**Discussion Questions for "Global reference mapping of human transcription factor footprints" by Vierstra et al.**

1. What is a DNA footprint? How is it connected through statistics to a transcription factor (TF)?

2. How was the empirical false discovery rate for the number of footprints per biosample estimated? (See second paragraph under "Global mapping of TF footprints".)

3. What is the Jaccard similarity? Does a Jaccard similarity of 0.43 vs. 0.29 for consensus vs. non-consensus footprints (Extended Data Fig. 3a) seem meaningful? Why or why not?

4. What factors determine the power to detect chromatin altering variants (CAVs) in the section "Functional DNA variants in TF footprints"?

5. In evaluating the overlap of GWAS variants with TF footprints, how was the null distribution calculated? Why is it important to account for linkage disequilibrium, minor allele frequency, and proximity to genes? Is the enrichment shown in Fig. 6A more or less than you would have expected? Why?