

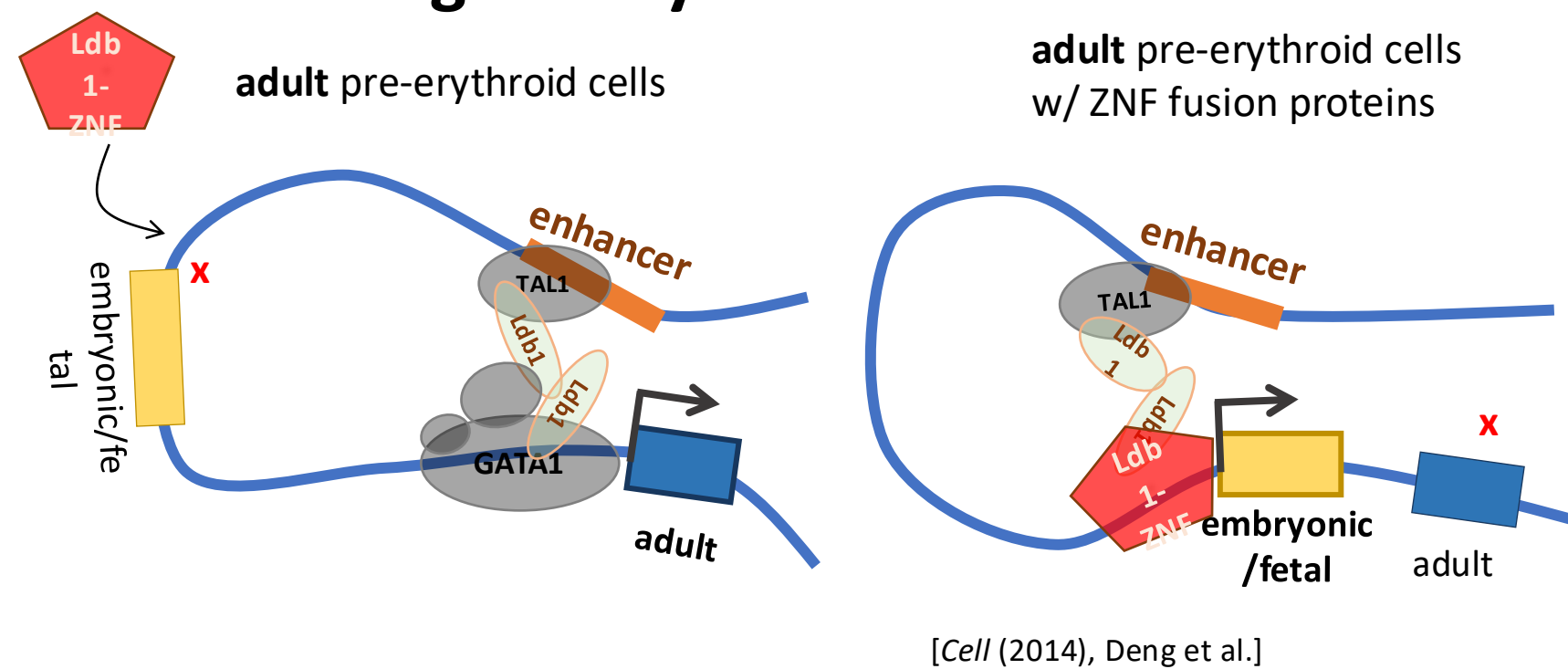
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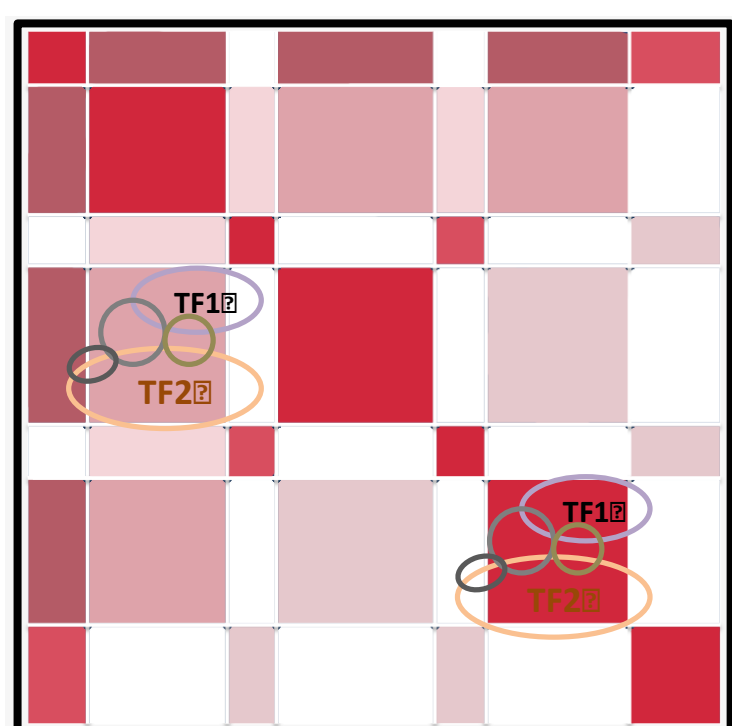
LONG-RANGE REGULATORY INTERACTIONS

Protein complexes mediate enhancer-promoter and other regulatory interactions



Regulatory interactions and mediating protein complexes in the Hi-C data?

Hi-C contact matrix



Can we find
1) DNA physically-interacting regions (PIRs)
2) regulatory interactions
3) mediating protein complexes?

