ISSN 0026-8933, Molecular Biology, 2006, Vol. 40, No. 4, pp. 541–550. © Pleiades Publishing, Inc., 2006.
Original Russian Text © M.S. Gelfand, 2006, published in Molekulyarnaya Biologiya, 2006, Vol. 40, No. 4, pp. 609–619.

UDC 577.2

Bacterial *cis*-Regulatory RNA Structures

M. S. Gelfand[a, b]

[a] *Institute of Information Transmission Problems, Russian Academy of Sciences, Moscow, 127994 Russia; e-mail: gelfand@iitp.ru*

[b] *Department of Bioengineering and Bioinformatics, Moscow State University, Moscow, 119992 Russia*

Received December 21, 2005

Abstract—The review considers the mechanism regulating bacterial gene expression with the use of alternative RNA structures, such as riboswitches, attenuators, T-boxes, etc. These structures are classified by the mechanism of action. Evolution and interactions of regulatory systems are discussed.

DOI: 10.1134/S0026893306040066

Key words: regulation, transcription, translation, attenuator, riboswitch, evolution

INTRODUCTION

One of the main mechanisms regulating gene expression in bacteria is linked with the generation of alternative structures in mRNA. In one of the conformations the gene is repressed as a result of premature transcription termination or inhibition of translation initiation. Selection of the conformation is determined by the concentration of a target metabolite. Depending on how the concentration of a target metabolite acts on the formation of structural elements, several mechanisms are distinguished in the regulation involving classic attenuators, which use the ratio of transcription and translation rates; protein-binding elements; tRNA-binding elements (T-boxes); and riboswitches, which directly, without any mediator, bind small molecules.

A regulatory element contains a sensory structure, which indirectly defines the concentration of a metabolite, and a regulatory structure, which directly acts on gene expression. The regulatory structures are divided into two major groups (Table 1): terminators (their generation results in repression due to premature termination of transcription) and sequesters (hairpins that overlap the Shine–Dalgarno box or the start codon and prevent translation initiation). RNA regulatory structures may function as activators or repressors, depending on the location of sensory and regulatory structures and the presence of other structures (Fig. 1, Table 2). In the simplest case the sensory structure coincides with the regulatory one (Fig. 1a). The binding with a coregulatory molecule stabilizes the structure and prevents translation of the gene. If the sensory structure is alternative to the regulatory one, the whole element functions as an activator: the binding with a coregulator stabilizes the sensory structure and prevents the generation of a regulatory hairpin (Fig. 1b). Finally, if there is a hairpin that is alternative to the regulatory one (antiterminator or

Table 1. Classification of regulatory structures and examples

Type of regulation	Premature termination of transcription	Inhibition of translation initiation
Repression: A sensory structure coincides with a regulatory one	Does it not exist?	Riboswitches in actinobacteria. Thermosensors. Ribosomal proteins regulating their own operons. TRAP (several genes of *Bacillus* spp.)
Activation: A sensory structure is alternative to a regulatory one	Activating riboswitches (lysine catabolism, purine export). Proteins of the BglA family, acting as antiterminators of catabolic operons	Operons of resistance to macrolide antibiotics and chloramphenicol
Repression: A sensory structure is alternative to an antiregulatory one	Riboswitches of bacteria from the *Bacillus*/*Clostridium* group. PyrR, a regulator of the *Bacillus subtilis* pyrimidine operon T-boxes of bacteria from the *Bacillus*/*Clostridium* group Attenuators of the amino acid operons	Riboswitches of proteobacteria. TRAP (the *trp* operon in *Bacillus* spp.) T-boxes of actinobacteria

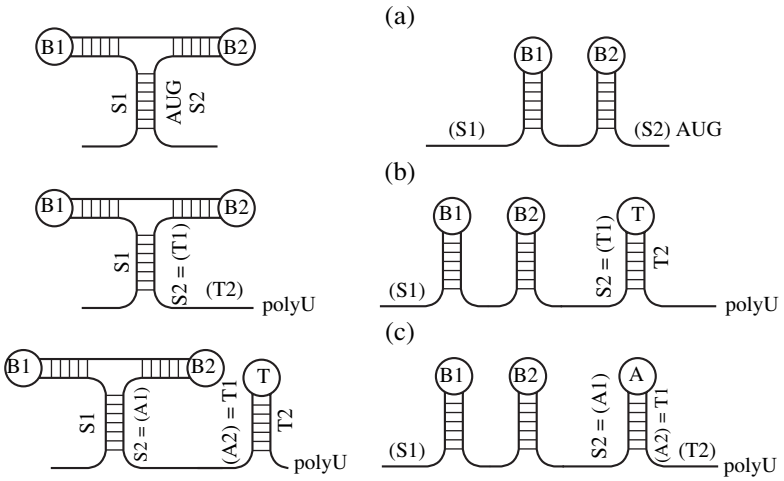

Fig. 1. Scheme of the repressor and activator RNA structures. (a) Repressor: The sensory structure coincides with the regulatory one; binding with a coregulatory molecule stabilizes the structure and prevents translation. (b) Activator: The sensory structure is alternative to the regulatory one; binding with a coregulator stabilizes the sensory structure and prevents the formation of the regulatory hairpin. (c) Repressor: The sensory structure (antiterminator, antisequester) is alternative to the antiregulatory one; the sensory regulator functions as a repressor. Left column, the sensory structure is stabilized by binding with a ligand, protein, or tRNA. Right column, an alternative structure is formed. B1 and B2 are elements of the sensory structure; T is the terminator; and A is the antiterminator. Regions unpaired in the given conformation are shown in brackets. AUG is the start codon; polyU is the polyuridine sequence in the terminator. A sequester of translation initiation may play the role of a regulatory hairpin instead of a terminator.

antisequester) and a sensory structure that is alternative to this hairpin, the regulator functions as a repressor (Fig. 1c).

RIBOSWITCHES

Riboswitches were recently discovered, but are the most widespread and, possibly, the most ancient RNA regulatory elements. Computational analysis has played an important role in their discovery. In 1999, it was found that highly conserved structures precede the operons of riboflavin biosynthetic genes and function as regulators, binding directly with small molecules [1]. Further analysis has revealed that the structures contain sites complementary to potential regulatory hairpins, terminators or sequesters. Therefore, it

