Bacmethy: a novel and convenient tool for investigating bacterial DNA methylation pattern and their transcriptional regulation effects

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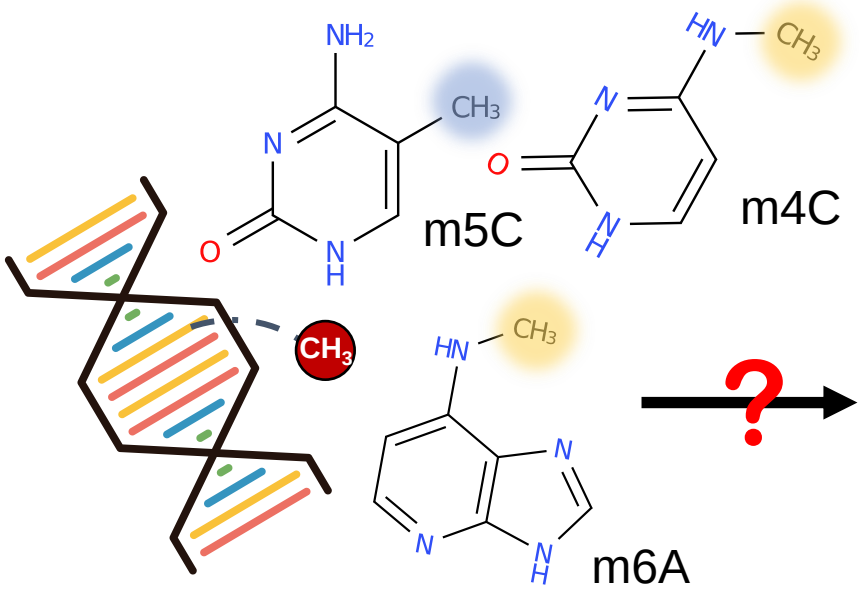
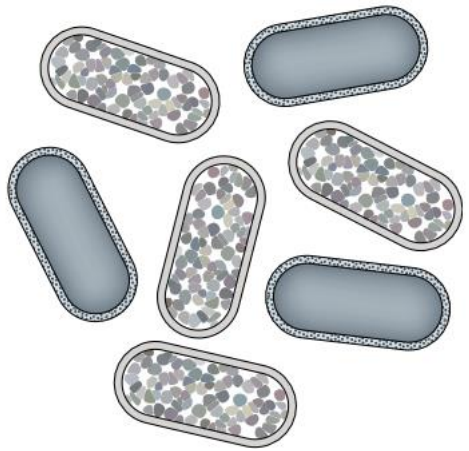
Introduction



? Gene ?

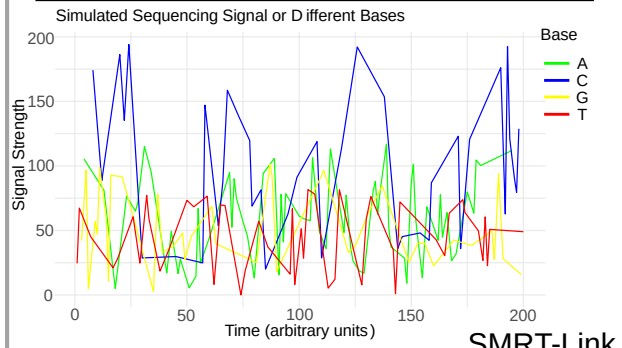


Phenotype

Bacmethy

A user- friendly tools for bacterial methylation analysis

Prerequisite step. Base Modification Analysis of PacBio Sequence Data

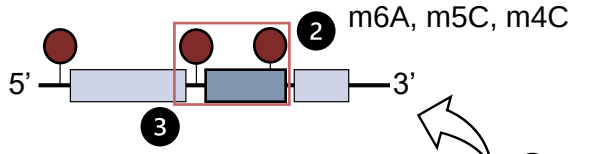


SMRT-Link

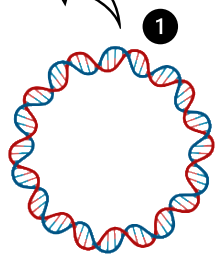
Raw Data → HGAP4 Genome assemble

Raw Data → Base Modification Modification detection

1. Bacmethy Basic Analysis



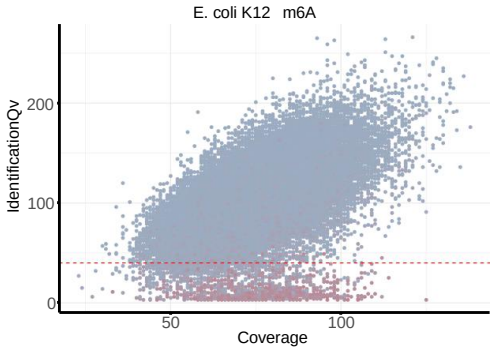
1. Genome annotation
2. DNA methylation sites
3. Filter candidate region