HiPIE2 software

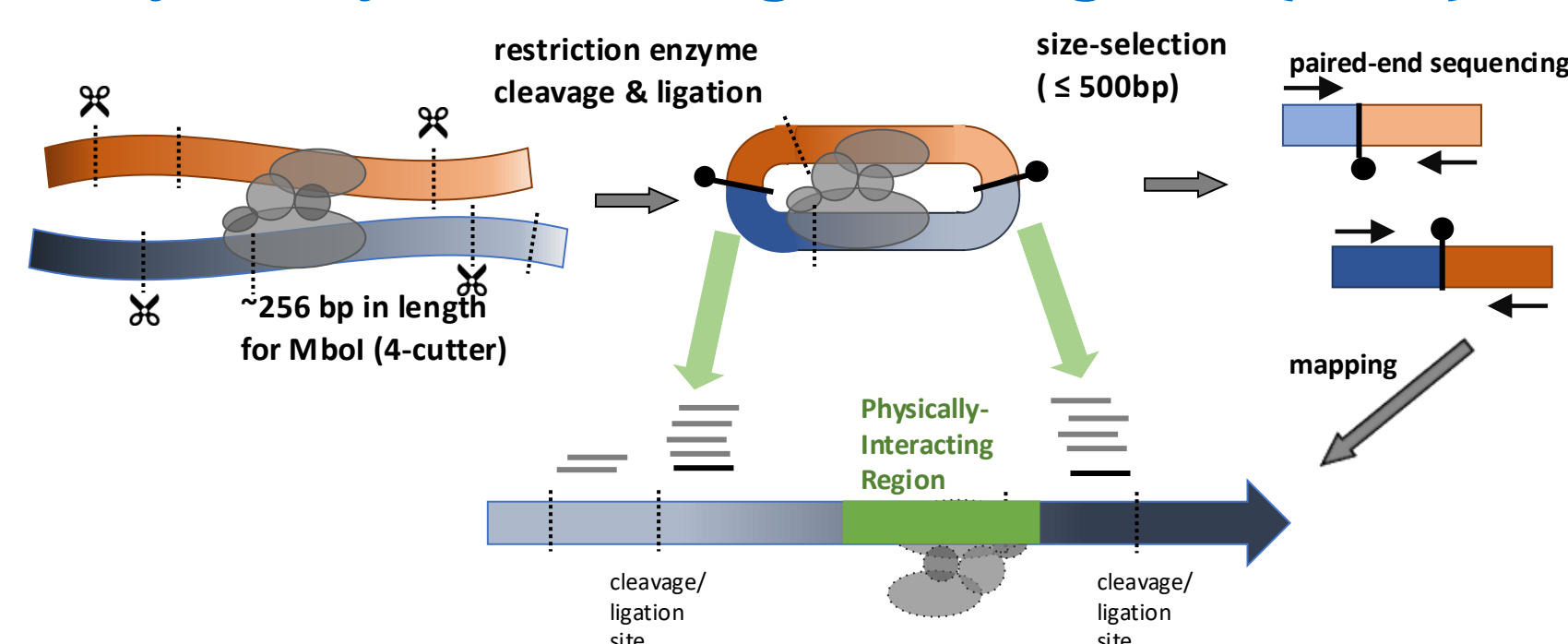
<https://bitbucket.com/wanglab-upenn/HIPPIE2>

HiPIE2 pipeline analyzes Hi-C data from raw reads to significant PIR interactions to functional genomics annotation

PHYSICALLY-INTERACTING DNA REGIONS

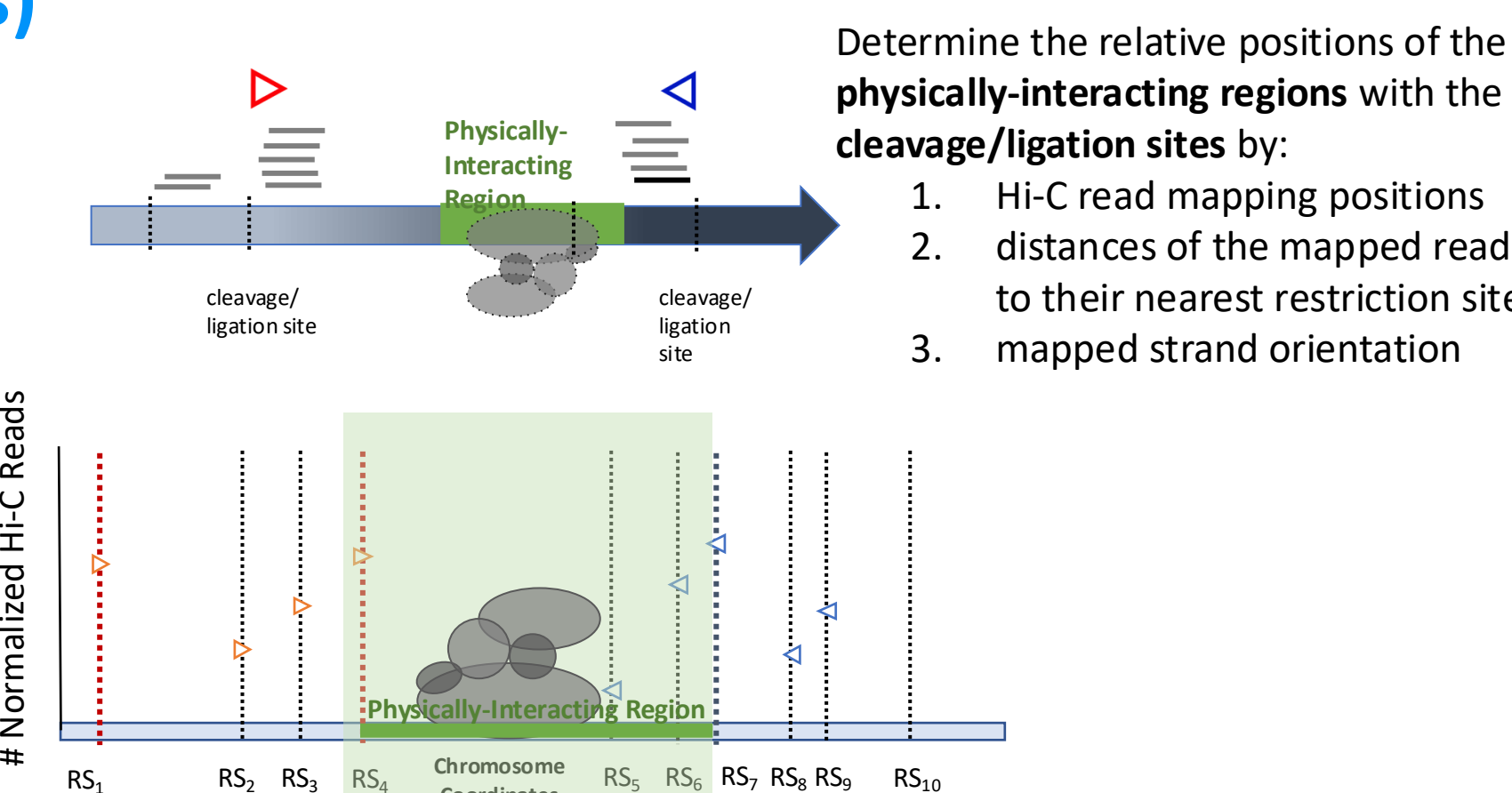
Identify physically interacting regions (PIRs) for high-resolution identification of enhancer-promoter interactions

