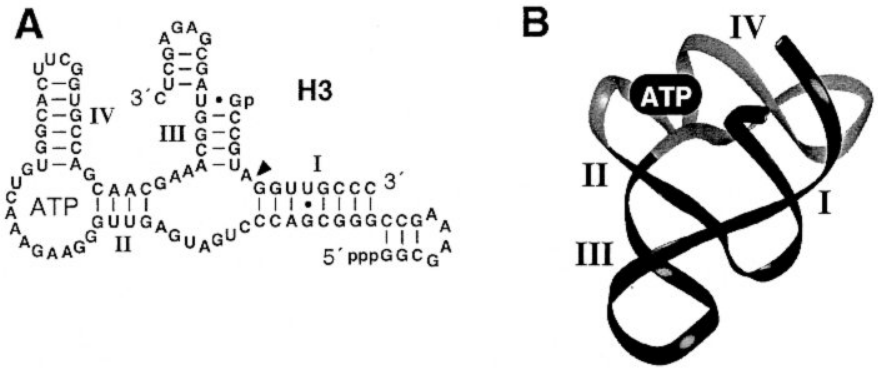
Breaker Laboratory

Molecule of the Year

1997

ATP-dependent Allosteric Ribozyme

Fig. 1. Structural features of an ATP-inactivated ribozyme.[1] (**A**) Sequence and secondary structure of H3, a conjoined ATP-aptamer/hammerhead-ribozyme. The arrowhead identifies the site of RNA cleavage. (**B**) Overlaid molecular models depicting the steric-clash mechanism for ATP-mediated ribozyme inhibition.



In recognition of the first discovery of allosteric modulation of ribozymes by small organic effectors, the status of Breaker Laboratory "Molecule of the Year" has been conferred upon the ATP-dependent ribozyme (H3) based on the hammerhead motif.

Allosteric function is a kinetic feature of protein enzymes that is critical to metabolic regulation. Ribozymes in the putative "RNA World" would have had need of similar regulatory principles to control the primitive, yet complex, metabolism that presumably emerged billions of years ago. The demonstration that RNA can exhibit true allosteric[2] modulation supports theories that advocate the ancient existence of a sophisticated metabolic state that was guided entirely by RNA. Moreover, these findings indicate that new allosteric ribozymes could be made to function inside cells and that such "molecular switches" could be used to modulate gene expression using various effector molecules.

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[1] Tang, J. and Breaker, R. R. (1997) Rational design of allosteric ribozymes. *Chem. Biol.* **4**, 453-459.
[2] The function of allosteric ribozymes are regulated by the binding of an effector molecule at location distinct from that of the active site.