Gene-bender proteins may sway to DNA

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Among the many genes packed into each cell of our body, those that get turned on, or expressed, are the ones that make us who we are. Certain proteins do the job of regulating gene expression by clasping onto key spots of DNA -- the nucleic acid that contains the genetic instructions.

How does the protein recognize a particular binding site" Structural changes in both the protein and DNA, sometimes with the DNA within the complex kinked or sharply bent, allow for the specific contacts needed for a tight DNA-protein fit.

Scientists think DNA is largely passive in this genetic tango. But new findings by Anjum Ansari, associate professor of biophysics at the University of Illinois at Chicago, suggest DNA may not be the wallflower that many had assumed.

To follow in real time the structural changes that accompany protein-DNA binding, Ansari and her UIC colleagues used a test protein from bacteria and applied a laser pulse lasting about 10 billionths of a second to heat up and disturb the protein-DNA complex. They watched the dynamics of the bound DNA in response to this perturbation.

Ansari's group was the first to apply the laser temperature-jump technique to study the dynamics of a protein-DNA complex.

The studies were done in collaboration with Donald Crothers, Sterling Professor Emeritus of chemistry at Yale University, who examined the protein-DNA interaction with the more traditional stopped-flow technique.

"While stopped-flow technique can capture dynamics of biomolecules occurring on millisecond time-scales or longer, the goal of this study was to extend the time-resolution down to sub-microseconds. It gave us a new time window on probing protein-DNA interactions," Ansari said.

That broader time window, obtained in combination with the stopped-flow measurements, provided the first direct observation of DNA bending when bound to a DNA-bending protein.

"We found that the time-scales on which DNA was bending were very similar to previously reported time-scales on which individual base-pairs that hold the two DNA strands together were transiently breaking. That led us to conclude that the DNA is able to bend or kink on its own, at weak points created by the transient opening of base-pairs, and that the protein recognizes and binds tightly to the bent DNA conformation."

Conclusions by Ansari and her colleagues deviate slightly from the conventional dogma that it is the protein that bends the DNA. She said the results raise important questions about the role that the DNA "bendability" plays in guiding the correct bending protein to the appropriate site on the DNA.

Ansari said the research adds to the basic understanding of how proteins recognize a specific binding site.

"Gaining better insights into protein-DNA interactions that control all aspects of gene regulation may prove useful for rational design of drugs to target specific sites on the DNA, whereby one can ultimately develop better gene-based therapies," she said.

Source: University of Illinois at Chicago