ChIP-exo interrogation of Crp, DNA, and RNAP holoenzyme interactions - DTU Orbit (06/11/2019)

ChIP-exo interrogation of Crp, DNA, and RNAP holoenzyme interactions
Numerous in vitro studies have yielded a refined picture of the structural and molecular associations between Cyclic-AMP receptor protein (Crp), the DNA motif, and RNA polymerase (RNAP) holoenzyme. In this study, high-resolution ChIP-exonuclease (ChIP-exo) was applied to study Crp binding in vivo and at genome-scale. Surprisingly, Crp was found to provide little to no protection of the DNA motif under activating conditions. Instead, Crp demonstrated binding patterns that closely resembled those generated by σ70. The binding patterns of both Crp and σ70 are indicative of RNAP holoenzyme DNA footprinting profiles associated with stages during transcription initiation that occur post-recruitment. This is marked by a pronounced advancement of the template strand footprint profile to the +20 position relative to the transcription start site and a multimodal distribution on the nontemplate strand. This trend was also observed in the familial transcription factor, Fnr, but full protection of the motif was seen in the repressor ArcA. Given the time-scale of ChIP studies and that the rate-limiting step in transcription initiation is typically post recruitment, we propose a hypothesis where Crp is absent from the DNA motif but remains associated with RNAP holoenzyme post-recruitment during transcription initiation. The release of Crp from the DNA motif may be a result of energetic changes that occur as RNAP holoenzyme traverses the various stable intermediates towards elongation complex formation.

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