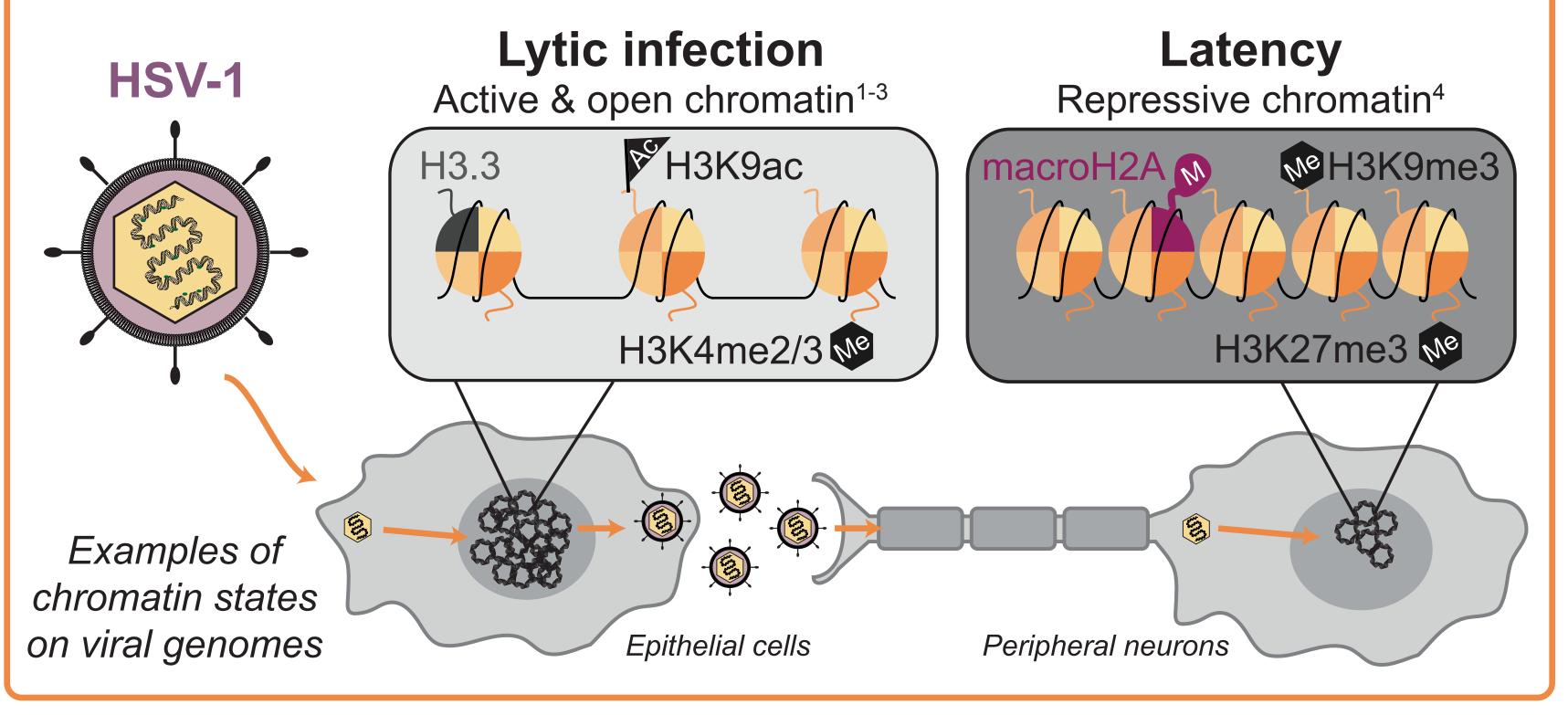
The function of histone variant macroH2A1 during HSV-1 infection