HiPIE2 Hi-C model and identification of Physically-Interacting DNA Regions (PIRs)

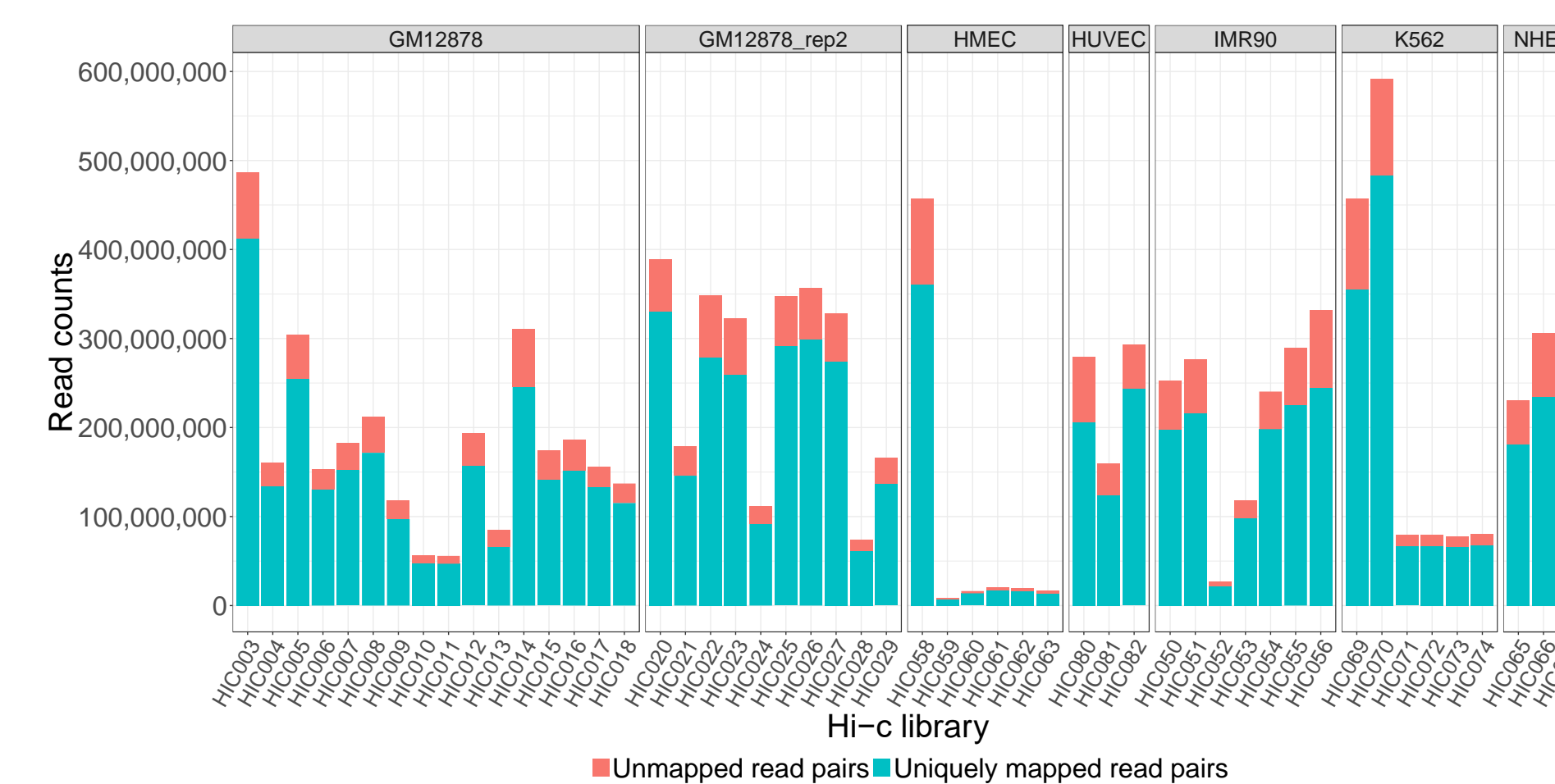


PIR is identified with two converging and consistently cut cleavage/ligation sites