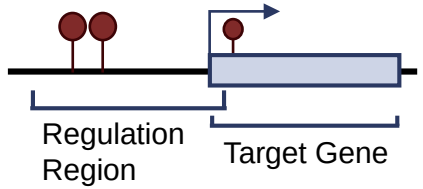
PROKKA, bedtools, FIMO

2. Bacmethy Result

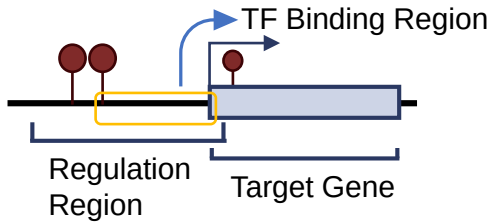
Methylation Ratio Plot



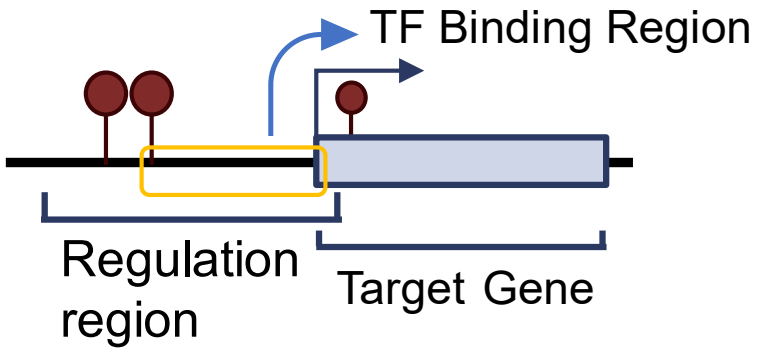
Methylation and Gene Features Table



TFs Binding Integration Table

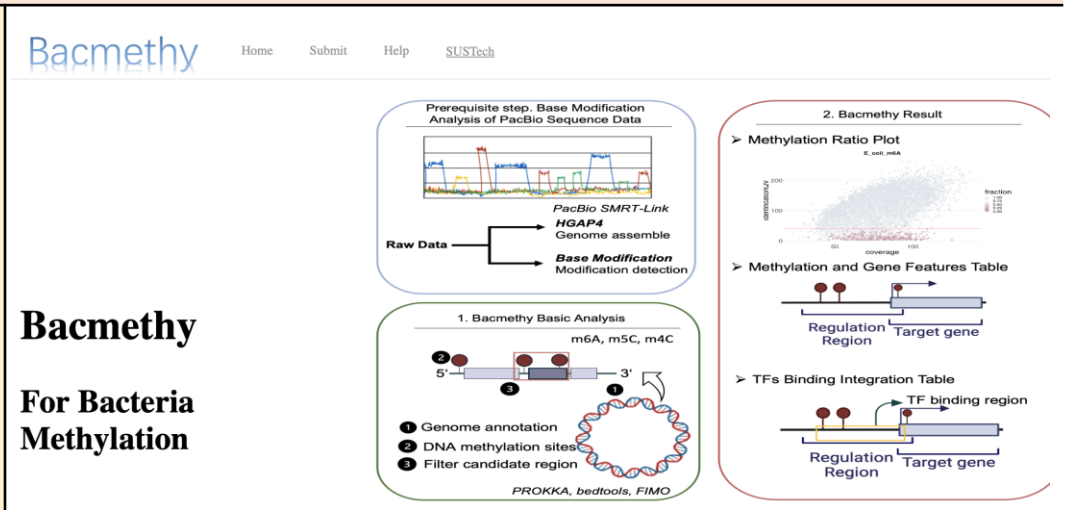


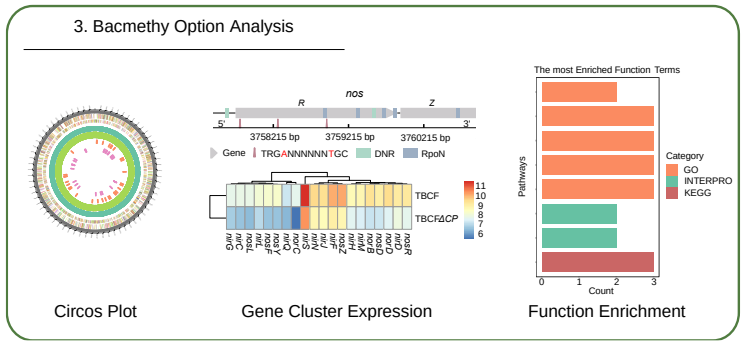
Highlights



Bacmethy tool provides a one-stop analysis and visualization pipeline for effectively characterizing