Table 2. Riboswitches

Riboswitch	Methabolic system	Cofactor	Genome	Reference
RFN element	Riboflavin biosynthesis and transport	FMN (flavin mononucleotide)	*Bacillus*/*Clostridium* group, proteobacteria, actinobacteria, other bacteria	[1–4]
THI element	Biosynthesis and transport of thiamine and precursors	TPP (thiamine pyrophosphate)	*Bacillus*/*Clostridium* group, proteobacteria, actinobacteria, cyanobacteria, other bacteria, archaebacteria (thermoplasmata), plants, fungi	[3, 7, 8, 34, 38]
B12 element	Cobalamine biosynthesis, cobalt transport, cobalamine-dependent enzymes	Coenzyme B12 (adenosylcobalamine)	*Bacillus*/*Clostridium* group, proteobacteria, actinobacteria, cyanobacteria, spirochetes, other bacteria	[11, 12, 30, 33]
S-box (SAM-I)	Methionine and cysteine metabolism	SAM (S-adenosylmethionine)	*Bacillus*/*Clostridium* group, other bacteria	[20–23, 29, 32]
SAM-II	Methionine metabolism	S-adenosylmethionine	α-proteobacteria	[25]
LYS element, L-box	Lysine metabolism	Lysine	*Bacillus*/*Clostridium* group, Enterobacteriae, other bacteria	[18, 19, 31]
G-box	Purine metabolism	Purines	*Bacillus*/*Clostridium* group, other bacteria	[14, 15, 37]
gcvT	Glycine catabolism	Glycine	*Bacillus*/*Clostridium* group	[27]
glmS (ribozyme)	Glucosamine 6-phosphate synthesis	Glucosamine 6-phosphate	*Bacillus*/*Clostridium* group	[28]

Table 3. Ribosomal proteins acting as autoregulators

Protein	Position of the regulator gene in the operon	Operon	Gene whose upstream region harbors the regulatory element	Position of this gene in the operon	Genome	Reference
S8	5	*spc*	*rplE* (*L5*)	3	*E. coli*	[46, 47]
L1	2	L11 (*rplKA*)	*rplK*	1	Enterobacteria	[48–50]
L1	2	L11 (*rplKA*)	*rplK*	1	*Thermotoga maritima*	[51, 52]
L1	1	*MvaL1* (L1-L10-L12)	*L1*	1	Archaebacteria *Methanococcus vannielii*, *Halobacterium cutirubrum*	[53, 54]
L10	1	*beta*	*rplJ* (*L10*)	1	Enterobacteria	[55, 56]
L10	1	*rplJL*	*rplJ* (*L10*)	1	*Thermotoga maritima*	[51, 52]
L20	3	IF3-L35-L20	*L35*	2	*E. coli*	[57, 58]
S15	1	*rpsO* (S15)	*rpsO*	1	*E. coli*	[59, 60]
L4	1	S10	*S10*	1	*E. coli*	[62]

has been proposed that regulation is based on repression, resulting from a disbalance in the formation of terminators–antiterminators or sequesters–antisequesters [2]. This suggestion has been proven experimentally [3]. Breaker and colleagues [4] obtained similar results independently. Another approach was used in this case: from a study of synthetic aptamers (RNA structures able to bind small molecules) to a search of natural ones [5].

These results stimulated a search for novel riboswitches. At first the cases with uncertain or poorly known regulatory mechanisms were considered. That made it possible to reveal thiamine [6–8], cobalamine [9–12], purine [13–15], and lysine [16–19] riboswitches. Investigations of S-boxes, regulating the methionine biosynthesis genes in *Bacillus subtilis* and related bacteria, are the most demonstrative. These structures were initially identified by a comparative analysis of the *met* regulatory regions [20], but the mechanism of regulation was unclear. After the first publications on riboswitches, the same mechanism was proposed for S-boxes and was promptly confirmed [21–23].

Since all known riboswitches have highly conserved primary and secondary structures, comparative genomics approaches were applied for the search for novel classes of riboswitches. Bacterial intergenic spacers were compared within [24, 25] and between taxonomic groups [26]. This revealed several novel classes of riboswitches: glycine [27] and glucosamine [28] riboswitches in Gram-positive bacteria and another class of S-adenosylmethionine riboswitches in α-proteobacteria [25]. Moreover, the conservation and length of a signal makes it possible to identify novel riboswitches in different genomes, thereby, allowing a prediction of the function of their target genes coding for enzymes and, especially, transporters [1, 2, 7, 12, 29–33]. Thiamine riboswitches were found in the genomes of archaebacteria [7] and eukaryotes, including plants and fungi [34]. The presence of riboswitches in the metagenome of the Sargasso Sea was predicted [35]. As expected, thiamine (THI) elements were most frequent, lysine (LYS) elements and cobalamine (B12) elements were significantly more infrequent, and the riboflavine (RFN) elements and methionine S-boxes were very rare (M. Kazanov, personal communication). However, it is not always possible to predict the cofactor from only the functions of the regulated genes, and several classes of putative riboswitches remain experimentally uncharacterized [5, 24].

The combination and functional specificity of riboswitches differ among taxonomic groups [36]. The repressor structures causing premature transcription termination predominate in bacteria from the *Bacillus*/*Clostridium* group, which demonstrate the largest variety of riboswitches. Repressors with sequester hairpins, which inhibit translation initiation, are found more often in proteobacteria; repressor structures directly overlapping the translation start site are most common in actinobacteria.

Experiments following a computational analysis revealed other mechanisms of regulation. Activators, the structures alternative to regulatory (terminator) hairpins, were found in two classes of riboswitches, lysine [31], and purine [37]. The thiamine riboswitches predicted for eukaryotic genomes regulate splicing [38], and a riboswitch regulating the glucosamine 6-phosphate metabolism operon functions as a ribozyme and cleaves its own mRNA [28].

The high selectivity of riboswitches toward their cofactors was demonstrated in experiments [4, 8, 15, 19, 21, 27, 28]. The selectivity was explained after the spatial structure of the purine-responsive riboswitches was established by X-ray analysis [39, 40] and NMR

[41]. As expected [36], numerous conserved nucleotides that are not included in the secondary structure are involved in tertiary interactions and the formation of the recognizing site. Guanine/hypoxanthine and adenine are specifically recognized by the corresponding riboswitches, owing to Watson–Crick pairing with cytidine and uracil, respectively [37, 39, 40], as predicted earlier [15]. The spatial structures solved for two purine riboswitches were nearly identical, although their primary structures differed in about 40% of the nucleotides [42].

A special variant of riboswitches is thermosensors, which sequester the ribosome-binding region. The thermosensor that induces the virulence genes of *Listeria monocytogenes* after infection of a host, and the resulting increase in temperature to 37°C was studied experimentally [43]. An analogous sensor has been proposed to regulate the heat shock σ factor gene in *Escherichia coli* [44].

RNA-BINDING PROTEINS

Regulatory mechanisms based on RNA–protein interactions can be divided in two groups. In one case an RNA-binding protein autoregulates its own gene by binding to a structure resembling its main substrate. In another a special regulatory protein controls the expression of other genes.

The best-known example of mimicking structures is provided by the structures that imitate rRNA in the regulatory regions of ribosomal protein genes. The mRNA region with the translation start site and the Shine–Dalgarno box folds into a structure similar to the binding site for a given protein on rRNA [45]. Such structures were found in the S8, S15, L1, L4, L10, and L20 mRNAs. In the case of L1 the structures were revealed in various bacteria and even in archaebacteria (Table 3). The sequence similarity of such structures is sometimes poor and is restricted to a small site, whereas the secondary [62] and, especially, spatial structures of the protein-binding sites are virtually identical on mRNA and rRNA. For instance, the regulatory element of the S10 operon and the L4-binding site of the 23S rRNA [63] lack similarity at the levels of the primary and secondary structures and nearly fully coincide in their spatial determinants [61]. However, in the case of S4 [64] and S14 [65], the determinants of regulatory and functional binding of ribosomal proteins with mRNA and rRNA, respectively, are completely different. It is worth noting that regulation can take place not only at the translational level. Thus, the binding of L4 with the leader region of the S10 operon results in premature transcription termination [61].

