

Defining the Role of the Sas5 YEATS Domain in Histone Acetylation and Chromatin-State Regulation

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How Chromatin Context Regulates SAS-I Activity

- Histone H4K16 acetylation (H4K16ac) is an important regulator of chromatin accessibility. In budding yeast, this mark is deposited primarily by the SAS-I complex.
- SAS-I activity varies across histone and nucleosome substrates, indicating regulation by chromatin context.
- We asked whether the Sas5 YEATS domain mediates this regulation through canonical acetyl-lysine recognition or broader histone engagement.

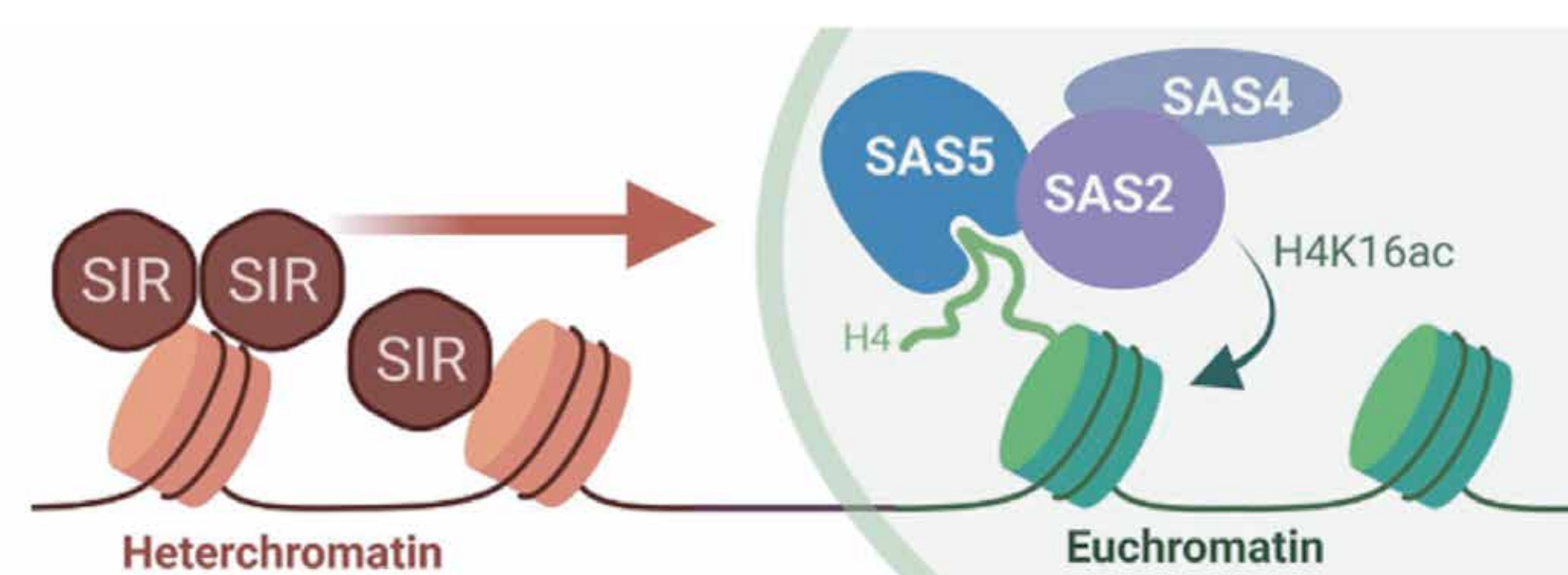
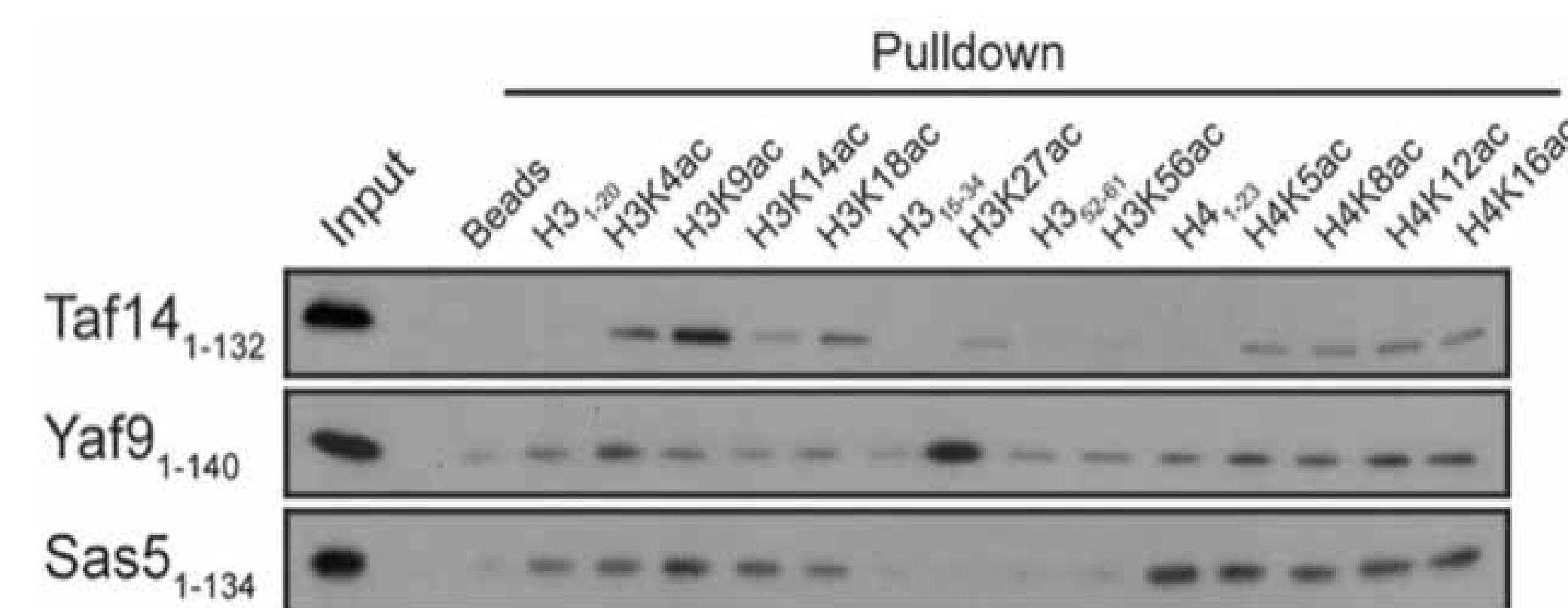