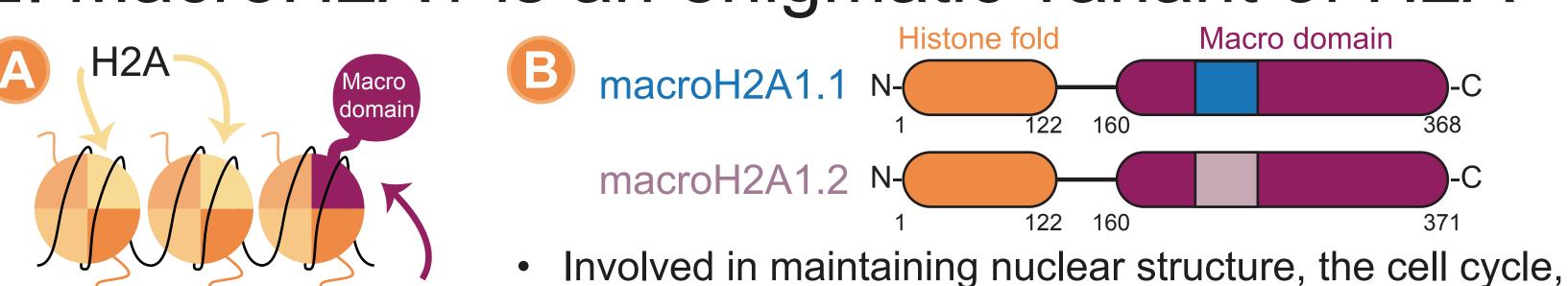
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1. Herpes simplex virus hijacks host chromatin factors to facilitate infection and persistence



