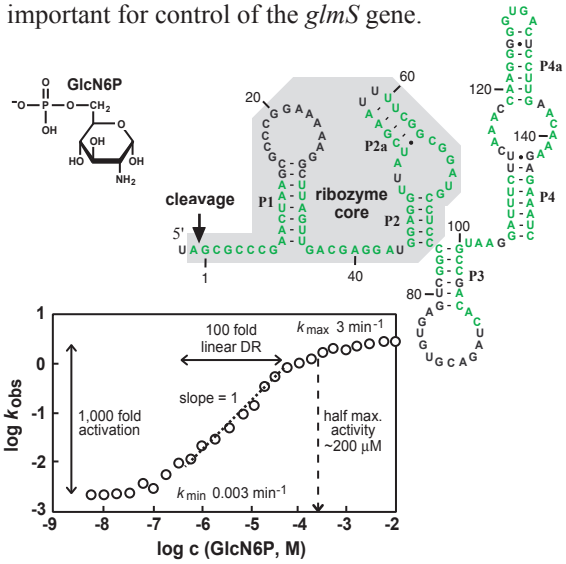
Breaker Laboratory

Molecule of the Year 2003

glmS Ribozyme Riboswitch

Fig. 1. Structure and function of the glmS ribozyme from *B. subtilis.* The ribozyme is activated by the presence of glucosamine-6-phosphate (GlcN6P), and this activation is important for control of the *glmS* gene.



BLISS

Fig. 2. The discovery of new riboswitch candidates is enabled by a bioinformatics approach called BLISS (Breaker Laboratory Intergenic Sequence Server). This web-based system permits comparison of intergenic DNA sequences to search for sequence similarities between different organisms that might be indicative of structured RNAs. Sequence alignments like the one shown below for inter-genic regions associated with the *glmS* genes of Gram-positive bacteria have proven to be novel riboswitches.

IGR + 199833 200262 (430) 3 * Bsu_NP_388059
NP_388059.1 glmS COG0449 L-glutamine-D-fructose-6-phosphate amidotransferase
1 Classifications: B/C (3) ; 3 Organisms: Bsu (1), Cte (1), Oih (1)
COG0449 3 1 glmS Glucosamine 6-phosphate synthetase, contains amidotransferase and phosphosugar isomerase domains

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0  CGGAAA__AAGGCTTAGTTGACGAGGATGGAGGTTATCGAAT_TT
1  CGGATAGGAAGGAT-AGTTGACGAGGTAGGAGGTTATCGAAT-TT
2  GGGGTG--TCACTTAAGTTGACGAGGATGGGGAGTATCGAATCTT

0  __CG_CGGAT_CCTCCCGGCTGAGTGTGCAGATCACAGCCGTAAG
1  TCGG-CGGGTGCCTCCCGGCTGTC-------ATCACAGTCGAAAC
2  --CGGCGGGT-GCCCCACGGT-ACTG-------CACTACCGTTAA
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In recognition of the first ribozyme riboswitch and in recognition of the establishment of a bioinformatics tool for riboswitch discovery, the status of Breaker Laboratory "Molecule of the Year" is conferred upon these two advances.

Ribozymes serve in key areas of modern metabolism. This implies that ribozymes once performed all the necessary reactions for early life forms, including many of the fundamental processes that are common to all modern cells. The *glmS* RNA is the first ribozyme to be discovered in 14 years, and broadens the known roles of ribozymes to include genetic control. This ribozyme controls gene expression by activation with the metabolite GlcN6P, and thereby serves as a novel form of riboswitch. The RNA was identified by using a web-based bioinformatics tool called BLISS, which compares the intergenic regions (IGRs) from a given genome to all other IGRs from this and many other genomes. To date, BLISS has been used to examine more than 100 bacterial genomes and has provided numerous new RNA motifs that most likely reflect the existence of new riboswitches.

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