

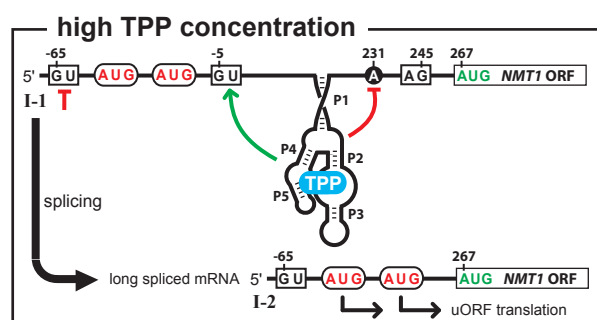
Breaker Laboratory

Molecule of the Year

2007a

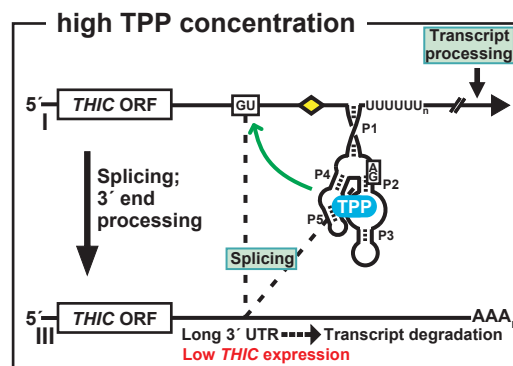
Fungal Riboswitch Splicing

Fig. 1. Proposed mechanism for riboswitch control of the expression of the *NMT-1* gene from *Neurospora crassa*. TPP binding causes activation (green line) of the second 5' splice site, and deactivation (red lines) of the first 5' splice site and the branch site. This alternative splice product yields a processed mRNA that carries two upstream open reading frames (uORFs) that prevent ribosomes from initiating at the main ORF, thus preventing expression of NMT1 protein.



Plant Riboswitch Splicing

Fig. 2. A model for *THIC* TPP riboswitch function in plants involves the control of splicing and alternative processing of the 3' terminus of the mRNA. TPP binding causes activation of splicing by modulating the structure of the 5' splice site. TPP-induced splicing removes a processing site in the 3' untranslated region (UTR) of the mRNA to yield extended mRNAs that are poorly expressed.



In recognition of the precision splicing control achieved by eukaryotic TPP riboswitches in fungi¹ and plants², the status of Breaker Laboratory “Molecule of the Year” is conferred upon these mechanisms.

The vast majority of riboswitch classes have been identified in bacteria, where they typically control gene expression by modulating transcription termination or translation initiation processes. Although representatives of the TPP riboswitch class are the only metabolite-sensing RNAs proven to exist in eukaryotes to date, they were predicted to control mRNA splicing. Indeed, a fungal TPP riboswitch controls alternative splicing and a plant TPP riboswitch* controls splicing to regulate gene expression by uORF or by mRNA stability mechanisms, respectively. These findings reveal how other eukaryotic riboswitches discovered in the future might function.

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1. Cheah, M.T., Wachter, A., Sudarsan, N., Breaker, R.R. 2007. Control of alternative RNA splicing and gene expression by eukaryotic riboswitches. *Nature* **447**:497-501. 2. Wachter, A., Tunc-Ozdemir, M., Grove, B.C., Green, P.J., Shintani, D.K., Breaker, R.R. 2007. Riboswitch control of gene expression in plants by splicing and alternative 3' end processing of mRNAs. *The Plant Cell* (in press).

*Related works: Bocobza, S., Adato, A., Mandel, T., Shapira, M., Nudler, E., Aharoni, A. 2007. Riboswitch-dependent gene regulation and its evolution in the plant kingdom. *Genes Dev.* **21**:2874-2879. Croft, M.T., Moulin, M., Webb, M.E., Smith, A.G. 2007. Thiamine biosynthesis in algae is regulated by riboswitches. *Proc. Natl. Acad. Sci. USA.* (in press).