The impact of Foxp1 on chromatin accessibility

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Introduction

This project focuses on understanding the role of the transcription factor (TF) Foxp1 in motor neuron development. Previous research has shown that Foxp1 may be involved in the regulation of two Hox genes, Hoxc6 and Hoxc10, which are involved in upper limb development.

ATAC-seq

The data for this experiment is an Assay for Transposase-Accessible Chromatin (ATAC-seq). This technique employs a mutant transposase that inserts a sequence into regions of the genome that are open to regulatory elements and cuts the strand.
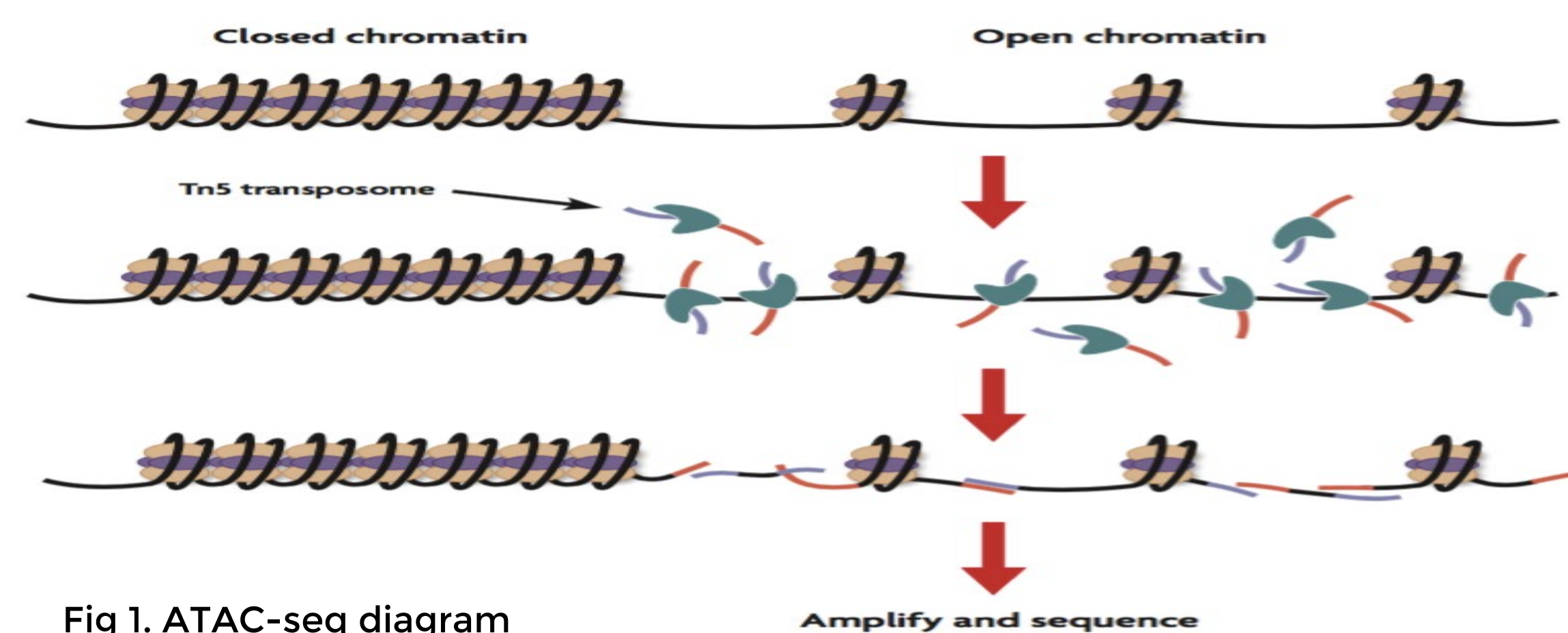

