LETTER TO THE EDITOR

An important RNA tertiary interaction of group I and group II introns is implicated in Gram-positive RNase P RNAs

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An RNA tertiary interaction involving a GAAA terminal loop and an 11-nt RNA motif [CCUAAG . . . UAUGG] was identified in group I and group II introns by Costa and Michel (1995). They found that a GAAA loop has high affinity for the motif while other GNRA loops could not restore wild-type affinity or activity. We find both elements present in the RNase P RNA component of *Bacillus megaterium*, where their interaction would join L12 with P10.1a (see Fig. 1). Only *Bacillus* and related Gram-positive bacteria have a P10.1a pairing; 9 out of the 10 that have been sequenced have a GAAA loop at L12 and the conserved motif in P10.1a (James et al., 1988; Brown et al., 1994; additional sequences from James Brown, personal communication).

Bacillus brevis is the only *Bacillus* species that lacks the GAAA loop at the end of P12, having instead a GCGA loop. Significantly, it is also the only one that lacks the 11-nt motif in P10.1a. Conceivably L12 and P10.1a still interact in the *B. brevis* RNA, but now through the sort of GNRA tetraloop-minor groove of a helix interaction first proposed by Michel and Westhof (1990) and observed in atomic detail in the X-ray structure of Pley et al. (1994). Indeed, the phylogenetically preferred partner of a GYGA loop [CU...AG] (Michel and Westhof, 1990) is found in stem P10.1a of the *B. brevis* RNA.

While the presence of the GAAA tetraloop and 11-nt motif in the *Bacillus* RNAs only suggests that they might interact, there are already data that support this proposal. Chemical probing of the *Bacillus subtilis* RNA with dimethyl sulfate shows protection of the last two A's of the GAAA loop (LaGrandeur et al., 1994), and probing with Fe(II)-EDTA shows protection around the 3' side of the GAAA loop and protection of part of the

Reprint requests to: Thomas R. Cech, Department of Chemistry and Biochemistry, Howard Hughes Medical Institute, University of Colorado, Boulder, Colorado 80309-0215, USA. motif in P10.1a (Pan, 1995). The protection data closely resemble the pattern found for the GAAA and 11-nt motif of the P4–P6 domain of the *Tetrahymena* group I intron (Murphy and Cech, 1993), where biochemical experiments pointed to the interaction of these two elements (Murphy and Cech, 1994).

An interesting variation of the motif is the substitution of an $A \cdot C$ for the more frequently used $G \cdot U$ wobble pair in sequences from group I introns. Such a change is also found in one of the RNase P sequences, that of *Heliobacillus mobilis*.

Because a small number of long-range tertiary contacts can define the global architecture of a folded RNA, this new tertiary interaction, if experimentally confirmed, should be helpful in modeling the 3D structure of the *Bacillus* RNase P RNAs. In addition, now

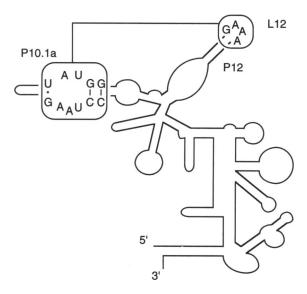


FIGURE 1. RNase P of Bacillus megaterium.

that it has been found in all three classes of large catalytic RNAs, the motif identified by Costa and Michel (1995) seems likely to be even more widespread.

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