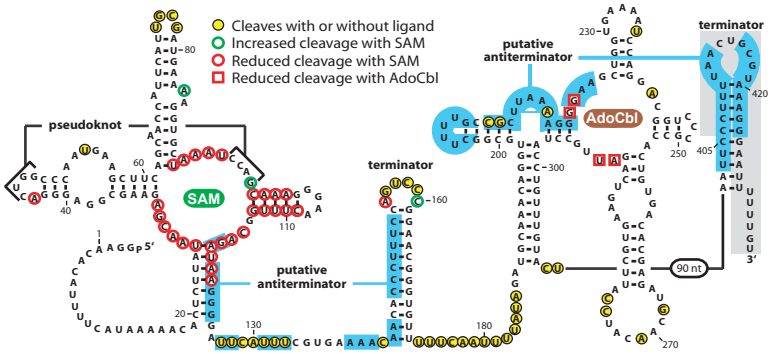
Breaker Laboratory

Molecule of the Year 2006a

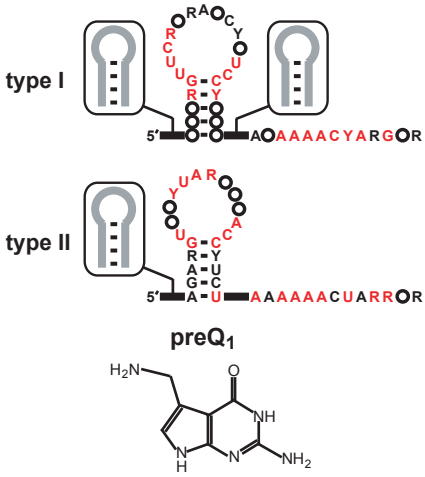
Complex Riboswitch Systems

Fig. 1. Tandom arrangement of two riboswitches representing two different metabolite-binding classes. The riboswitches function independently to terminate transcription, and together function as a two-input Boolean NOR gate. Either SAM or coenzyme B_{12} repress the expression of the *metE* gene in *Bacillus clausii*. These and other tandem riboswitch arrangements reveal how the assembly of simple riboswitches in series can yield complex gene control systems made only of RNA.



$preQ_1$ Riboswitches

Fig. 2. Consensus sequence and structural models for type I and type II forms of aptamers that selectively bind the nucleobase analog $preQ_1$. The aptamers can be formed from as few as 34 nucleotides, yet exhibit tight and selective binding to their target ligand.



In recognition of the complex functions that can be achieved by tandem riboswitch arrangements[1,2], and in recognition of the existence of strikingly small aptamers for some riboswitches[3], the status of Breaker Laboratory "Molecule of the Year" is conferred upon these systems.

Most riboswitches usually occur alone and control the expression of adjacent genes by binding a single defined metabolite. However, far more complex gene control characteristics can emerge when Riboswitches are arranged in tandem, including digital gene control characteristics and Boolean logic gate functions. In another extreme, riboswitches do not require large stretches of nucleotides to form precision metabolite sensors, indicating that relatively small and simple RNA elements can be used to achieve exceptional sensitivity, specificity and complexity in metabolite sensing and gene control.

Yale University Investigators: Dr. Narasimhan Sudarsan, Ph.D.; Dr. Ming C. Hammond, Ph.D.; Kirsten F. Block; Dr. Rudiger Welz, Ph.D.; Inbal Jona; Jeffrey E. Barrick; Dr. Adam Roth, Ph.D.; Dr. W.C. Winkler, Ph.D.; Elizabeth E. Regulski; Dr. Jinsoo Lim, Ph.D.; Ankita Ritwik; Jane N. Kim; Dr. R. R. Breaker, Ph.D.

1. Sudarsan, N., Hammond, M.C., Block, K.F., Welz, R., Barrick, J.E., Breaker, R.R. 2006. Tandem riboswitch architectures exhibit complex gene control functions. *Science* **314:**300-304. **2.** Welz, R., Breaker, R.R. 2007. Ligand binding and gene control characteristics of tandem riboswitches in *Bacillus anthracis*. **3.** Roth, A., Winkler, W.C., Regulski, E.E., Lee, B.W.K., Lim, J., Jona, I., Barrick, J.E., Ritwik, A. Breaker, R.R. 2007. A eubacterial riboswitch selective for the queosine precursor $preQ_1$ contains an unusually small aptamer domain. *RNA* (in press).