Apart from the ribosomal proteins, an analogous autoregulatory mechanism was observed for *E. coli thr*S of tryptophanyl-tRNA synthase. The leader region has a tRNA-like structure, by binding with which ThrS represses translation initiation [66].

The other class of regulators includes special RNA-binding proteins. In particular, this class includes the BglG/SacY family of transcriptional antiterminators. The membrane-bound protein of the PTS system phosphorylates the antiterminator protein, enabling it to bind with an antiterminatory hairpin and activate transcription of the target operon [67, 68]. The regulator contains two homologous domains, one of which is phosphorylated in the presence of glucose, and the other is posphorylated in the presence of different sugar. The regulator binds with RNA and activates expression only when the second domain is phosphorylated, while the first is not. This mechanism regulates the expression of numerous operons involved in catabolism of saccharides and polysaccharides in Gram-positive and Gram-negative bacteria. For instance, *Bacillus subtilis* LevR regulates the levanase operon [69]; LicT regulates the *bgl*PH operon, involved in utilization of aryl-β-glucosides, and the *bgl*S gene for β-glucanase [70]; GlcT regulates the *pts*GHI operon of the phosphotransferase system [71]; *Streptococcus mutans* LicT regulates the aesculin locus [72]; *Lactococcus plantarum* BglG regulates the *bgl*GPT operon [73]; and *E. coli* BglG regulates catabolism of aromatic β-glucosides [74].

The binding of PyrR with an anti-antiterminator hairpin facilitates the formation of a terminator with the subsequent repression of the *pyr* operon in *B. subtillis* [75, 76]. The spatial structure of the complex of PyrR with RNA and the ligands suggests dual regulation by pyrimidines and purines [77].

TRAP is one of the most unusual RNA-binding regulatory proteins. TRAP consists of 11 identical subunits binding to (G/U)AG repeats in the 5' leader region of mRNA [78], and forms a spool on which mRNA is twisted [79]. Multimerization is regulated by the accessibility of tryptophan and by another protein, AT (anti-TRAP) [80]. The group of TRAP-binding repeats forms a sensory structure, and regulation involves either sequestration of the translation initiation site (i.e., the sensory structure coincides with the regulatory one), as in *pab*A/*trp*G, *trp*P/*yha*G, and *ycb*K [81, 82], or competition with the antisequester hairpin, as in the *trp*EDCFBA operon [81, 83]. This operon is also regulated at the transcriptional level; this mechanism is conserved in related *Bacillus haloduranS*, whereas transnational regulation is not [82, 83].

T-BOXES: RNA–RNA INTERACTIONS

A high concentration of nonaminoacylated tRNAs is one of the indicators of a lack of amino acids in the medium. There are regulatory structures called T-boxes that directly interact with uncharged tRNAs. Initially T-boxes were revealed in the genes encoding

aminoacyl-tRNA synthases, whose low activity results in the appearance of nonaminoacylated tRNAs [84]. It was shown more recently that T-boxes regulate the genes encoding amino acid synthesis enzymes and amino acid transporters [85–87]. The tRNA for a certain amino acid is recognized specifically by an anti-anticodon, which is an unpaired sequence that is fixed in the conserved secondary structure and is complementary to the tRNA anticodon. The nonaminoacylated state of tRNA is recognized owing to a conserved sequence complementary to unpaired CCA in the tRNA acceptor loop: pairing with the T-box is possible only with nonaminoacylated tRNA.

As the T-box is an antiregulatory structure, the binding with tRNA stabilizes it and facilitates the progress of transcription (in bacteria of the *Bacillus*/*Clostridium* group) or translation initiation (in actinobacteria) [88].

Bacteria have other small RNAs that presumably regulate gene expression via *trans*-RNA–RNA interactions. However, the mechanism of such regulation is as of yet unclear; this binding is thought to act on mRNA translation and stability [89, 90].

ATTENUATORS AND LEADER PEPTIDES

In attenuators alternative structures appear dynamically, and the ratio between the rates of transcription and cotranscriptional translation has an important role [91, 92]. The attenuators of the amino acid operons consist of the gene for a leader peptide, which contains one (for rare amino acids) or several codons for a certain amino acid (this sequence is a sensor), and several hairpins, including the essential terminator and antiterminator ones. The region of the antiterminator hairpin overlaps the gene encoding the leader peptide. The hairpins are alternative: either the former or the latter is formed in mRNA.

The rate of translation yielding the leader peptide depends on the concentration of the given amino acid. When the concentration of the amino acid, or, more exactly, aminoacylated tRNA, is sufficient, the rate of translation is high and the translating ribosome prevents the formation of the antiterminator hairpin. This allows the formation of the terminator hairpin, and structural genes of the operon are not transcribed.

Attenuators were revealed initially in *E. coli* and other enterobacteria [93–98] and then in other bacteria both experimentally [99, 100] and by comparative genomic analysis [101–103].

There are other variants of regulation based on coupling the rates of operon transcription and translation yielding the leader peptide. Instead of a ribosome, RNA polymerase may be paused. This mechanism is used in the case of attenuators of the *E. coli* pyrimidine biosynthesis operons *pyr*E [104] and *pyr*BI [105, 106]. The regulation of other genes can thereby involve the choice of a transcription start, which leads to the formation of alternative structures in the *pyr*C leader region [107] and re-iterative transcription initiation on the *pyr*BI [108], *cod*BA [109], *upp* [110], and *car*AB [111] operons. This results in unproductive transcription yielding short oligonucleotides NUU…UU instead of the full-length transcripts.

In addition to translational attenuation of the leader peptides of the amino acid operons on hungry codons (codons whose cognate aminoacylated tRNAs occur at a low concentration) and transcriptional attenuation on thymines of the leader peptide-coding sequences of the pyrimidine operons, there are other mechanisms coupling the rates of translation and transcription. Stalling or pausing the "venenate" ribosome during translation of the leader peptide sequence results in the formation of an antiterminator in the *erm*K erythromycin resistance gene [112, 113] and the *tet*(*M*) tetracycline resistance gene of *Enterococcus faecalis* Tn916 [114], and releases the Shine–Dalgarno region in *ermC* [115] and the *ermD* [116], determining resistance to macrolide antibiotics, and *cat* for chloramphenicol resistance [117], and the tetracycline resistance gene of *Bacteroides fragilis* CTnDOT [118]. Finally, the ribosome translating *rtp*LP for the leader peptide of *B. subtilis rtp*A, which encodes anti-TRAP, covers the Shine–Dalgarno region, whereas a stalling of the ribosome on tryptophan codons of the leader peptide promotes translation initiation and anti-TRAP synthesis [119].