bacterial DNA methylation modification features and predicting the regulation patterns.

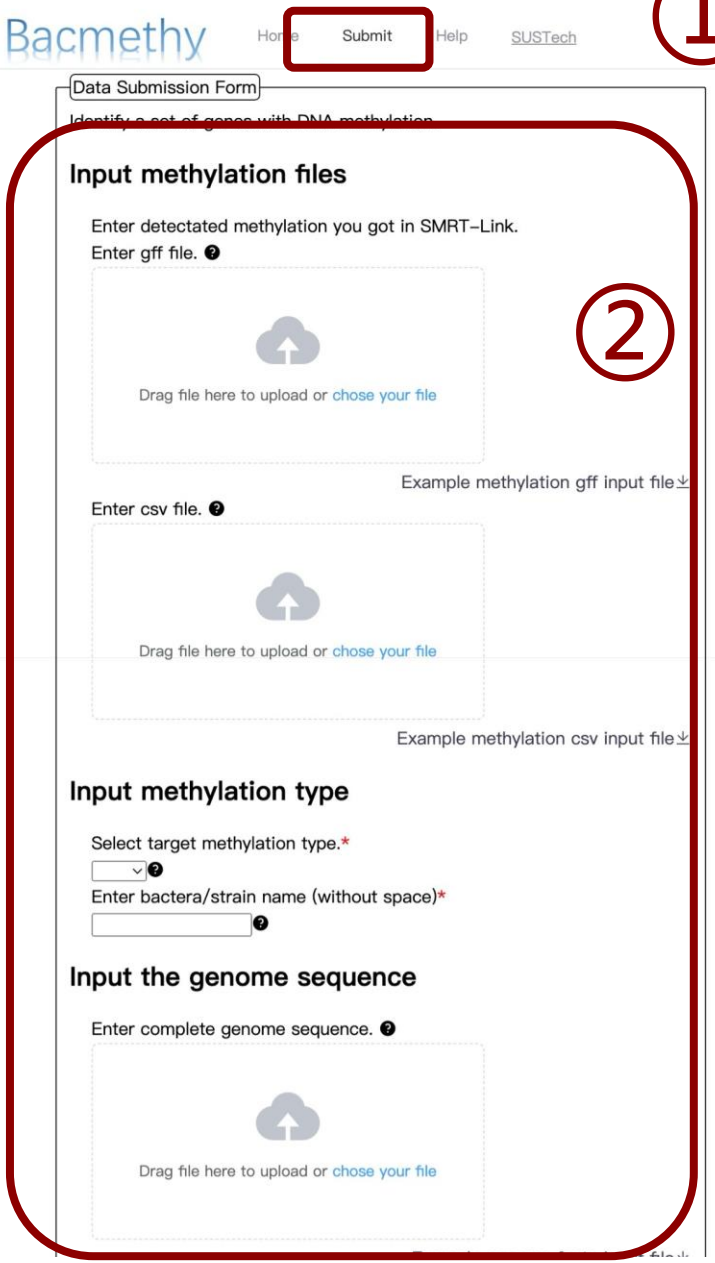
Bacmethy offers both a local run function and an online interface analysis service, providing significant convenience for researchers without coding abilities.





Bacmethy provides useful information for decoding the underlying molecular mechanisms of how DNA methylation regulates bacterial cellular and physiological functions.

