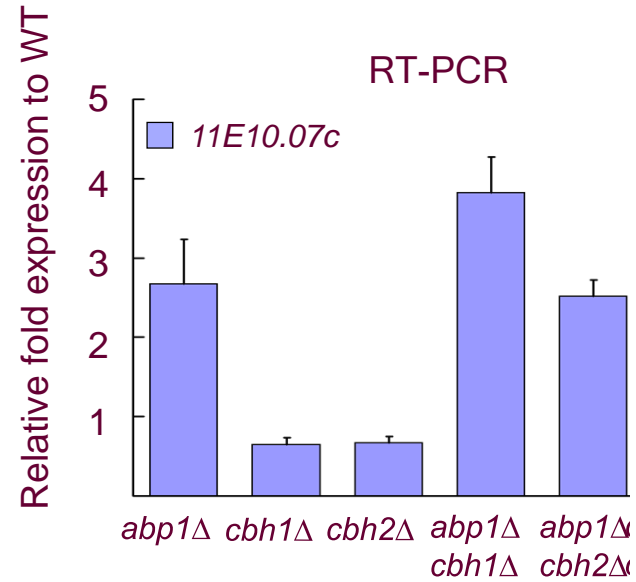
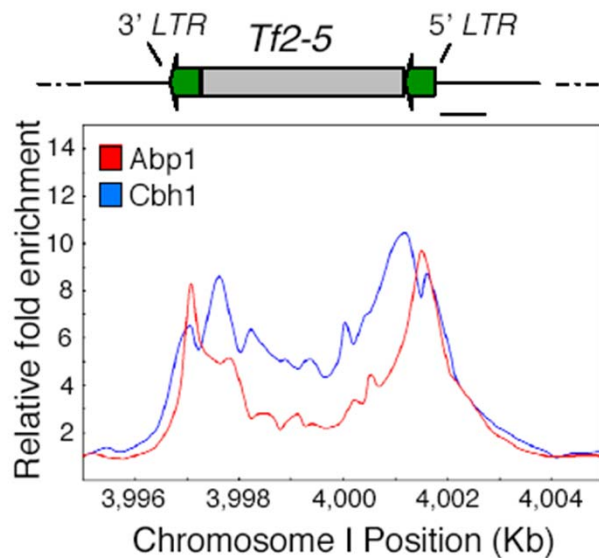
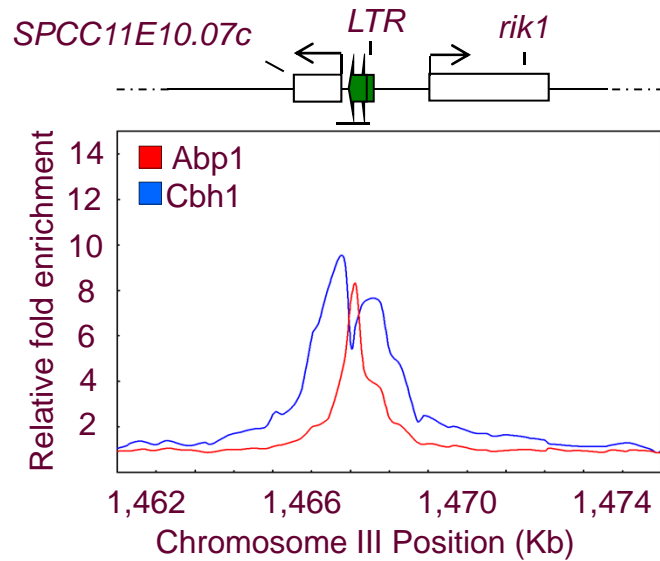
- CENP-Bs are conserved proteins that contain DNA binding and dimerization domains
- CENP-Bs are derived from transposases of POGO DNA transposons
- *S. pombe* genome encodes three CENP-Bs that have redundant roles in centromere chromatin assembly



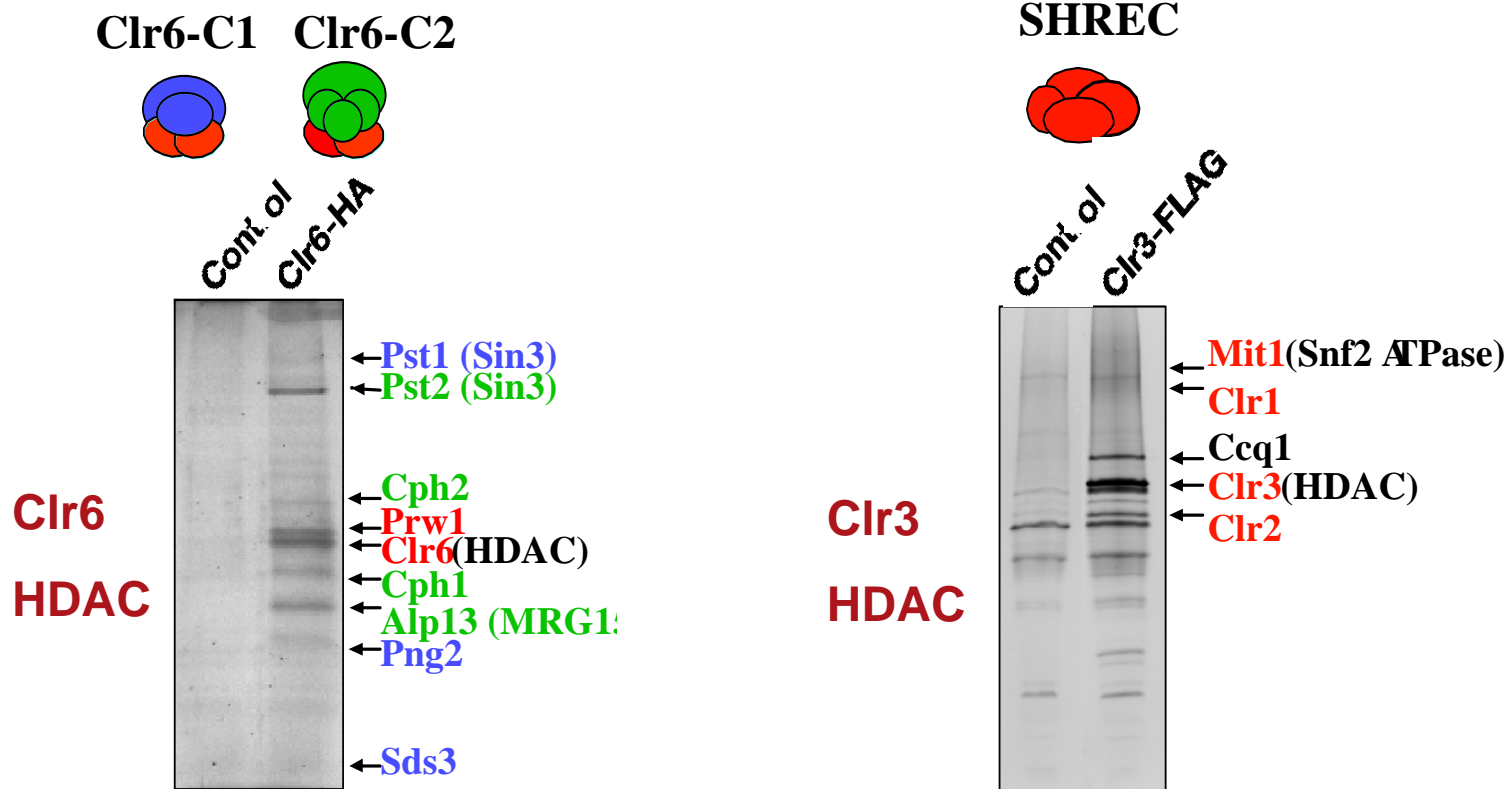
CENP-Bs localize to retrotransposons and their remnants in the *S. pombe* genome



