Biophysics : When chromosomes stretch

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Biophysicists at the Institut Curie/CNRS (France), in collaboration with CNRS and University Pierre et Marie Curie physicists and biologists, have just demonstrated the remarkable elasticity of chromatin, the DNA-protein complex that makes up the chromosomes.

Observed by nanomanipulation of individual DNA molecules, this resilience facilitates the work of the enzymes that “read” the genetic material and of those that repair it if damaged. When alterations – mutations – remain in the DNA, there is a risk that defective, even tumor cells may arise. The elasticity of chromatin is therefore of crucial importance in the life of the cell.

The genetic material has clearly not yet divulged all its secrets. Hitherto, only its chemical composition and spatial organization were taken into account. The role of the physical properties of DNA, such as its mechanical response to torsion, is now beginning to be understood. These discoveries were published in the May 2006 issue of *Nature Structural & Molecular Biology*.

Each of our cells contains all the information needed for correct functioning of the body. This information, which directs the synthesis of all proteins, is written in the DNA in the form of a genetic code, a “book” of huge complexity containing some three thousand million letters. The spatial organization of this genetic code in the nucleus is not random: in addition to the information contained in the genetic code, there is also information implicit in the three-dimensional arrangement of the genetic material. So, the reading and expression of DNA depend on both the genetic code and how it is organized spatially. Any error in this ultrasophisticated arrangement can lead to disorganization of the genome, changes in gene expression, and cellular dysfunction.

Chromatin limbers up

The highly ordered organization of DNA (see box) is based first and foremost on histones. The DNA double helix wraps around these "condensing" proteins to form a bead necklace – chromatin. By varying the condensation, it is possible to modulate how accessible DNA is to proteins, thereby influencing its transcription, repair and so forth. In particular, chromatin organization is involved in the regulation of gene expression.

At the Institut Curie, the CNRS team of Jean-Louis Viovy, MMBM began to be interested in chromatin condensation during a collaboration with the group of Geneviève Almouzni, a specialist in the field. The MMBM group is now investigating in depth the mechanics of chromatin dynamics in collaboration with the biologists of Ariel Prunell’s team at the Institut Jacques Monod, Jean-Marc Victor’s group of theoreticians at the University Paris VI, and Vincent Croquette’s team at the Ecole Normale Supérieure in Paris.

By using “molecular adhesive tape”, a bead a few microns across is attached to one end of the DNA. This bead can be observed under the microscope, and so the position of the end of the DNA can be deduced. The other end of the DNA is attached to the wall of a recipient. Using magnets, a force is applied to the bead, thereby stretching the DNA molecule.

Using these “magnetic tweezers”, it is possible to hold the ends of an individual DNA fiber and apply torsion and forces comparable to those exerted by biological molecules. This experiment demonstrated that the chromatin fiber is extremely flexible in torsion and can be twisted clockwise and anticlockwise without changing its length. This plasticity, which is five times greater than that of naked DNA, can be explained by a theoretical model in which there is a state of equilibrium between three different configurations of the nucleosomes.

This great flexibility of the DNA bead necklace is vital for the cell's functions. In particular, it enables the chromatin fiber to withstand the twisting forces exerted by the enzymes in charge of DNA transcription, without being damaged, and without the need for other proteins. Because of its flexibility, the chromatin fiber transmits the resulting structural changes as "information" on how these enzymes work.

In conclusion, the flexibility of the chromatin fiber facilitates and accelerates DNA's reaction to changes in its environment. This flexibility plays a vital role in the regulation of gene expression and in cellular functions. Only biophysical approaches on the scale of a single DNA molecule can yield such observations, which are indispensable to a better and multifaceted understanding of DNA, its interactions and cell function.

Source: Institut Curie

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