Two converging cleavage/ligation sites enclose a physically-interacting region (PIR)

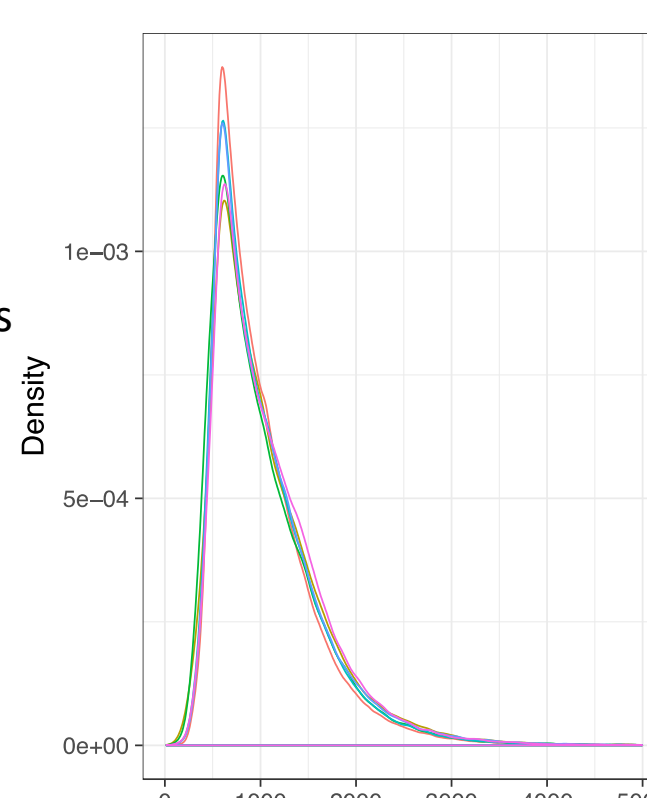


Hi-C DATASETS

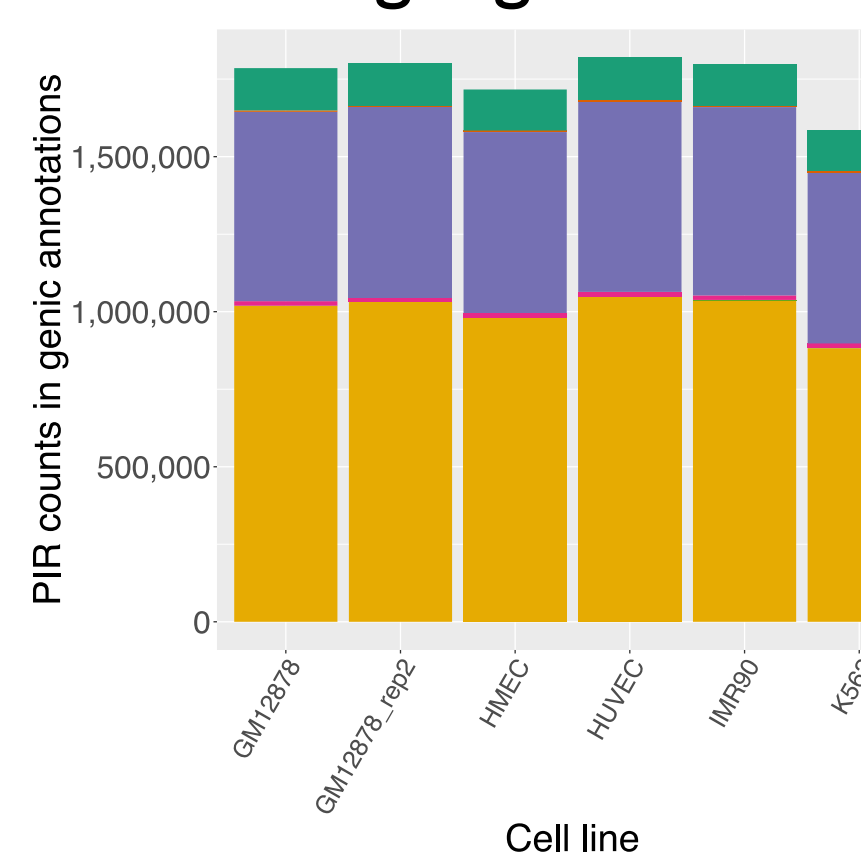


