

Evaluating the chromatin state activity of the K562 cell line by leveraging CRISPR-Cas9 based epigenetic regulatory element screening (CERES)

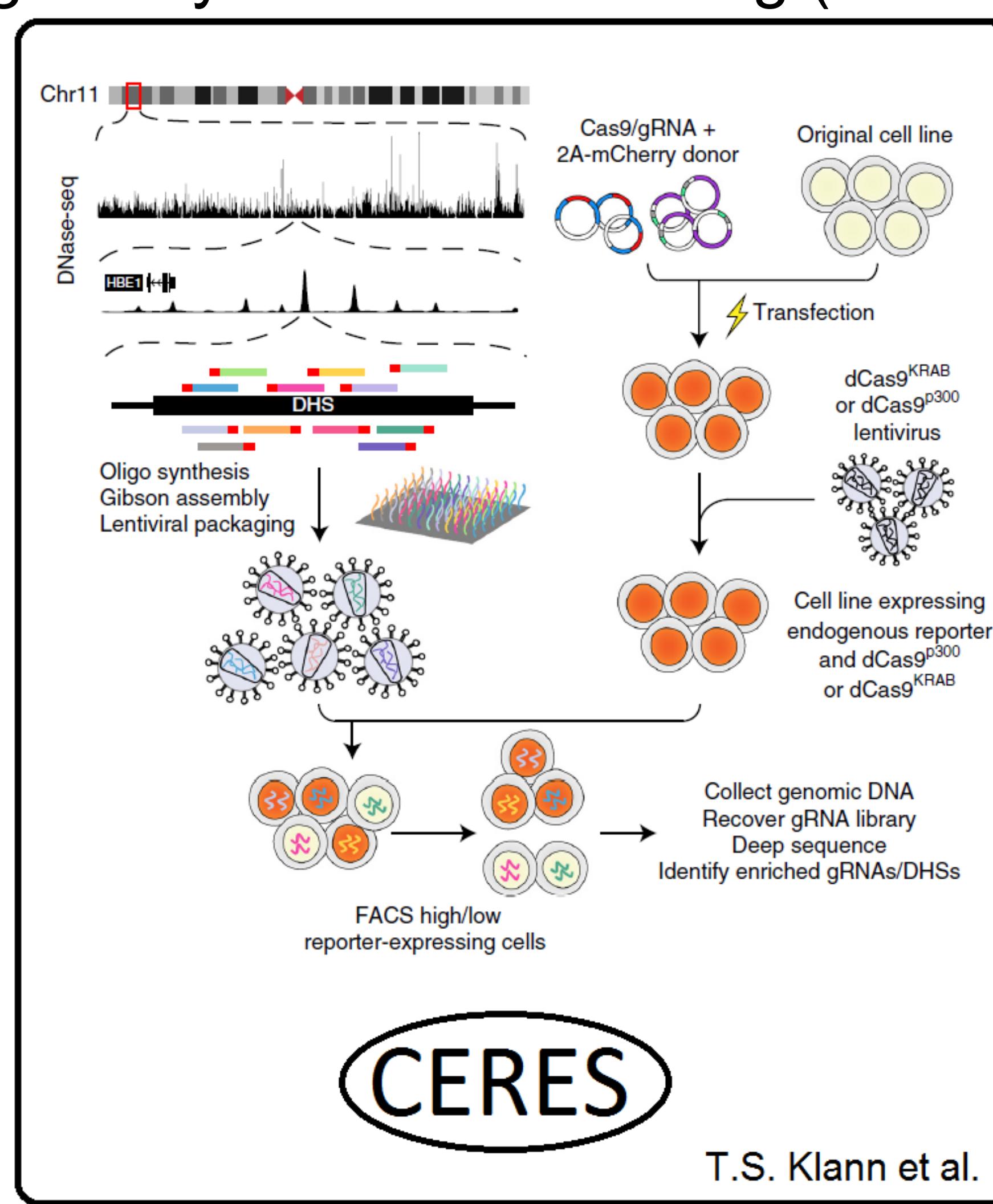


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Introduction

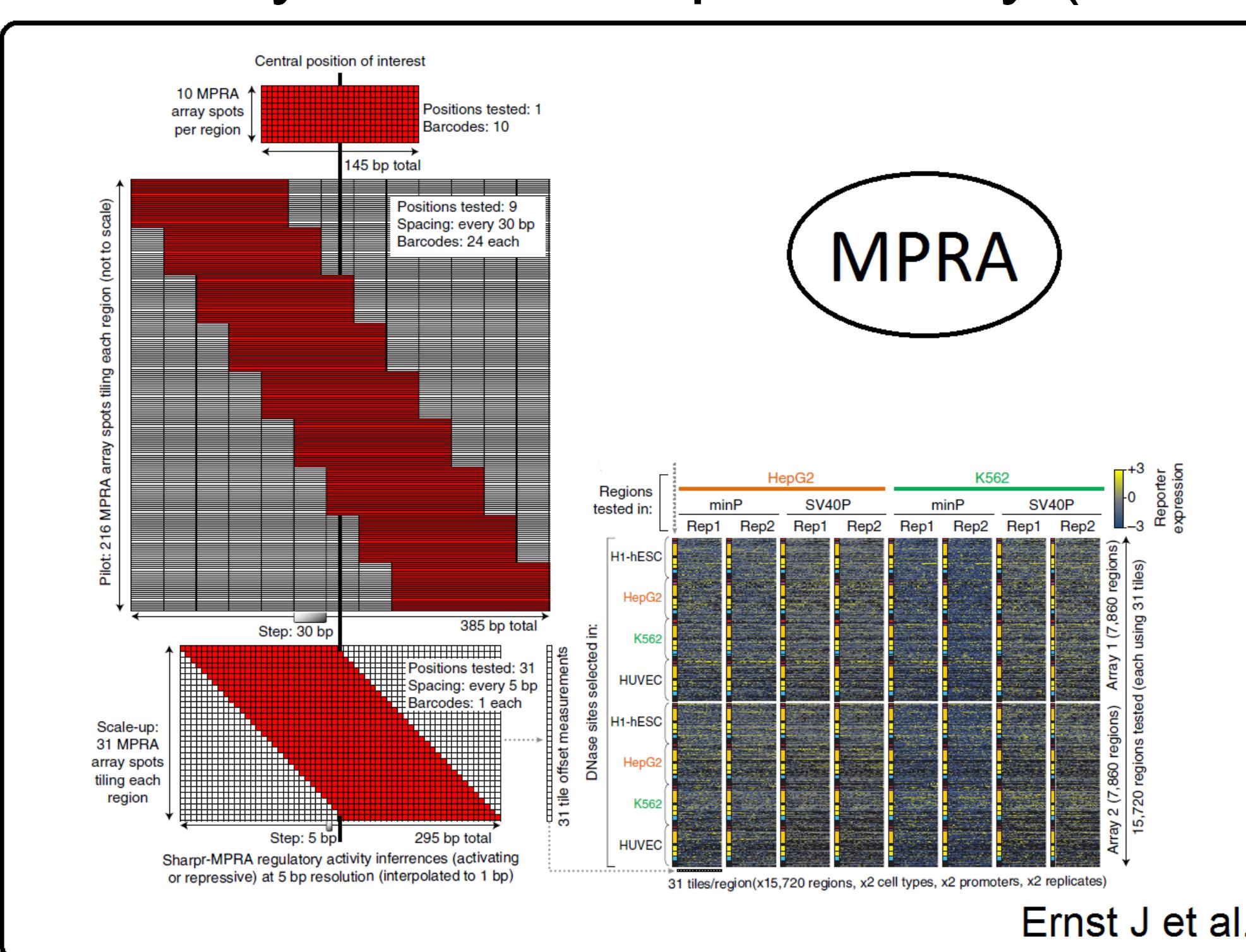
- CRISPR-Cas9 based genome editing technology can be leveraged to advance our understanding of functional activity of the non-coding genome in its native context.

CRISPR-Cas9 based epigenetic regulatory element screening (CERES)



T.S. Klann et al.

Massively Parallel Report Assay (MPRA)



Ernst J et al.