2. MacroH2A1 is an enigmatic variant of H2A

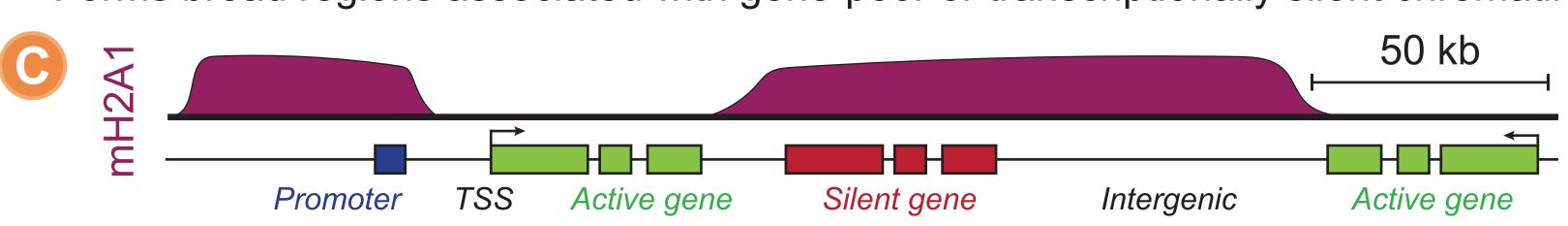


Expression and splicing is dysregulated in many cancers⁷

macroH2A1

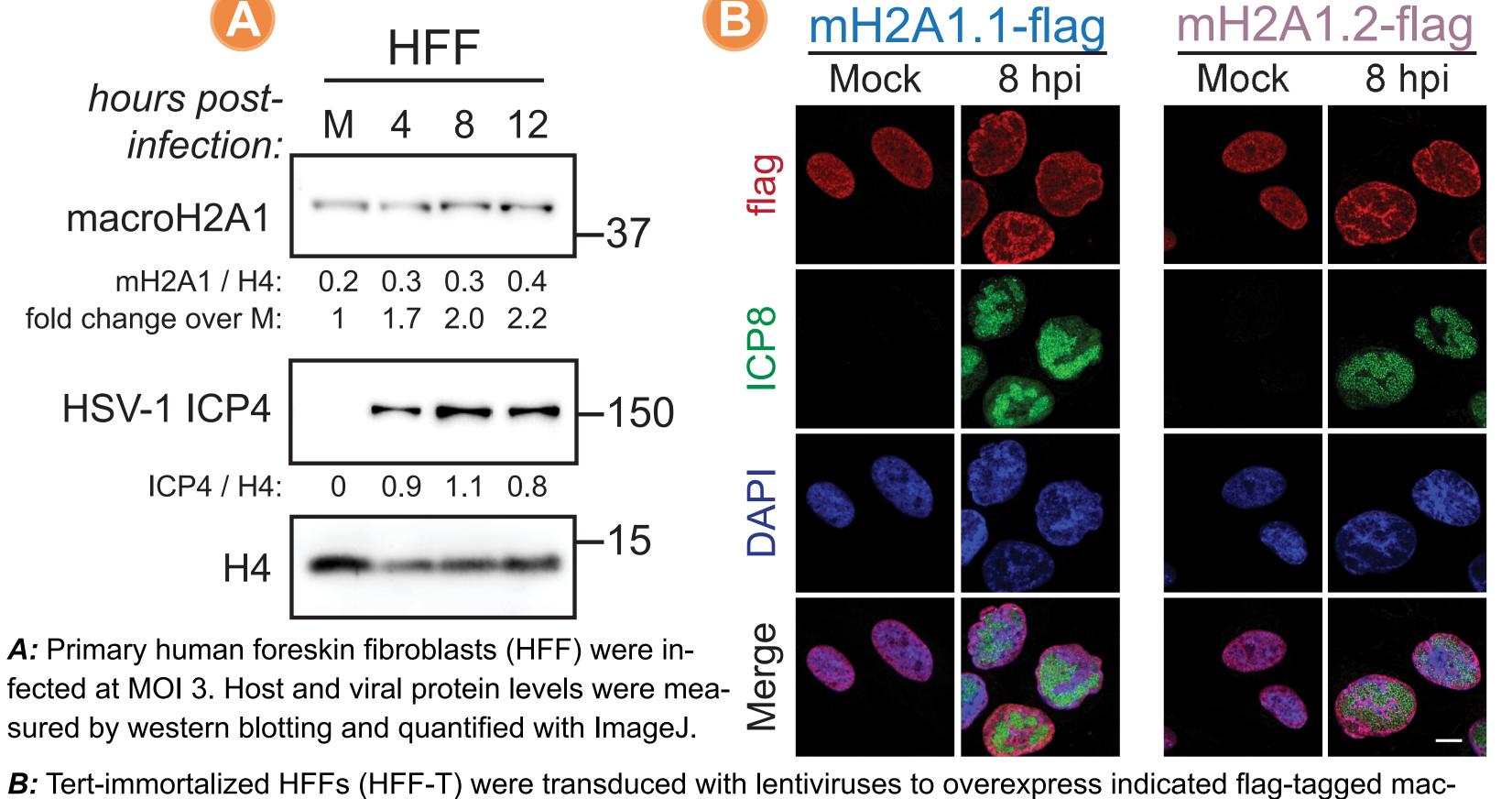
- Implicated in transcriptional repression of latent HSV-1 genomes⁴
- Forms broad regions associated with gene-poor or transcriptionally silent chromatin8

