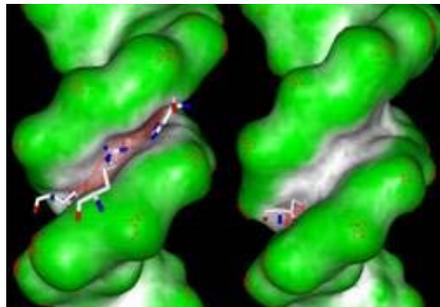


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DNA Gets Its Groove On

The simple act of living requires that each of our 25,000 genes is turned on at the right time and in the right place.

The genetic code is thought to control the activation of genes, but a new paper from Columbia scientists has found that the shape of the DNA helix may be just as important. The finding should improve the understanding of how disease-causing genes are turned on, as well as lead to new therapies that turn them off.



The width of DNA's grooves helps control the activation of genes. The finding will help scientists find how disease-causing genes are turned on and how to turn them off.

The process of turning on a gene is an enormous physical challenge. A DNA-binding protein must scan through 3 billion base pairs of DNA to find a precise spot, approximately six bases long, where it attaches and turns on the gene. For decades the linear sequence of bases (i.e. AATCGCTATGC) were thought to tell the protein where to attach.

In a paper published in the Oct 29. issue of *Nature*, Richard Mann, Barry Honig, Remo Rohs, Sean West, and Peng Liu, all in the Department of Biochemistry & Molecular Biophysics, found that DNA-binding proteins often use the width of the DNA helix's minor groove to recognize their binding sites.

The finding may explain why all computer modeling attempts to locate every binding site in the genome have failed. "When proteins read DNA, they're reading more than a string of letters, they're reading the shape of the DNA helix," Mann says. "And people haven't paid enough attention to that in the past."

The researchers say that by incorporating shape, computer models may become more accurate in the future. And with more accurate predictions, researchers will make faster progress in understanding how disease-causing genes are turned on, as well as discovering new therapies to turn them off.

For more information about the study, go to <http://www.hhmi.org/news/honig20091029.html>.
Barry Honig is an investigator with Howard Hughes Medical Institute and director of the Center for Computational Biology and Bioinformatics.

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