Structure watch

ON THE DNA–RNA PIVOT

The RNA-induced silencing complex (RISC) mediates RNA cleavage by forming a complex with DNA and nascent RNA. The catalytic residues for RNA cleavage lie in the PIWI domain of the RISC component Argonaute (Ago). Now, Wang *et al.* define the molecular basis for RNA cleavage by solving the crystal structures of *Thermus thermophilus* Ago catalytic mutants bound to guide DNA and complementary target RNAs; this enables the cleavage site to be monitored. They show that the DNA and RNA form an A-form helix that spans up to 15 base pairs, with both ends of the DNA strand anchored to Ago. As DNA–RNA duplex formation proceeds, domains in Ago undergo pivot-like movements, and duplex zippering occurs beyond one turn of the helix and requires the release of the 3′ DNA end from the PAZ pocket of Ago. Furthermore, they show that cleavage occurs at the phosphate that bridges the 10′ and 11′ bases of the RNA, with Mg^{2+} positioned on either side, and requires three catalytic Asp residues in the PIWI domain. These high-resolution structures provide insight into RNA cleavage, with potential applications in RNA interference-based therapeutics.

ORIGINAL RESEARCH PAPER Wang, Y. *et al.* Nucleation, propagation and cleavage of target RNAs in Ago silencing complexes. *Nature* **461**, 754–761 (2009)

TRANSLATION MECHANISMS EMERGE

Two studies provide structural insight into the mechanism by which co-translational translocation of nascent polypeptides from the ribosome to specific cellular locations occurs, and how translational stalling might be induced during this process. SEC61 is part of the protein-conducting channel (PCC), which acts as a receptor for ribosomes to target them to the membrane. Becker *et al.* determined cryo-electron microscopy structures of mammalian SEC61 and its yeast homologue Ssh1 bound to ribosomes. They show that a single copy of the SEC61 or Ssh1 complex is recruited to the ribosome, and a nascent polypeptide is located in this complex. The PCC forms a central pore that might be a channel for the polypeptide. The PCC binds the ribosome at the ribosome tunnel exit and also contacts the emerging nascent polypeptide. Seidelt *et al.* used cryo-electron microscopy and single-particle reconstruction to study stalled ribosomes during translation of the *Escherichia coli* tryptophanase leader peptide TnaC. They suggest that interactions between the nascent polypeptide and the ribosome might mediate translational stalling of the polypeptides in the ribosome tunnel. Free tryptophan-induced translational stalling results in an extended nascent TnaC chain and high polypeptide density in the tunnel. Furthermore, nascent polypeptides show many distinct interactions with the tunnel wall and adopt individual conformations, implying a role in initial protein folding and protein translocation.

ORIGINAL RESEARCH PAPERS Becker, T. *et al.* Structure of monomeric yeast and mammalian Sec61 complexes interacting with the translating ribosome. *Science* 29 Oct 2009 (doi:10.1126/science.1178535) | Seidelt, B. *et al.* Structural insight into nascent polypeptide chain-mediated translational stalling. *Science* 29 Oct 2009 (doi:10.1126/science.1177662)