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Structure watch

ELONGATION STOPPED IN ITS TRACKS

Transcriptional elongation involves the rapid extension of RNA chains by DNA-dependent RNA polymerases, but structural information on the mechanistic basis of this process has been lacking. Vassylyev *et al*. determined the first high-resolution structure of a bacterial transcription elongation complex (EC) that comprises the RNA polymerase core enzyme bound to a nucleic-acid scaffold that contains 14 base pairs (bp) of downstream DNA, a 9-bp RNA–DNA hybrid and seven nucleotides of the displaced RNA transcript. The most notable rearrangement of the core enzyme in the EC is the closure of the pincers of the crab-claw-like structure of RNA polymerase, which substantially reduces the size of the main channel that accommodates the downstream DNA and the RNA–DNA hybrid. The channel closure might increase the surface complementarity between the polymerase and nucleic-acid chains, favouring high stability and processivity of the EC.

Each elongation cycle involves the separation of 1 bp of the downstream DNA, accompanied by the displacement of one nucleotide of the nascent RNA from the DNA template at the upstream edge of the RNA–DNA hybrid. The structure reveals that DNA-strand separation occurs one position downstream of the active site, which implies that only one substrate at a time can bind to the EC. The upstream edge of the 9-bp RNA–DNA hybrid interacts with the so-called lid loop, which is thought to sterically block further growth of the hybrid while stabilizing the upstream hybrid base pair. The first displaced RNA from the DNA template is trapped in a hydrophobic protein pocket, providing a clue to the possible mechanism of RNA separation.

In a separate paper, Vassylyev *et al*. also elucidated the structural basis for substrate loading in bacterial multisubunit RNA polymerases. Their findings suggest a universal substrate-loading mechanism for all RNA polymerases; they reported a two-step mechanism for substrate loading that is conceptually similar to that used for loading of a substrate into the active site of single-subunit RNA polymerases (such as in phage T7). First, the substrate binds to an open, inactive ('preinsertion') configuration. This is followed by the substrate-induced refolding of the so-called trigger loop into two trigger α-helices, which stabilizes the closed, catalytically active ('insertion') intermediate. The authors also demonstrated that antibiotics may be used to stabilize the preinsertion state, which has important implications for future drug design.

The highly processive elongation process can pause and finally terminates. Modelling studies showed that a pause hairpin could form within the RNA exit channel without major alterations to the enzyme structure, whereas the termination hairpin destabilized the EC, presumably abrogating the transcription process. Given that the core enzymes that carry out elongation in eukaryotes are highly homologous to bacterial ECs, the overall findings are also expected to be of great interest to the eukaryotic transcription community.

ORIGINAL RESEARCH PAPERS Vassylyev, D. G. *et al*. Structural basis for transcription elongation by bacterial RNA polymerase. *Nature* **448**, 157–162 (2007) | Vassylyev, D. G. *et al*. Structural basis for substrate loading in bacterial RNA polymerase. *Nature* **448**, 163–168 (2007)

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