RNase-L inhibitor (RLI) and RNA interference (RNAi).

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In mammals, RLI acts in the regulation of RNA turnover and stability by inhibiting RNase-L. However, the role of RLI is unknown in a great variety of *Eukaryota* and *Archaea* that do not have RNase-L. The high degree of sequence conservation observed for RLI is indicative of its ancient and probably conserved biological role. It is interesting to observe that RLI and the enzyme it inhibits, the RNase- L, have some common properties besides the association with 2-5A: both proteins possess a P-loop or Walker A in their NB domains; RLI probably also uses Mg^{2+} and ATP, both necessary for optimal RNase-L activity. RLI also has a Fe-S domain that can be involved in protein-RNA or protein-protein interactions. Curiously, RNase-L was only reported in *Tetrapods* and no typical sequence was found in other organisms. This raised a question about the role RLIs have in all other systems where they have been found. RLIs could be implicated in another system of mRNA regulation induced by dsRNA, common to all these organisms. The system that fits in this scenario is RNAi, a conserved biological response to dsRNA found in eukaryotes, and like RNase-L/RLI pathway, can mediate viral resistance and regulate the expression of cellular mRNAs. In RNAi, an enzymatic complex (RISC) cleaves targets mRNA using siRNAs as a guide. RNase-L can be guided by small antisense oligonucleotides linked to an oligo2-5A. Association of *Arabidopsis* RLIs to the RNAi pathway was demonstrated. Despite the modest increase in expression, it was consistently observed in three different transgenic plant lines from two ecotypes showing posttranscriptional silencing. It would be expected that plants producing high amounts of siRNAs should have an increase in the activities of their Dicer-like and RISC complexes. We speculate that the increase in RLI2 transcripts may reflect a cellular response to regulate this increase in RNase activity. As RNAi and miRNA production are associated processes, it would be expected that the expression of genes directly involved in the RNAi process should be tightly regulated, not allowing great variations in their concentration.

This work was supported by CNPq.