EVOLUTION AND INTERACTIONS BETWEEN REGULATORY SYSTEMS

In contrast to the binding sites for transcriptional factors, the RNA regulatory systems with their conserved primary and secondary structures allow efficient computational analysis. A range of novel classes of riboswitches has been discovered as a result of mass analysis of genome sequences [24–28]. There are many more examples of successful analysis of certain systems in the whole set of bacterial genome and in separate taxa [1, 2, 7, 12, 15, 20, 30–34, 56, 85, 87, 88, 101, 102, 120–122], including analysis of metagenomes.

Many regulatory RNA structures, mainly identified by computational analysis, are available from the RFAM database [123]. It should be noted that the leader regions of operons regulated at the level of premature transcription termination are often revealed in a search for relatively short regulatory mRNAs [124]. This makes it possible to apply the analysis of regulatory RNAs for annotating genes (e.g., see [36]) and, which is more pertinent to this review, to describe the interactions between different regulators, the events of complicated regulation, and the evolution of regula-

tory systems. It is known that regulatory structures form tandems. This is characteristic of thymine riboswitches of δ-proteobacteria [120], several T-boxes [125], and the all glycine riboswitches [27]. A case was described that the S-box regulates the antisense transcript of the *ubi*G*yrh*AB operon involved in synthesis of cysteine from methionine in *Clostridium acetobutylicum* [32]. As a result, the expression of the operon is depressed in methionine deficiency. Moreover, this operon is regulated by the cysteine T-box, which represses transcription in the conditions of a cysteine excess. Preliminary experimental evidence for this prediction has been obtained (I. Martin-Verstaete, personal communication).

The relatively large sizes of riboswitches and other regulatory structures allow a study of their evolution, since the information they contain is sufficient for constructing phylogenetic trees. Thus, riboflavin-sensitive riboswithces of *ypa*A transporters have been assumed to result from independent duplications in different genomes [2]. Horizontal transfer of regulatory elements has also been described [2]. Several local duplications have been observed in T-boxes (A.G. Vitreschak, personal communication), which might be one of the mechanisms extending the corresponding regulons.

Comparative genome analysis makes it possible to describe cases where a regulatory system is fully changed. Since RNA regulation is especially important in Gram-positive bacteria, most observations were obtained in this group.

Thus, the ancient system regulating methionine metabolism by S box-like riboswitches was lost in a common ancestor of lactobacilli and streptococci. The S-box regulon was absorbed by the expanded methionine T-box system in lactobacilli and by the system of the transcriptional regulator MtaR in streptococci [32]. On the other hand, the tryptophan T boxes that regulated the main operon tryptophan synthesis in the *Bacillus*/*Clostridium* group were substituted with a TRAP-binding system in *Bacillus subtillis* and its close relatives [125]. Transcription factors substituted the tyrosine T-boxes and came to play a significant role in regulating the genes of the metabolic system of aromatic amino acid synthesis in streptococci and lactococci, which resembles the regulation using the methionine pathway [87].

ACKNOWLEDGMENTS

I thank A. Mironov, D. Rodionov, and A. Vitreschak for the long-term collaboration; M. Kazanov and I. Martin-Verstraete for preliminary experimental data; and N. Sadovskaya for assistance in the manuscript preparation.

The studies mentioned in this review were supported by the Howard Hughes Medical Institute, the Russian Foundation for Basic Research, and the programs Molecular and Cell Biology and Origin and Evolution of the Biosphere of the Russian Academy of Sciences. In addition, I am grateful to the Foundation for the Support of Russian Science.

REFERENCES

1. Gelfand M.S., Mironov A.A., Jomantas J., Kozlov Y.I., Perumov D.A. 1999. A conserved RNA structure element involved in the regulation of bacterial riboflavin synthesis genes. *Trends Genet*. **15**, 439–442.
2. Vitreschak A.A., Rodionov D.A., Mironov A.A., Gelfand M.S. 2002. Regulation of riboflavin biosynthesis and transport genes in bacteria by transcriptional and translational attenuation. *Nucleic Acids Res*. **30**, 3141–3151.
3. Mironov A.S., Gusarov I., Rafikov R., Lopez L.E., Shatalin K., Kreneva R.A., Perumov D.A., Nudler E. 2002. Sensing small molecules by nascent RNA: A mechanism to control transcription in bacteria. *Cell*. **111**, 747–756.
4. Winkler W.C., Cohen-Chalamish S., Breaker R.R. 2002. An mRNA structure that controls gene expression by binding FMN. *Proc. Natl. Acad. Sci. USA*. **99**, 15,908–15,913.
5. Mandal M., Breaker R.R. 2004. Gene regulation by riboswitches. *Nature Rev. Mol. Cell Biol*. **5**, 451–463.
6. Miranda-Rios J., Navarro M., Soberon M. 2001. A conserved RNA structure (thi box) is involved in regulation of thiamin biosynthetic gene expression in bacteria. *Proc. Natl. Acad. Sci. USA*. **98**, 9736–9741.
7. Rodionov D.A., Vitreschak A.A., Mironov A.A., Gelfand M.S. 2002. Comparative genomics of thiamin biosynthesis in procaryotes. New genes and regulatory mechanisms. *J. Biol. Chem*. **277**, 48 949–48 959.
8. Winkler W., Nahvi A., Breaker R.R. 2002. Thiamine derivatives bind messenger RNAs directly to regulate bacterial gene expression. *Nature*. **419**, 952–956.
9. Nou X., Kadner R.J. 2000. Adenosylcobalamin inhibits ribosome binding to btuB RNA. *Proc. Natl. Acad. Sci. USA*. **97**, 7190–7195.
10. Ravnum S., Andersson D.I. 2001. An adenosyl-cobalamin (coenzyme-B12)-repressed translational enhancer in the cob mRNA of *Salmonella typhimurium. Mol. Microbiol*. **39**, 1585–1594.
11. Nahvi A., Sudarsan N., Ebert M.S., Zou X., Brown K.L., Breaker R.R. 2002. Genetic control by a metabolite binding mRNA. *Chem. Biol*. **9**, 1043.
12. Vitreschak A.G., Rodionov D.A., Mironov A.A., Gelfand M.S. 2003. Regulation of the vitamin B12 metabolism and transport in bacteria by a conserved RNA structural element. *RNA*. **9**, 1084–1097.
13. Christiansen L.C., Schou S., Nygaard P., Saxild H.H. 1997. Xanthine metabolism in *Bacillus subtilis*: Characterization of the *xpt-pbuX* operon and evidence for purine- and nitrogen-controlled expression of genes involved in xanthine salvage and catabolism. *J. Bacteriol*. **179**, 2540–2550.
14. Johansen L.E., Nygaard P., Lassen C., Agerso Y., Saxild H.H. 2003. Definition of a second *Bacillus subtilis*

pur regulon comprising the *pur* and *xpt-pbuX* operons plus *pbuG*, *nupG* (*yxjA*), and *pbuE* (*ydhL*). *J. Bacteriol*. **185**, 5200–5209.

