

Nanoscale Structure of a Transcriptional Condensate

Abstract

Clusters of enhancers regulate genes that play prominent roles in cell identity. These enhancers and their target genes coalesce into assemblies of protein and RNA called transcriptional condensates. The components and structures of transcriptional condensates have yet to be defined in terms of the individual transcription factors (TFs), RNA molecules and DNA sequences that contribute to the assembled compartment. We present an approach that produces this information at nanoscale resolution, revealing that enhancers are bound by multiple small clusters of TFs, that these TF-enhancer assemblies co-occur with nascent enhancer RNA molecules, and that the enhancer assemblies coalesce to form the composite transcriptional compartment. The approach described here reveals how TFs populate enhancers at base-pair resolution, indicates that TFs, nascent RNA molecules and DNA elements together govern the relationship between gene regulation and genome structure, and provides a foundation for high-resolution maps of regulatory architecture across the genome.