DNA topoisomerases: Vital multitasking enzymes

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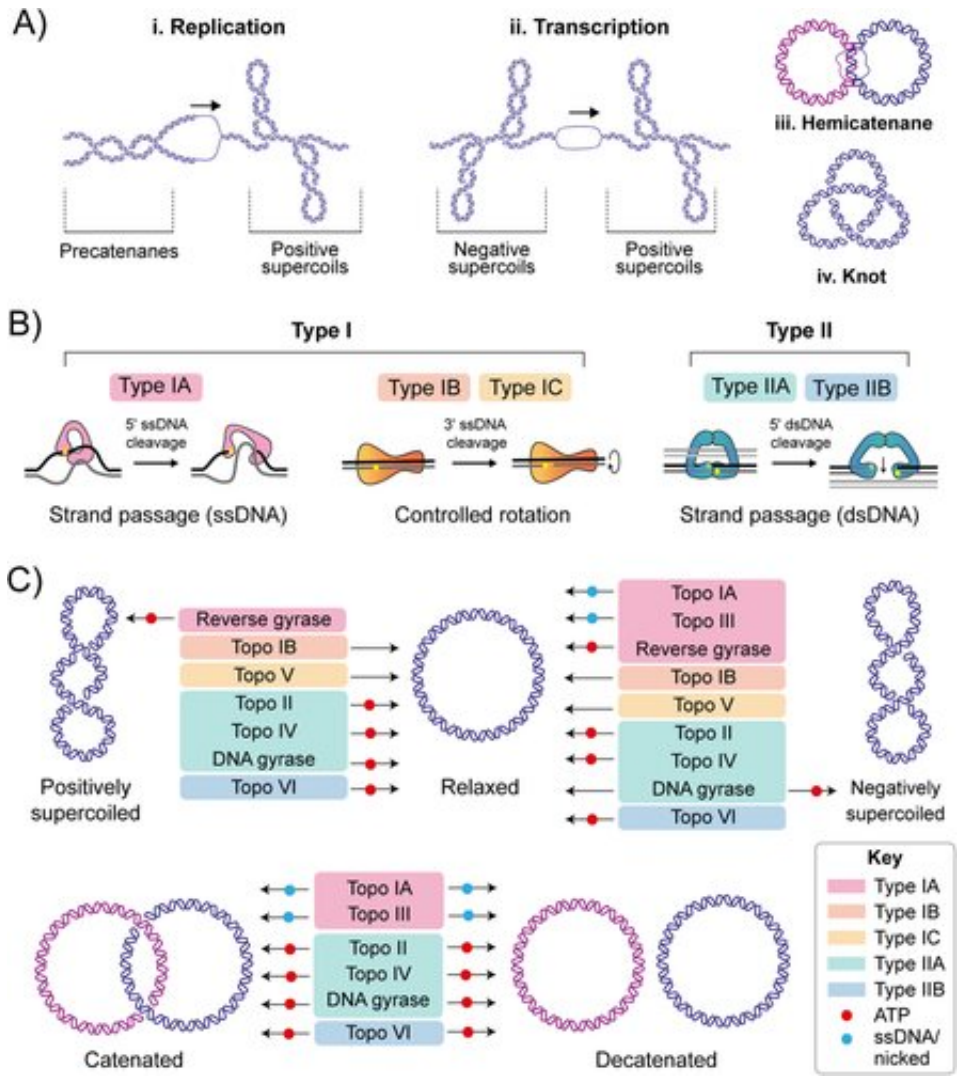

DNA topology and DNA topoisomerase mechanisms. (A) Topological consequences of DNA metabolism. i) During DNA replication, strand separation leads to positive supercoiling ahead of the advancing protein machinery, and precatenane formation behind. Precatenanes form as the newly-synthesised

duplexes wrap around one and other, and, if not removed prior to complete of replication, catenated DNA molecules are formed. ii) During transcription, strand separation leads to positive supercoiling ahead of the advancing protein machinery, and negative supercoil formation behind. iii) Hemicatenanes are a possible end result of replication, in which the parental strands of the replicated duplexes remain base-paired. iv: DNA knotting can also occur as a result of DNA replication in which a DNA molecule is intramolecularly linked. (B) Summary of topo categories and mechanism. The topos are categorised based on whether they catalyse single- (type I) or double-stranded (type II) DNA breaks. The type I topos are further subdivided to type IA, IB and IC. Type IA form a transient covalent bond to the 5′ DNA phosphate and function via a strand passage mechanism. Type IB and IC form a transient covalent bond to the 3′ DNA phosphate and function via a controlled-rotation mechanism. Type II topos are further subdivided into type IIA and IIB. Both form a transient covalent bond to the 5′ DNA phosphate of both strands of the duplex and function via a strand-passage mechanism. (C) Summary of the topological manipulations performed by DNA topoisomerases, namely relaxation of positive and negative supercoils and decatenation. Type IA topos are colour-coded pink, type IB are orange, type IC are yellow, type IIA are green, and type IIB are blue. Requirement of ATP or ssDNA for activity is denoted using a red or blue circle, respectively

Important advances in the understanding of DNA topoisomerases are discussed in a new review led by John Innes Centre researchers.

DNA topoisomerases are vital enzymes with important roles in numerous processes such as transcription, replication, chromosome segregation and DNA repair.

In the article, which appears in *BioEssays*, researchers review recent findings from structural as well as single-molecule studies that help to advance the understanding of these versatile enzymes in living organisms and as drug targets.

The team investigated some recently identified topoisomerases and discussed the importance of topoisomerase interaction with accessory proteins.

"New findings in this area of research are advancing our understanding of DNA-related processes and the vital functions that topoisomerases fulfill, demonstrating their indispensability in virtually every aspect of DNA metabolism," said corresponding author Professor Tony Maxwell.

"Application of novel structural technologies, such as cryo-EM, has given us new insight into how these enzymes work and will contribute towards the development of new treatments for bacterial disease and cancer," he added.

"DNA topoisomerases: Advances in understanding of cellular roles and multi-protein complexes via structure-function analysis)" was written by Shannon McKie, Keir Neuman and Tony Maxwell and appears in *BioEssays*.

More information: Shannon J. McKie et al. DNA topoisomerases: Advances in understanding of cellular roles and multi-protein complexes via structure-function analysis, *BioEssays* (2021). DOI: 10.1002/bies.202000286

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