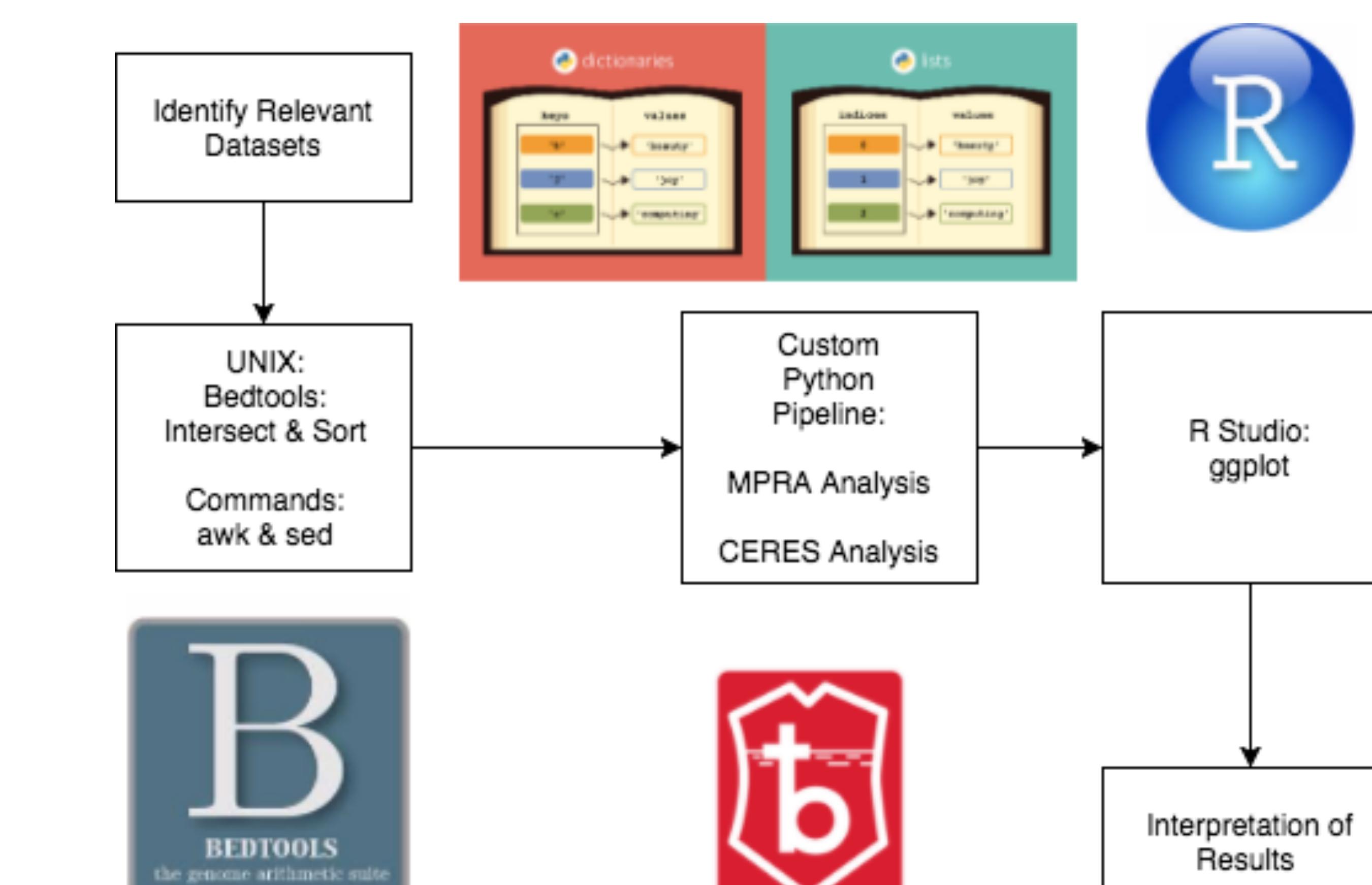
Aim and Significance

- Aim of this project is to understand how the chromatin state annotations for the K562 cell line relate to functional activity as reported by CERES.
- Significance of this project is that it provides a comparison of regulatory activity as measured by MPRA and CERES in the context of chromatin state.

Datasets

- CRISPR-Cas9 based epigenetic regulatory element screening (CERES) for K562 cell line
 - Data from Klann et al.
 - <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE96875>
- MPRA-SHARPR comparison:
 - K562 Scaled-Up combined design
 - <http://www.biolchem.ucla.edu/labs/ernst/SHARPR/>
- ChromHMM segmentations
 - 25-state Genome Segmentations from ChromHMM for the K562 cell line
 - <https://genome.ucsc.edu/cgi-bin/hgFileUi?db=hg19&g=wgEncodeAwgSegmentation>

