RNAi MACHINERIES IN ANCIENT EUKARYOTES

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The “classical” RNA interference (RNAi) pathway regulates gene expression through mRNA degradation. In certain organisms, including *Trypanosoma brucei*, RNAi is initiated in response to double-stranded RNA, which is cleaved into small interfering RNAs (siRNAs) by Dicer, an RNase III-like enzyme. In a second step, siRNAs are incorporated into a ribonucleoprotein complex termed the RNA-induced silencing complex (RISC), which contains the RNAi endonuclease or “slicer”, a member of the Argonaute (Ago) protein family. The RNAi pathway is strictly regulated and the *T. brucei* Ago1 protein is central to this regulation Argonaute and Dicer are the hallmark of RNAi. Recent genome database searches have revealed that members of the *Leishmania (Viannia)* subgenus, which evolutionarily represents the oldest Leishmanias, possess the RNAi genes and are most likely endowed with a functional RNAi pathway. This finding has allowed us to determine that the loss of the RNAi pathway in *L. major* has occurred by a combination of genetic mechanisms, including genetic drift. Furthermore, our findings open the possibility of exploiting the power of RNAi to study gene function in these important parasites. Lastly, we have discovered that in trypanosomes a second member of the Ago family is localized to the mitochondrion, thus suggesting that the RNAi pathway extends its tentacles into this organelle. Since certain prokaryotes posses Ago-like proteins, it is possible that the trypanosome mitochondrial Ago-like protein is a remnant of the genome of the symbiotic bacterium which was the progenitor of mitochondria in eukaryotes.

Key words: RNA interference, Leishmania, trypanosome