Co-ChIP enables genome-wide mapping of histone mark co-occurrence at single-molecule resolution

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Background

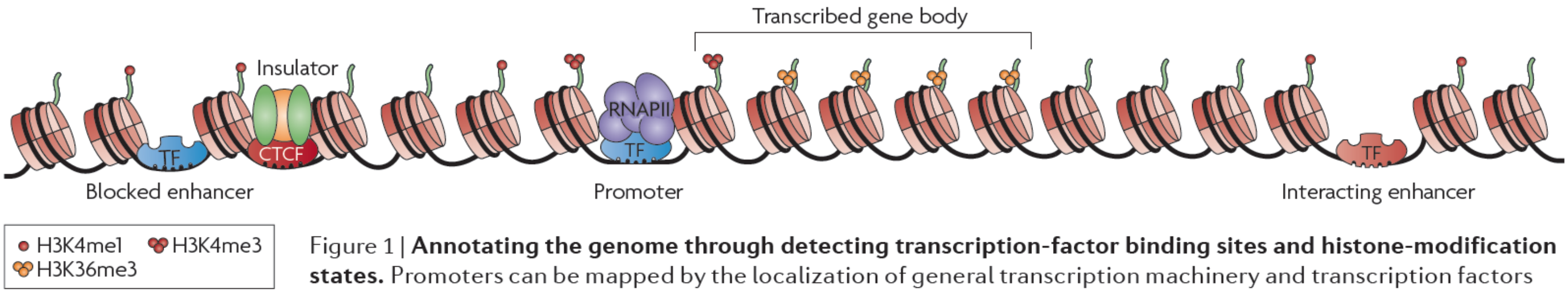
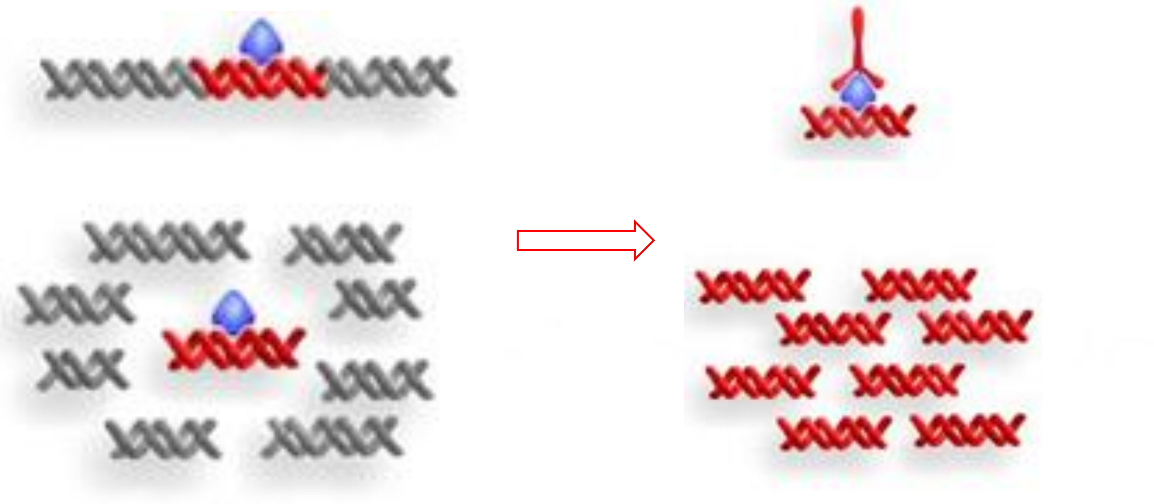
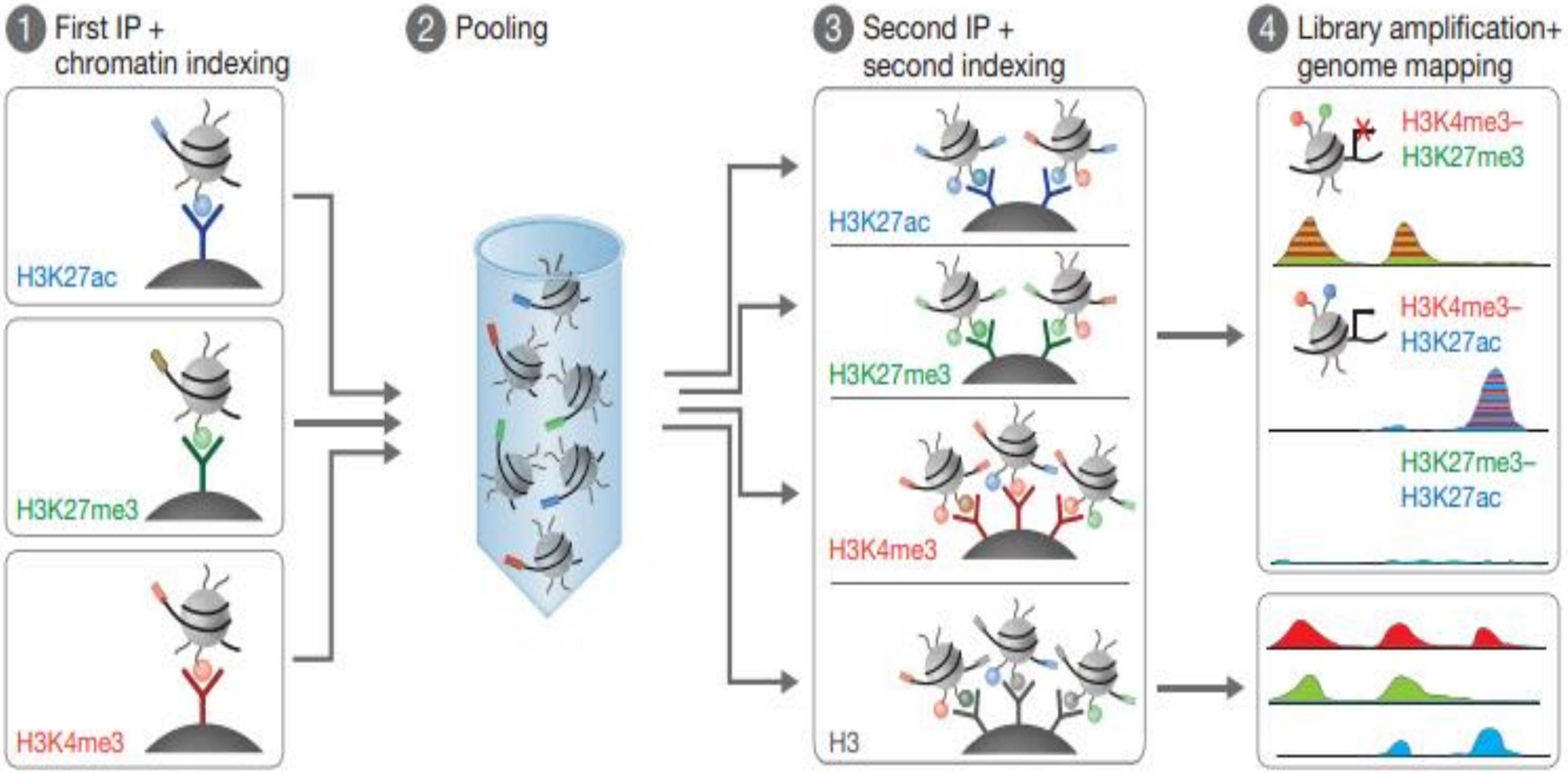