transcriptional repression, and other processes⁵



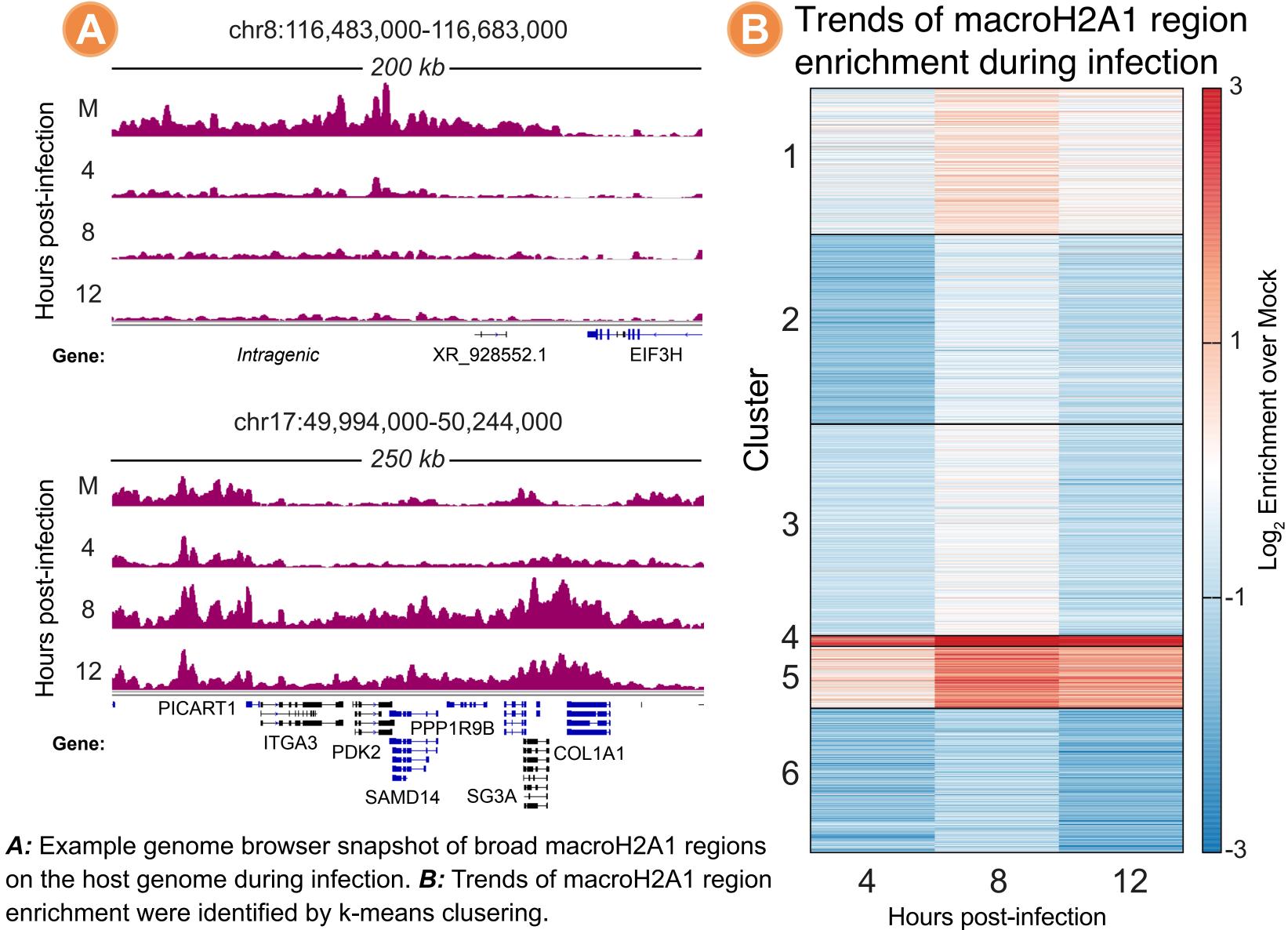
A: MacroH2A1 replaces H2A in nucleosomes. B: Alternate splicing results in mutually exclusive exons between isoforms macroH2A1.1 and 1.2. C: Cartoon depicting macroH2A1 regions in chromatin. Figure adapted from reference 8.

