

Structural basis of ribosomal RNA transcription regulation

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Ribosomal RNA (rRNA) is the most highly expressed gene in rapidly growing bacteria and is drastically downregulated under stress conditions by the global transcriptional regulator DksA and the alarmone ppGpp. To reveal the mechanism of highly regulated rRNA transcription, we determined cryo-electron microscopy structures of the *Escherichia coli* RNA polymerase (RNAP) σ 70 holoenzyme at different steps of rRNA promoter recognition with and without DksA/ppGpp. RNAP contacts the UP element of rRNA promoter using the dimerized α subunit carboxyl-terminal domain and scrunches the template DNA with the σ finger and β 'lid to select a transcription start site favorable for rRNA expression. Promoter DNA binding to RNAP induces conformational change of the σ domain 2 that opens a gate for DNA loading and ejects σ 1.1 from the RNAP cleft to facilitate open complex formation. DksA/ppGpp binding to RNAP also opens the DNA loading gate, but it is not coupled to σ 1.1 ejection and impedes the open complex formation of the rRNA promoter due to its G+C rich discriminator sequence. Mutations in σ 1.1 or the β 'lid stabilize the RNAP and rRNA promoter complex and decrease its sensitivity to DksA/ppGpp. These results provide a molecular basis for exceptionally active rRNA transcription and for its vulnerability to DksA/ppGpp. (<https://www.biorxiv.org/content/10.1101/2020.06.05.136721v1>)