

RNA polymerase II clustering through carboxy-terminal domain phase separation.

Journal: Nat Struct Mol Biol

Publication Year: 2018

Authors: Marc Boehning, Claire Dugast-Darzacq, Marija Rankovic, Anders S Hansen, Taekyung Yu, Herve Marie-Nelly, David T McSwiggen, Goran Kokic, Gina M Dailey, Patrick Cramer, Xavier Darzacq, Markus Zweckstetter

PubMed link: 30127355

Funding Grants: Single Molecule Biophysics and Biology of Cellular Identity

Public Summary:

The carboxy-terminal domain (CTD) of RNA polymerase (Pol) II is an intrinsically disordered low-complexity region that is critical for pre-mRNA transcription and processing. The CTD consists of hepta-amino acid repeats varying in number from 52 in humans to 26 in yeast. Here we report that human and yeast CTDs undergo cooperative liquid phase separation, with the shorter yeast CTD forming less-stable droplets. In human cells, truncation of the CTD to the length of the yeast CTD decreases Pol II clustering and chromatin association, whereas CTD extension has the opposite effect. CTD droplets can incorporate intact Pol II and are dissolved by CTD phosphorylation with the transcription initiation factor IIH kinase CDK7. Together with published data, our results suggest that Pol II forms clusters or hubs at active genes through interactions between CTDs and with activators and that CTD phosphorylation liberates Pol II enzymes from hubs for promoter escape and transcription elongation.

Scientific Abstract:

The carboxy-terminal domain (CTD) of RNA polymerase (Pol) II is an intrinsically disordered low-complexity region that is critical for pre-mRNA transcription and processing. The CTD consists of hepta-amino acid repeats varying in number from 52 in humans to 26 in yeast. Here we report that human and yeast CTDs undergo cooperative liquid phase separation, with the shorter yeast CTD forming less-stable droplets. In human cells, truncation of the CTD to the length of the yeast CTD decreases Pol II clustering and chromatin association, whereas CTD extension has the opposite effect. CTD droplets can incorporate intact Pol II and are dissolved by CTD phosphorylation with the transcription initiation factor IIH kinase CDK7. Together with published data, our results suggest that Pol II forms clusters or hubs at active genes through interactions between CTDs and with activators and that CTD phosphorylation liberates Pol II enzymes from hubs for promoter escape and transcription elongation.

Source URL: <https://www.cirm.ca.gov/about-cirm/publications/rna-polymerase-ii-clustering-through-carboxy-terminal-domain-phase>