3. MacroH2A1 protein levels and localization are disrupted during lytic HSV-1 infection



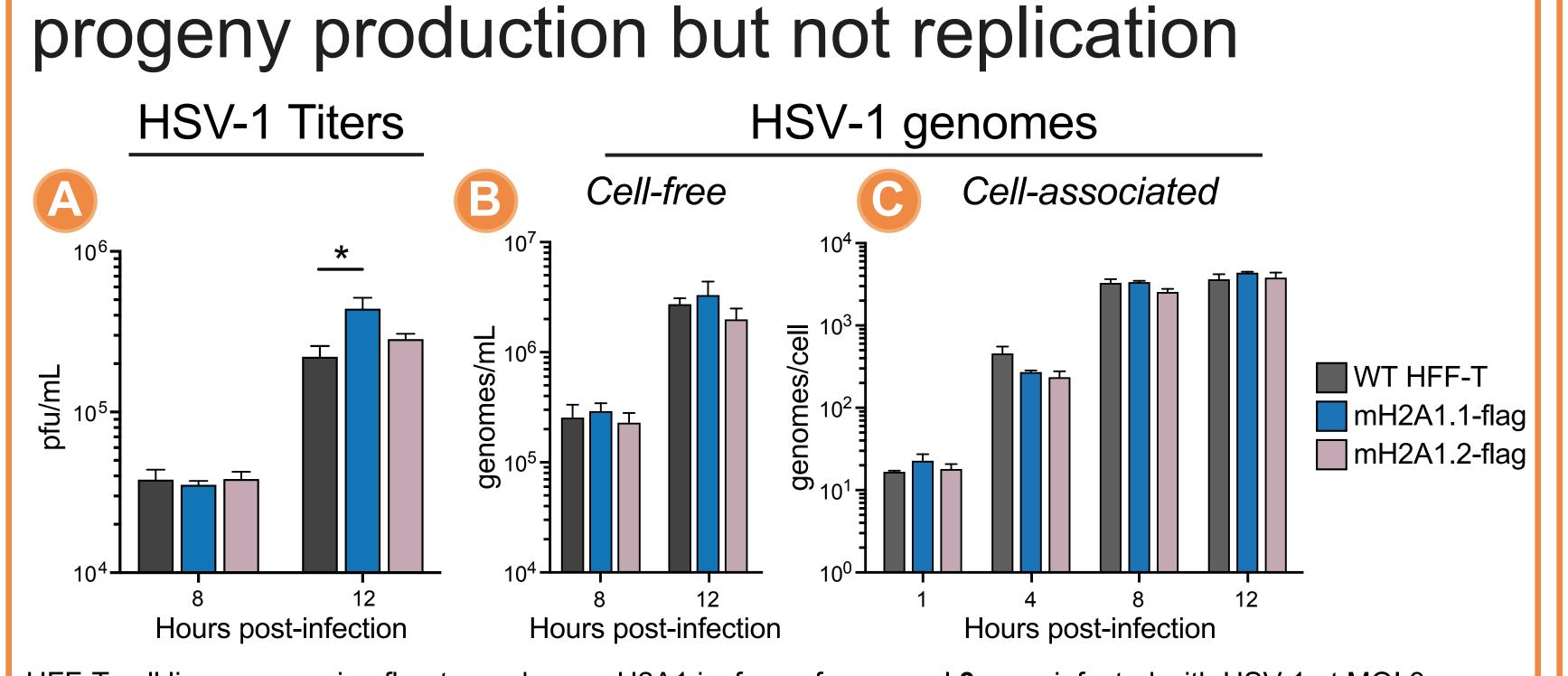
roH2A1 isoforms. Immunofluorescence was performed during mock or MOI 3 infection against indicated targets.

4. Broad macroH2A1 regions in chromatin are dynamic during infection



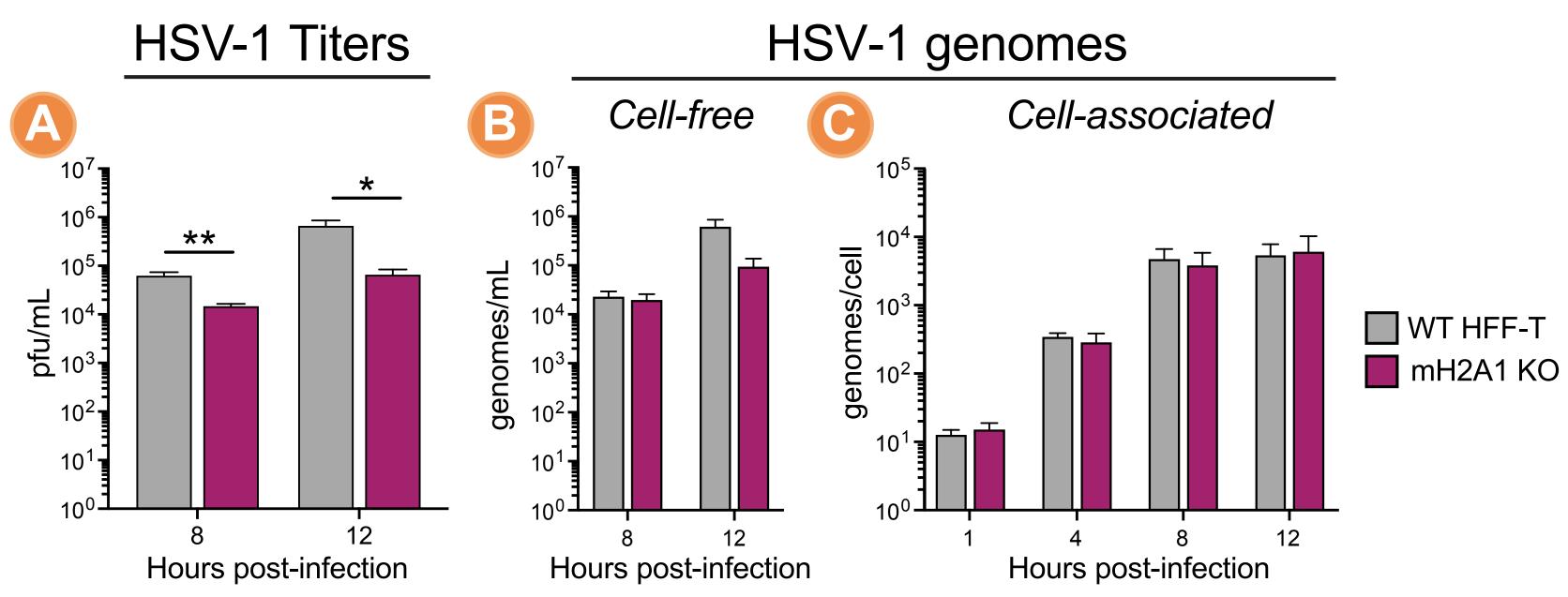
Hypothesis: macroH2A1 promotes HSV-1 lytic infection by reorganizing host chromatin