Fig 1. ATAC-seq diagram

Data and Analysis

A good indication of the ATAC-seq quality is determined by a paired-end histogram, which identifies insert sizes. Each peak represents a fragment of DNA.
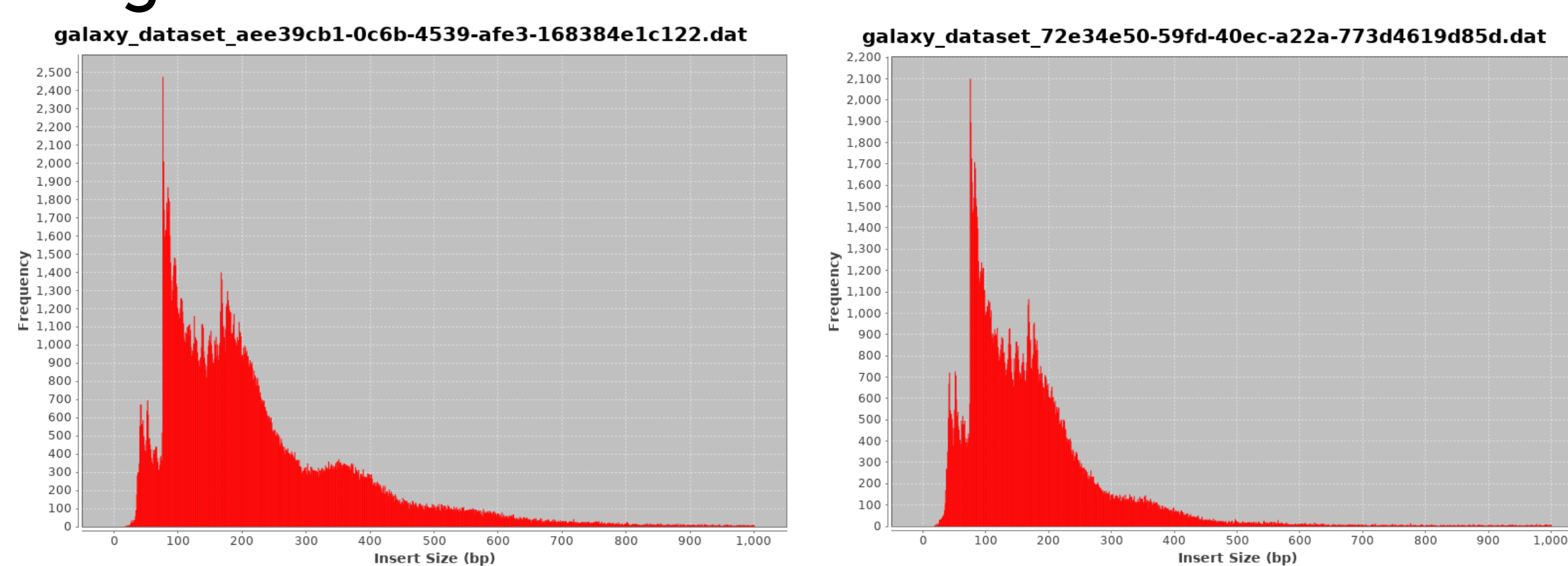

