be regulated from within. In the case of the SIN mutation, condensation of the chromatin fiber is drastically reduced; in the case of H2A.Z, the condensed fiber is actually stabilized to some extent, however, interfiber interactions are inhibited, presumably affecting the stability of higher-order structures. Thus activities that use DNA as a substrate can be influenced in biologically significant ways by altering the equilibria at multiple levels above the wrapping of DNA about the nucleosome.

The work of Horn *et al.*[5] and Fan *et al.*[6] raises a number of interesting questions. First, it remains to be demonstrated that H2A.Z is present exclusively in long contiguous stretches of nucleosomes. Thus, what is the minimum H2A.Z content required to observe a drastic reduction in interfiber interactions? What is the effect of either SIN mutants or H2A.Z in arrays containing linker histones? Do all SIN mutants result in a drastic reduction in the stability of the condensed chromatin fiber or are there multiple ways in which these mutants can affect chromatin? Analysis of other histone mutants is an obvious target. In addition, the fact that a single amino acid substitution in the H4 SIN mutation causes such a drastic effect on structure suggests that small numbers of specific post-translational modifications may also have similar effects.

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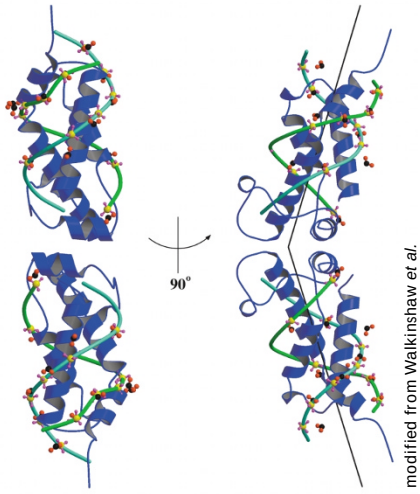
A DNA look-alike

There are many examples of mimicry in the natural world — insects that resemble a twig or leaf, butterfly wings that look like the face of an owl or a cobra poised to strike, harmless snakes that resemble their poisonous cousins — all are directed toward a common goal; distract the predator so as to increase the chances for survival of the individual and ultimately the species. What is becoming increasingly evident in the world of structural biology is the degree to which the concept of mimicry exists on a molecular level. In a recent issue of *Molecular Cell*, Walkinshaw *et al.* (*Molecular Cell*, **9**, 187–194; 2002.) present a striking example of molecular mimicry in the bacteriophage T7.

Bacteriophage propagate through infection of a host bacterial colony. They inject their DNA into the host bacterium and rely on the replication machinery of the host for phage replication. Ultimately, lysis of the host bacterium releases copies of the phage for further infection of the bacterial population. In turn, bacteria have several mechanisms of defense against phage attack, one of which is the possession of restriction enzymes that are designed to recognize and bind to certain sequences in foreign DNA, provoking cleavage and ultimately destroying the foreign DNA.

In order to avoid destruction by restriction enzymes, phage employ molecular mimicry in the form of antirestriction proteins. The X-ray crystal structure determined by Walkinshaw *et al.* of the ocr (overcome classical restriction) protein encoded by gene 0.3 of bacteriophage T7 reveals a structure (blue ribbon) that very closely resembles ~24 base pairs of B-form DNA (left, shown with overlay of DNA phosphate backbone, green coil with phosphate groups in yellow and purple), even down to the arrangement of negative charges from the side chain carboxyl groups (shown in red and black) of several aspartate and glutamate residues along the mimicked phosphate backbone. The protein forms a dimer, with the individual subunits arranged to resemble bent DNA (right). This bend is almost identical to the bend in DNA that is observed when the type I restriction enzyme *Eco*KI binds to its target sequence. This suggests a mechanism whereby the ocr dimer is able to bind any of several type I restriction enzymes — regardless of their target DNA sequence



modified from Walkinshaw *et al.*

— preventing these enzymes from exerting their destructive effects on phage DNA.

This structure presents a nice example of molecular mimicry and adds insight into the mechanism of action of type I restriction enzymes. For all their differences, it is possible to achieve structural similarity between proteins and DNA, well enough in fact to fool some of the restriction enzymes some of the time.

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