5. MacroH2A1 overexpression enhances viral



HFF-T cell lines expressing flag-tagged macroH2A1 isoforms from panel 3 were infected with HSV-1 at MOI 3. A: Progeny were titered on Vero cells. Absolute cell-free HSV-1 genomes (B) and cell-associated HSV-1 genomes (C) were quantified by droplet digital PCR. N=3

6. MacroH2A1 knockout results in defective progeny production



WT and macroH2A1 knockout HFF-T were infected at MOI 3.

A: Progeny were titered on Vero cells. Absolute cell-free HSV-1 genomes (B) and cell-associated HSV-1 genomes (C) were quantified by droplet digital PCR. N=3

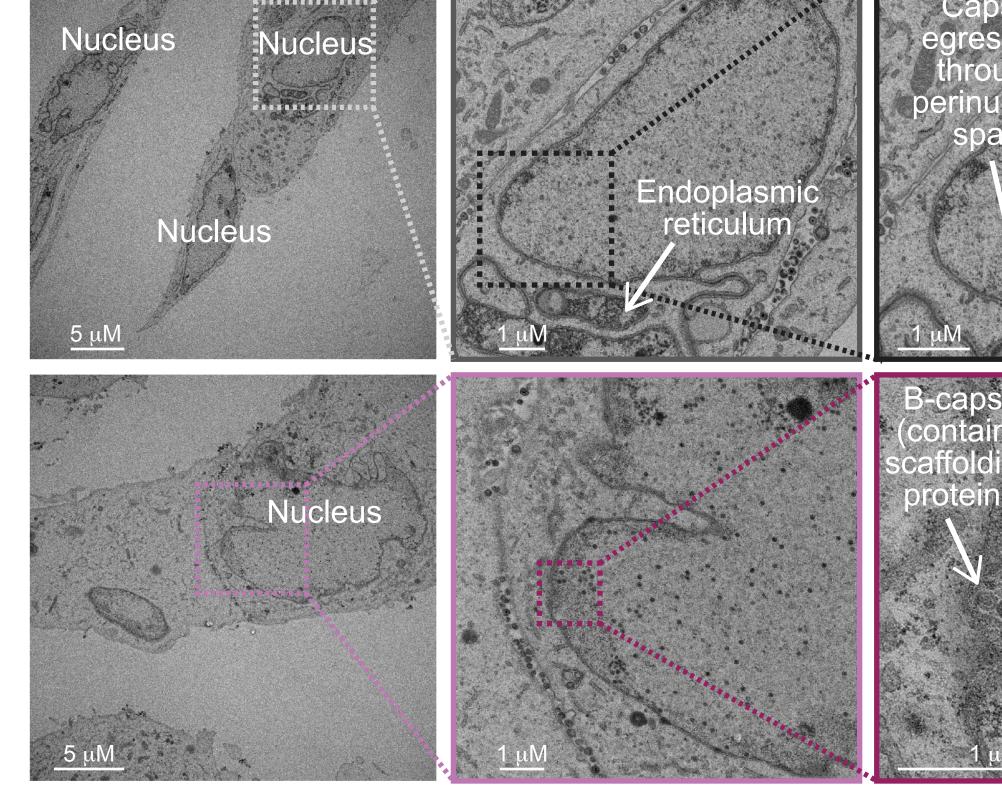
18 hours post-infection

7. MacroH2A1 loss may impact nuclear size and lead to a defect in HSV-1 nuclear egress

Current questions:

- 1) How does nuclear size differ between WT and macroH2A1 KO cells?
- 2) How does number of capsids per μm² nucleus differ between cell types?
- 3) How many A, B or C capsids are in each nucleus? How does this proportion differ between cell types?