CENP-Bs silence LTR-associated genes and Tf retroelements

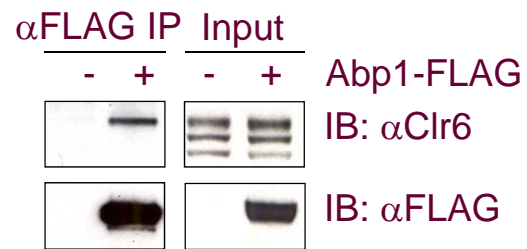
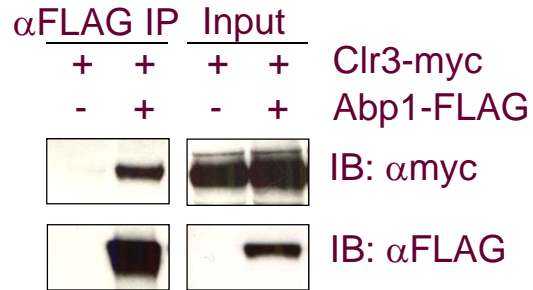


Transcriptional gene silencing effector protein complexes

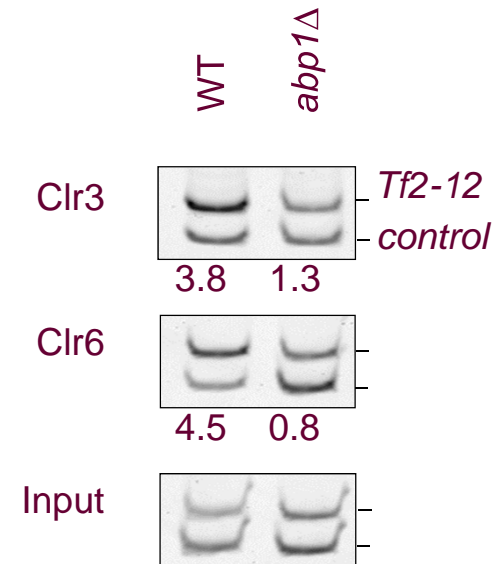


CENP-Bs recruit Clr3 and Clr6 histone deacetylases to repress Tf2 retroelements

Co-Immunoprecipitation



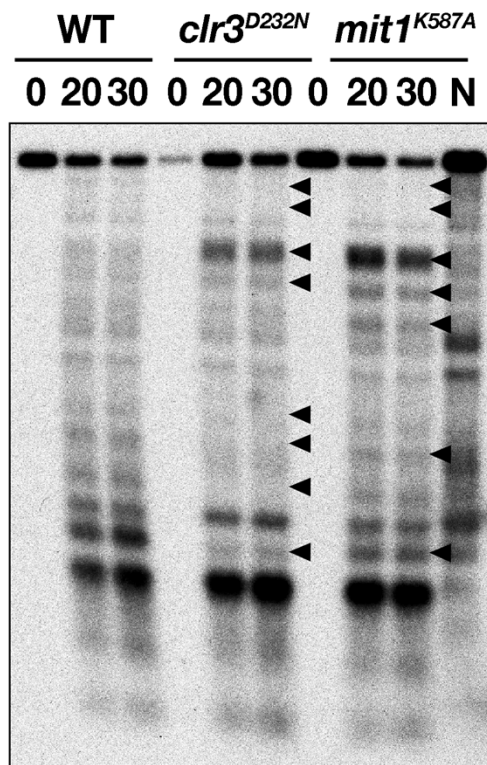
ChIP



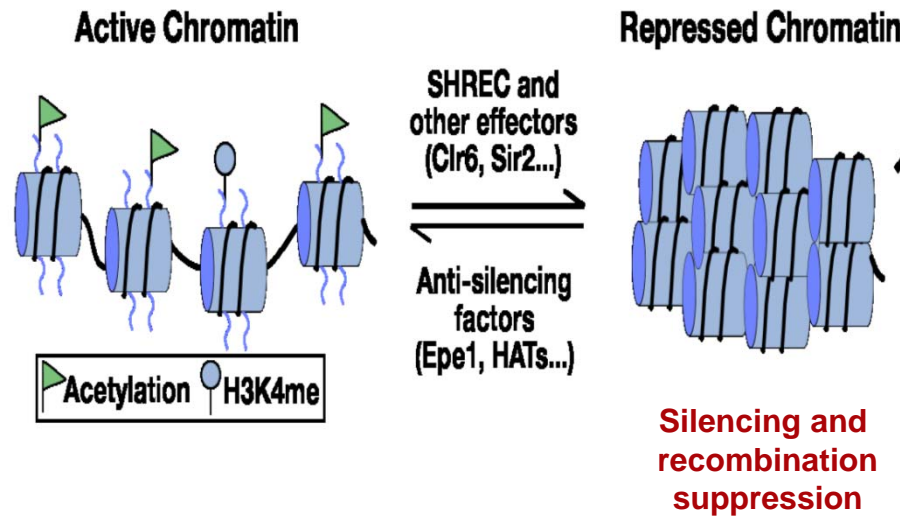
Clr3 = SHREC

Clr6 = Clr6 HDAC

SHREC activities facilitate positioning of nucleosomes required for higher-order chromatin assembly



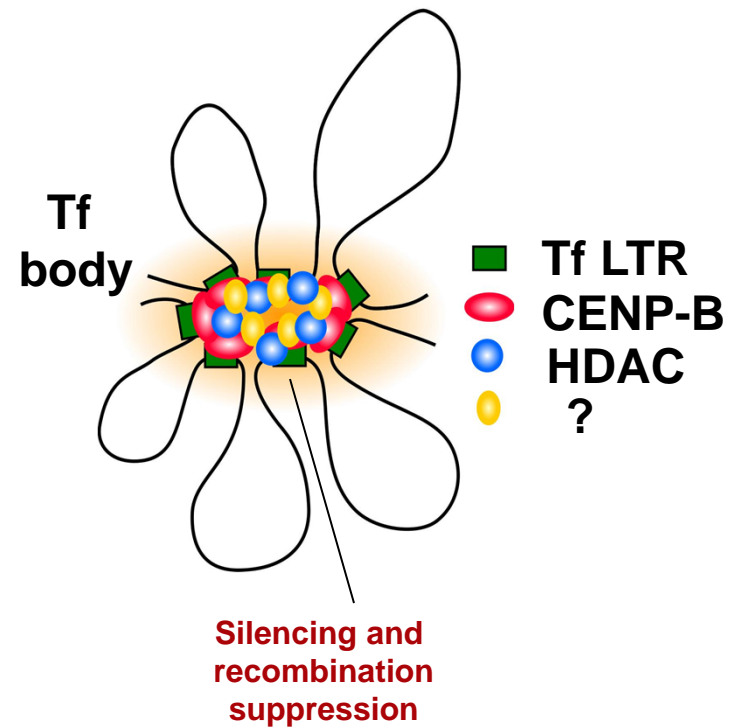
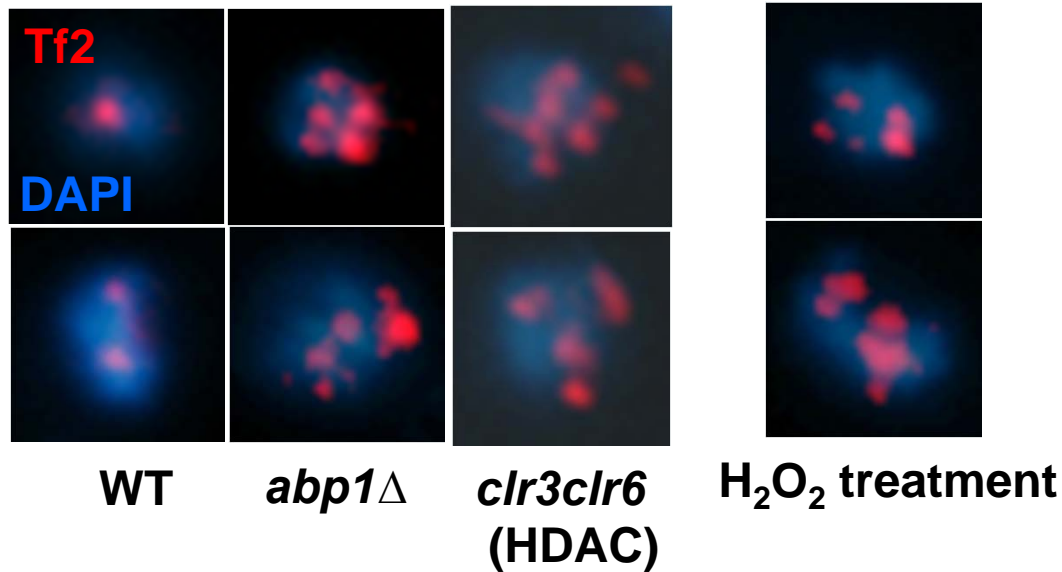
Micrococcal nuclease digestion patterns