15. Mandal M., Boese B., Barrick J.E., Winkler W.C., Breaker R.R. 2003. Riboswitches control fundamental biochemical pathways in *Bacillus subtilis* and other bacteria. *Cell*. **113**, 577–586.
16. Kochhar S., Paulus H. 1996. Lysine-induced premature transcription termination in the *lys*C operon of *Bacillus subtilis. Microbiology.* **142**, 1635–1639.
17. Lu Y., Shevtchenko T.N., Paulus H. 1992. Fine-structure mapping of *cis*-acting control sites in the *lys*C operon of *Bacillus subtilis. FEMS Microbiol. Lett*. **71**, 23–27.
18. Grundy F.J., Lehman S.C., Henkin T.M. 2003. The L box regulon: Lysine sensing by leader RNAs of bacterial lysine biosynthesis genes. *Proc. Natl. Acad. Sci. USA*. **100**, 12,057–12,062.
19. Sudarsan N., Wickiser J.K., Nakamura S., Ebert M.S., Breaker R.R. 2003. An mRNA structure in bacteria that controls gene expression by binding lysine. *Genes Dev.* **17**, 2688–2697.
20. Grundy F.J., Henkin T.M. 1998. The S box regulon: A new global transcription termination control system for methionine and cysteine biosynthesis genes in Gram-positive bacteria. *Mol. Microbiol*. **30**, 737–749.
21. Winkler W.C., Nahvi A., Sudarsan N., Barrick J.E., Breaker R.R. 2003. An mRNA structure that controls gene expression by binding S-adenosylmethionine. *Nature Struct. Biol*. **10**, 701–707.
22. McDaniel B.A., Grundy F.J., Artsimovitch I., Henkin T.M. 2003. Transcription termination control of the S box system: Direct measurement of S-adenosylmethionine by the leader RNA. *Proc. Natl. Acad. Sci. USA*. **100**, 3083–3088.
23. Epshtein V., Mironov A.S., Nudler E. 2003. The riboswitch-mediated control of sulfur metabolism in bacteria. *Proc. Natl. Acad. Sci. USA*. **100**, 5052–5056.
24. Barrick J.E., Corbino K.A., Winkler W.C., Nahvi A., Mandal M., Collins J., Lee M., Roth A., Sudarsan N., Jona I., Wickiser J.K., Breaker R.R. 2004. New RNA motifs suggest an expanded scope for riboswitches in bacterial genetic control. *Proc. Natl. Acad. Sci. USA*. **101**, 6421–6426.
25. Corbino K.A., Barrick J.E., Lim J., Welz R., Tucker B.J., Puskarz I., Mandal M., Rudnick N.D., Breaker R.R. 2005. Evidence for a second class of S-adenosylmethionine riboswitches and other regulatory RNA motifs in alpha-proteobacteria. *Genome Biol*. **6**, R70.
26. Abreu-Goodger C., Ontiveros-Palacios N., Ciria R., Merino E. 2004. Conserved regulatory motifs in bacteria: Riboswitches and beyond. *Trends Genet*. **20**, 475–479.
27. Mandal M., Lee M., Barrick J.E., Weinberg Z., Emilsson G.M., Ruzzo W.L., Breaker R.R. 2004. A glycine-dependent riboswitch that uses cooperative binding to control gene expression. *Science*. **306**, 275–279.
28. Winkler W.C., Nahvi A., Roth A., Collins J.A., Breaker R.R. 2004. Control of gene expression by a natural metabolite-responsive ribozyme. *Nature*. **428**, 281–286.
29. Murphy B.A., Grundy F.J., Henkin T.M. 2002. Prediction of gene function in methylthioadenosine recycling from regulatory signals. *J. Bacteriol*. **184**, 2314–2318.
30. Rodionov D.A., Vitreschak A.G., Mironov A.A., Gelfand M.S. 2003. Comparative genomics of the vitamin B12 metabolism and regulation in prokaryotes. *J. Biol. Chem*. **278**, 41,148–41,159.
31. Rodionov D.A., Vitreschak A.G., Mironov A.A., Gelfand M.S. 2003. Regulation of lysine biosynthesis and transport genes in bacteria: Yet another RNA riboswitch? *Nucleic Acids Res*. **31**, 6748–6757.
32. Rodionov D.A., Vitreschak A.G., Mironov A.A., Gelfand M.S. 2004. Comparative genomics of the methionine metabolism in Gram-positive bacteria: A variety of regulatory systems. *Nucleic Acids Res*. **32**, 3340–3353.
33. Nahvi A., Barrick J.E., Breaker R.R. 2004. Coenzyme B12 riboswitches are widespread genetic control elements in prokaryotes. *Nucleic Acids Res*. **32**, 143–150.
34. Sudarsan N., Barrick J.E., Breaker R.R. 2003. Metabolite-binding RNA domains are present in the genes of eukaryotes. *RNA*. **9**, 644–647.
35. Venter J.C., Remington K., Heidelberg J.F., Halpern A.L., Rusch D., Eisen J.A., Wu D., Paulsen I., Nelson K.E., Nelson W., Fouts D.E., Levy S., Knap A.H., Lomas M.W., Nealson K., White O., Peterson J., Hoffman J., Parsons R., Baden-Tillson H., Pfannkoch C., Rogers Y.H., Smith H.O. 2004. Environmental genome shotgun sequencing of the Sargasso Sea. *Science*. **304**, 66–74.
36. Vitreschak A.G., Rodionov D.A., Mironov A.A., Gelfand M.S. 2004. Riboswitches: The oldest mechanism for the regulation of gene expression? *Trends Genet*. **20**, 44–50.
37. Mandal M., Breaker R.R. 2004. Adenine riboswitches and gene activation by disruption of a transcription terminator. *Nature Struct. Mol. Biol*. **11**, 29–35.
38. Kubodera T., Watanabe M., Yoshiuchi K., Yamashita N., Nishimura A., Nakai S., Gomi K., Hanamoto H. 2003. Thiamine-regulated gene expression of *Aspergillus oryzae thiA* requires splicing of the intron containing a riboswitch-like domain in the 5'-UTR. *FEBS Lett*. **555**, 516–520.
39. Batey R.T., Gilbert S.D., Montange R.K. 2004. Structure of a natural guanine-responsive riboswitch complexed with the metabolite hypoxanthine. *Nature*. **432**, 411–415.
40. Serganov A., Yuan Y.R., Pikovskaya O., Polonskaia A., Malinina L., Phan A.T., Hobartner C., Micura R., Breaker R.R., Patel D.J. 2004. Structural basis for discriminative regulation of gene expression by adenine- and guanine-sensing mRNAs. *Chem. Biol*. **11**, 1729–1741.
41. Noeske J., Richter C., Grundl M.A., Nasiri H.R., Schwalbe H., Wohnert J. 2005. An intermolecular base triple as the basis of ligand specificity and affinity in the guanine- and adenine-sensing riboswitch RNAs. *Proc. Natl. Acad. Sci. USA*. **102**, 1372–1377.
42. Lescoute A., Westhof E. 2005. Riboswitch structures: Purine ligands replace tertiary contacts. *Chem. Biol*. **12**, 10–13.
43. Johansson J., Mandin P., Renzoni A., Chiaruttini C., Springer M., Cossart P. 2002. An RNA thermosensor

controls expression of virulence genes in Listeria monocytogenes. *Cell.* **110**, 551–561.

