Structure watch

TERNARY ARGONAUTE COMPLEX

After determining the crystal structure of eubacterial *Thermus thermophilus* Argonaute (Ago) protein bound to guide DNA (which has higher affinity than guide RNA), the groups of Thomas Tuschl and Dinshaw J. Patel crystallized the ternary complex, which also contains target RNA. Both ends of the guide DNA remain anchored in their respective binding pockets in Ago as they do in the binary complex, and the seed region of the guide DNA adopts an A-form helix Watson–Crick paired duplex with the target RNA. An Arg residue, which is inserted between guide-strand nucleotides 10 and 11 in the binary complex and locks it into an inactive conformation, is released following ternary complex formation. The nucleic-acid-binding channel between the PAZ- and PIWI-domain-containing lobes of the Ago widens in the ternary complex, facilitating the insertion and pairing of the target RNA.
By assessing the effects of single mismatches, insertions, deletions and 2′-*O*-methyl modifications on cleavage activity of the ternary complex, the researchers found that a surprising number of single-site mutations in the target RNA, but not the guide DNA, can be accommodated without interference with cleavage activity, provided that sufficient base pairing is retained around the cleavage site.

ORIGINAL RESEARCH PAPER Wang, Y. *et al.* Structure of an argonaute silencing complex with a seed-containing guide DNA and target RNA duplex. *Nature* **456**, 921–926 (2008)

RECOGNIZING UV DAMAGE

How various ultraviolet (UV)-induced DNA lesions are recognized by the DNA damage-binding protein 1 (DDB1)–DDB2 complex has been puzzling. But structural work from Scrima *et al.* provides insight into damage recognition in chromatin and recruitment of the nucleotide excision repair (NER) machinery. The crystal structure of the DDB1–DDB2 complex bound to DNA containing either a 6–4 pyrimidine–pyrimidone photodimer (6–4PP) or an abasic lesion reveals that the DNA is unwound and bent, and that two nucleotides of the photolesion are flipped out of the double helix.
The WD40 β-propeller domain of DDB2 binds the damage-containing DNA duplex by a three-residue hairpin that inserts into the minor groove. Recognition by DDB2 is DNA-sequence independent and is probably based on distortion of the double helix, and the same mechanism seems to apply to both types of DNA lesion. The ~40° angle of the kinked DNA resembles the nucleosomal DNA curvature, which suggests that DDB1–DDB2 might recognize DNA lesions in chromatin. On the basis of modelling studies, the authors suggest that the DDB1-associated CUL4 ubiquitin ligase targets DNA-bound substrates that surround the lesion, including histones, for ubiquitylation, thereby destabilizing the local nucleosome structure and enabling the recruitment of the NER machinery.

ORIGINAL RESEARCH PAPER Scrima, A. *et al.* Structural basis of UV DNA-damage recognition by the DDB1–DDB2 complex. *Cell* **135**, 1213–1223 (2008)