Figure 1 | **Annotating the genome through detecting transcription-factor binding sites and histone-modification states.** Promoters can be mapped by the localization of general transcription machinery and transcription factors

Chromatin Immunoprecipitation (ChIP)

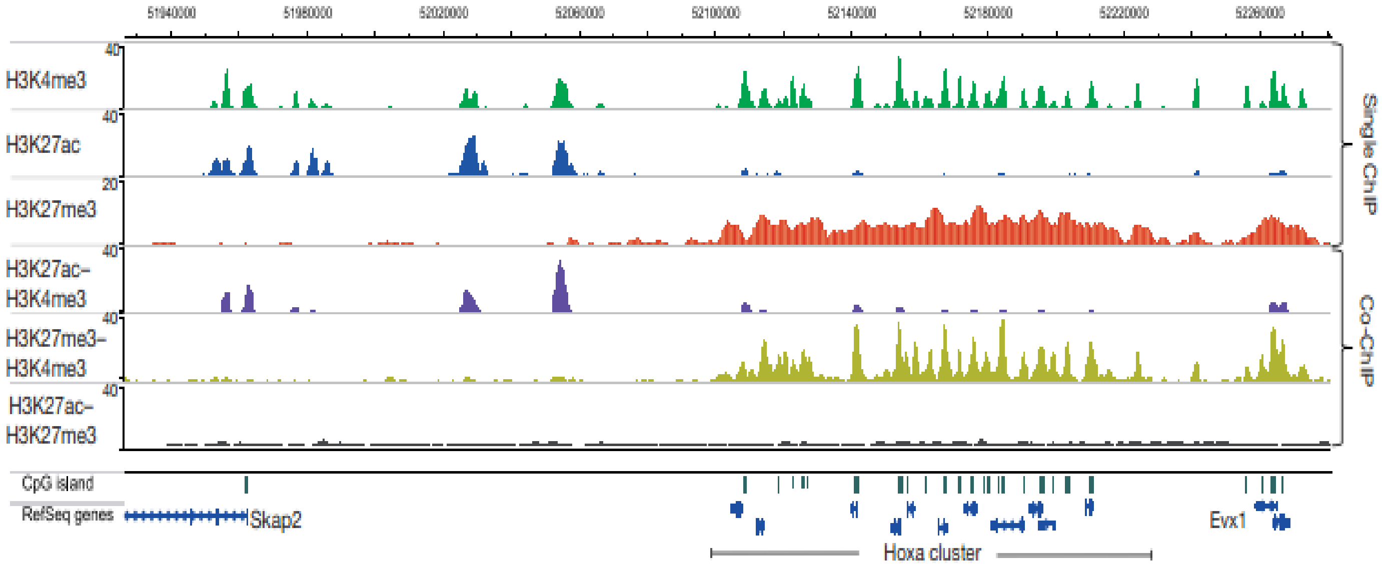


Co-ChIP

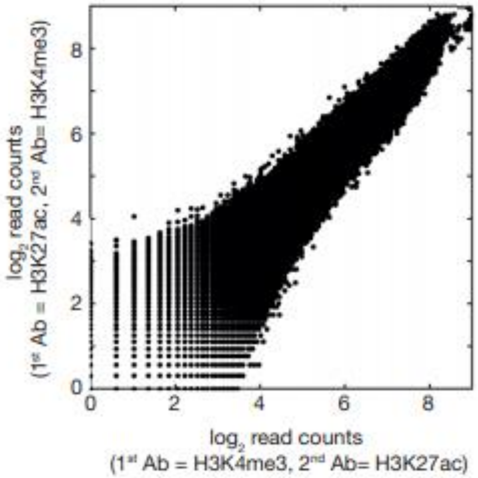


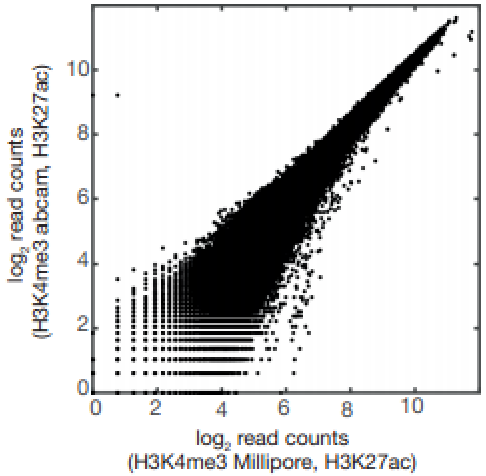
为了探究全基因组范围内组蛋白修饰对同时发生时，它们之间的相互作用，我们发展了co-ChIP。

