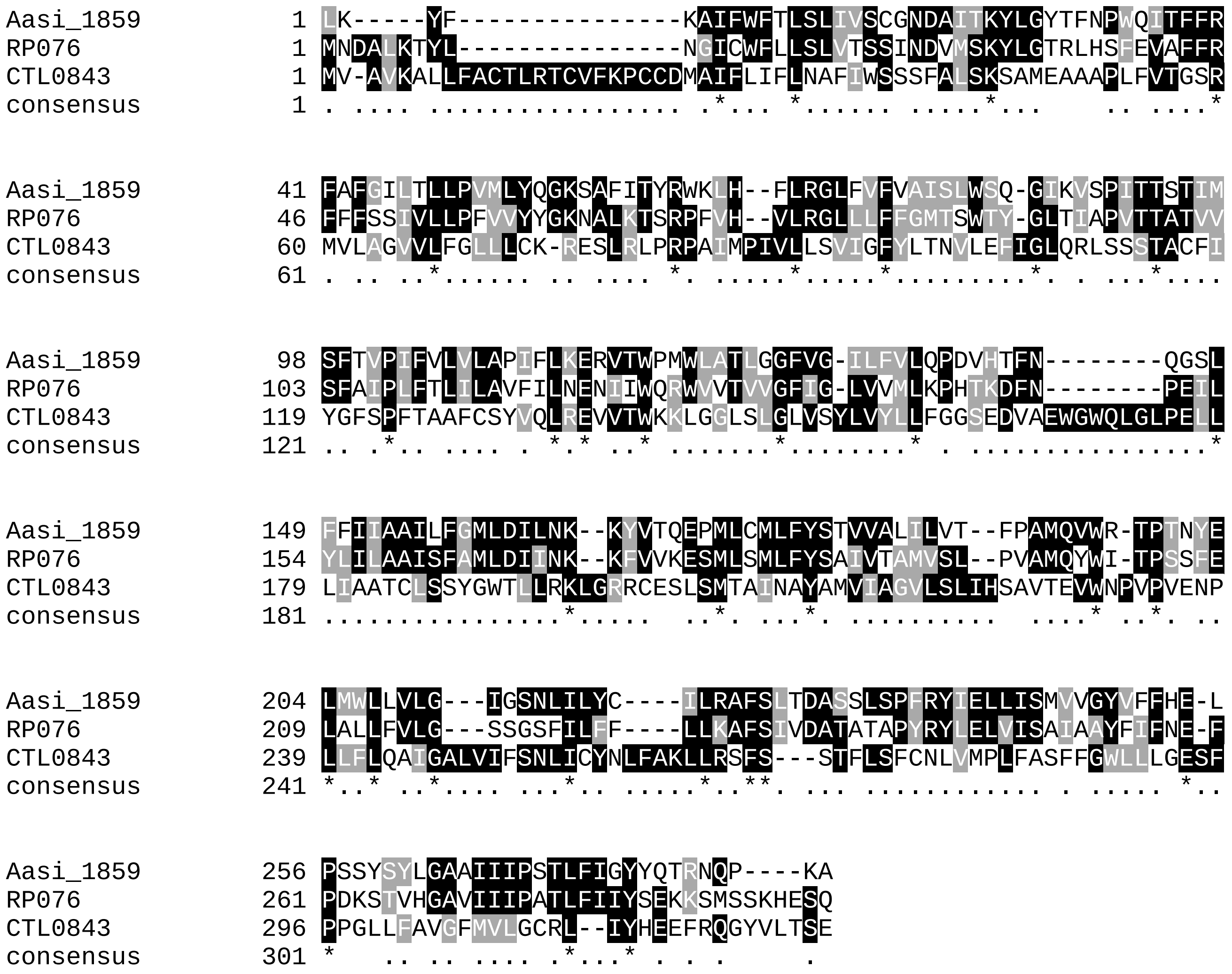
Table S1: Enzymes proposed to require SAM as cofactor encoded in the *A. asiaticus* genome.

