SPECIFICITY OF THE ARGONAUTE PROTEIN FROM *ARCHAEOGLOBUS FULGIDUS* TO THE 5‘-END OF THE GUIDE

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Argonaute proteins (Agos) are widespread in all three domains of life (bacteria, archaea and eukaryotes) [1]. In eukaryotic organisms, eAgos are the functional core of the RNA-silencing machinery, which is critical for regulation of gene expression, silencing of mobile genome elements, and defence against viruses. Prokaryotic Ago proteins (pAgo), in contrast, remain poorly understood and might hold a potential for development of novel genome editing tools, discovering new intracellular mechanisms and pathways.

In Agos, target recognition is facilitated by specific recognition of complementarity between the target and the Ago-bound strand (RNA or DNA). The 5’-end of the guide strand is anchored in the evolutionarily conserved pocked of the MID domain. eAgos and pAgos usually show a preference for a specific 5’-nucleotide of the guide strand (e.g. human Ago2 for a 5’-U, while bacterial TtAgo and CbAgo for a 5’-dC and 5‘-dA, respectively).

The Argonaute protein from an archaeaon *Archaeoglobus fulgidus* (AfAgo) has previously been well crystallographically characterized and provided initial information on the molecular mechanism of RNA interference (RNAi) in eukaryotes [2-5]. In this work we present biochemical and structural studies showing that AfAgo has specificity for a 5‘-dATT base pairs at the end of the DNA duplex, interacting with the nucleobases from both the guide and the target strands.

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