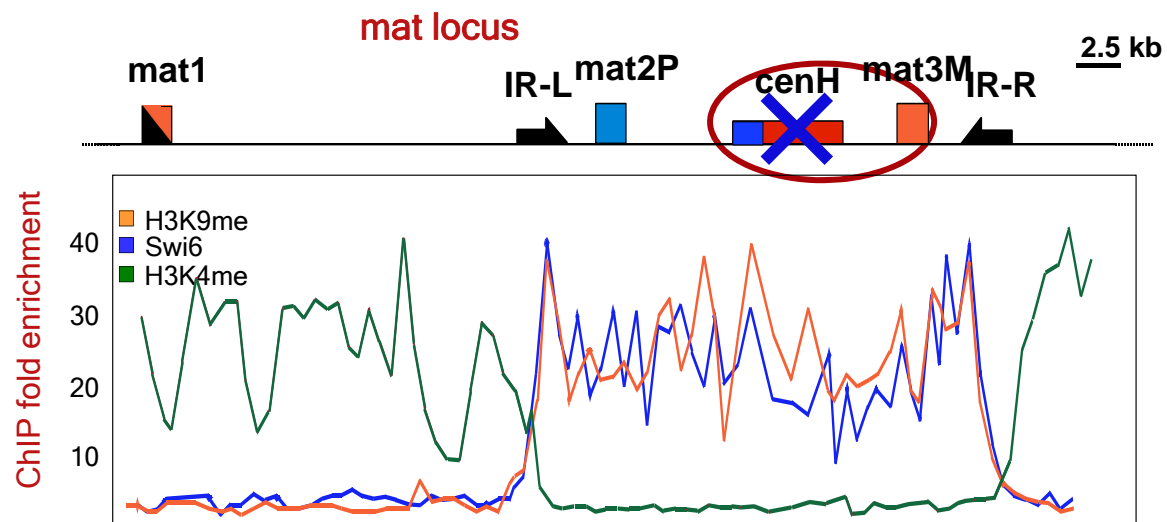
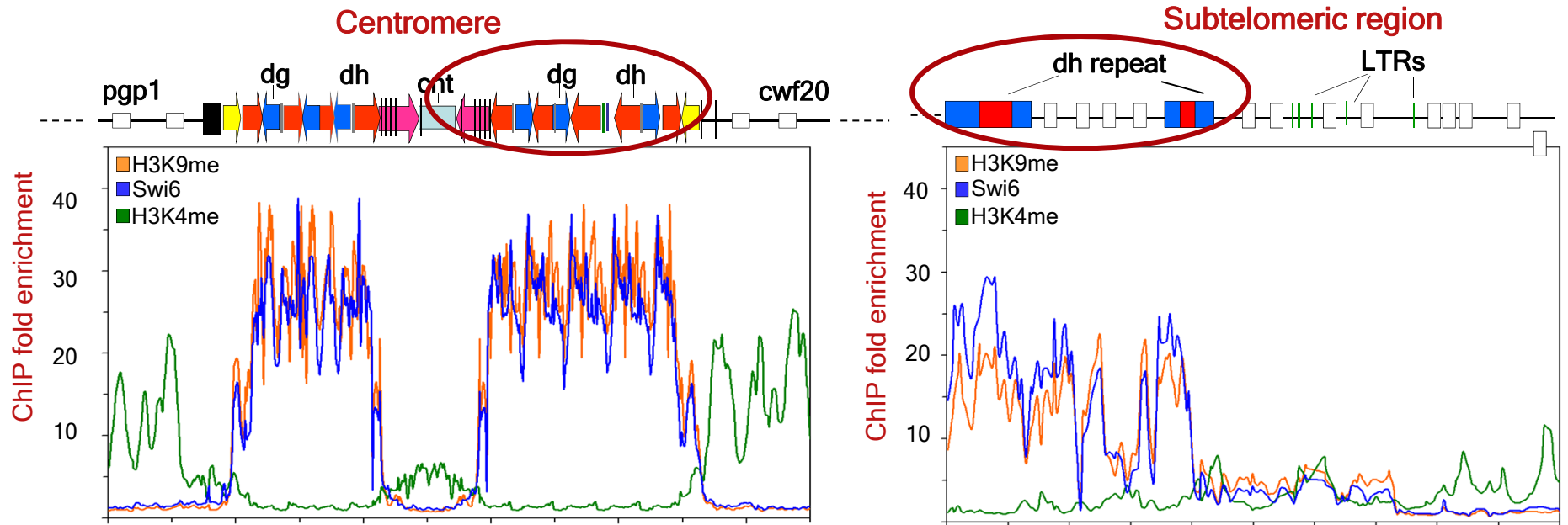
Silencing and recombination suppression

CENP-Bs and their associated HDACs are required for clustering of retrotransposon elements

FISH using Tf2 retroelement probe

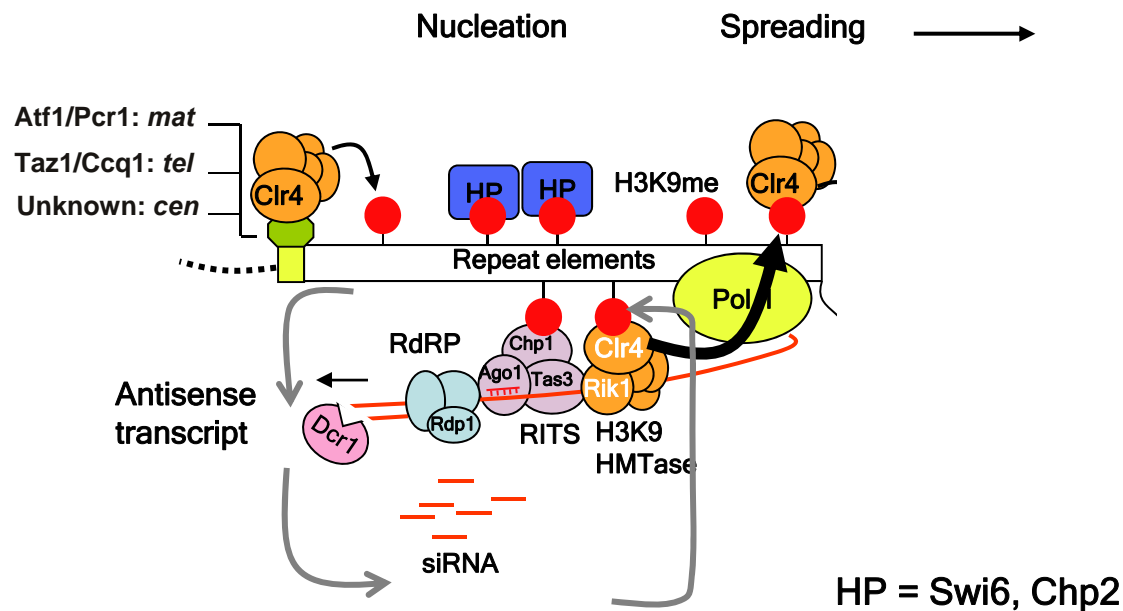


Heterochromatin coats extended domains associated with a specific classes of repeat elements in *S. pombe*