A. asiaticus **locus_tag**	**Description**	**Best hit in UniProtKB/Swiss-Prot (considering only functionally characterized proteins), (GenBank accession number, % amino acid identity)**	**PFAM family**
Aasi_0005	TrmA family tRNA (Uracil-5-)-methyltransferase	RlmCD *Bacillus subtilis* 168 (CAB12493.1., 31%)	tRNA (Uracil-5-)-methyltransferase (PF05958)
Aasi_0010	TrmD; tRNA (guanine-N(1)-)-methyltransferase [EC: 2.1.1.228]	TrmD *E. coli* (YP_490830.1 ,40%)	tRNA (Guanine-1)-methyltransferase (PF01746)
Aasi_0020	HemK/PrmC family modification methylase	PrmB *E. coli* (AAC75390.2 ,33%)	Methyltransferase small domain (PF05175)
Aasi_0275	GlyA Serine hydroxymethyltransferase [EC: 2.1.2.1]	GlyA *B. subtilis* (CAA86110.1, 54%)	Serine hydroxymethyltransferase (PF00464)
Aasi_0280	Putative 6-O-methylguanine DNA methyltransferase	Ogt *E. coli* (CAA68548.1, 34%)	6-O-methylguanine DNA methyltransferase, DNA binding domain (PF01035)
Aasi_0286	Methylated-DNA-protein-cysteine methyltransferase [EC: 2.1.1.63]	Ada *E. coli* (AAA23412.1, 29%)	6-O-methylguanine DNA methyltransferase, DNA binding domain (PF01035); 6-O-methylguanine DNA methyltransferase, ribonuclease-like domain (PF02870)
Aasi_0466	GidB/rsmG; ribosomal RNA small subunit methyltransferase G [EC: 2.1.1.-]	RsmG *B. subtilis* (CAA44405.1, 34%)	rRNA small subunit methyltransferase G (PF02527)
Aasi_0566	Putative O-methyltransferase	COMTD1 *H. sapiens* (AAQ88840.1, 30%)	O-methyltransferase (PF01596)
Aasi_0584	Tetrapyrrole methylase family protein	Rsml *E. coli* (AAC76180.1, 30%)	Tetrapyrrole (Corrin/Porphyrin) Methylases (PF00590)
Aasi_0766	RNA methyltransferase	RlmB *E. coli* (AAA97076.1, 29%)	SpoU rRNA Methylase family (PF00588)
Aasi_1616	RlmN; ribosomal RNA large subunit methyltransferase N [EC: 2.1.1.192]	RlmN *E. coli* (AAA21359.1, 44%)	Radical SAM superfamily (PF04055)
Aasi_0780	QueA; S-adenosylmethionine:tRNA ribosyltransferase-isomerase	QueA *B. subtilis* (CAB75332.1, 39%)	Queuosine biosynthesis protein (PF02547)
Aasi_1647	RNA methyltransferase, TrmH family	RlmB *E. coli* (AAA97076.1, 26%)	SpoU rRNA Methylase family (PF00588)
Aasi_0908	RsmH; Ribosomal RNA small subunit methyltransferase H [EC: 2.1.1.199]	RsmH *E. coli* (CAA36283.1, 41%)	MraW methylase family (PF01795)