Fig 2. ATAC-seq WT paired end histogram

Fig 3. ATAC-seq WT paired end histogram

Heat maps

Comparison of peaks to known mouse genes. Blue areas show maximum enrichment,
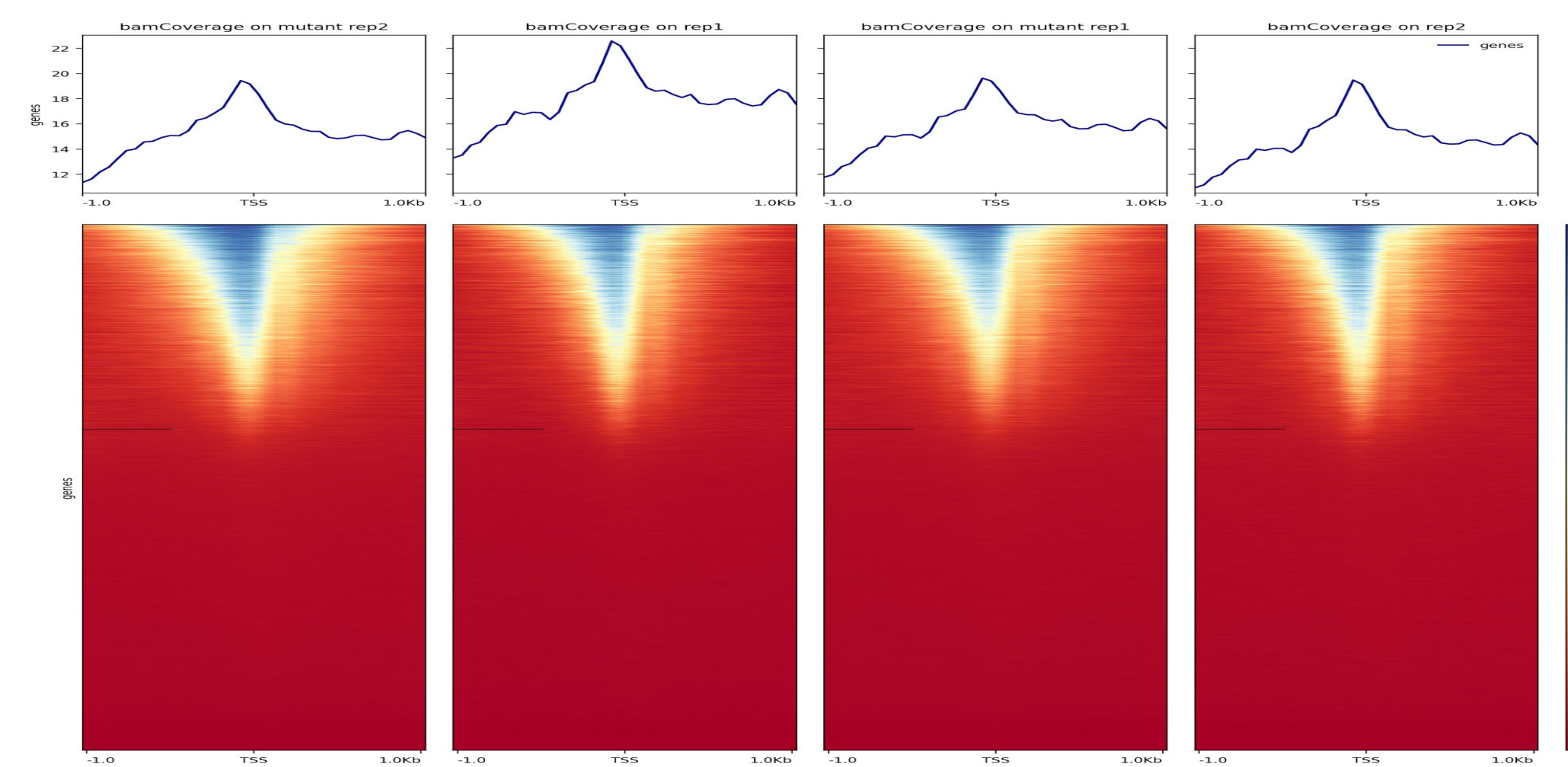

