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Poster #123: ATP-dependent oligomerization triggers tRNA degradation by Schlafen-fused prokaryotic Argonaute proteins

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Organisms from all domains of life are under constant attack from selfish genetic elements including viruses, plasmids, and transposons. To defend against these invaders, a myriad of immune systems has evolved. Argonautes (Agos) are a heavily diversified family of immune proteins that are conserved from prokaryotes to eukaryotes. In general, Agos use small nucleic acid guides to recognize invader sequences, after which immunity is conferred through one of various mechanisms. Specific prokaryotic Agos (pAgos) are fused to Schlafen (Slfn) proteins, another immune protein found in all domains of life. In other systems, Schlafen proteins can cleave tRNA to restrict viral replication. However, the importance of the association of Slfn and pAgos proteins has remained unclear.

Here, we show that Slfn-pAgos form a novel major clade of pAgos that act as immune systems: Slfn-pAgo from *Runella zaea* (RzAgo) defends *E. coli* from several phages of the BASEL collection. *In vitro* biochemical experiments reveal that, upon RNA-guided DNA targeting by RzAgo, its Slfn domain is catalytically activated through ATP-dependent oligomerization, which results in tRNA cleavage. Combined, these results provide a foundational understanding of the mechanisms by which Slfn-pAgo systems provide immunity and further highlights the conservation of immune mechanisms across different domains of life.

Reference #1

Reference #2

Reference #3

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