MCM molecules impede the formation of DNA loops

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How is it put into loops? Packaging and unpacking are also dynamic processes that must run quickly and smoothly.

Now Kikuë Tachibana, new director of the department "Totipotency" at the Max Planck Institute of Biochemistry, and her team discovered that a protein complex well known for its function in DNA replication has an unexpected role in genome folding. "During a symposium at our institute, it emerged that my new colleague Karl Duderstadt and I shared a common interest. We decided to join forces to use complementary approaches to investigate these initial observations at a mechanistic level." Karl Duderstadt is head of the research group "Structure and Dynamics of Molecular Machines."

New class of barriers

In this current study, they have now jointly identified the minichromosome maintenance (MCM) complex as a new class of barriers in the formation of DNA loops. In the process of DNA loop formation, also called loop extrusion, three proteins or protein complexes are mainly involved: first cohesin, second the zinc finger protein CTCF, and third the MCM complex. Cohesin binds to DNA and initiates the formation of a loop. Cohesin coils the DNA and this results in the progressive growth of a loop.

Loop extrusion stops when cohesin encounters the DNA-bound protein CTCF, which was the only known loop extrusion barrier prior to this work. "Although the details differ, one can imagine that it is a little like placing a ring on a ribbon and threading the ribbon through the ring, which remains at the base of the loop," says Matthias Scherr, co-first author of the study. Kikuë Tachibana explains: "Unlike CTCF, which is a vertebrate-specific barrier, MCMs are conserved across eukaryotes and archaea. It is therefore fascinating to consider that this might be an ancestral barrier to loop extrusion." The work raises
the possibility that the encounters of loop extruding cohesin complexes with MCM complexes are part of a fundamental mechanism that organizes the genome folding of a wide variety of organisms.

Karl Duderstadt summarizes, "Our discovery was only possible through the formation of an amazing international team with expertise in a broad range of areas. This work is a testament to what is possible when you build bridges between fields. I am convinced many more surprises are in store for us as we explore deeper into the network of interactions that control chromosome organization."

The study is published in Nature.


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