44. Narberhaus F. 2002. mRNA-mediated detection of environmental conditions. *Arch. Microbiol*. **178**, 404–410.
45. Draper D.E. 1989. How do proteins recognize specific RNA sites? New clues from autogenously regulated ribosomal proteins. *Trends Biochem. Sci*. **14**, 335–338.
46. Cerretti D.P., Mattheakis L.C., Kearney K.R., Vu L., Nomura M. 1988. Translational regulation of the *spc* operon in *Escherichia coli*. Identification and structural analysis of the target site for S8 repressor protein. *J. Mol. Biol*. **204**, 309–329.
47. Merianos H.J., Wang J., Moore P.B. 2004. The structure of a ribosomal protein *S8/spc* operon mRNA complex. *RNA*. **10**, 954–964.
48. Said B., Cole J.R., Nomura M. 1988. Mutational analysis of the L1 binding site of 23S rRNA in *Escherichia coli. Nucleic Acids Res*. **16**, 10,529–10,545.
49. Sor F., Nomura M. 1987. Cloning and DNA sequence determination of the L11 ribosomal protein operon of *Serratia marcescens* and *Proteus vulgaris*: Translational feedback regulation of the *Escherichia coli* L11 operon by heterologous L1 proteins. *Mol. Gen. Genet*. **210**, 52–59.
50. Nevskaya N., Tishchenko S., Gabdoulkhakov A., Nikonova E., Nikonov O., Nikulin A., Platonova O., Garber M., Nikonov S., Piendl W. 2005. Ribosomal protein L1 recognizes the same specific structural motif in its target sites on the autoregulatory mRNA and 23S rRNA. *Nucleic Acids Res*. **33**, 478–485.
51. Liao D., Dennis P.P. 1992. The organization and expression of essential transcription translation component genes in the extremely thermophilic eubacterium *Thermotoga maritima. J. Biol. Chem*. **267**, 22787–22797.
52. Paton E.B., Zhivolup A.N. 1996. Presence of the binding site for the ribosomal protein L10 in the untranslated leader sequence upstream from the *rpl*J gene in *Thermotoga maritima* is evidence for autogenous control of the expression of this gene. *Genetika*. **32**, 140–145.
53. Shimmin L.C., Dennis P.P. 1989. Characterization of the L11, L1, L10 and L12 equivalent ribosomal protein gene cluster of the halophilic archaebacterium *Halobacterium cutirubrum. EMBO J*. **8**, 1225–1235.
54. Hanner M., Mayer C., Kohrer C., Golderer G., Grobner P., Piendl W. 1994. Autogenous translational regulation of the ribosomal MvaL1 operon in the archaebacterium *Methanococcus vannielii. J. Bacteriol*. **176**, 409–418.
55. Climie S.C., Friesen J.D.1987. Feedback regulation of the *rplJL-rpoBC* ribosomal protein operon of *Escherichia coli* requires a region of mRNA secondary structure. *J. Mol. Biol*. **198**, 371–381.
56. Zhyvolup A.N., Kroupskaya I.V., Lyaskovsky I.M., Paton E.B. 1994. Comparison of nucleotide sequences of the rplJ leader in enterobacteria. *Biopol. Cell*. **10**, 37–40.
57. Guillier M., Allemand F., Raibaud S., Dardel F., Springer M., Chiaruttini C. 2002. Translational feedback regulation of the gene for L35 in *Escherichia coli* requires binding of ribosomal protein L20 to two sites in its leader mRNA: A possible case of ribosomal RNA–messenger RNA molecular mimicry. *RNA*. **8**, 878–889.
58. Guillier M., Allemand F., Dardel F., Royer C.A., Springer M., Chiaruttini C. 2005. Double molecular mimicry in *Escherichia coli*: Binding of ribosomal protein L20 to its two sites in mRNA is similar to its binding to 23S rRNA. *Mol. Microbiol*. **56**, 1441–1456.
59. Mathy N., Pellegrini O., Serganov A., Patel D.J., Ehresmann C., Portier C. 2004. Specific recognition of rpsO mRNA and 16S rRNA by *Escherichia coli* ribosomal protein S15 relies on both mimicry and site differentiation. *Mol. Microbiol*. **52**, 661–675.
60. Serganov A., Ennifar E., Portier C., Ehresmann B., Ehresmann C. 2002. Do mRNA and rRNA binding sites of *E. coli* ribosomal protein S15 share common structural determinants? *J. Mol. Biol*. **320**, 963–978.
61. Stelzl U., Zengel J.M., Tovbina M., Walker M., Nierhaus K.H., Lindahl L., Patel D.J. 2003. RNA-structural mimicry in *Escherichia coli* ribosomal protein L4-dependent regulation of the S10 operon. *J. Biol. Chem*. **278**, 28,237–28,245.
62. Vitreschak A.G., Bansal A.K., Titov I.I., Gelfand M.S. 1999. Computer analysis of regulatory signals in complete bacterial genomes. Initiation of translation of ribosomal protein operons. *Biofizika*. **44**, 601–610.
63. Li X., Lindahl L., Zengel J.M. 1996. Ribosomal protein L4 from *Escherichia coli* utilizes nonidentical determinants for its structural and regulatory functions. *RNA*. **2**, 24–37.
64. Tang C.K., Draper D.E. 1990. Evidence for allosteric coupling between the ribosome and repressor binding sites of a translationally regulated mRNA. *Biochemistry.* **29**, 4434–4439.
65. Philippe C., Eyermann F., Benard L., Portier C., Ehresmann B., Ehresmann C. 1993. Ribosomal protein S15 from *Escherichia coli* modulates its own translation by trapping the ribosome on the mRNA initiation loading site. *Proc. Natl. Acad. Sci. USA*. **90**, 4394–4398.
66. Romby P., Springer M. 2003. Bacterial translational control at atomic resolution. *Trends Genet*. **19**, 155–161.
67. Amster-Choder O. 2005. The *bgl* sensory system: A transmembrane signaling pathway controlling transcriptional antitermination. *Curr. Opin. Microbiol*. **8**, 127–134.
68. Declerck N., Minh N.L., Yang Y., Bloch V., Kochoyan M., Aymerich S. 2002. RNA recognition by transcriptional antiterminators of the BglG/SacY family: Mapping of SacY RNA binding site. *J. Mol. Biol*. **319**, 1035–1048.
69. Stulke J., Martin-Verstraete I., Charrier V., Klier A., Deutscher J., Rapoport G. 1995. The HPr protein of the phosphotransferase system links induction and catabolite repression of the *Bacillus subtilis* levanase operon. *J. Bacteriol*. **177**, 6928–6936.
70. Lindner C., Hecker M., Le Coq D., Deutscher J. 2002. *Bacillus subtilis* mutant LicT antiterminators exhibiting enzyme I- and HPr-independent antitermination affect catabolite repression of the *bgl*PH operon. *J. Bacteriol*. **184**, 4819–4828.
71. Schmalisch M.H., Bachem S., Stulke J. 2003. Control of the *Bacillus subtilis* antiterminator protein GlcT by phosphorylation. Elucidation of the phosphorylation

chain leading to inactivation of GlcT. *J. Biol. Chem*. **278**, 51,108–51,115.