LANDSCAPE OF PHYSICALLY-INTERACTING DNA REGIONS

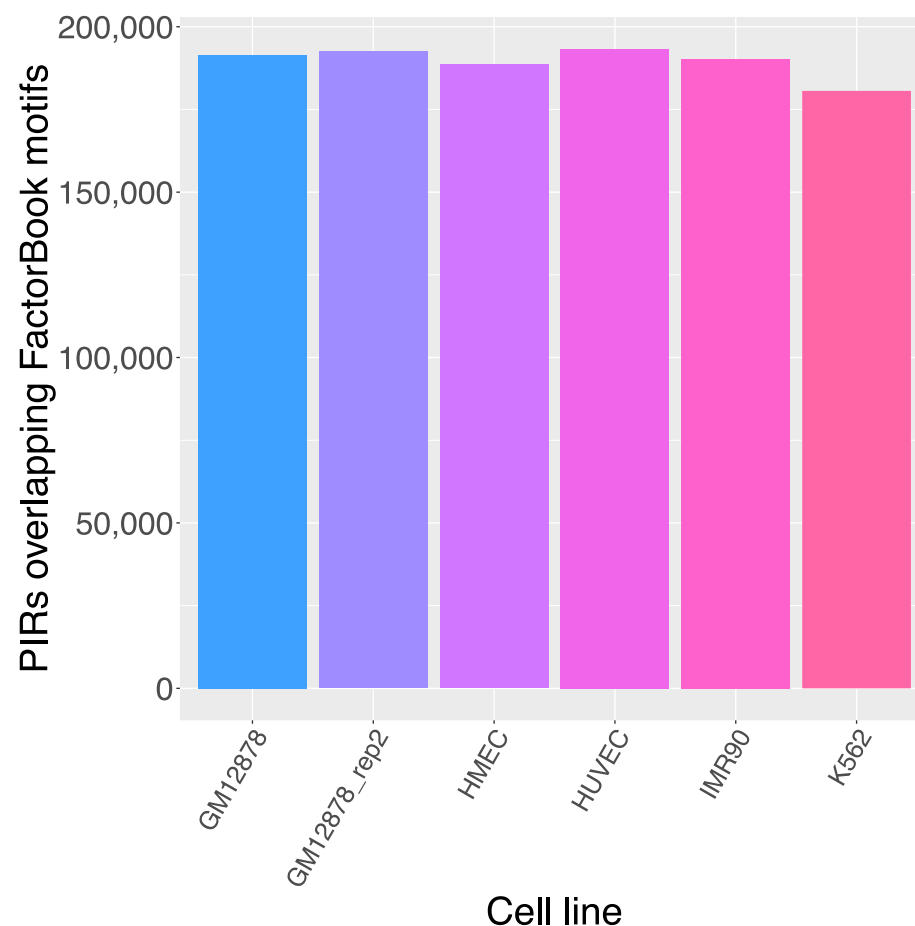
PIRs provide sub-1K resolution of chromatin interactions