Co-ChIP

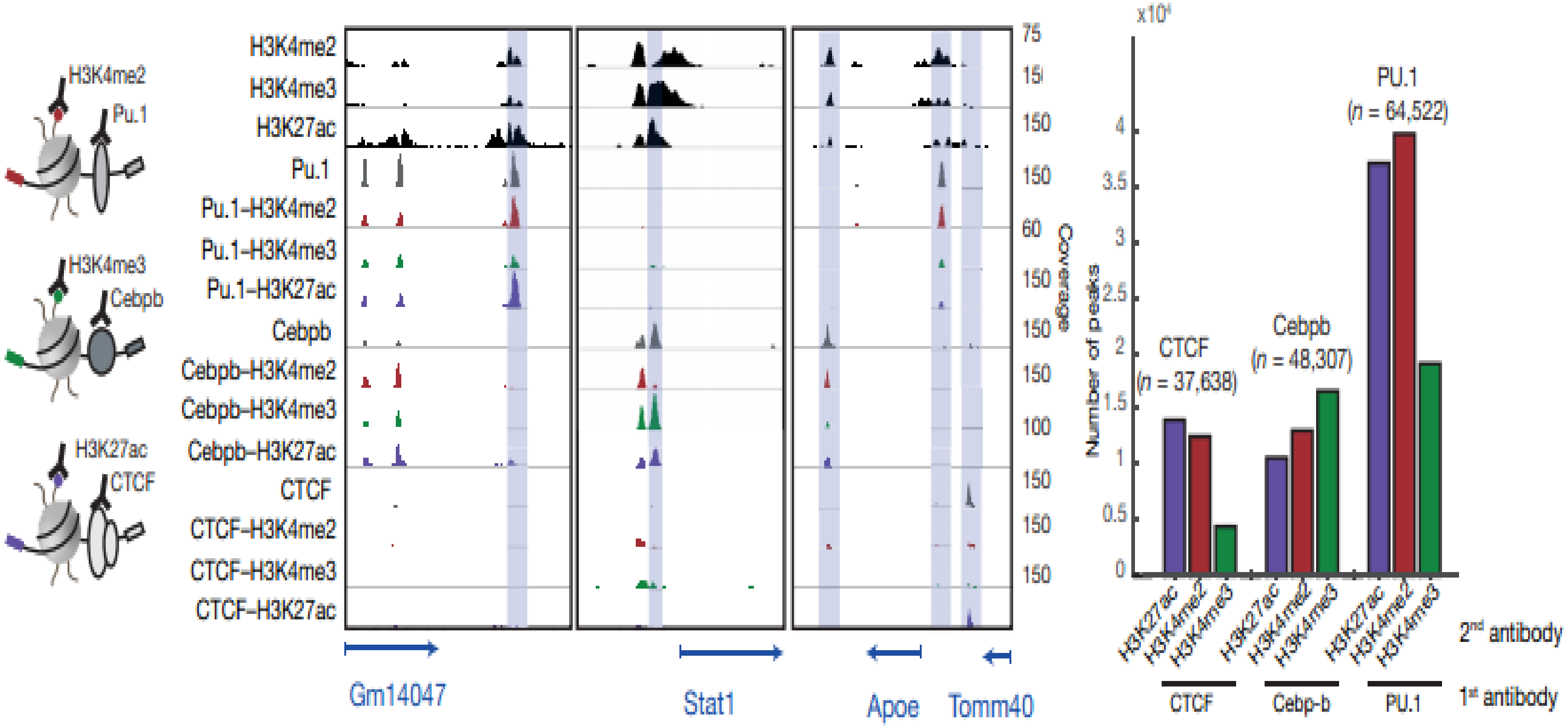


结果表明，抗体使用的顺序以及不同抗体的使用并没有显著影响组蛋白翻译后修饰共同修饰区域的识别。



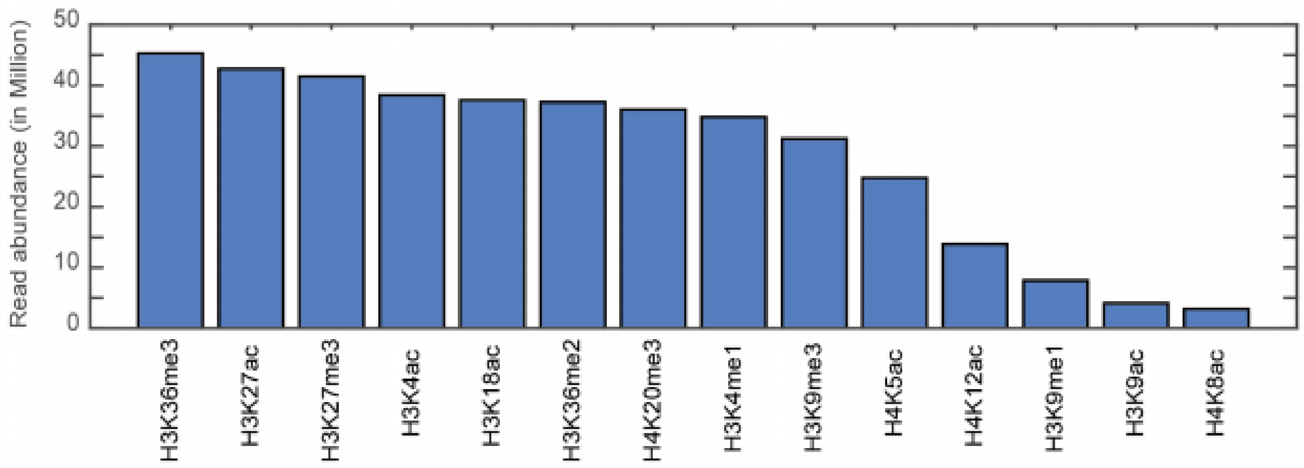


Co-ChIP

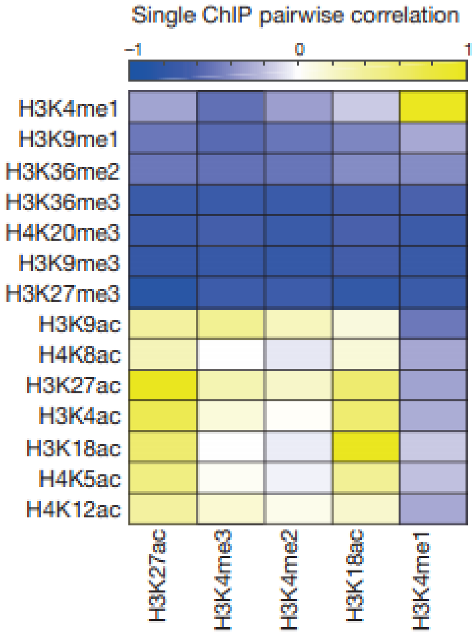


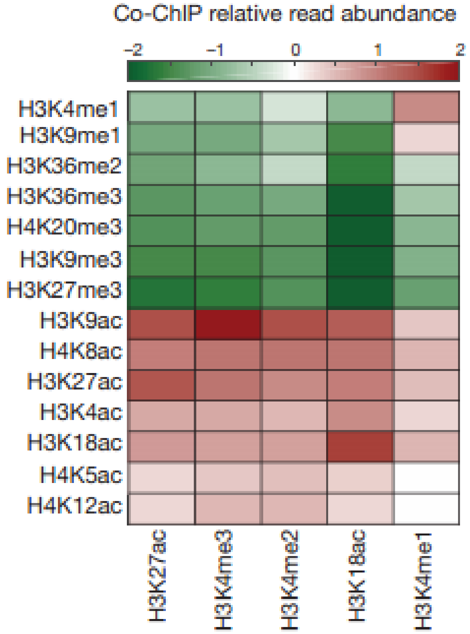
Co-ChIP在全基因组范围内对于组蛋白翻译后修饰以及转录因子的同现性有很好的描述。

