Comparative Epigenomic Annotation of Regulatory Elements in Multiple Tissues Across Vertebrates

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A comprehensive characterization and comparison of *cis*-regulatory elements across tissues and species can help us understand the genetic and evolutionary basis of complex phenotypes. Yet, attempts to dissect the evolution of regulatory elements have generally been small, both regarding the number of tissues and species compared. Here, we provided the most comprehensive atlas of *cis*-regulatory elements to date, including 25 tissues across seven species (i.e., human, mouse, pig, cow, horse, chicken, and zebrafish), by integrating 1,028 epigenomes including ChIP-seq for 4 histone marks, ATAC-seq, CTCF-seq, RNA-seq, and Hi-C datasets. We predicted a total of 15 chromatin states (e.g., promoters, enhancers and repressors) based on these epigenomic data. The relationship between epigenetic conservation and DNA sequence conservation showed distinct patterns across chromatin states, such as S shape for strong promoters and V shape for strong enhancers in mammals. Further analysis suggests that the regulators were significantly enriched in evolutionary breakpoint regions (EBRs) in a tissue-specific and regulator-specific manner. For example, human-specific EBRs are significantly enriched for human cortex-specific repressors. Enhancers were also significantly enriched in transposable elements in a species-specific and tissue-specific manner. For instance, in liver, strong enhancers were significantly enriched in SINE (tRNA-RTE) in pig. Next, we will integrate these findings with results from genome-wide association studies (GWAS) of complex traits and eQTLs to provide novel insights into the genetic

and evolutionary basis of complex traits in livestock and humans. Our current datasets and analysis will provide not only a compendium of regulatory elements for the entire community of biology and genetics, but also a prototype for harnessing comparative 'Omics' for understanding complex trait genetics.