Aasi_1135	Protein-L-isoaspartate(D-aspartate) O-methyltransferase [EC: 2.1.1.77]	Pcm *E. coli* (AAA24302.1, 34%)	Protein-L-isoaspartate(D-aspartate) O-methyltransferase (PCMT) (PF01135)
Aasi_1164	RNA methyltransferase, TrmH family	RlmB *E. coli* (AAA97076.1, 37%)	SpoU rRNA Methylase family (PF00588)
Aasi_1234	Putative methyltransferase	UbiE *E. coli* (AAA67628.1, 22%)	Methyltransferase domain (PF13847)



```
Aasi_1859        1 LK-----YF---------------KAIFWFTLSLIVSCGNDAITKYLGYTFNPWQITFFR
RP076            1 MNDALKTYL---------------NGICWFLLSLVTSSINDVMSKYLGTRLHSFEVAFFR
CTL0843          1 MV-AVKALLFACTLRTCVFKPCCDMAIFLIFLNAFIWSSSFALSKSAMEAAAPLFVTGSR
consensus        1 . .... ................. .*... *...... .....*...    .. ....*

Aasi_1859       41 FAFGILTLLPVMLYQGKSAFITYRWKLH--FLRGLFVFVAISLWSQ-GIKVSPITTSTIM
RP076           46 FFFSSIVLLPFVVYYGKNALKTSRPFVH--VLRGLLLFFGMTSWTY-GLTIAPVTTATVV
CTL0843         60 MVLAGVVLFGLLLCK-RESLRLPRPAIMPIVLLSVIGFYLTNVLEFIGLQRLSSSTACFI
consensus       61 . .. ..*...... .. .... *. .....*.....*.........*. . ...*....

Aasi_1859       98 SFTVPIFVLVLAPIFLKERVTWPMWLATLGGFVG-ILFVLQPDVHTFN--------QGSL
RP076          103 SFAIPLFTLILAVFILNENIIWQRWVVTVVGFIG-LVVMLKPHTKDFN--------PEIL
CTL0843        119 YGFSPFTAAFCSYVQLREVVTWKKLGGLSLGLVSYLVYLLFGGSEDVAEWGWQLGLPELL
consensus      121 .. .*.. .... . *.* ..* .......*........* . ................*

Aasi_1859      149 FFIIAAILFGMLDILNK--KYVTQEPMLCMLFYSTVVALILVT--FPAMQVWR-TPTNYE
RP076          154 YLILAAISFAMLDIINK--KFVVKESMLSMLFYSAIVTAMVSL--PVAMQYWI-TPSSFE
CTL0843        179 LIAATCLSSYGWTLLRKLGRRCESLSMTAINAYAMVIAGVLSLIHSAVTEVWNPVPVENP
consensus      181 ................*.....  ..*. ...*. ..........  ....* ..*. ..

Aasi_1859      204 LMWLLVLG---IGSNLILYC----ILRAFSLTDASSLSPFRYIELLISMVVGYVFFHE-L
RP076          209 LALLFVLG---SSGSFILFF----LLKAFSIVDATATAPYRYLELVISAIAAYFIFNE-F
CTL0843        239 LLFLQAIGALVIFSNLICYNLFAKLLRSFS---STFLSFCNLVMPLFASFFGWLLLGESF
consensus      241 *..* ..*.... ...*.. .....*..**. ... ............ . ..... *..

Aasi_1859      256 PSSYSYLGAAIIIPSTLFIGYYQTRNQP----KA
RP076          261 PDKSTVHGAVIIIPATLFIIYSEKKSMSSKHESQ
CTL0843        296 PPGLLFAVGFMVLGCRL--IYHEEFRQGYVLTSE
consensus      301 *   .. .. .... .*...* . . .     .
```

