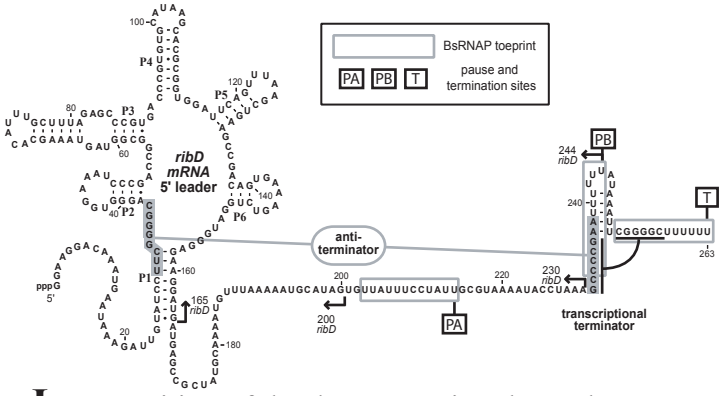
Breaker Laboratory

Molecule of the Year 2005

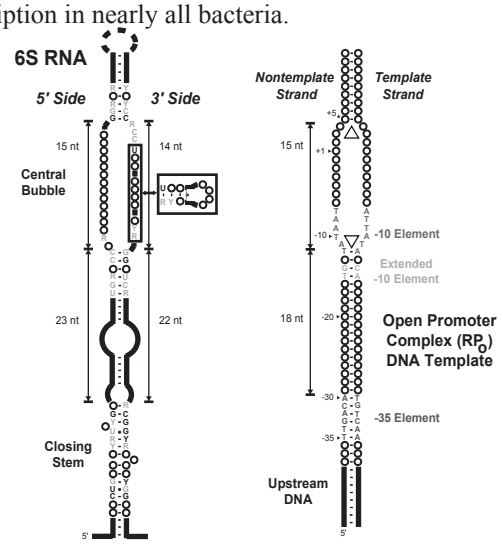
Kinetics-driven Riboswitches

Fig. 1. Configuration of an FMN riboswitch highlighting components that are important for establishing the speed of RNA polymerase as it proceeds to a terminator stem (the point of decision for gene expression). Ligand binding does not reach equilibrium before polymerase makes its genetic decision, and therefore kinetics, and not thermodynamic equilibrium constants, are most important for establishing the conentration of metabolite needed to trigger riboswitch function.



6S RNA

Fig. 2. Consensus structural model for 6S RNAs and its similarity to a DNA open-promoter complex with RNA polymerase. This near universally-conserved structure and other data suggest that 6S RNA is an important regulator of transcription in nearly all bacteria.



In recognition of the demonstration that at least some riboswitches are kinetically driven[1] and in recognition of the establishment of 6S RNA as a widespread and highly-conserved non-coding RNA in bacteria,[2] the status of Breaker Laboratory "Molecule of the Year" is conferred upon these systems.

Riboswitches usually appear to be simple metabolite sensing and genetic control elements. However, the characteristics of some riboswitches reveal that RNA can perform complex gene control tasks. A possible widespread example of this is their reliance on kinetic parameters to establish the actual concentration of metabolite needed to trigger modulation of gene expression. The importance of RNA in bacterial gene control is further demonstrated by the structure and function of 6S RNA, which was first discovered decades ago in a few closely related bacteria. Bioinformatics and biochemical studies by several laboratories recently* reveal that 6S RNAs are nearly universally distributed in bacteria. The pattern of sequence and structure conservation is consistent with a role for 6S RNA as a mimic of the open promoter structure of DNA, suggesting that the RNA is a decoy ligand for RNA polymerase.

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**See also the work of the Wassarman (U.W. Madison) and Hartmann (Philipps-Universität Marburg) laboratories.*

1. Wickiser, J.K., Winkler, W.C., Breaker, R.R., Crothers, D.M., 2005. The speed of RNA transcription and metabolite binding kinetics operate an FMN riboswitch. *Mol. Cell* **18:**49-60. **2.** Barrick, J.E., Sudarsan, N., Weinberg, Z., Ruzzo, W.L., Breaker, R.R. (2005) 6S RNA is a widespread regulator of eubacterial RNA polymerase that resembles an open propoter RNA. **11:**774-784.