

P047 Topo-II α controls the kinetics of reactivated rRNA gene transcription

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Various human Pol-I complexes with distinct compositions and functions have been identified, including initiation-competent Pol-I and the more abundant Pol-I. Initiation of rRNA gene transcription requires the recruitment of Pol-I by promoter-bound SL1, through the interaction of SL1 with Pol-I-associated RRN3. Little is known of the roles of other Pol-I-associated factors.

Topoisomerase-II has been identified by mass spectrometry in purified Pol-I but not Pol-I complexes. The association of Topoll with Pol-I is stoichiometric and has been substantiated by co-immunoprecipitation. ChIP demonstrated Topoll at the rDNA in cells, and this association is dependent upon promoter-bound SL1. Inhibitors of Topoll activity affect rRNA gene expression in cells. There is a transient effect of Topoll-inhibitors on rDNA transcription, which is likely to be the consequence of activation ATM-dependent DNA damage response pathways, as reported recently. Intriguingly, in addition to this transient effect, we have observed an ATM-independent effect of Topoll-inhibitors on the kinetics of reactivation of Pol-I transcription in cells first starved (Pol-I transcription downregulated), then refed (Pol-I transcription reactivated). We propose a requirement for Topoll activity in cells at 'de novo' productive preinitiation complex formation in this reactivation of Pol-I transcription.