Figure S1. Amino acid sequence alignment of SAM-transport proteins. The alignment was done with MAFFT (35), shading of conserved amino acid residues was performed with Boxshade available at the Swiss EMBnet server (http://www.ch.embnet.org/index.html). Identical amino acid residues are highlighted in black and similar residues in grey. A consensus line is displayed at the bottom of each alignment block, an asterisk indicates identical positions, and a dot indicates similar positions.

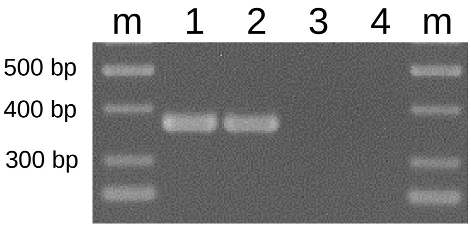
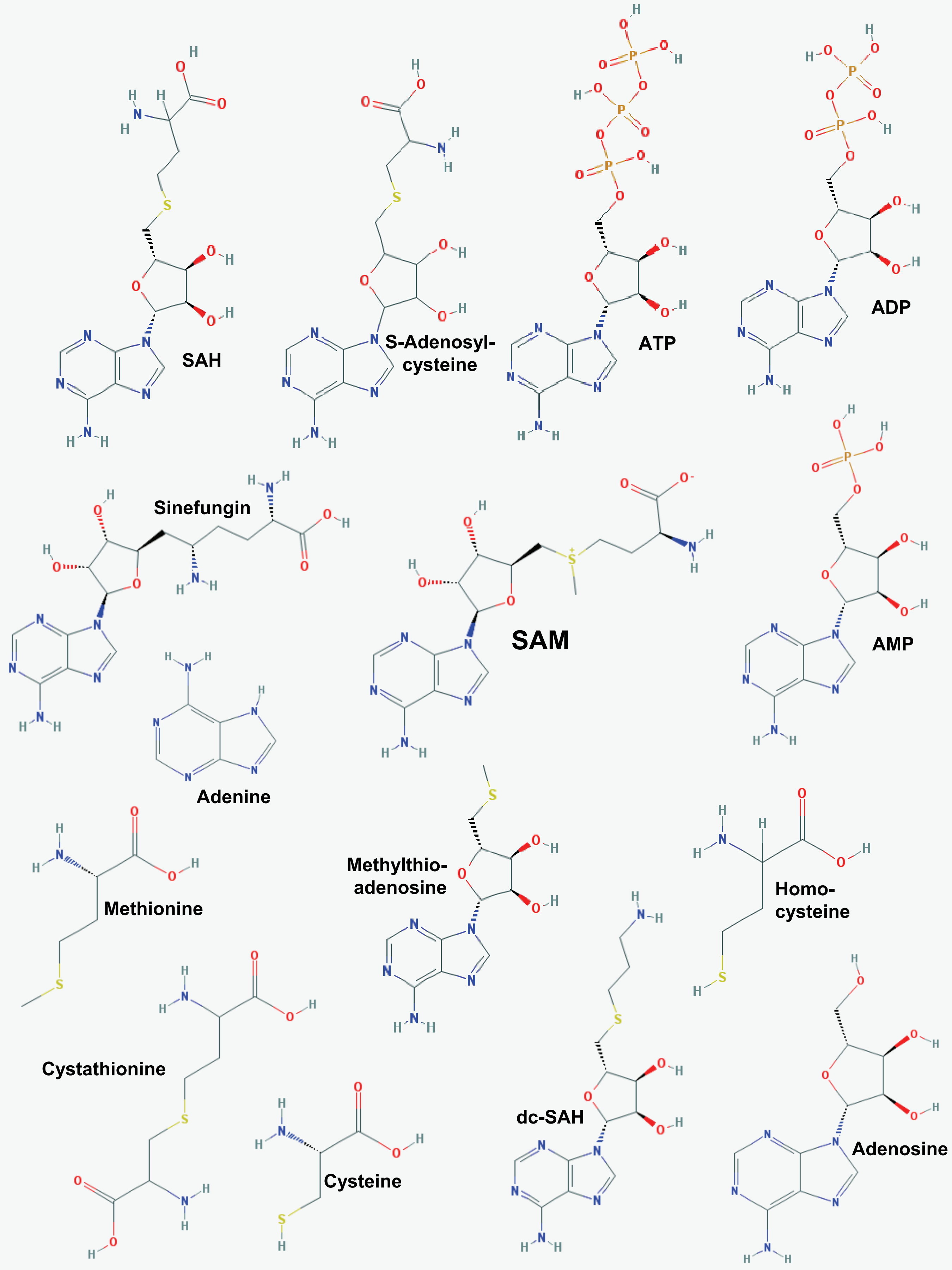


Figure S2. Transcription of *Aasi_1859* during intracellular growth of *A. asiaticus* within its *Acanthamoeba* host. Transcription of *Aasi_1859* was analyzed with reverse transcriptase PCR. Lane **1**: PCR positive controls using *A. asiaticus* DNA; lane **2**: amplification products of cDNA synthesized from whole RNA from amoebae harboring *A. asiaticus;* lane **3**: PCR using whole RNA from amoebae containing *A. asiaticus* (control for the absence of DNA in the RNA preparation, no reverse transcriptase added); lane **4**: PCR negative control (no DNA added); **m**: molecular-size marker. The RT-PCR products shown in lane 2 are derived from two biological replicates.

Figure S3: Structure of potential substrates/inhibitors tested in the effector analysis. Structures were obtained from PubChem (http://pubchem.ncbi.nlm.nih.gov/search/).



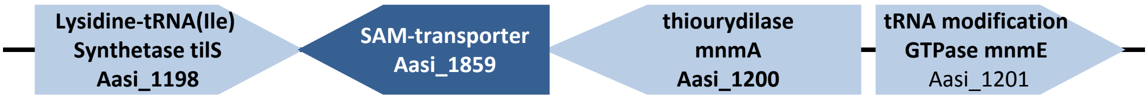


Fig. S4: Genomic organization of Aasi_1859 and surrounding genes