PIRs are located mostly in non-coding regions



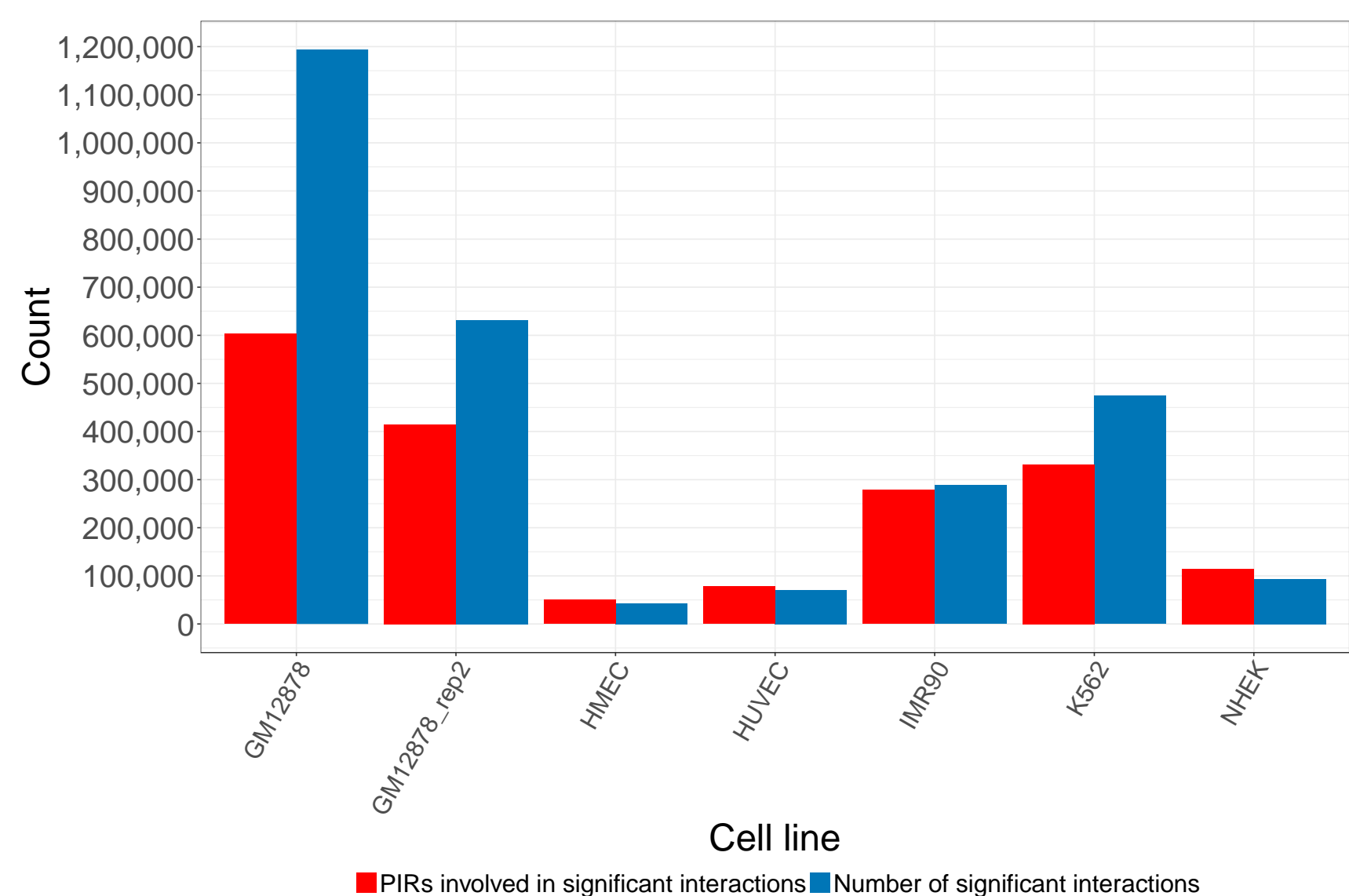
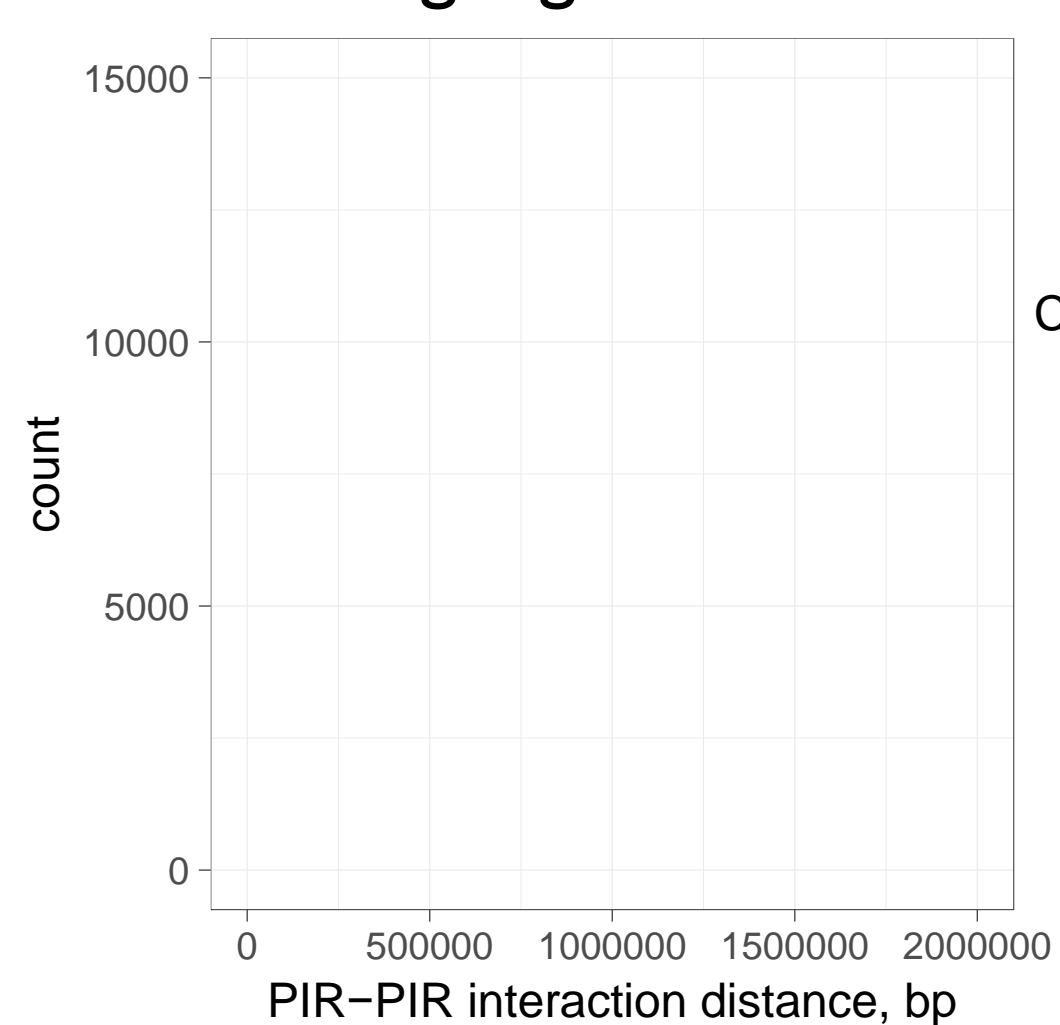
PIRs are enriched for TFBS (ChIP-seq)