Figure 1. SAS-I and Sir complexes have opposing roles in chromatin regulation. Sir promotes heterochromatin, while SAS-I acetylates H4K16 to support euchromatin.

Sas5 YEATS May Recognize Histone Tails Differently from Canonical YEATS Domains

- Canonical YEATS domains typically recognize specific acetylated lysines on histone tails.
- Compared with Taf14 and Yaf9, Sas5 binds a broader range of H3 and H4 peptides, indicating reduced site specificity.
- Sas5 also shows detectable binding to unmodified histone tails, suggesting that it may not function as a strictly canonical acetyl-lysine reader.

Figure 2. Taf14, Yaf9, and Sas5 YEATS domains were tested by histone peptide pulldown using biotinylated H3 and H4 peptides, and bound protein was detected by immunoblot.



Sas5 Histone-Peptide Recovery Was Retained Following F85A Substitution

- Sas5 WT and F85A were recovered with modified and unmodified histone peptides, whereas F85A reduced Taf14 recovery, particularly with modified peptides.

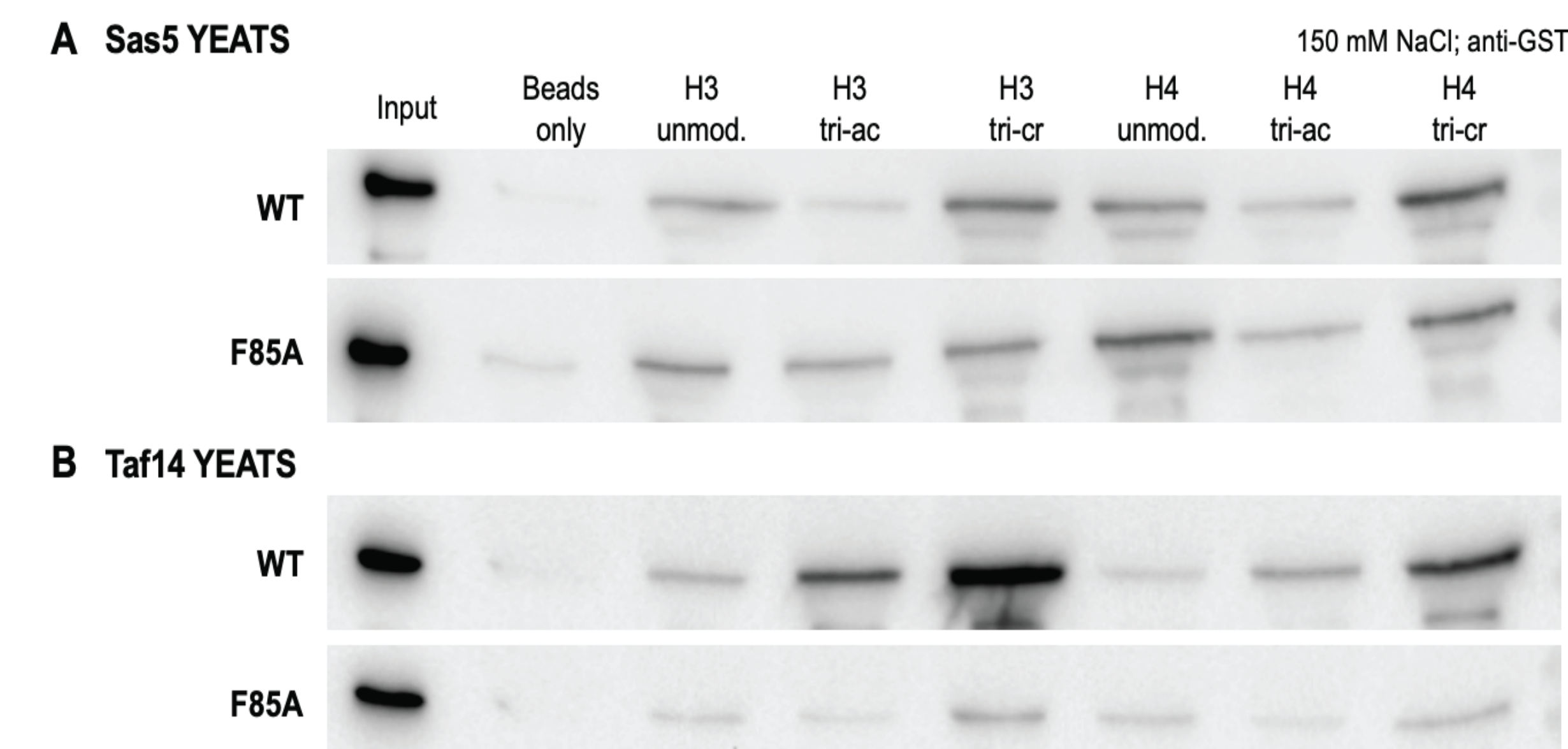


Figure 3. Sas5 (A) and Taf14 (B) WT and F85A YEATS domains were tested by pulldown with biotinylated unmodified, tri-acetylated, and tri-crotonylated H3/H4 peptides at 150 mM NaCl. Recovered proteins were detected by anti-GST immunoblotting. Input and beads-only controls were included.

SAS-I Activity Depends on Chromatin Substrate Context

- SAS-I shows stronger H4K16 acetylation on nucleosomal substrates, supporting chromatin context dependence.