Overview of Bacmethy websever

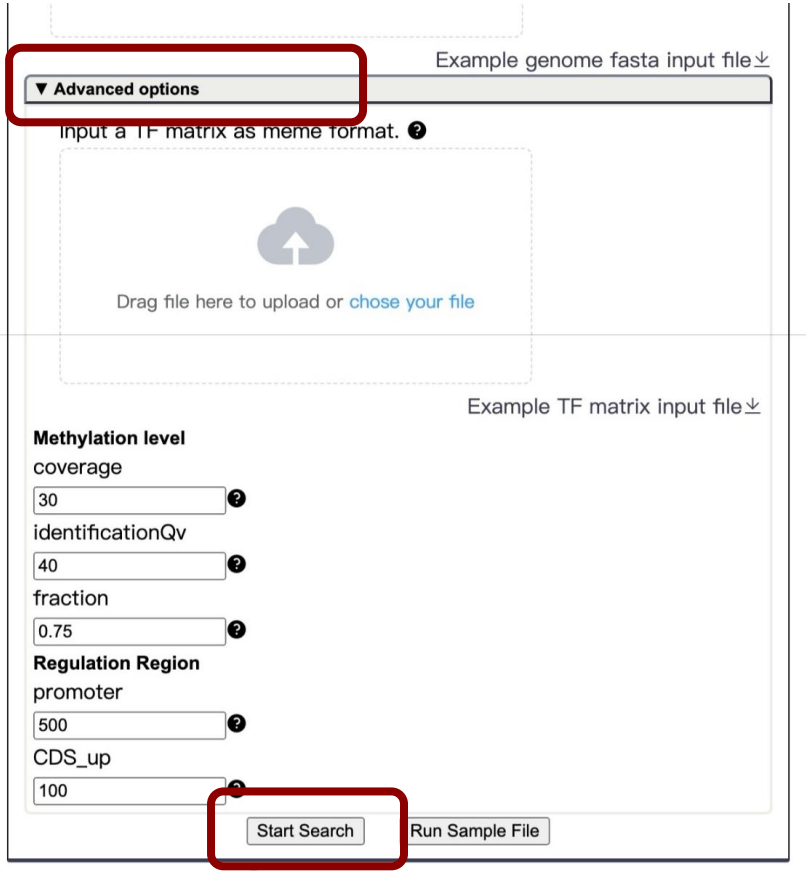


① Click "submit" to enter the task submission page.

②

- Upload modification detection files (motifs.csv and motifs.gff), and a complete genome sequence (fasta file).
- Select target methylation type and typing the name of the sample

③ Click ”Advance options" to add transcription factor analysis and modify other parameters.



④ Click ”Start Search" to submit the task.

