

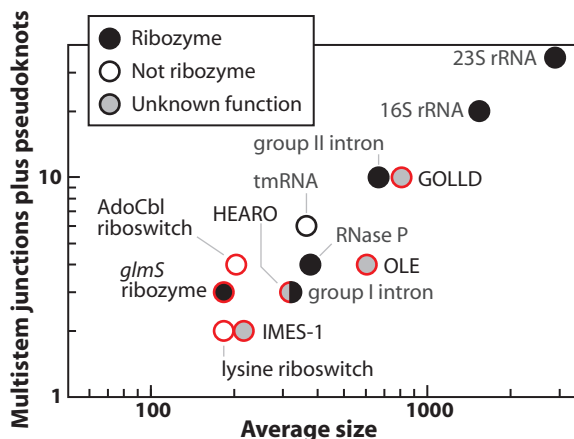
# Breaker Laboratory

## Molecule of the Year

### 2009

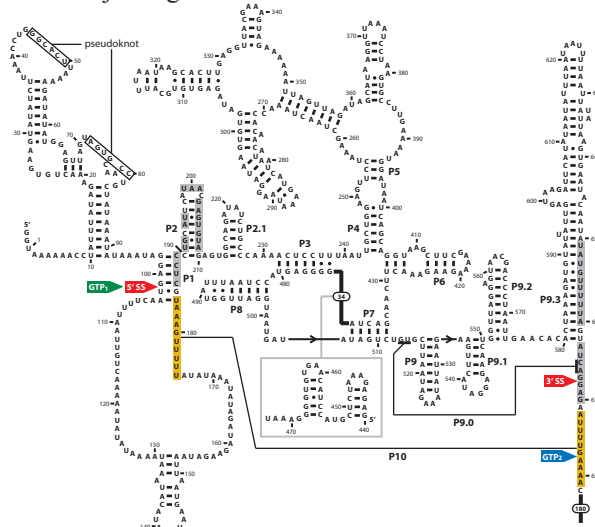
### Huge Structured ncRNAs

**Fig. 1.** Plot of the size and structural complexity of 13 largest structured RNAs present in diverse species of bacteria. RNAs depicted with red circles designate seven that have been identified or functionally validated by the Breaker laboratory.



### Allosteric Self-splicing Ribozyme

**Fig. 2.** Sequence and secondary structure of a natural allosteric ribozyme. Both c-di-GMP and GTP are necessary for ribozyme-mediated joining of 5' and 3' exons.



In recognition of the discovery of noncoding RNAs of exceptional size and structural complexity<sup>1</sup>, and in recognition of the discovery and validation of the first natural allosteric ribozyme<sup>2</sup>, the status of Breaker Laboratory “Molecule of the Year” is conferred upon these findings.

Computational search strategies will continue to yield novel classes of structured RNAs as long as unique DNA sequences are made available. The emergence of “metagenomic DNA” data derived by sequencing DNA from environmentally-derived samples promises to supply many orders of magnitude of new sequences for computational screening. Among the newfound RNA classes revealed by these efforts include strikingly large structured RNAs such as GOLLD and HEARO, which rival the largest known ribozymes in size and complexity. Future searches are certain to yield additional RNAs that will continue to expand the collection of sophisticated RNAs, and some of these may reflect the functions of RNAs from the earliest forms of life. One complex RNA whose functions may represent those from the RNA World carries a c-di-GMP-II riboswitch aptamer in tandem with a group II self-splicing ribozyme. This RNA from the bacterial pathogen *Clostridium difficile* functions as an allosteric ribozyme whose splicing is regulated by second messenger binding.

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1. Z. Weinberg, J. Perreault, M. M. Meyer and R. R. Breaker (2009) Exceptional structured noncoding RNAs revealed by bacterial metagenome analysis. *Nature* 462:656-659.

2. E. R. Lee, J. Baker, N. Sudarsan and R. R. Breaker. (unpublished data).