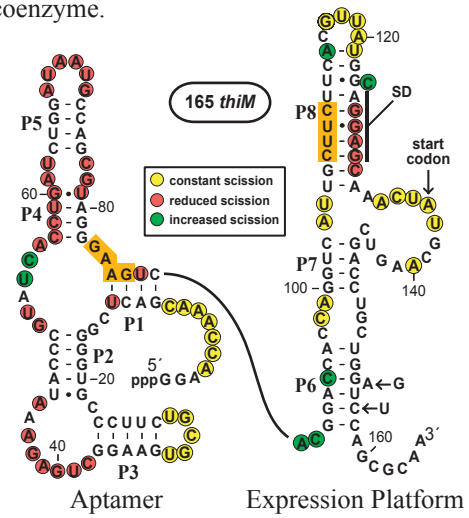
Breaker Laboratory

Molecule of the Year 2002

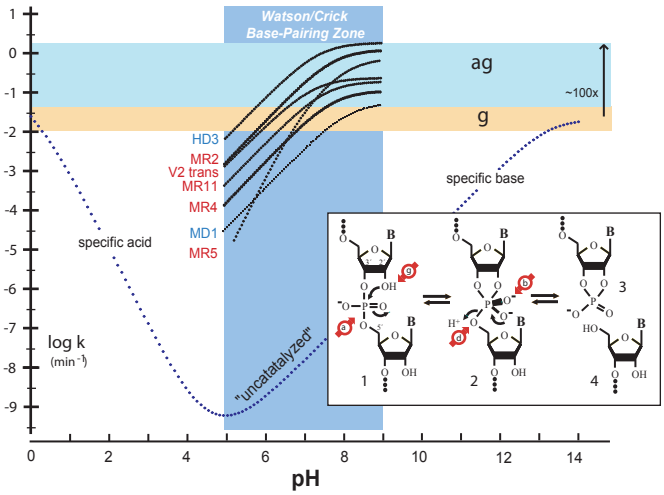
Riboswitches

Fig. 1. Sequence and secondary structure of a representative riboswitch from *E. coli* that binds thiamine pyrophosphate (TPP). Encircled bases identify positions that undergo alteration in their structure upon binding the coenzyme.



Ribozyme Speed Limits

Fig. 2. Composite plot comparing the kinetic profiles of seven RNA-cleaving ribozymes and deoxyribozymes to the pH profile for the spontaneous degradation of RNA. These enzymes maximize two of four possible catalytic strategies for internal phosphoester transfer (see inset).



In recognition of the detection of metabolite-sensing riboswitches and in recognition of the establishment of ribozyme speed limits, the status of Breaker Laboratory "Molecule of the Year" has been jointly conferred upon these two discoveries.

Metabolite sensing by biological systems is essential to maintain metabolic stasis and to respond to various biochemical processes. The discovery of mRNAs that directly bind metabolites for the purpose of genetic control provides new understanding of the mechanisms by which cells maintain a complex metabolic state. In a related display of biochemical sophistication, the observation that RNA and DNA enzymes can maximally exploit multiple catalytic strategies to achieve enormous rate enhancements proves that nucleic acid enzymes can utilize the same level of catalytic power that is typically generated by protein enzymes. Together, these findings indicate that life in the RNA World was most likely of a highly sophisticated form. Furthermore, both discoveries facilitate the pursuit of new drugs by serving as drug targets (riboswitches) or as new biochemcial tools (enzymes).

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