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DNA Shape Directs Proteins

Sensing the shape of DNA's minor grove, not simply following DNA's sequence, helps DNA-binding proteins find their proper place

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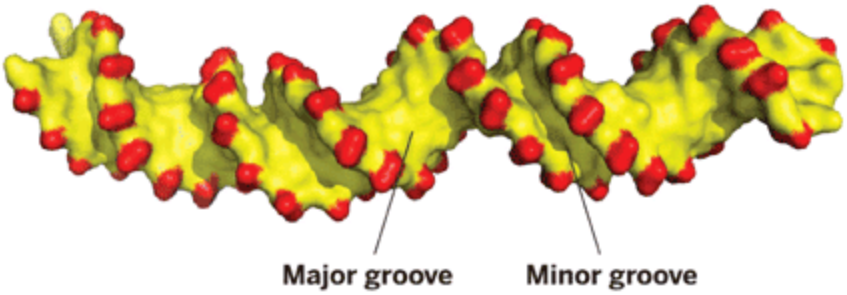

Nature

Negatively charged phosphate groups (red) line the edges of DNA's major and minor grooves.

The shape of DNA, not simply its sequence, helps DNA-binding proteins find their proper place. That's the conclusion a Columbia University team reached after sifting through high-resolution structures of more than 1,000 protein-DNA complexes (*Nature* **2009,** *461,* 1248). Barry Honig, Richard S. Mann, and coworkers found that many such proteins dip a positively charged arginine "finger" into DNA's minor groove to detect local variations in DNA shape and electrostatic potential. Short tracts of as few as three adenine or thymine nucleotides are sufficient to narrow the minor groove and thus boost the local electrostatic potential, they note. Unlike DNA's major groove, the minor groove offers proteins few, if any, opportunities to make sequence-specific hydrogen bonds with DNA bases. That has left the minor groove largely in the shadows when scientists consider how proteins recognize specific DNA binding sites. But sensing the shape of the minor groove by way of its electrostatic potential "might help a protein find its binding site in the midst of all the other DNA sequences in a genome, without directly sampling every possible major-groove hydrogen bond," comments Tom Tullius, who studies DNA recognition at Boston University.

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