

DNA conformational dynamics and DNA molecular Motors: New nanomedicine research targets

La dinámica de la conformación de ADN y motores moleculares de ADN: Nuevos objetivos en la investigación de la nanomedicina

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DNA supercoiling is a feature of almost all DNA molecules inside the cell. It is a powerful thermodynamic force that drives and directs many DNA associated processes *in vivo*. The level of supercoiling or DNA spatial conformation is constantly changing by the activities of proteins and the environmental conditions of the cell. Several proteins, such as DNA topoisomerases, are responsible for maintaining the steady state of supercoiling essential for the cell viability. Local and temporal changes in DNA supercoiling affect many cellular processes such as replication, transcription recombination and chromosome organization.

In prokaryotes, DNA supercoiling is expected to play an important role in site-specific recombination, a fundamental process to achieve resolution of dimeric chromosomes, allowing plasmids and chromosome segregation and consequently cell division.

During this process, DNA undergoes to multiple conformational changes due by the activity of Xer tyrosine recombinases and accessory proteins like FtsK translocase, that so far have not been characterized.

Here we use a combination of biochemical and biophysical techniques to study the biological role of DNA topology. We characterize at the single molecule level the nature of the forces that drive relevant DNA conformational changes perse or after protein interaction.

Using high-resolution AFM in physiological buffer we characterize the structure of individual chromosomes and plasmid molecules.

Additionally the dynamics of DNA and the conformational changes of DNA are imaged by High-Speed AFM at time resolutions up to 20 ms and sub-nm spatial resolution, allowing label-free studies of single- molecule processes in physiological conditions that can not be visualized by any other technique.

We are developing nanostructures that selectively recognize prokaryotic/ eukaryotic cells and directly deliver drugs to block particular proteins such anti-topoisomerase drugs (eg ciprofloxacin, etoposide). A nanoscale approach could offer further advantages over traditional antibiotics, as nanostructures could be programmed to act more precisely.