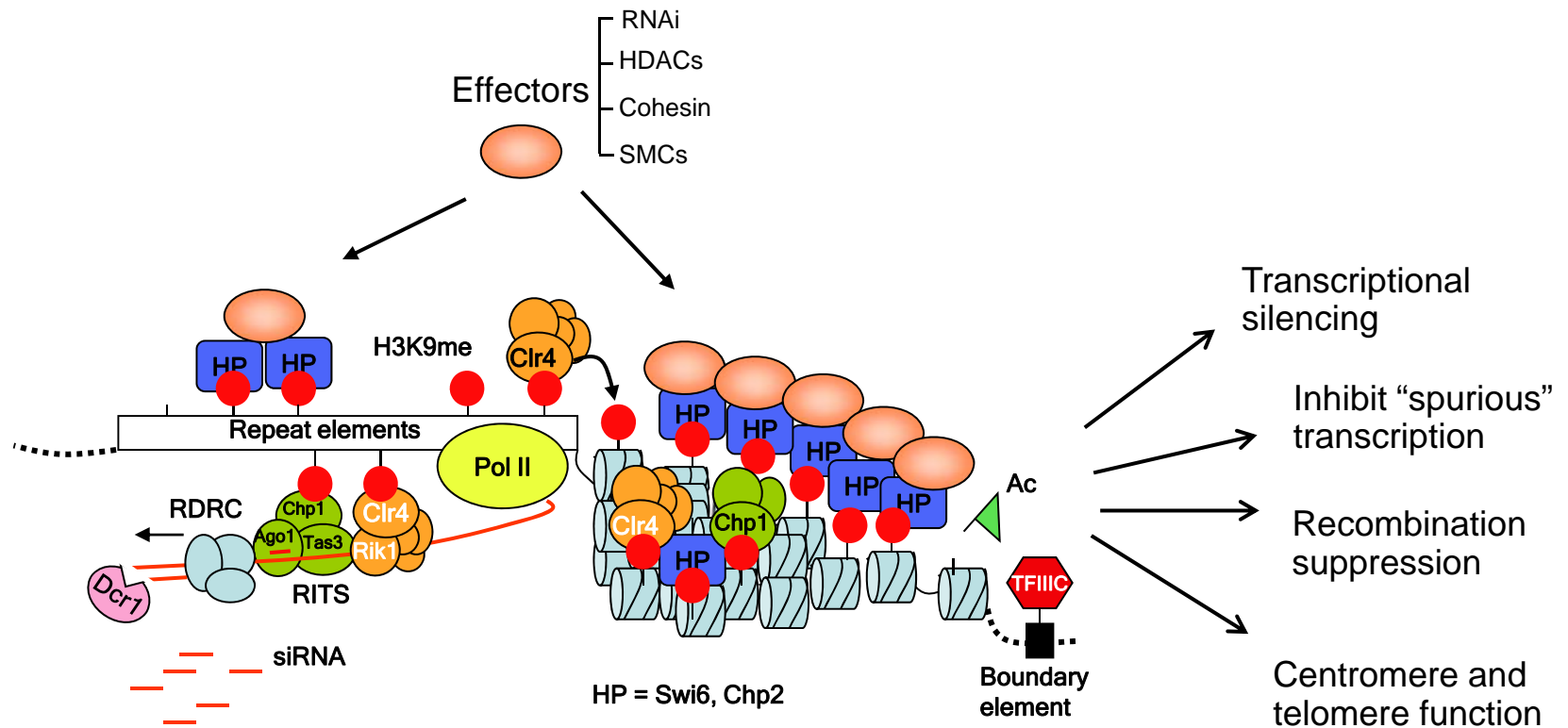
Grewal and Klar
Cell 1996

Nucleation and spreading of heterochromatin

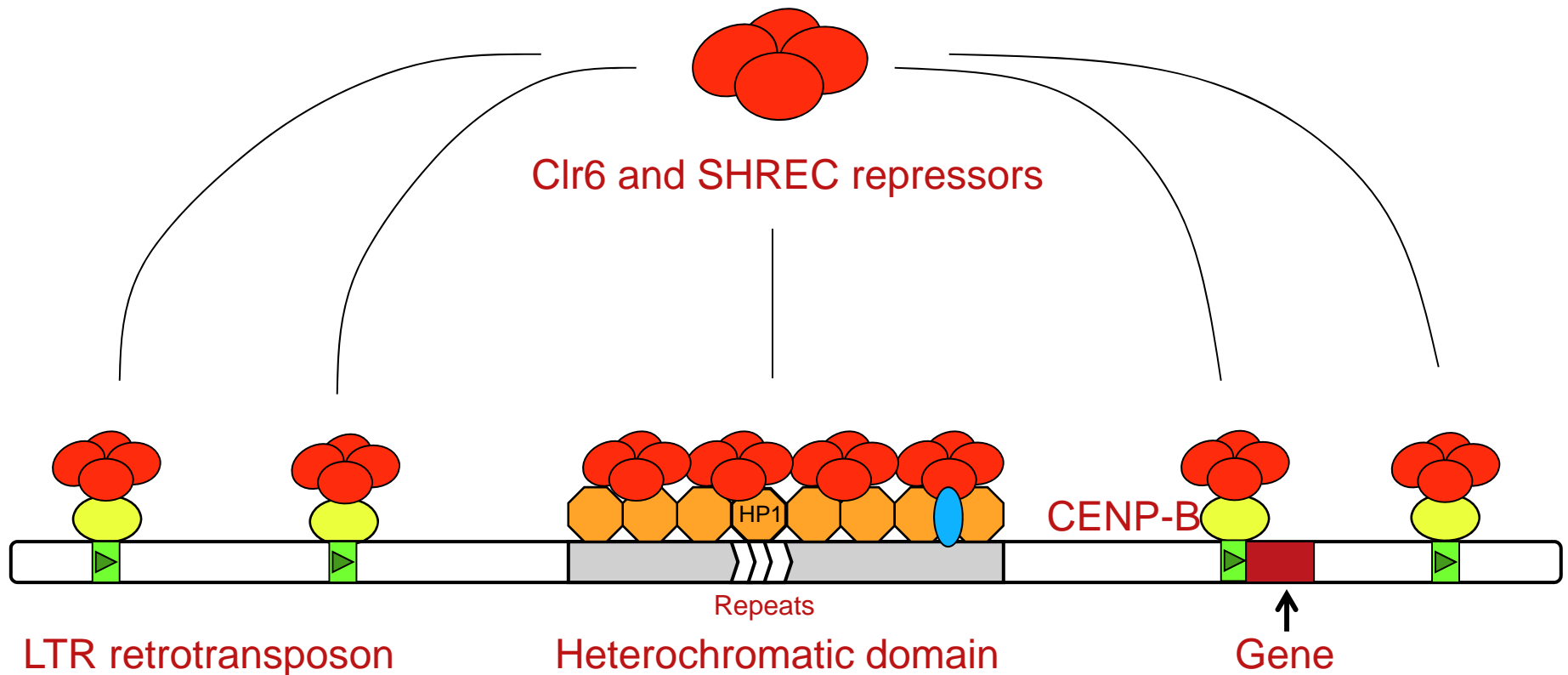


Spreading of heterochromatin requires Clr4 chromodomain binding to methylated H3K9

