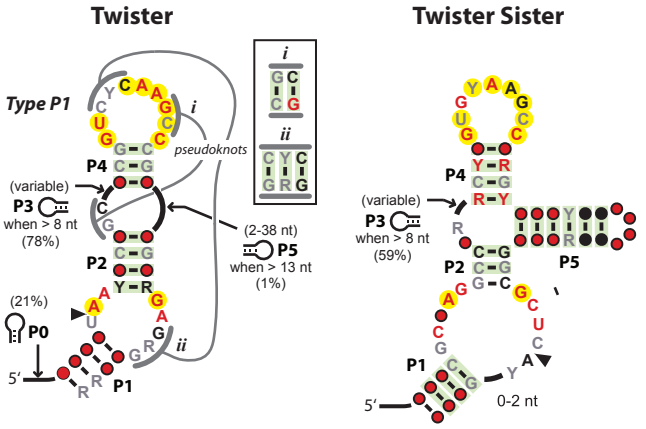
Breaker Laboratory

Molecule of the Year

2013

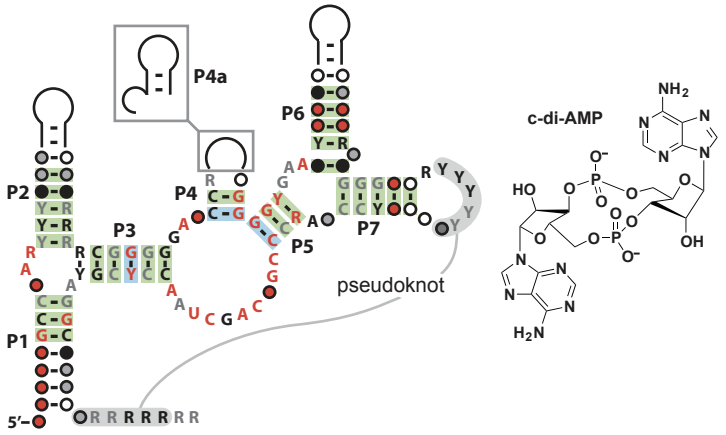
Twister Sister Ribozymes

Fig. 1. Consensus sequence and secondary-structure models of twister and twister sister ribozymes. Arrowhead marks the sites of RNA cleavage. Yellow shading indicates nucleotide similarity between the two ribozymes. Red, black, and gray nucleotides are conserved at >97%, 90% and 75%.



C-di-AMP Riboswitches

Fig. 2. (Left) Consensus sequence and secondary structure of c-di-AMP riboswitches (formerly known as *ydaO* motif RNAs). (**Right**) Chemical structure of c-di-AMP).



In recognition of the discovery[1] of twister sister ribozymes, only the 12th natural class of catalytic RNA known, and in recognition of the validation[2] *ydaO* motif RNAs as c-di-AMP riboswiches, the status of Breaker Laboratory "Molecule of the Year" is conferred upon these findings.

Twister sister ribozymes are named due to their similarity in sequence, structure and catalytic mechanism relative to that of twister ribozymes. As with several other self-cleaving ribozymes, many twister sister RNAs exist, which highlights the puzzling fact that many cells express such ribozymes but there is little or no understanding of why biology employs so many.

Orphan riboswitches are RNA regulatory elements whose ligands remain mysterious. One very common orphan riboswitch, called *ydaO*, associates with genes for cell wall metabolism and osmotic shock. Its ligand was known to be both common and present in cells under normal conditions, however it was not clear what signaling compound triggered the biological responses associated with *ydaO* motif RNAs. Through a series of biochemical purifications and analyses, c-di-AMP was discovered to function as the ligand for this riboswitch class, thus solving this long-standing genetic mystery.

Yale University Investigators: Peter Kim; Adam Roth, Ph.D.; Zasha Weinberg, Ph.D.; T. Chen; James N. Nelson; Narasimhan Sudarsan, Ph.D.; Dr. Kazuhiro Furukawa, Ph.D.; Dr. Joy X,. Wang, Ph.D.; Ronald R. Breaker, Ph.D.

1. *P. B. Kim, A. Roth, Z. Weinberg, T. Chen, R. R. Breaker. A class of self-cleaving RNAs mimics twister ribozymes)in preparation).*

2. *J. W. Nelson, N. Sudarsan, K. Furukawa, Z. Weinberg, J. X. Wang, R. R. Breaker. Riboswitches in eubacteria sense the second messenger c-di-AMP. Nat. Chem. Biol. 9:834 (2013).*