GENOME ORGANIZATION

Supercoiled roles

“supercoiling has a role in the generation of genome organization features and may also contribute actively to gene regulation”

The transcribing RNA polymerase induces torsional strain in the DNA; in front of the polymerase, DNA is overwound (referred to as positive supercoiling), and behind it DNA is underwound (referred to as negative supercoiling). However, the precise nature of the supercoiling *in vivo* and the details of how it is relieved by topoisomerases is unknown, as is the relationship between supercoiling and higher-order chromatin structure. Two recent studies describe new techniques for studying DNA supercoiling genome-wide and provide initial answers to these questions.

Kouzine *et al.* and Naughton *et al.*, both using human cell lines, developed techniques for probing supercoiling of DNA using compounds that intercalate and crosslink negatively supercoiled DNA on exposure to ultraviolet light. The crosslinked DNA is then isolated and assayed using arrays to determine its location.

Kouzine *et al.* investigated changes in supercoiling at promoters when transcription is induced. They

found that supercoiling spreads ~1.5 kb upstream of the transcriptional start site and that increased transcriptional activity correlated with negative supercoiling. Furthermore, highly expressed genes dissipate supercoiling by the recruitment of topoisomerase (Topo) II to the promoter, whereas moderately expressed genes recruit Topo I in a more diffuse way.

Naughton *et al.* focused on the effects of supercoiling on genome organization. They found that the boundaries of negatively supercoiled domains were associated with those of higher-level chromatin architecture, as determined by previous studies using Hi-C (an unbiased method for mapping chromosomal interactions), and with the chromatin organizer protein CTCF at a more local level, as also determined by previous studies. These authors also found that negatively supercoiled domains were highly transcribed and contained a high proportion of Topo I and DNase I — a mark of ‘open’ chromatin — but were depleted in Topo II.

Furthermore, such domains were cytologically decondensed. The role of transcription and topoisomerases in maintaining these domains was demonstrated using inhibitors.

The studies thus show that supercoiling has a role in the generation of genome organization features and may also actively contribute to gene regulation.

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ORIGINAL RESEARCH PAPERS Kouzine, F. *et al.* Transcription-dependent dynamic supercoiling is a short-range genomic force. *Nature Struct. Mol. Biol.* 17 Feb 2012 (doi:10.1038/nsmb.2517) | Naughton, C. *et al.* Transcription forms and remodels supercoiling domains unfolding large-scale chromatin structures *Nature Struct. Mol. Biol.* 17 Feb 2012 (doi:10.1038/nsmb.2509)