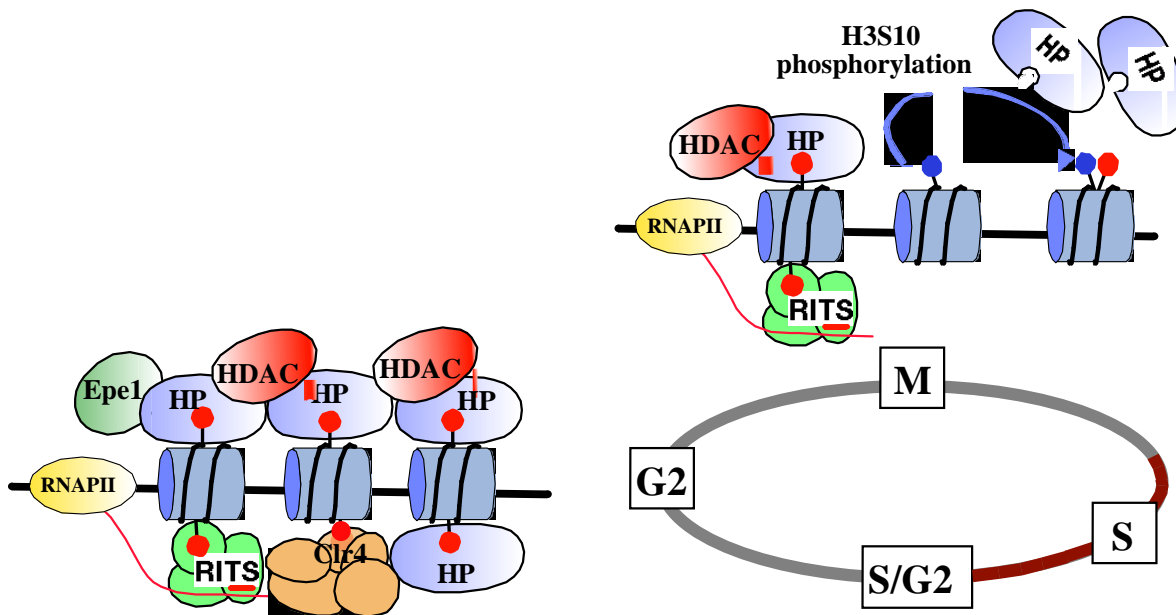
Heterochromatin serves as versatile recruiting platform to regulate diverse chromosomal processes



CENP-Bs and heterochromatin recruit same repressor complexes

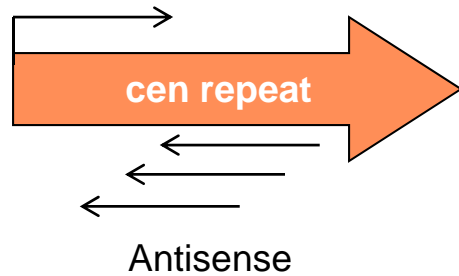


Cascade of events at heterochromatin during the cell cycle

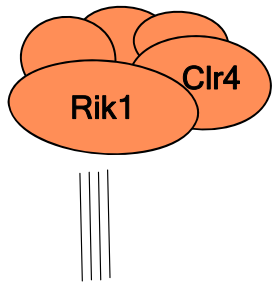


HP = chromodomain proteins **Swi6** and **Chp2**

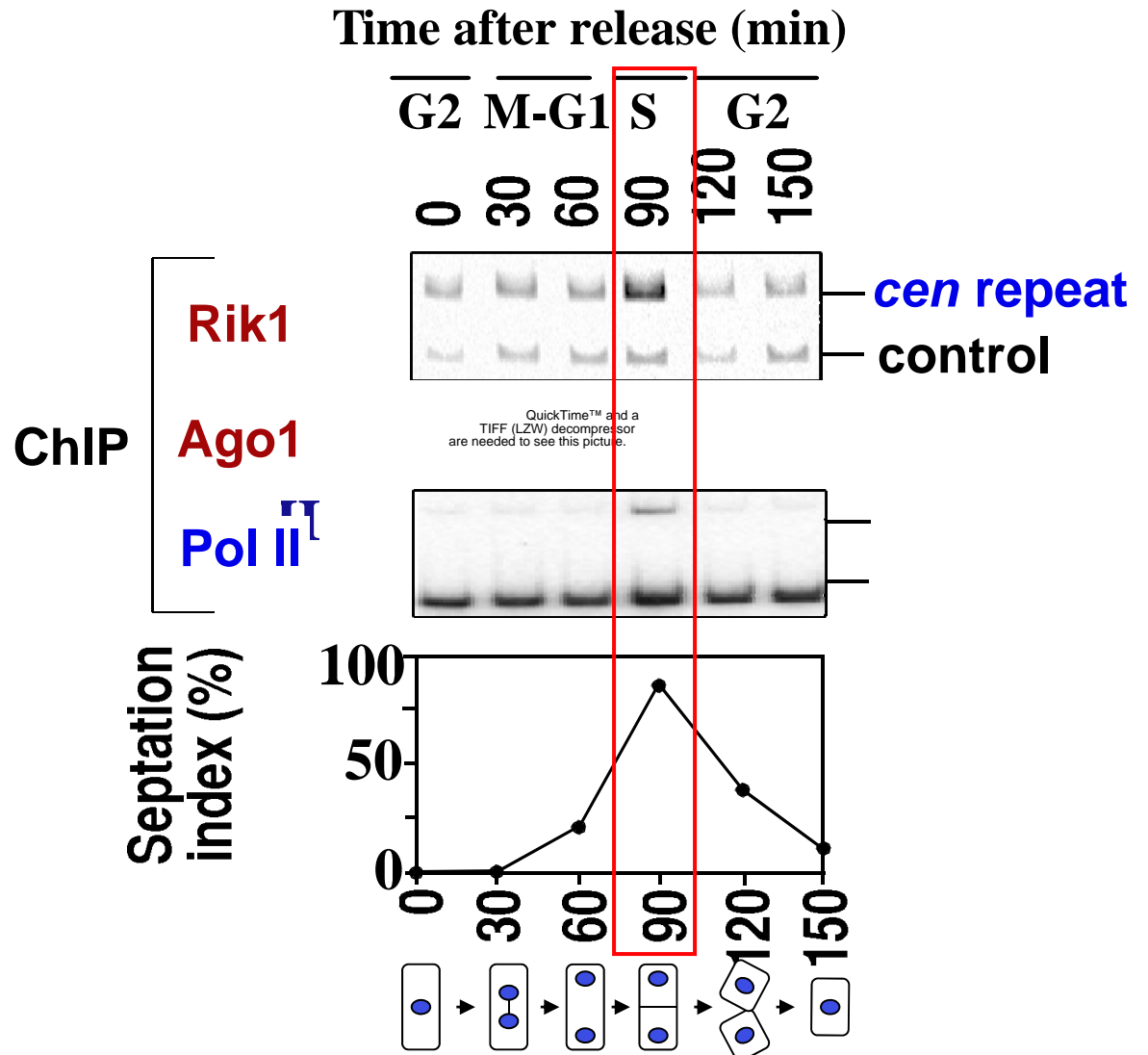
Rik1, a component of Ctr4 methyltransferase, is recruited to Pol II transcribed repeats during S-phase



