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Structure watch

SIMILAR RING, DIFFERENT ACTIVITIES

The eukaryotic RNA exosome is a 9–11-subunit 3′→5′ exoribonuclease complex that catalyses cellular RNA degradation. Liu *et al.* determined the structure of the reconstituted 9-subunit 286-kDa human exosome at 3.35-Å resolution. The human exosome complex forms a six-membered ring structure, which consists of six different proteins (Rrp41, Rrp45, Rrp46, Rrp43, Mtr3 and Rrp42). The remaining three proteins (Rrp4, Csl4 and Rrp40) form a cap structure that is thought to stabilize the exosome complex. Even though the structure is conserved among bacterial, archaeal and human exosomes, the enzymatic properties vary. Whereas the archaeal exosome has three active sites, the human exosome contains just one, which contains processive phosphorolytic activity provided by the Rrp41–Rrp45 dimer. The processive hydrolytic activity of the ten-subunit yeast exosome is contributed by the yeast-specific subunit Rrp44 (also known as Dis3). The human and yeast nuclear exosomes include a 10th and 11th subunit, respectively, known as Rrp6, which has distributive hydrolytic activity. As the individual catalytic subunits are also active by themselves, the authors suggest that other exosome components might provide regulatory functions.

REFERENCE Liu, Q. *et al.* Reconstitution, activities, and structure of the eukaryotic RNA exosome. *Cell* **127**, 1223–1237 (2006)
FURTHER READING Dziembowski, A. *et al.* A single subunit, Dis3, is essentially responsible for yeast exosome core activity. *Nature Struct. Mol. Biol.* **14**, 15–22 (2007)

AN EXCLUSIVE CAGE

Histone methylation has been implicated in the recruitment of the mammalian DNA-repair protein 53BP1 and its fission yeast homologue Crb2 to DNA double-strand breaks (DSBs). Binding studies revealed that the tandem tudor domains of 53BP1 and Crb2 interacted directly and specifically with histone H4 that was dimethylated on residue Lys20 (H4K20me2). The structural determination of 53BP1 alone and in complex with H4K20me2 uncovered a five-residue binding cage in the first tudor domain of 53BP1, which, following interaction with H4K20me2, undergoes a structural reordering that stabilizes the complex. This binding pocket best accommodates a dimethyl-lysine residue, but excludes a trimethyl-lysine, thereby providing a structural basis for the binding specificity. A 53BP1 mutant that lacked the H4K20me2-binding cage failed to be recruited to sites of DNA DSBs *in vivo*. Despite the low amino-acid sequence similarity, the structure of Crb2 is related to that of 53BP1 in that it also contains a conserved dimethyl-lysine-binding cage in its first tudor domain. The authors' discovery of the methylation-state-specific recognition of histone H4K20 "uncovers an added level of complexity in the DNA DSB repair process."

REFERENCE Botuyan, M. V. *et al.* Structural basis for the methylation state-specific recognition of histone H4-K20 by 53BP1 and Crb2 in DNA repair. *Cell* **127**, 1361–1373 (2006)