Co-occurrence measurements



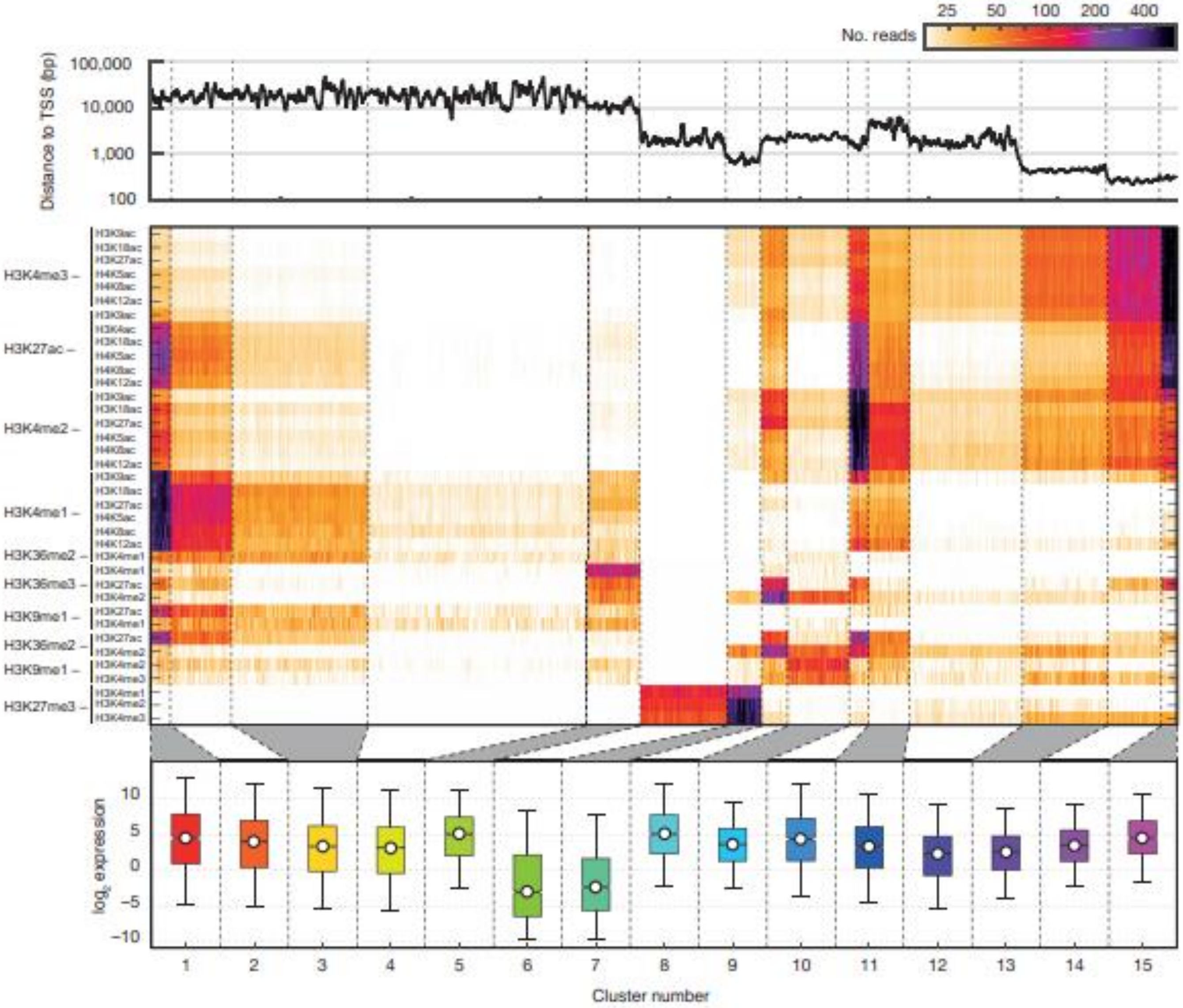
Comparing the relative abundances to the pairwise correlations of conventional single PTM ChIP revealed an overall agreement between these two measurements.