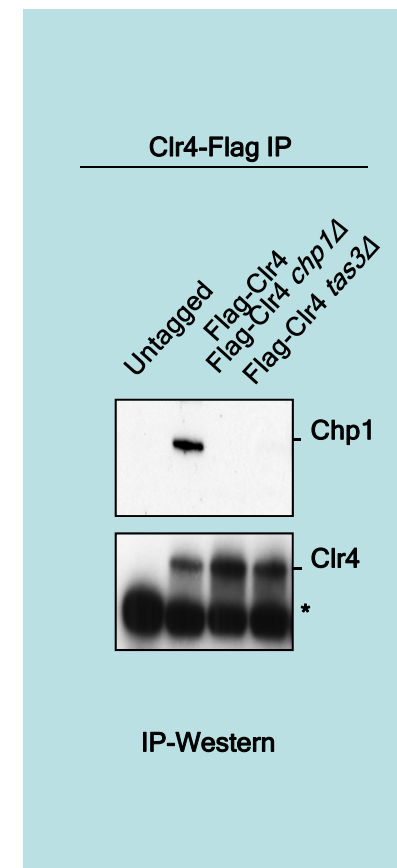
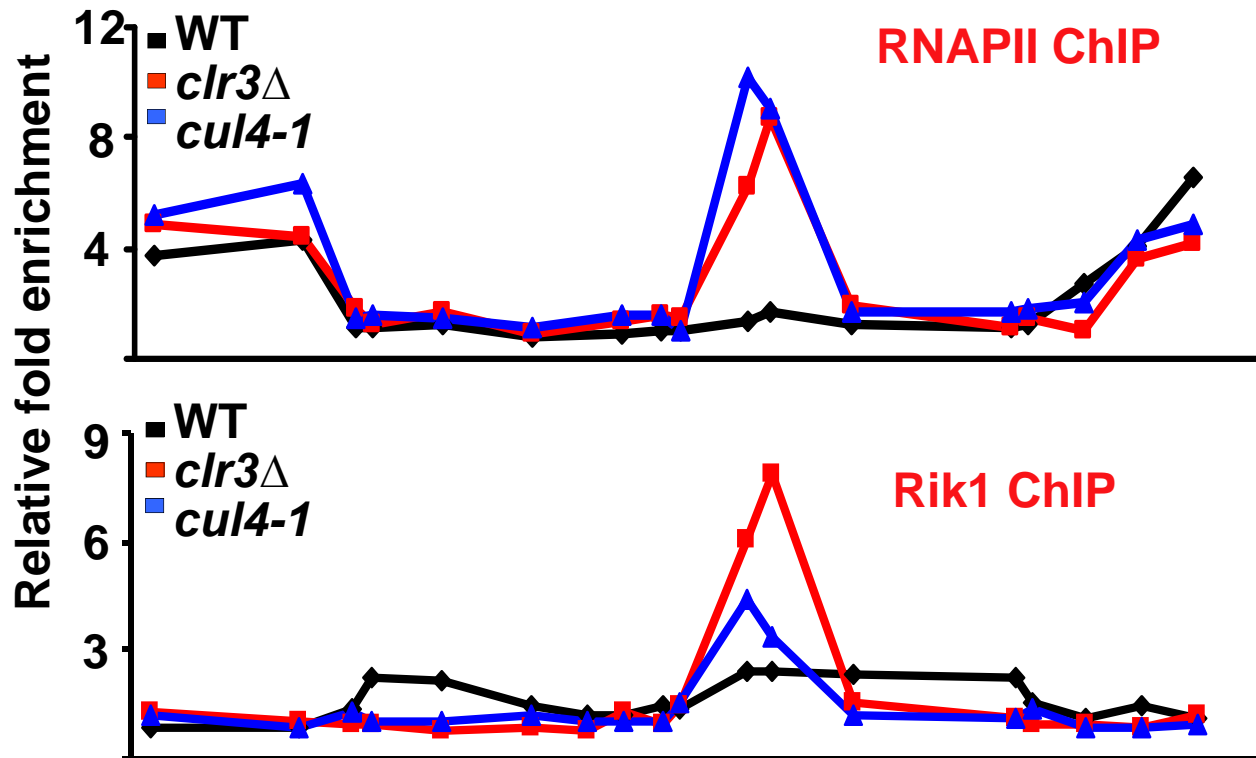
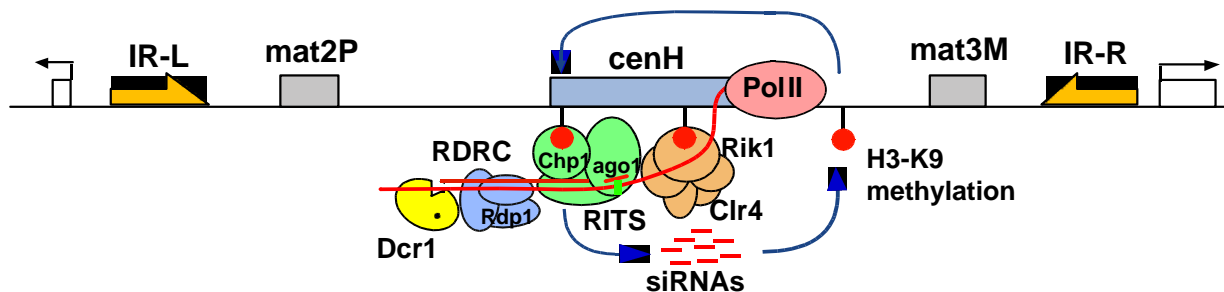
Clr4 complex