Fig 4. Heat map of the coverage for each replicate

Visualization in Genome Browser

Once the sequences are filtered and mapped against the mouse genome, areas of interest can be compared to known genes.
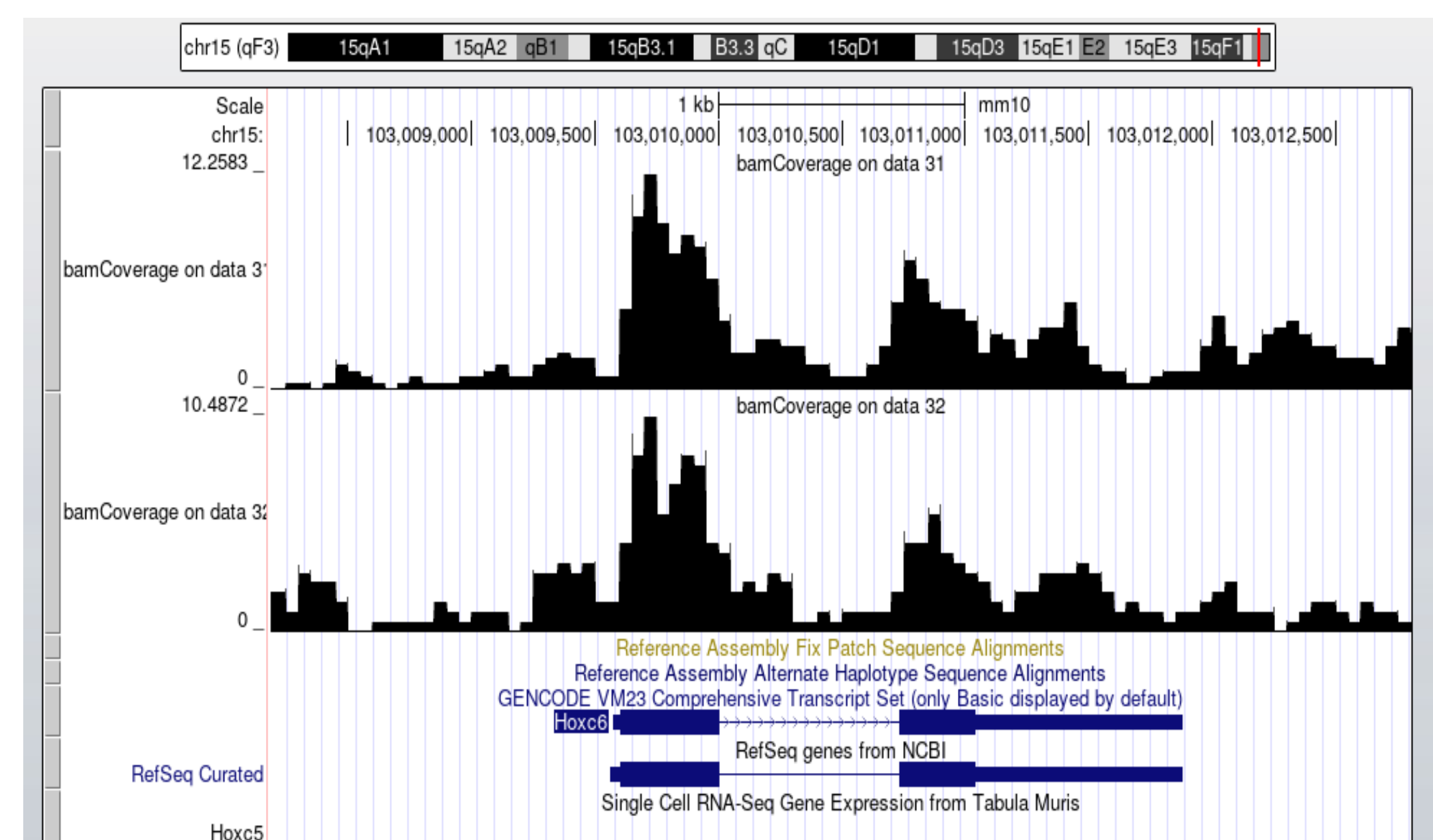

Fig 5. Mutant vs. Wild-Type in reference to Hox c6 gene on Chr 15

Differential Binding

ATAC-seq regions of accessibility vs. CHiP-seq Foxp1 binding sites

Regions of Increased Accessibility	508	Regions that overlap with Foxp1 bound site	49
Regions of Decreased Accessibility	1,284	Regions that overlap with Foxp1 bound site	129