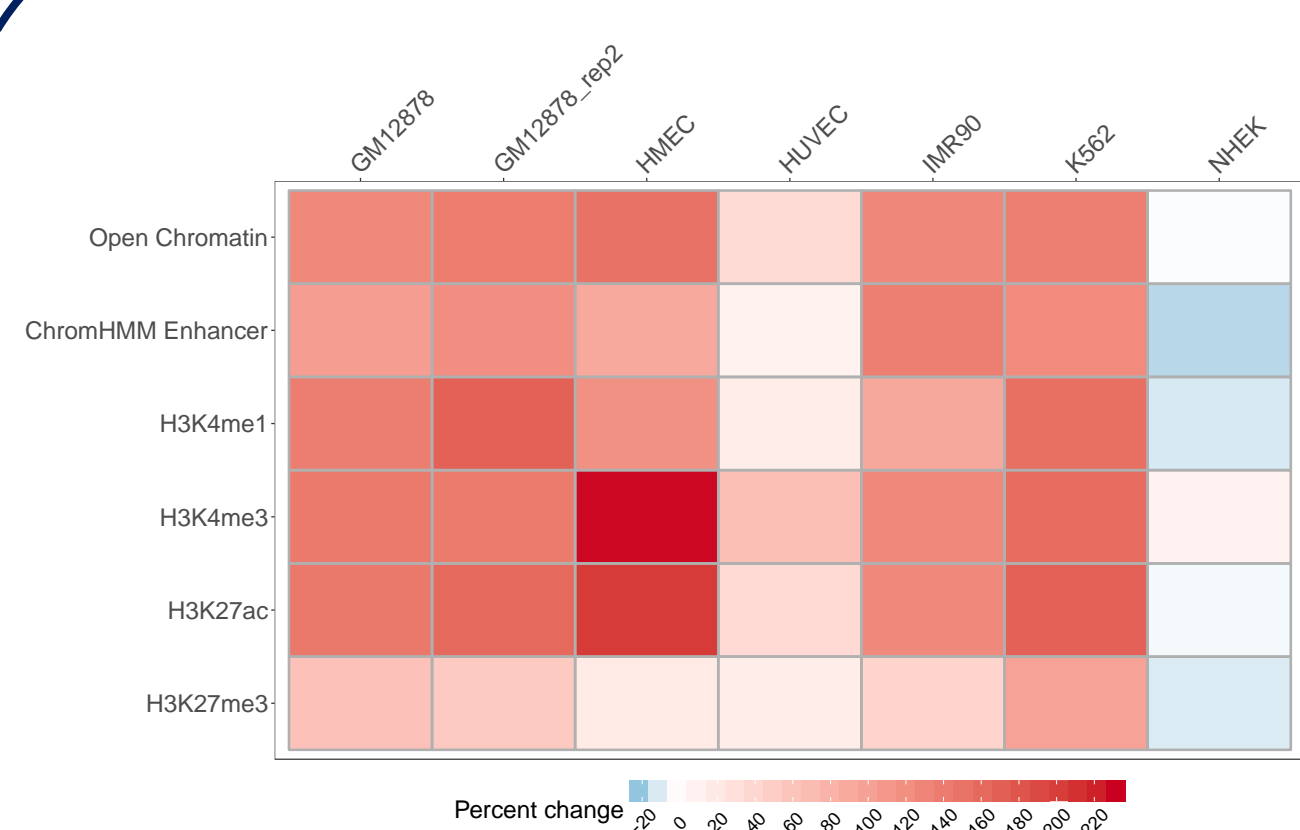
LANDSCAPE OF PIR-PIR INTERACTIONS

PIR-PIR interactions across cell lines

Genomic distance between physically-interacting regions

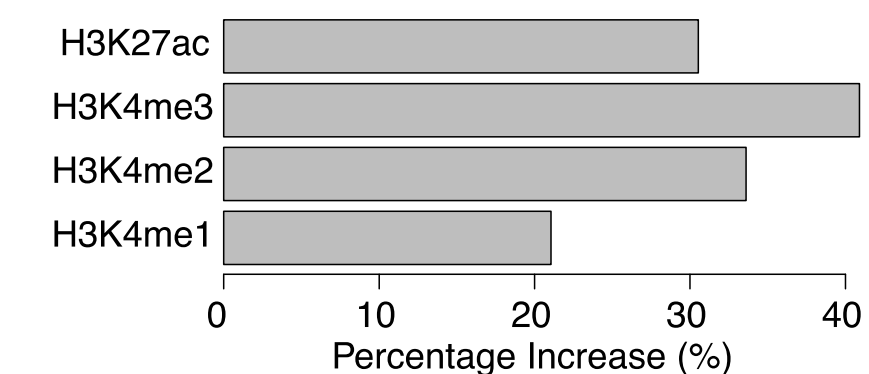


Functional enrichments in PIRs

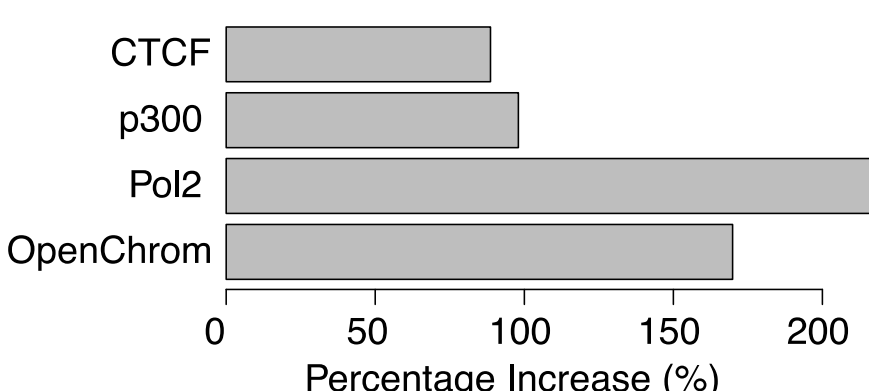


Promoter-touching PIRs are likely to be regulatory elements

Histone Mod Increase from All Interacting PIRs



TF Binding Increase from All Interacting PIRs

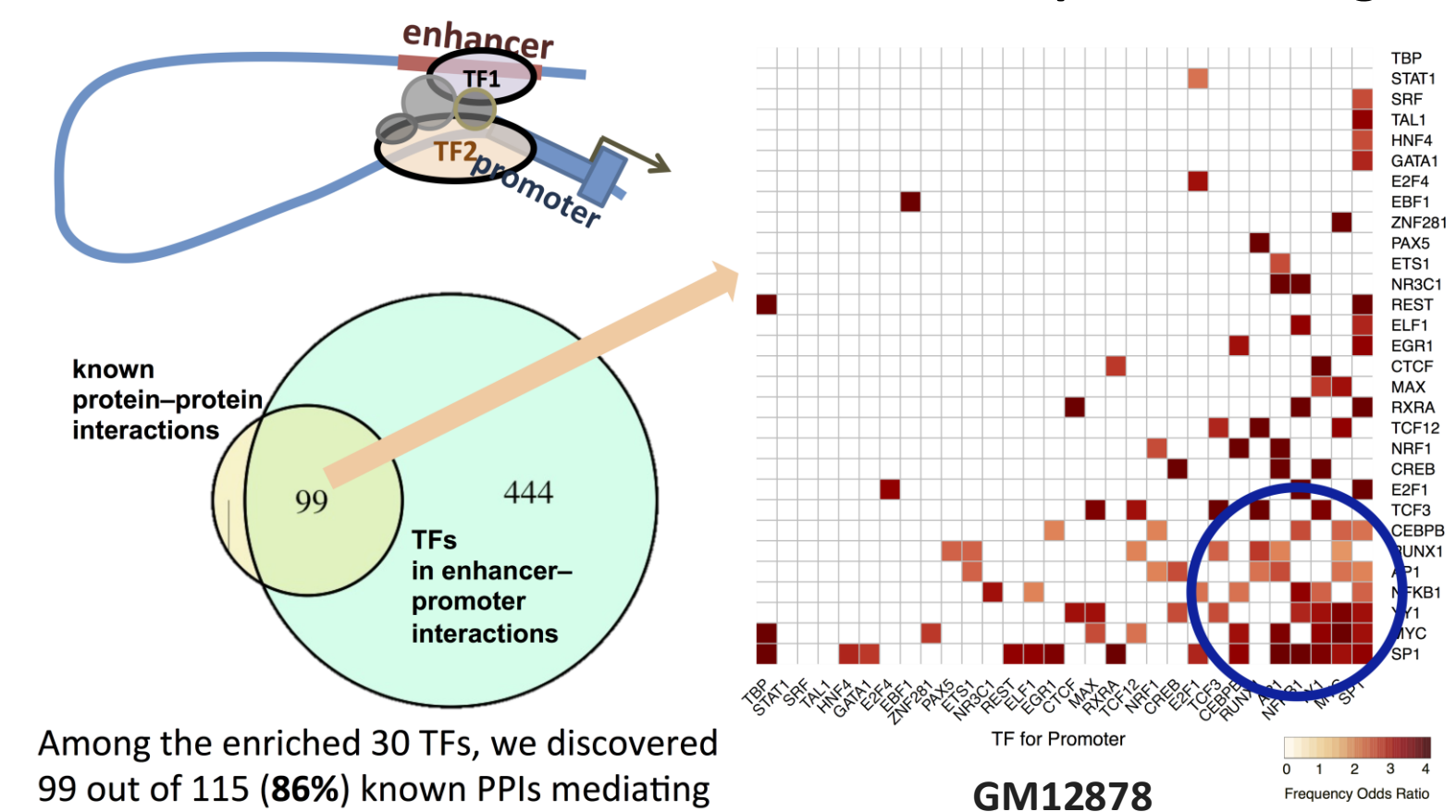


- promoters were defined upstream of annotated genes
- enhancers were defined by open chromatin, H3K27ac and/or H3K4me1, and lack of H3K4me3 and H3K27me3 in the matching cell types

Regulatory and other PIR-PIR interactions