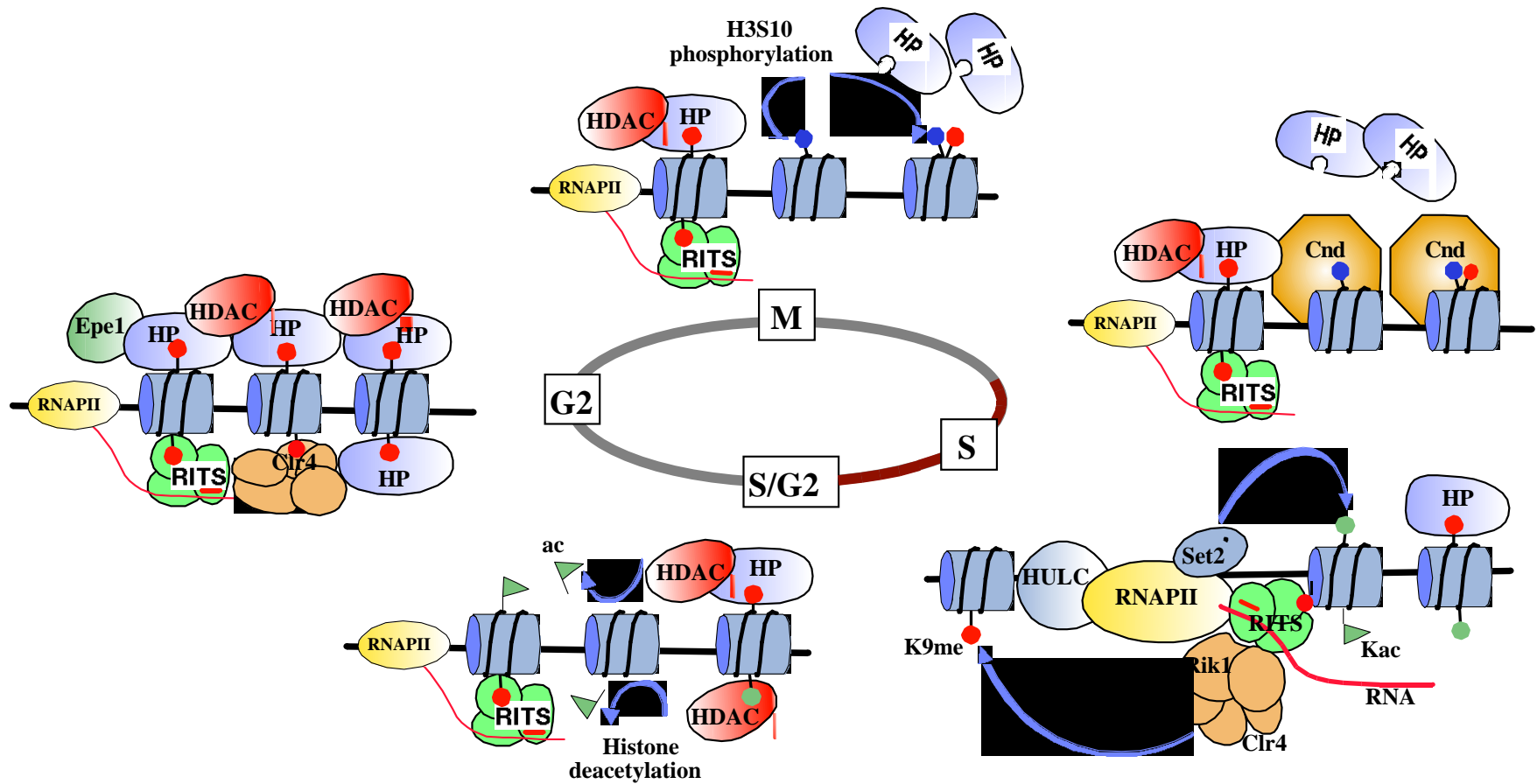
- 11 WD40-like repeats
- related to CPSF



Rik1 binding correlates with RNAPII transcription of *cen* repeat elements

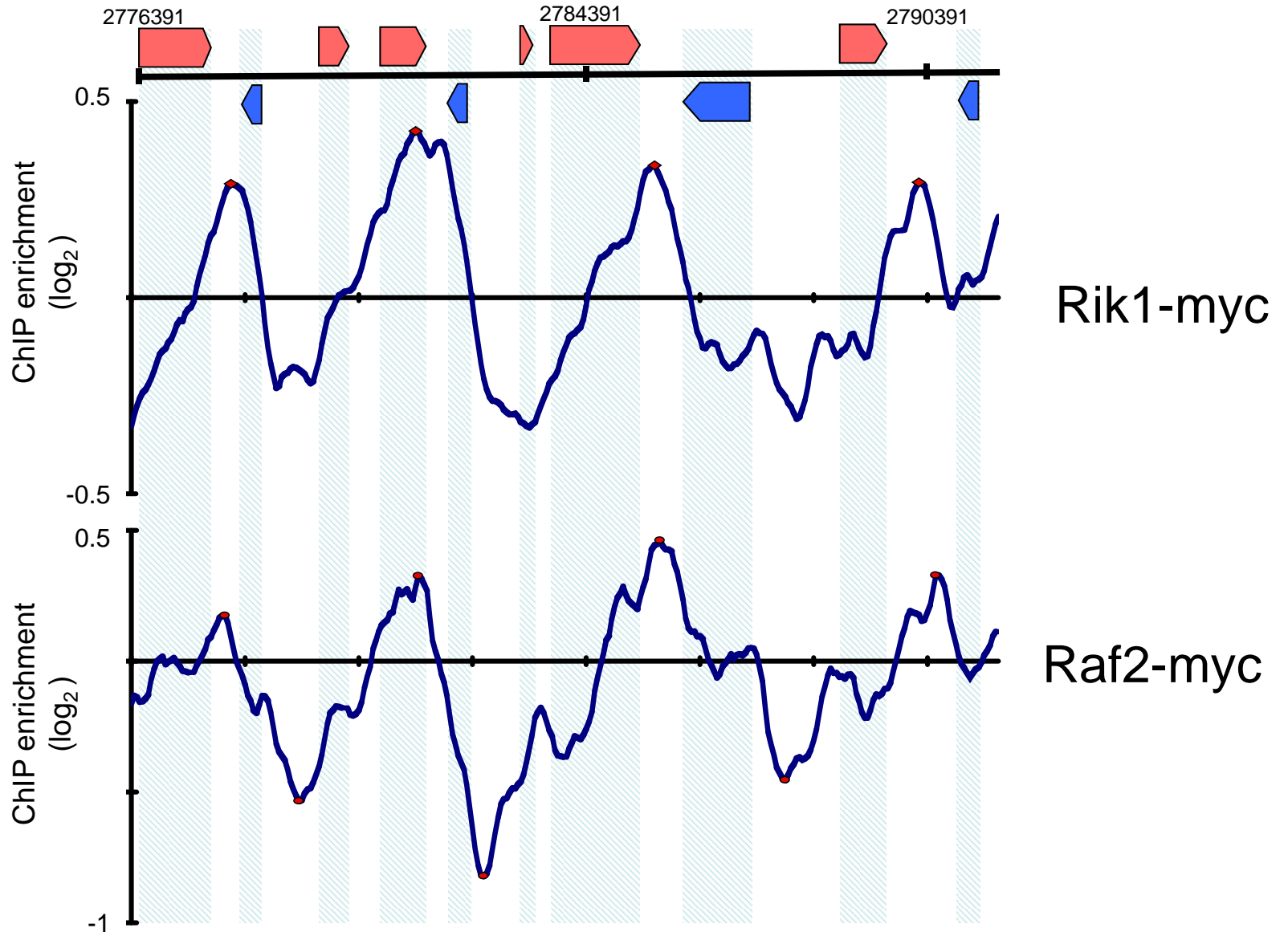
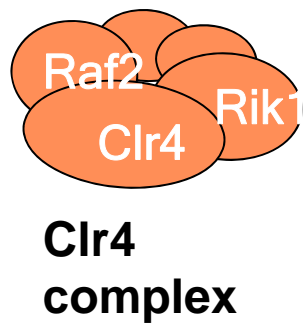


Transcription coupled loading of heterochromatin factors during S-phase

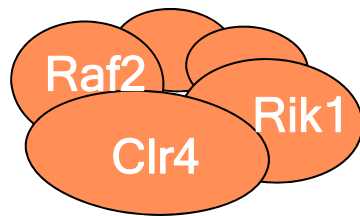


HP = chromodomain proteins **Swi6** and **Chp2**

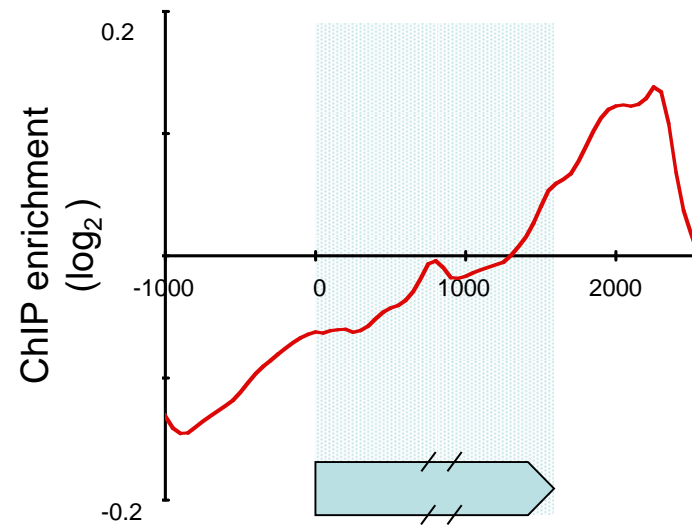
Clr4 complex components are distributed across euchromatic regions