Mock infection Heterochromat Heterochromatin



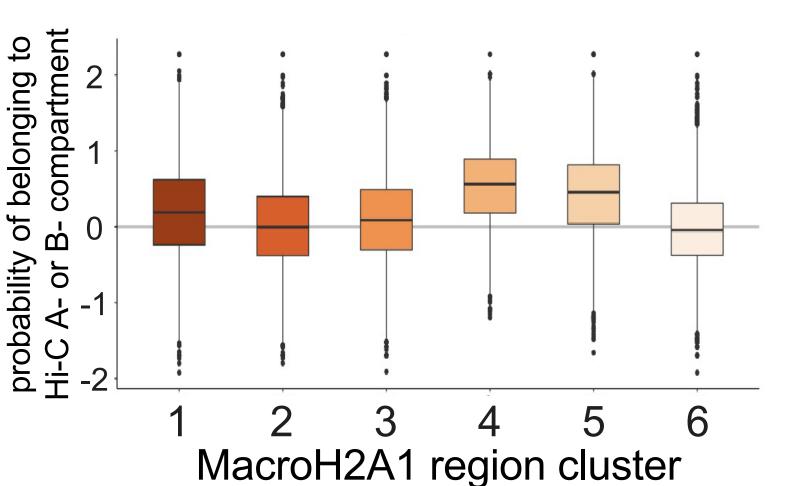
Transmission electron microscropy images of WT and macroH2A2 knockout HFF-T either mockinfected or infected with HSV-1 for 18 hours at MOI 10.

8. Future directions

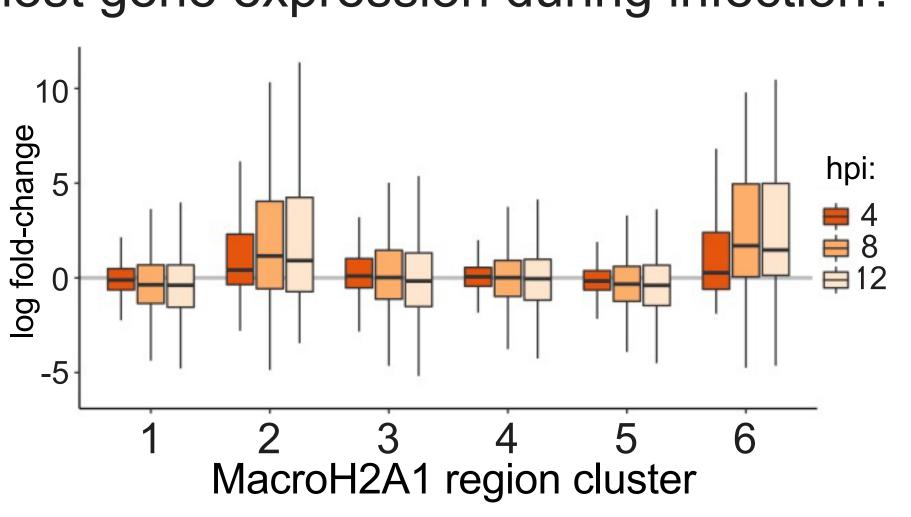
Working model: MacroH2A1 maintains

nuclear structure during infection and loss of macroH2A1 negatively impacts HSV-1 egress

1) Do macroH2A1 regions correlate more with eu- or heterochromatin?



2) How do macroH2A1 regions impact host gene expression during infection?



8. References &

Acknowledgements References: **Funding:** T32 Al083203

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Acknowledgements: We thank the Henikoff lab for providing reagents and technical assistance for CUT&Tag. We thank the Fred Hutch Bioinformatics core for assistance with analysis.