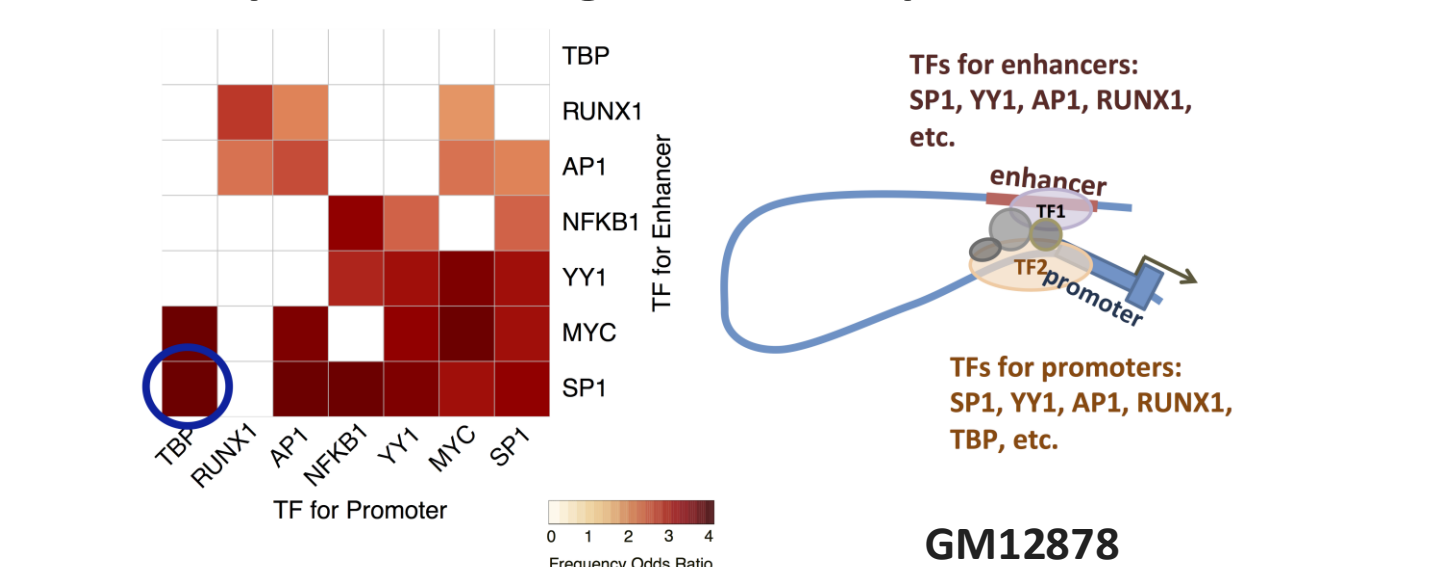


TF-TF interactions involved in enhancer-promoter regulations



Among the enriched 30 TFs, we discovered 99 out of 115 (86%) known PPIs mediating the enhancer-promoter interactions

TF complexes linking enhancer-promoter interactions



References

1. Kuksa PP, Amlie-Wolf A, Hwang Y-C et al. HIPPIE2 (In preparation)
2. Hwang Y-C et al. HIPPIE: A high-throughput identification pipeline for promoter interacting enhancer elements. *Bioinformatics* 2014
3. Hwang Y-C et al. High-throughput identification of long-range regulatory elements and their target promoters in the human genome. *Nucl. Acids Res.*, 2013.

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