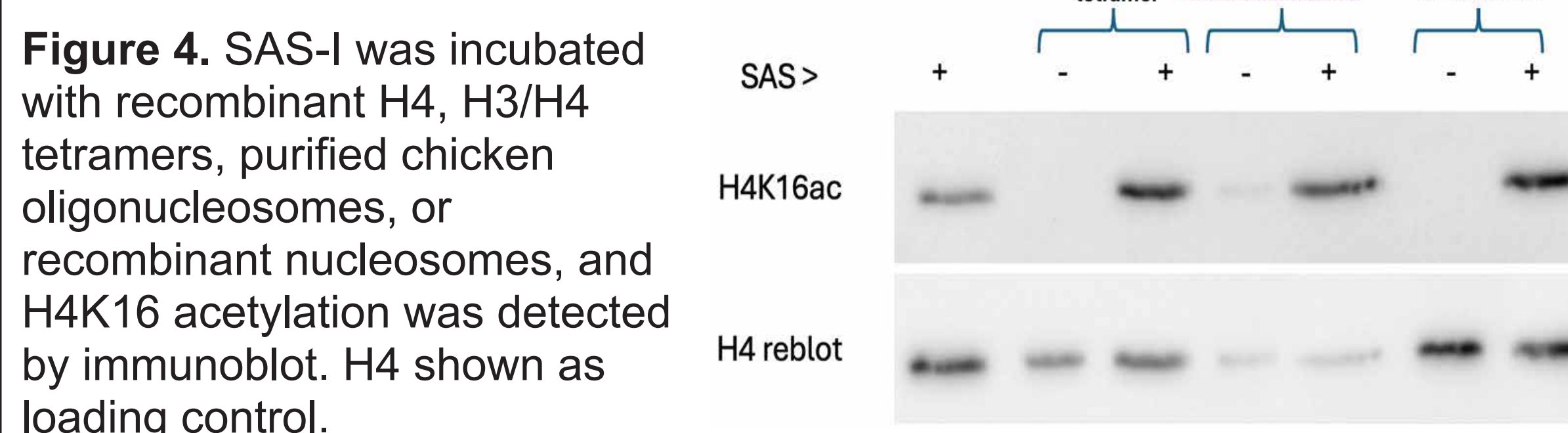
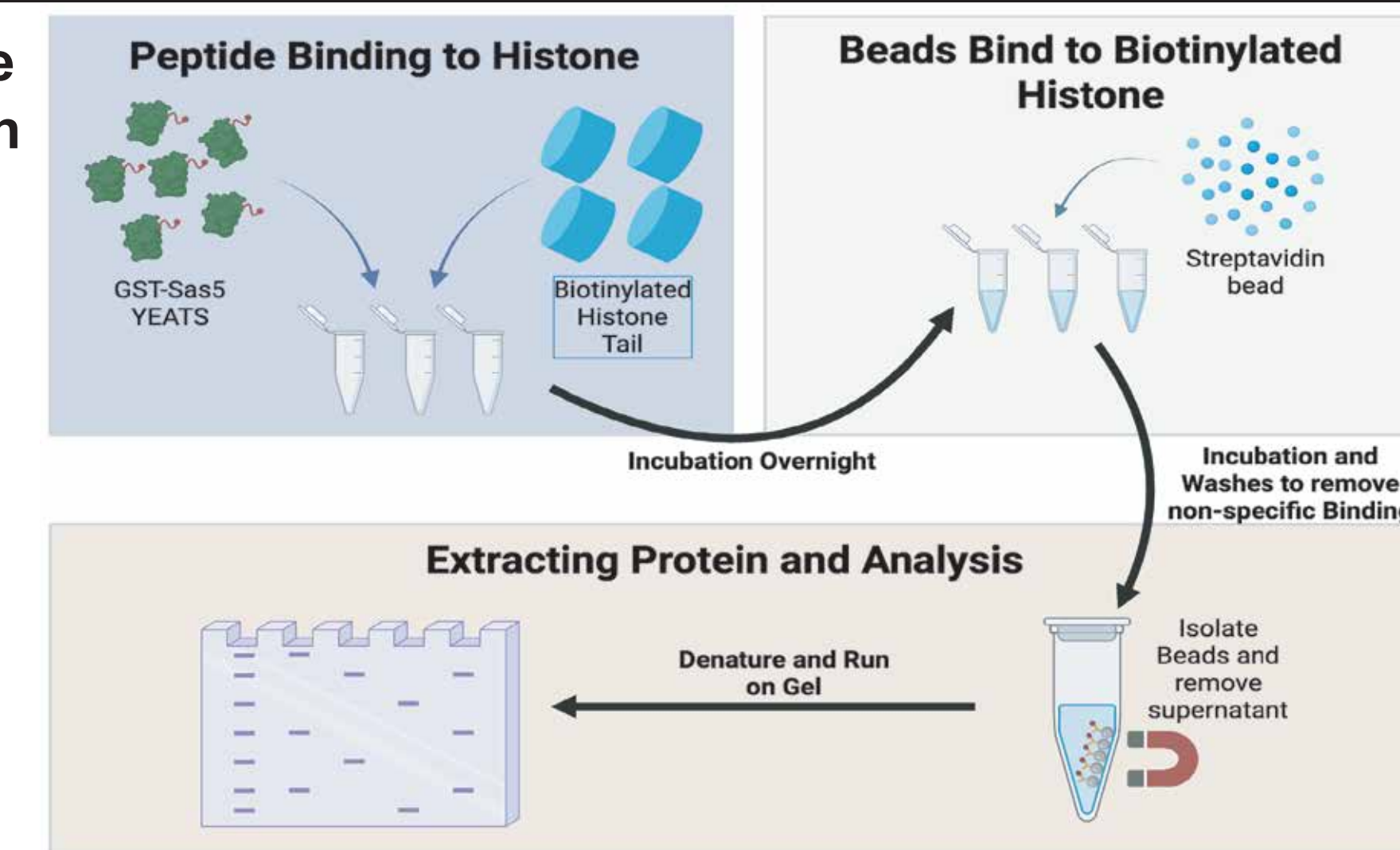


Figure 4. SAS-I was incubated with recombinant H4, H3/H4 tetramers, purified chicken oligonucleosomes, or recombinant nucleosomes, and H4K16 acetylation was detected by immunoblot. H4 shown as loading control.

Peptide Pulldown and Mutagenesis Strategy to Test Sas5 Binding Mechanism

Figure 5. Histone peptide pulldown assay workflow. Sas5 binding is assessed using biotinylated histone peptides and immunoblot detection.



Working Model and Next Steps

- We propose that Sas5 may promote SAS-I chromatin-state sensitivity through broad histone engagement.
- Future work will compare YEATS-only, full-length Sas5, test YEATS aromatic cage mutants, and nucleosome-based substrates.

References & Acknowledgments

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