72. Cote C.K., Honeyman A.L. 2003. The LicT protein acts as both a positive and a negative regulator of loci within the *bgl* regulon of *Streptococcus mutans. Microbiology.* **149**, 1333–1340.
73. Marasco R., Salatiello I., De Felice M., Sacco M. 2000. A physical and functional analysis of the newly-identified *bgl*GPT operon of *Lactobacillus plantarum. FEMS Microbiol. Lett*. **186**, 269–273.
74. Gulati A., Mahadevan S. 2000. Mechanism of catabolite repression in the *bgl* operon of *Escherichia coli*: Involvement of the anti-terminator BglG, CRP-cAMP and EIIAGlc in mediating glucose effect downstream of transcription initiation. *Genes Cells*. **5**, 239–250.
75. Lu Y., Turner R.J., Switzer R.L. 1996. Function of RNA secondary structures in transcriptional attenuation of the *Bacillus subtilis pyr* operon. *Proc. Natl. Acad. Sci. USA*. **93**, 14,462–14,467.
76. Zhang H., Switzer R.L. 2003.Transcriptional pausing in the *Bacillus subtilis pyr* operon in vitro: A role in transcriptional attenuation? *J. Bacteriol*. **185**, 4764–4771.
77. Chander P., Halbig K.M., Miller J.K., Fields C.J., Bonner H.K., Grabner G.K., Switzer R.L., Smith J.L. 2005. Structure of the nucleotide complex of PyrR, the *pyr* attenuation protein from *Bacillus caldolyticus*, suggests dual regulation by pyrimidine and purine nucleotides. *J. Bacteriol*. **187**, 1773–1782.
78. Barbolina M.V., Li X., Gollnick P. 2005. *Bacillus subtilis* TRAP binds to its RNA target by a 5' to 3' directional mechanism. *J. Mol. Biol*. **345**, 667–679.
79. Hopcroft N.H., Manfredo A., Wendt A.L., Brzozowski A.M., Gollnick P., Antson A.A. 2004. The interaction of RNA with TRAP: The role of triplet repeats and separating spacer nucleotides. *J. Mol. Biol*. **338**, 43–53.
80. Yang W.J., Yanofsky C. 2005. Effects of tryptophan starvation on levels of the trp RNA-binding attenuation protein (TRAP) and anti-TRAP regulatory protein and their influence on trp operon expression in *Bacillus subtilis. J. Bacteriol*. **187**, 1884–1891.
81. Babitzke P. 2004. Regulation of transcription attenuation and translation initiation by allosteric control of an RNA-binding protein: The *Bacillus subtilis* TRAP protein. *Curr. Opin. Microbiol*. **7**, 132–139.
82. Yakhnin H., Zhang H., Yakhnin A.V., Babitzke P. 2004. The trp RNA-binding attenuation protein of *Bacillus subtilis* regulates translation of the tryptophan transport gene *trp*P (*yha*G) by blocking ribosome binding. *J. Bacteriol*. **186**, 278–286.
83. Szigeti R., Milescu M., Gollnick P. 2004.Regulation of the tryptophan biosynthetic genes in *Bacillus halodurans*: Common elements but different strategies than those used by *Bacillus subtilis. J. Bacteriol*. **186**, 818–828.
84. Henkin T.M., Glass B.L., Grundy F.J. 1992. Analysis of the *Bacillus subtilis tyrS* gene: Conservation of a regulatory sequence in multiple tRNA synthetase genes. *J. Bacteriol*. **174**, 1299–1306.
85. Grundy F.J., Henkin T.M. 1994. Conservation of a transcription antitermination mechanism in aminoacyl-tRNA synthetase and amino acid biosynthesis genes in Gram-positive bacteria. *J. Mol. Biol*. **235**, 798–804.
86. Makarova K.S., Mironov A.A., Gelfand M.S. 2001. Conservation of the binding site for the arginine repressor in all bacterial lineages. *Genome Biol*. **2**, RESEARCH0013.
87. Panina E.M., Vitreschak A.G., Mironov A.A., Gelfand M.S. 2003. Regulation of biosynthesis and transport of aromatic amino acids in low-GC Gram-positive bacteria. *FEMS Microbiol. Lett*. **222**, 211–220.
88. Seliverstov A.V., Putzer H., Gelfand M.S., Lyubetsky V.A. 2005. Comparative analysis of RNA regulatory elements of amino acid metabolism genes in Actinobacteria. *BMC Microbiol*. **5**, 54.
89. Gottesman S. 2004. The small RNA regulators of *Escherichia coli*: Roles and mechanisms. *Annu. Rev. Microbiol*. **58**, 303–328.
90. Storz G., Opdyke J.A., Zhang A. 2004. Controlling mRNA stability and translation with small, noncoding RNAs. *Curr. Opin. Microbiol*. **7**, 140–144.
91. Kolter R., Yanofsky C. 1982. Attenuation in amino acid biosynthetic operons. *Annu. Rev. Genet*. **16**, 113–134.
92. Henkin T.M., Yanofsky C. 2002. Regulation by transcription attenuation in bacteria: How RNA provides instructions for transcription termination/antitermination decisions. *Bioessays*. **24**, 700–707.
93. Lee F., Yanofsky C. 1977. Transcription termination at the *trp* operon attenuators of *Escherichia coli* and *Salmonella typhimurium*: RNA secondary structure and regulation of termination. *Proc. Natl. Acad. Sci. USA*. **74**, 4365–4369.
94. Gemmill R.M., Wessler S.R., Keller E.B., Calvo J.M. 1979. *leu* operon of *Salmonella typhimurium* is controlled by an attenuation mechanism. *Proc. Natl. Acad. Sci. USA*. **76**, 4941–4945.
95. Keller E.B., Calvo J.M. 1979. Alternative secondary structures of leader RNAs and the regulation of the *trp, phe, his, thr*, and *leu* operons. *Proc. Natl. Acad. Sci. USA*. **76**, 6186–6190.
96. Blumenberg M., Yanofsky C. 1982. Evolutionary divergence of the *Citrobacter freundii* tryptophan operon regulatory region: Comparison with other enteric bacteria. *J. Bacteriol*. **152**, 57–62.
97. Hauser C.A., Sharp J.A., Hatfield L.K., Hatfield G.W. 1985. Pausing of RNA polymerase during in vitro transcription through the *ilv*B and *ilv*GEDA attenuator regions of *Escherichia coli* K12. *J. Biol. Chem*. **260**, 1765–1770.
98. Lynn S.P., Burton W.S., Donohue T.J., Gould R.M., Gumport R.I., Gardner J.F. 1987. Specificity of the attenuation response of the threonine operon of *Escherichia coli* is determined by the threonine and isoleucine codons in the leader transcript. *J. Mol. Biol*. **194**, 59–69.
99. Herry D.M., Dunican L.K. 1993. Cloning of the *trp* gene cluster from a tryptophan-hyperproducing strain of *Corynebacterium glutamicum*: Identification of a mutation in the *trp* leader sequence. *Appl. Environ. Microbiol*. **59**, 791–799.
100. Lin C., Paradkar A.S., Vining L.C. 1998. Regulation of an anthranilate synthase gene in *Streptomyces venezuelae* by a *trp* attenuator. *Microbiology.* **144**, 1971–1980.
101. Vitreshchak A.G., Gel'fand M.S. 2000. Computer analysis of signals of regulation in bacterial genomes.