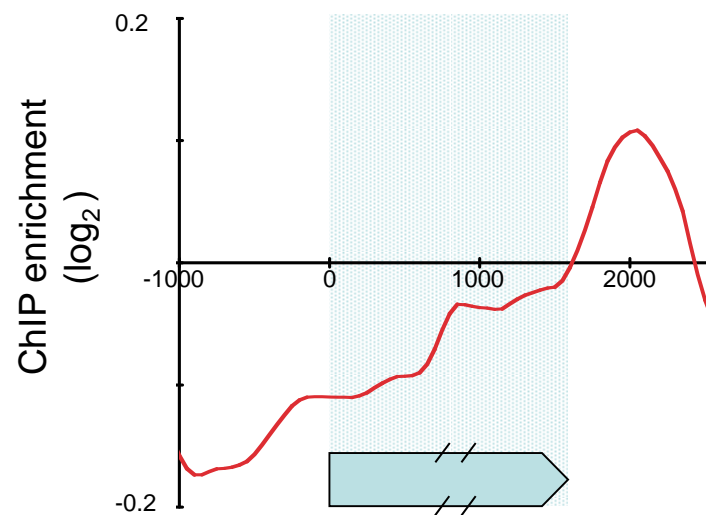
Clr4 complex subunits show similar distribution profiles at euchromatic genes



Clr4 complex

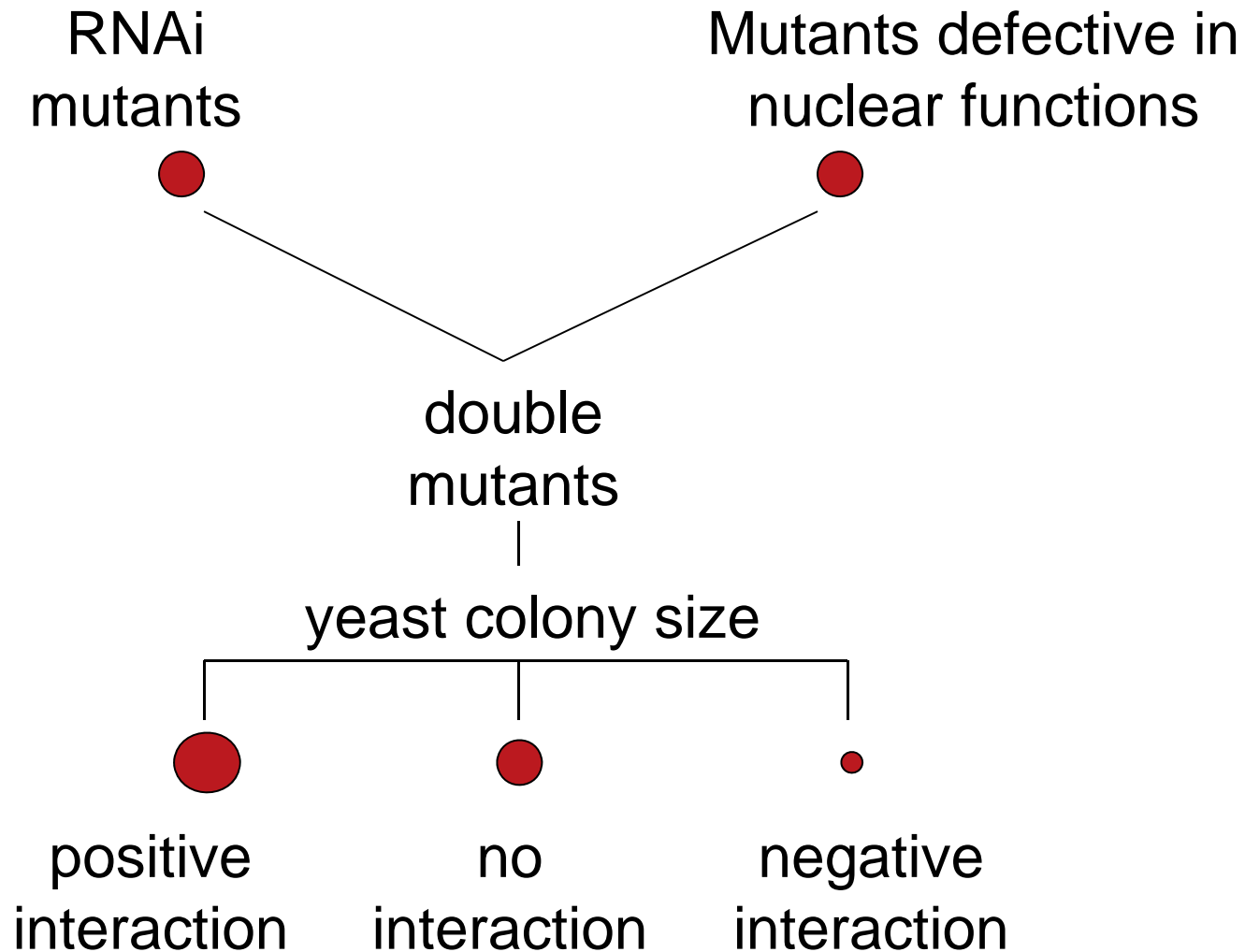


Rik1 profile



Raf2 profile

Exploring RNAi connections to other nuclear functions



RNAi and heterochromatin machineries positively interact with factors involved RNA Pol II transcription

QuickTime™ and a
TIFF (Uncompressed) decompressor
are needed to see this picture.

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(JmJc)
(HDAC)

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RNAi and heterochromatin factors show negative genetic interactions with DNA repair machinery

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Re-wiring of conserved functional modules in different organisms

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Acknowledgments

Grewal Lab

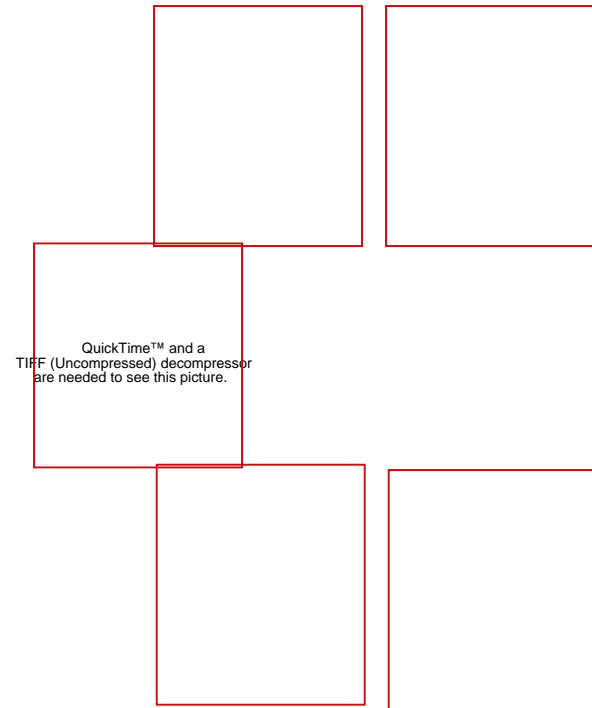
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Martin Zofall
Ke Zhang
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Bowen Cui
Natalia Kommissarova
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Wolfgang Fischle (Max Planck)
Peter FitzGerald (NCI)
Danesh Moazed (Harvard)
Nevan Krogan and Assen Roguev (UCSF)



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Post-transcriptional and transcriptional heterochromatic silencing

