

## Insights into mRNA Recognition from a PIWI–siRNA Complex

Mark S. Roe, James S. Parker, David Barford, *The Institute of Cancer Research, London, UK*. E-mail: Mark.Roe@icr.ac.uk

RNA interference (RNAi) and related RNA silencing phenomena use short antisense guide RNA molecules to repress expression of target genes. Argonaute proteins, containing N-terminal PAZ domains and C-terminal PIWI domains, are core components of these mechanisms. We present the native crystal structure<sup>1</sup> of a PIWI protein from *Archaeoglobus fulgidus* (AfPiwi) and also in complex with an siRNA-like duplex<sup>2</sup>, that mimics the 5' end of a guide RNA strand bound to an overhanging target mRNA.

The structures reveal a highly conserved and stable metal-binding site that anchors the 5' nucleotide of the guide RNA. The first base pair of the duplex is unwound, separating the 5' nucleotide of the guide from the complementary nucleotide on the target strand, which exits with the 3' overhang through a short channel. The remaining base-paired nucleotides assume an A-form helix, accommodated within a channel in the PIWI domain, which can be extended to place the scissile phosphate of the target strand adjacent to the putative slicer catalytic site. This study provides insights into mechanisms of target mRNA recognition and cleavage by an Argonaute-siRNA guide complex.

[1] Parker J. S., Roe S. M., Barford D., *Embo J.*, 2004, **23**, 4727-37. [2] Parker J. S., Roe S. M., Barford D., *Nature*, 2005, *in press*.

**Keywords:** RNA-protein complexes, siRNA, protein crystallography