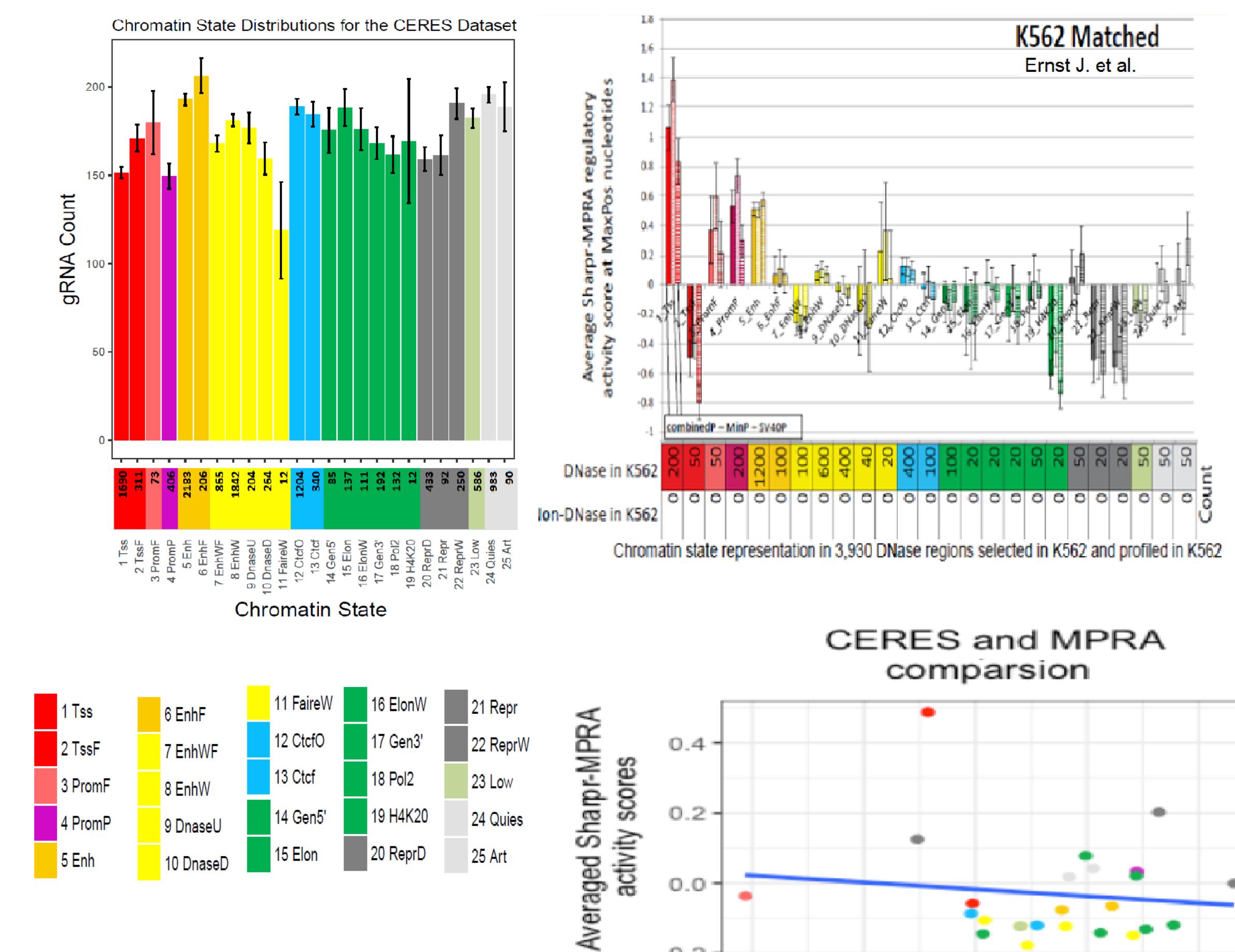
Methods



Observations

ChromHMM Chromatin State Annotations	nhW	Enh	EnhWF	Enh	Enh
CERES Data					
MPRA Data				133.5833333	110

Results



Conclusion

- We have observed poor correlation between the SHARPR-MPRA score and CERES gRNA count distributions for chromatin state.
- This could indicate that MPRA and CERES measure functional activity in fundamentally different ways in the context of chromatin state, or it could mean that there is an insufficient amount of points in the CERES data to make a call.

Future Directions

- An increase in the sample size could improve the error bars of our results.
- Multiple datasets could be utilized to obtain CRISPR-Cas9 data on more regions to better understand the role of chromatin states.

Acknowledgements

- Ernst Lab and B.I.G Summer Students

Works Cited

- T.S. Klann et al., "CRISPR-Cas9 epigenome editing enables high-throughput screening for functional regulatory elements in the human genome," *Nature Biotechnol.*, doi:10.1038/nbt.3853, 2017.
- Ernst J, Melnikov A, Zhang X, et al. Genome-scale high-resolution mapping of activating and repressive nucleotides in regulatory regions. *Nature biotechnology*. 2016;34(11):1180-1190. doi:10.1038/nbt.3678.