Breaker Laboratory

Molecule of the Year 2006b

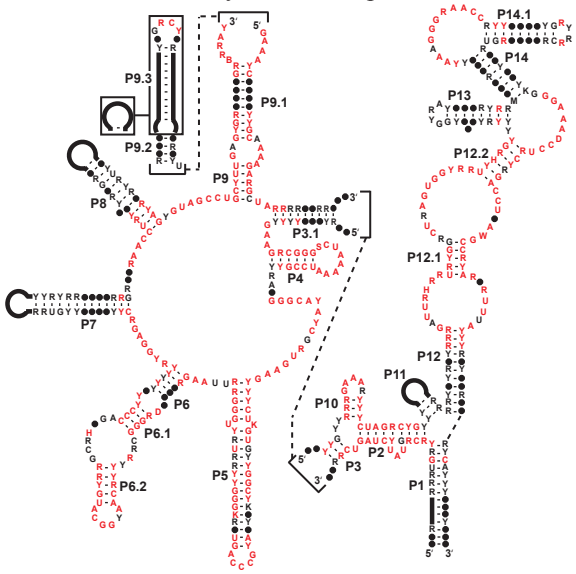
Riboswitches as Drug Targets

Fig. 3. The distribution of known riboswitch classes in various pathogenic bacteria. The wide distribution of numerous riboswitch classes provides opportunities to create metabolite analogs that kill pathogens by binding to riboswitches and deactivating expression of enzymes that participate in essential metabolic pathways.

	TPP	FMN	AdoCbl	Purine	SAM1	SAM2	SAM3	Lysine	GlcN6P	Glycine	PreQ$_1$
A. baumannii	1(3)	1(1)	1(1)	--	--	--	--	--	--	1*(1)	
B. anthracis	6(19)	2(5)	1(1)	6(9)	17(36)	--	--	4(4)	1(2)	1(1)	2(5)
B. melitensis	**2(11)**	1(1)	**2(5)**	--	--	1(1)	--	--	--	1*(3)	--
E. faecalis	2(5)	--	2(4)	1(2)	--	--	1(1)	1(1)	1(1)	--	2(3)
E. coli	3(11)	**1(1)**	**1(2)**	--	--	--	--	1(1)	--	--	--
F. tularensis	1(1)	1(5)	--	--	--	1(1)	--	--	--	--	1(1)
H. influenza	**3(11)**	1(1)	--	--	--	--	--	1(1)	--	1*(1)	1(1)
H. pylori	1(2)	--	--	--	--	--	--	--	--	--	--
L. monocytogenes	2(5)	1(1)	2(20)	2(3)	7(14)	--	--	1(1)	1(1)	1(3)	1(1)
M. tuberculosis	2(6)	--	2(4)	--	--	--	--	--	--	2*(3)	--
P. aeruginosa	1(1)	1(2)	5(24)	--	--	--	--	--	--	--	--
S. enterica	3(11)	**1(1)**	2(22)	--	--	--	--	--	--	--	--
S. aureus	2(7)	2(5)	--	1(2)	**4(6)**	--	--	2(2)	1(1)	1(3)	2(4)
S. pneumoniae	4(11)	1(4)	--	1(2)	--	--	1(1)	--	--	1(1)	--
V. cholera	2(7)	1(1)	1(1)	--	--	--	--	3(3)	--	1(1)	--
Y. pestis	3(8)	1(1)	1(2)	--	--	--	--	--	--	--	--

OLE RNAs

Fig. 4. Consensus sequence and structural model for OLE RNAs. OLE RNAs are strikingly complex and highly conserved RNAs that likely have a complex function.



In recognition of the possible utility of riboswitches as targets for novel classes of antibacterial drugs[1-3], and in recognition of the striking complexity and unusual phylogenetic distribution of OLE RNAs[4], the status of Breaker Laboratory "Molecule of the Year" is conferred upon these findings.

Analogs of metabolites recognized by riboswitches have proven to bind specific riboswitches and repress the expression of essential metabolic genes, thereby killing bacteria. These findings indicate that some riboswitches in bacterial or fungal pathogens might serve as useful targets for novel classes of antibiotics. Also, the discovery of OLR RNA (an ornate and large RNA that is found almost exclusively in extremophilic organisms) suggests that more noncoding RNAs with complex functions are likely to be discovered.

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