

We thank the reviewers for their comments. Please see our responses below.

Reviewer #1.

1. We have now included a table summarizing LCDs in transcriptional activation and repression. Please see Table 1.

2. We thank the reviewer for pointing out that cohesion-CTCF depicted in Figure 1 was not mentioned in the main text. We have now discussed the role of cohesion-CTCF in bringing enhancers to proximity to their target promoters, and provided two new references to support this statement.

3. Transcription activation requires a common set of transcription factors (e.g. general transcription factors, RNA polymerase II). It is known that the utilization of a few select cell-specific coactivators drives cell-type specific transcriptional activation. Therefore, Figure 1A and 1B are in fact similar, as expected. We aim to drive home the message that small differences in the composition of transcription factor assemblies can affect gene and cell-type selective transcriptional activation.

4. ABCF1 is involved in stem cell-specific transcriptional activation while HP1 is involved in general repression. They are involved in very different cellular processes. In addition, ABCF1 likely functions as a transcriptional coactivator in a cell-type specific manner, while HP1 functions as repressor across many cell types. Therefore, we would like to respectfully disagree with the reviewer that they should be summarized in one figure.