Attenuators of operons of aromatic amino acids metabolism. *Mol. Biol*. **34**, 545–552.

102. Vitreschak A.G., Lyubetskaya E.V., Shirshin M.A., Gelfand M.S., Lyubetsky V.A. 2004. Attenuation regulation of amino acid biosynthetic operons in proteobacteria: Comparative genomics analysis. *FEMS Microbiol. Lett*. **234**, 357–370.
103. Merino E., Yanofsky C. 2005. Transcription attenuation: A highly conserved regulatory strategy used by bacteria. *Trends Genet*. **21**, 260–264.
104. Poulsen P., Jensen K.F. 1987. Effect of UTP and GTP pools on attenuation at the *pyr*E gene of *Escherichia coli. Mol. Gen. Genet*. **208**, 152–158.
105. Roland K.L., Powell F.E., Turnbough C.L., Jr. 1985. Role of translation and attenuation in the control of *pyr*BI operon expression in *Escherichia coli* K-12. *J. Bacteriol*. **163**, 991–999.
106. Donahue J.P., Turnbough C.L., Jr. 1994. Nucleotide-specific transcriptional pausing in the *pyr*BI leader region of *Escherichia coli* K-12. *J. Biol. Chem*. **269**, 18,185–18,191.
107. Liu J., Turnbough C.L., Jr. 1994. Effects of transcriptional start site sequence and position on nucleotide-sensitive selection of alternative start sites at the *pyr*C promoter in *Escherichia coli. J. Bacteriol*. **176**, 2938–2945.
108. Liu C., Heath L.S., Turnbough C.L., Jr. 1994. Regulation of *pyr*BI operon expression in *Escherichia coli* by UTP-sensitive reiterative RNA synthesis during transcriptional initiation. *Genes Dev*. **8**, 2904–2912.
109. Qi F., Turnbough C.L., Jr. 1995. Regulation of *cod*BA operon expression in *Escherichia coli* by UTP-dependent reiterative transcription and UTP-sensitive transcriptional start site switching. *J. Mol. Biol*. **254**, 552–565.
110. Tu A.H., Turnbough C.L., Jr. 1997. Regulation of *upp* expression in *Escherichia coli* by UTP-sensitive selection of transcriptional start sites coupled with UTP-dependent reiterative transcription. *J. Bacteriol*. **179**, 6665–6673.
111. Han X., Turnbough C.L., Jr. 1998. Regulation of carAB expression in *Escherichia coli* occurs in part through UTP-sensitive reiterative transcription. *J. Bacteriol*. **180**, 705–713.
112. Kwak J.H., Choi E.C., Weisblum B. 1991. Transcriptional attenuation control of ermK, a macrolide-lincosamide-streptogramin B resistance determinant from *Bacillus licheniformis. J. Bacteriol*. **173**, 4725–4735.
113. Choi S.S., Kim S.K., Oh T.G., Choi E.C. 1997. Role of mRNA termination in regulation of *erm*K. *J. Bacteriol*. **179**, 2065–2067.
114. Su Y.A., He P., Clewell D.B. 1992. Characterization of the tet(M) determinant of Tn916: Evidence for regulation by transcription attenuation. *Antimicrob. Agents Chemother*. **36**, 769–778.
115. Dubnau D. 1984. Translational attenuation: The regulation of bacterial resistance to the macrolide-lincosamide-streptogramin B antibiotics. *CRC Crit. Rev. Biochem*. **16**, 103–132.
116. Hue K.K., Bechhofer D.H. 1992. Regulation of the macrolide-lincosamide-streptogramin B resistance gene *ermD. J. Bacteriol*. **174**, 5860–5868.
117. Harrod R., Gu Z., Lovett P.S. 1994. Analysis of the secondary structure that negatively regulates inducible cat translation by use of chemical probing and mutagenesis. *Gene*. **140**, 79–83.
118. Wang Y., Rotman E.R., Shoemaker N.B., Salyers A.A. 2005. Translational control of tetracycline resistance and conjugation in the *Bacteroides* conjugative transposon CTnDOT. *J. Bacteriol*. **187**, 2673–2680.
119. Chen G., Yanofsky C. 2004. Features of a leader peptide coding region that regulate translation initiation for the anti-TRAP protein of *B. subtilis. Mol. Cell*. **13**, 703–711.
120. Rodionov D.A., Dubchak I., Arkin A., Alm E., Gelfand M.S. 2004. Reconstruction of regulatory and metabolic pathways in metal-reducing delta-proteobacteria. *Genome Biol*. **5**, R90.
121. Axmann I.M., Kensche P., Vogel J., Kohl S., Herzel H., Hess W.R. 2005. Identification of cyanobacterial noncoding RNAs by comparative genome analysis. *Genome Biol*. **6**, R73.
122. Chopin A., Biaudet V., Ehrlich S.D. 1998. Analysis of the *Bacillus subtilis* genome sequence reveals nine new T-box leaders. *Mol. Microbiol*. **29**, 662–664.
123. Griffiths-Jones S., Bateman A., Marshall M., Khanna A., Eddy S.R. 2003. Rfam: An RNA family database. *Nucleic Acids Res*. **31**, 439–441.
124. Vogel J., Bartels V., Tang T.H., Churakov G., Slagter-Jager J.G., Huttenhofer A., Wagner E.G. 2003. RNomics in *Escherichia coli* detects new sRNA species and indicates parallel transcriptional output in bacteria. *Nucleic Acids Res*. **31**, 6435–6443.
125. Gutierrez-Preciado A., Jensen R.A., Yanofsky C., Merino E. 2005. New insights into regulation of the tryptophan biosynthetic operon in Gram-positive bacteria. *Trends Genet*. **21**, 432–436.