

Structural and functional analyses of RNA polymerase I and III transcription complexes

C.W. Müller

EMBL Heidelberg, Structural and Computational Biology Unit, Meyerhofstrasse 1, DE - 69117
HEIDELBERG, Germany, christoph.mueller@embl.de

RNA polymerases (Pol) I and Pol III mainly synthesize the non-coding RNA components required for ribosome assembly and protein synthesis in eukaryotes. Pol I synthesizes precursor ribosomal RNA, whereas Pol III produces small RNAs such as tRNA, 5S RNA and U6 snRNA. Pol I and Pol III transcription is carefully regulated in healthy cells, while misregulation of the Pol I and Pol III transcription machinery is observed in a variety of cancers. In the last years, we determined the crystal structure of the 14-subunit Pol I at 3.0 Å resolution, the cryo-EM structure of elongating Pol I at 3.8 Å resolution as well as cryo-EM structures of the 17-subunit elongating Pol III at 3.9 Å resolution and of apo Pol III in two different conformations at 4.6 and 4.7 Å resolution. The molecular structures of Pol I and Pol III in their bound and unbound states reveal the dynamics of both transcription machineries as well as their specific adaptations allowing them to fulfill their distinct transcription tasks. The Pol I and Pol III structures now also serve as starting points for assembling the Pol I and Pol III pre-initiation complexes (PIC). In yeast, the minimal PIC includes Pol I, the transcription factor Rrn3 and Core Factor (CF) composed of subunits Rrn6, Rrn7 and Rrn11. Our recently solved cryo-EM structure of a minimal 18-subunit yeast Pol I PIC bound to DNA transcription scaffold at 4.4 Å resolution reveals an unexpected arrangement of the DNA and CF subunits relative to Pol I. The Pol I PIC will be compared with the cryo-EM reconstruction of a Pol III PIC that comprises the heterotrimeric transcription factor TFIIB and an open DNA complex.