Single ChIP pairwise correlation

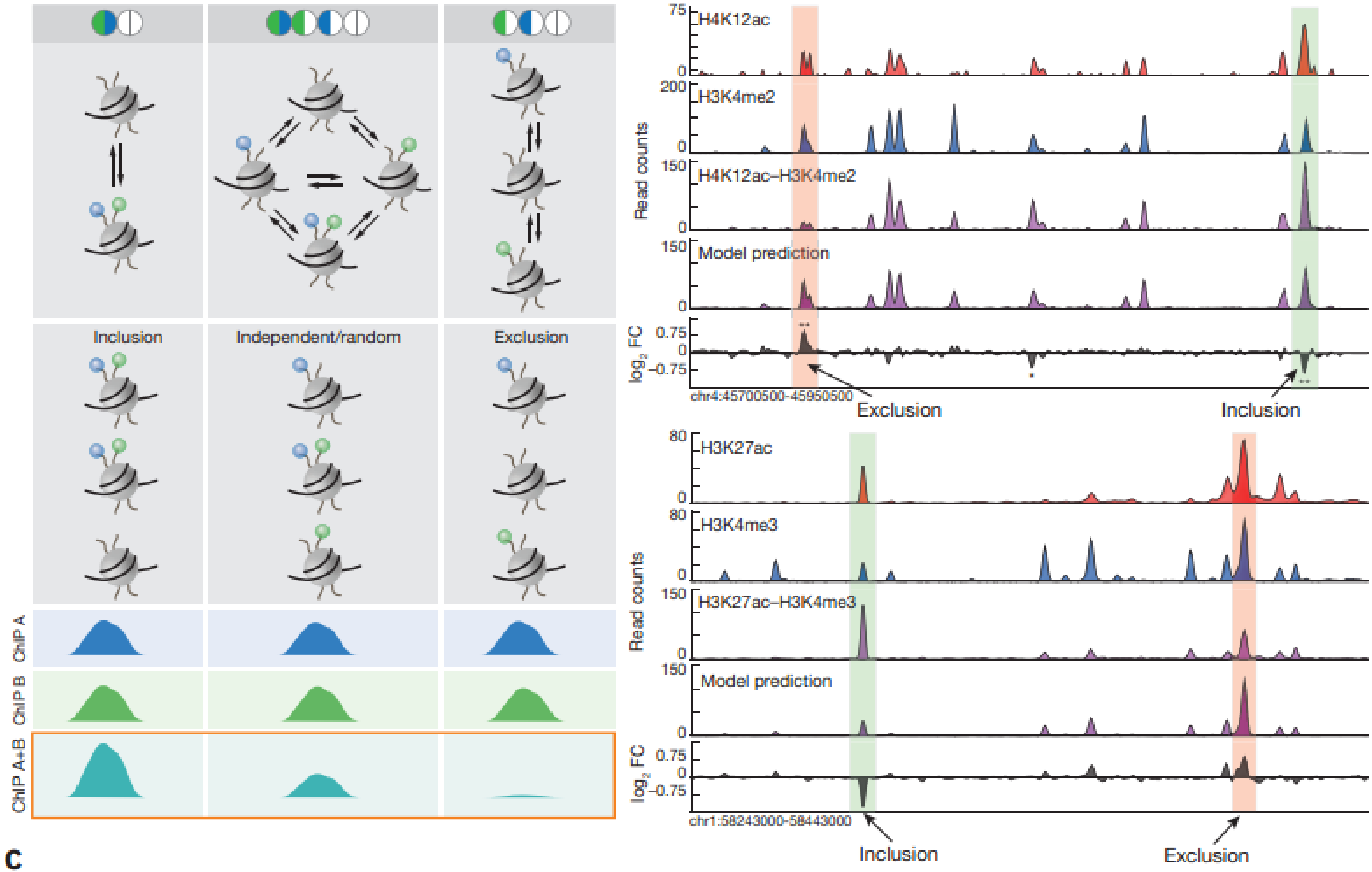

Co-ChIP relative read abundance

Co-occurrence measurements

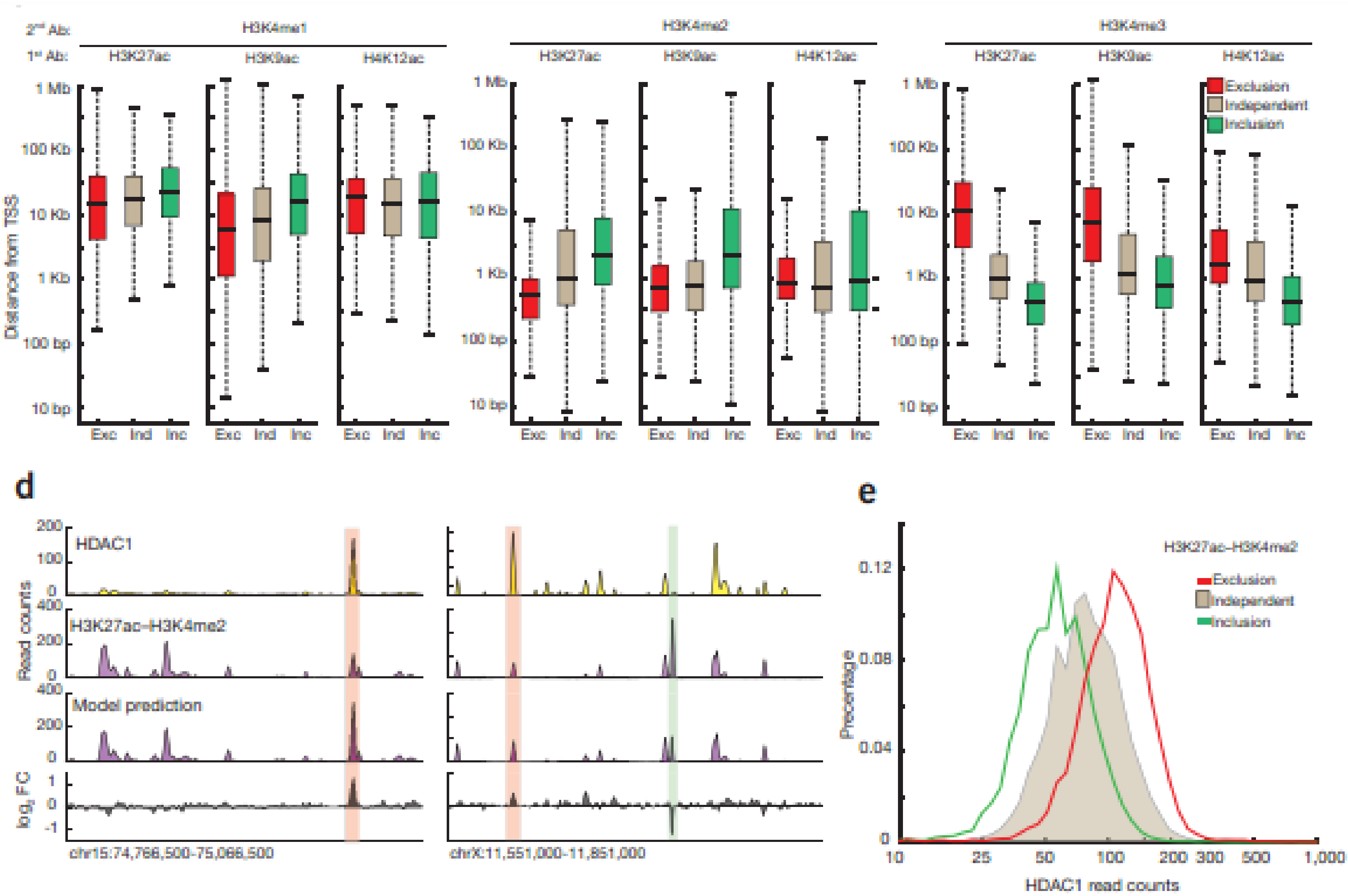
Clustering of the histone modification pairs revealed 15 distinct clusters corresponding to specific chromatin states that varied by genomic position and the expression profiles of neighboring genes.



