

Structures and Mechanisms of Transcription Initiation and Its Regulation

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Gene transcription is a fundamental cellular process that is carried out by the multi-subunit RNA polymerase (RNAP), which is conserved from bacteria to human. Transcription process contains multiple steps including initiation, elongation and termination. Transcription is highly controlled and many regulatory factors/strategies act on initiation, which involves the opening up the double strand DNA into single strands and the delivery of the DNA template into the RNAP active centre. Transcription initiation involves multiple intermediate states but is a highly dynamic process, and has thus been difficult to be studied structurally. We use a special form of bacterial RNAP, which allows us to trap intermediate states, to study the transcription initiation process. Bacterial RNA polymerase is directed to specific promoter DNA via sigma factors. Sigma54, responsible for transcribing stress-related genes, recruits RNAP to its promoter site and forms a transcriptionally incompetent closed complex and requires ATP-dependent activators to actively remodel the protein-DNA complex in order for transcription to proceed. In the last few years, using cryoEM and X-ray crystallography combined with biochemical studies, we have uncovered how sigma54 inhibits RNAP and the exact roles of the activator proteins. Using this unique system, we have now started to unravel the detailed molecular mechanism of transcription initiation process.