Table 1: Differential binding in Mutant vs. Wild-Type

DNA motifs

The differential binding sites have a preference for different DNA motifs. The decreased areas of accessibility were representative of known Foxp1 motifs.
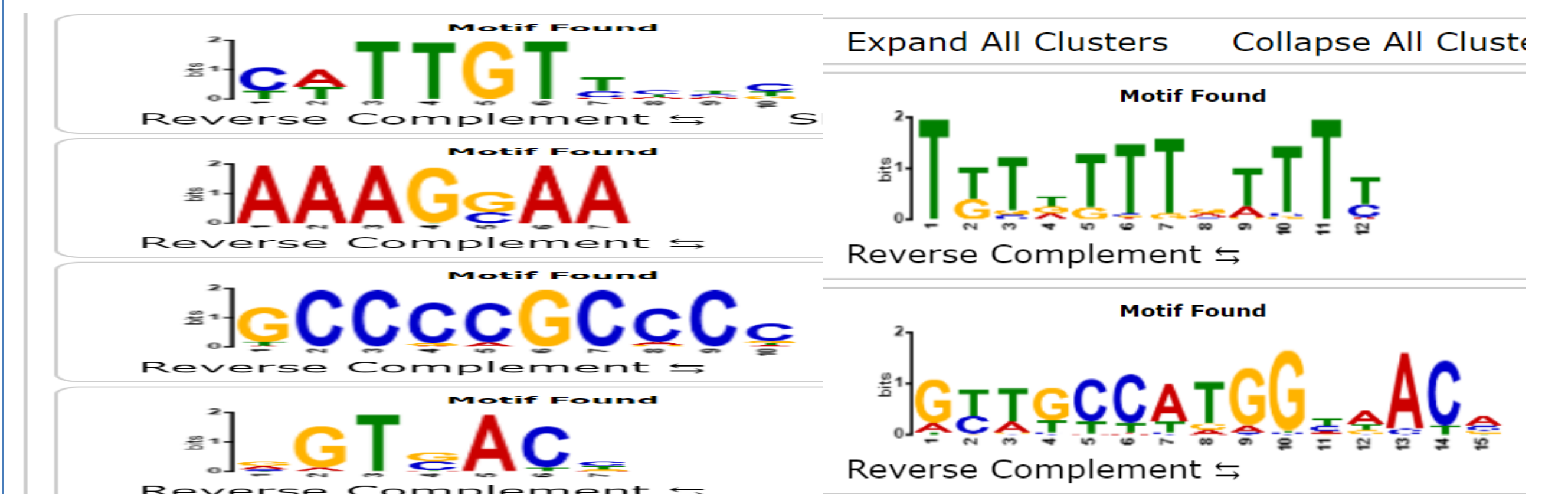

Fig 6. DNA Motifs of decreased accessibility

Fig 7. DNA Motifs of increased accessibility

Conclusion

The results suggested knocking out Foxp1 did decrease accessibility in 1,284 regions., however, there was an increase in accessibility in 508 regions. Next, comparing the CHiP-seq data of Foxp1 binding sites to the ATAC-seq data showed that only about 10% of the regions overlapped. This suggests that FoxP1 is not a pioneer factor for Hoxc6.

Acknowledgements

References

Yan, F., Powell, D.R., Curtis, D.J. et al. From reads to insight: a hitchhiker's guide to ATAC-seq data analysis. Genome Biol 21, 22 (2020). https://doi.org/10.1186/s13059-020-1929-3

Saskia Hiltemann ,Helena Rasche ,Simon Gladma Hotz HR, Lariviere D, et al. Galaxy Training:A powerful framework for teaching! PLOS Computational Biology. 2023 Jan 9: 19(1): e1010752. https://doi.org/10.1371/journal.pcbi.1010752