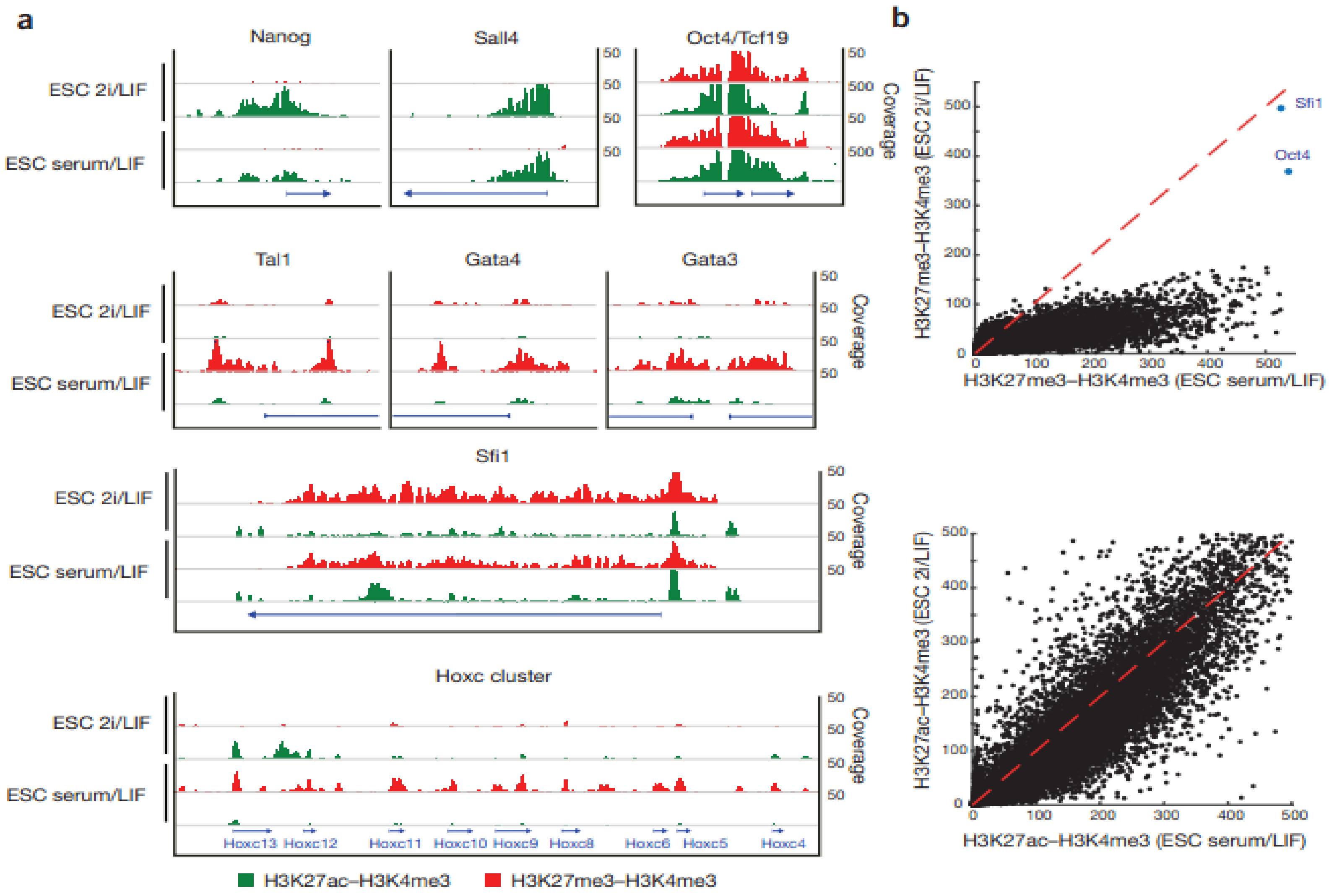
Exclusion or inclusion interactions



Exclusion or inclusion interactions



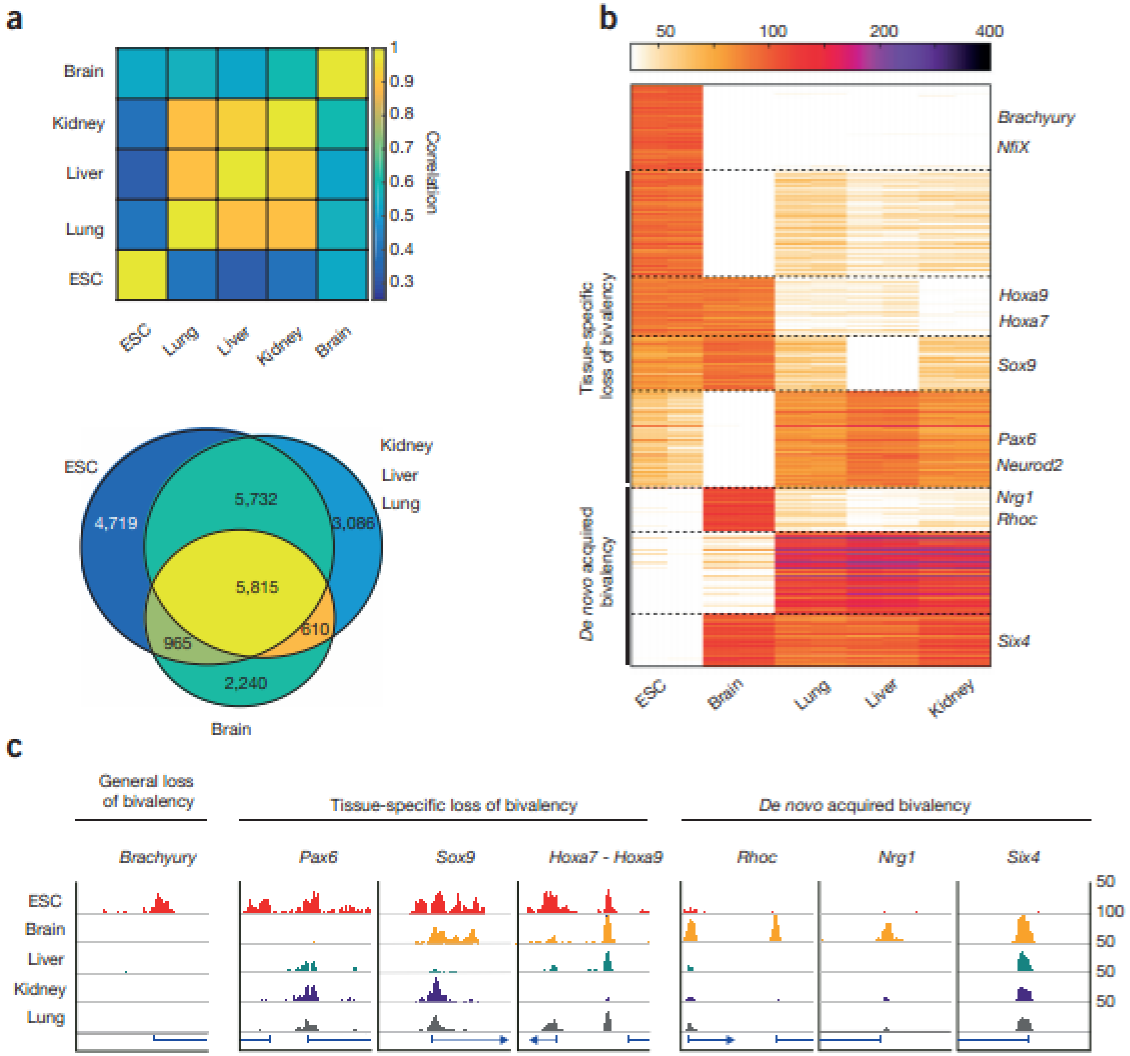
Characterization of bivalent domains



Characterization of bivalent domains

为了探究成年组织中的二价状态，我们选择了4种小鼠的组织：大脑、肝脏、肺和肾脏，并且在全基因组范围内测得H3K27me3-H3K4me3在同一个细胞核内的共发生。

这些结果显示出Co-ChIP在系统生物学以及干细胞生物学应用上的巨大潜力。



Discussion

- 本文最重要的创新点在于打破了传统ChIP的限制，发展了一种全新的Co-ChIP技术，使我们能够在同一个细胞核内观察到两种不同的组蛋白修饰共同起作用，以更好地使我们了解染色质的结构以及转录调控的过程。

- 此研究中的Co-ChIP这项新技术可能对于进一步揭示染色质三维结构有较大意义，也给我们的研究提供了新的思路，我们在研究染色质的相互作用时，大可不必局限于染色质两两之间的交互，也有可能是多条染色质之间共同的交互作用来调节染色质的活动以对转录、翻译等过程产生影响。

- 我认为此研究中Co-ChIP技术的应用与转录因子的调控作用结合得比较少，可以多多往转录调控方向发展；另外，抗体的寻找可能是限制该技术发展的重要因素。

Thank you!