https://bacmethy.med.sustech.edu.cn

Distribution of the methylated and un(der)methylated motifs

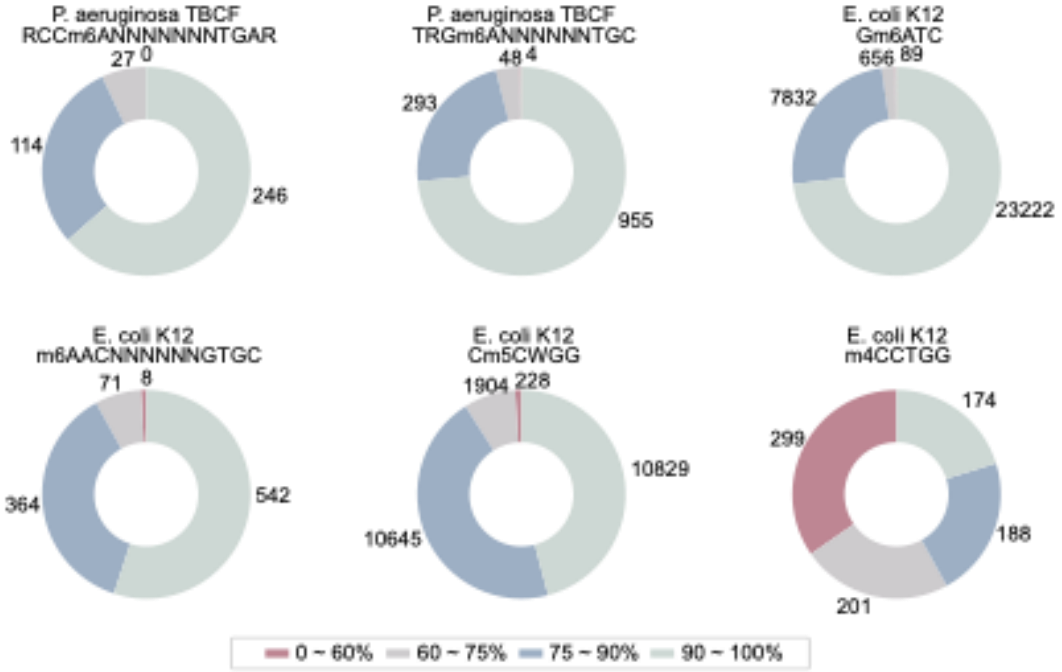
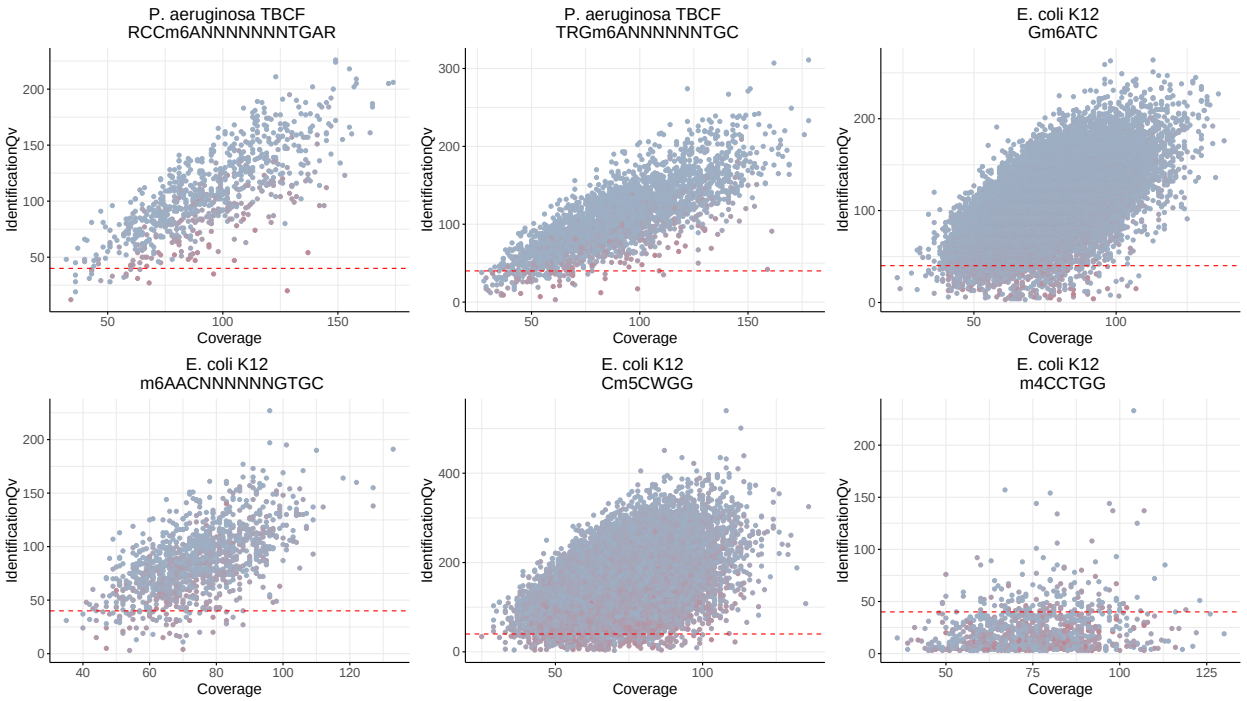


Figure 2 The distribution of metylation fraction and sequencing quality.

(A) The distribution of methylation fraction per motif in the bacterial stains, where the title of each circle includes the strain name and recognition motif, and the counts indicate the number of motifs with diverse ratios of 0 - 60% (red), 60 - 75% (grey), 75 - 90% (blue), and 90 - 100% (green).

(B) The scatter plots for the quality distribution of methylated and un(der)methylated motifs across the strains per MTase motif (6 MTase motifs for *P.aeruginosa* TBCF and *E.coli* K12). The x-axis shows the reads coverage, and the y-axis shows the identificationQV. The methylation fraction is represented by dot color, with blue indicating a high methylation fraction and red indicating a low fraction. MTase, methytransferase; QV, quality value.



Distribution of methylation sites in the regulation region

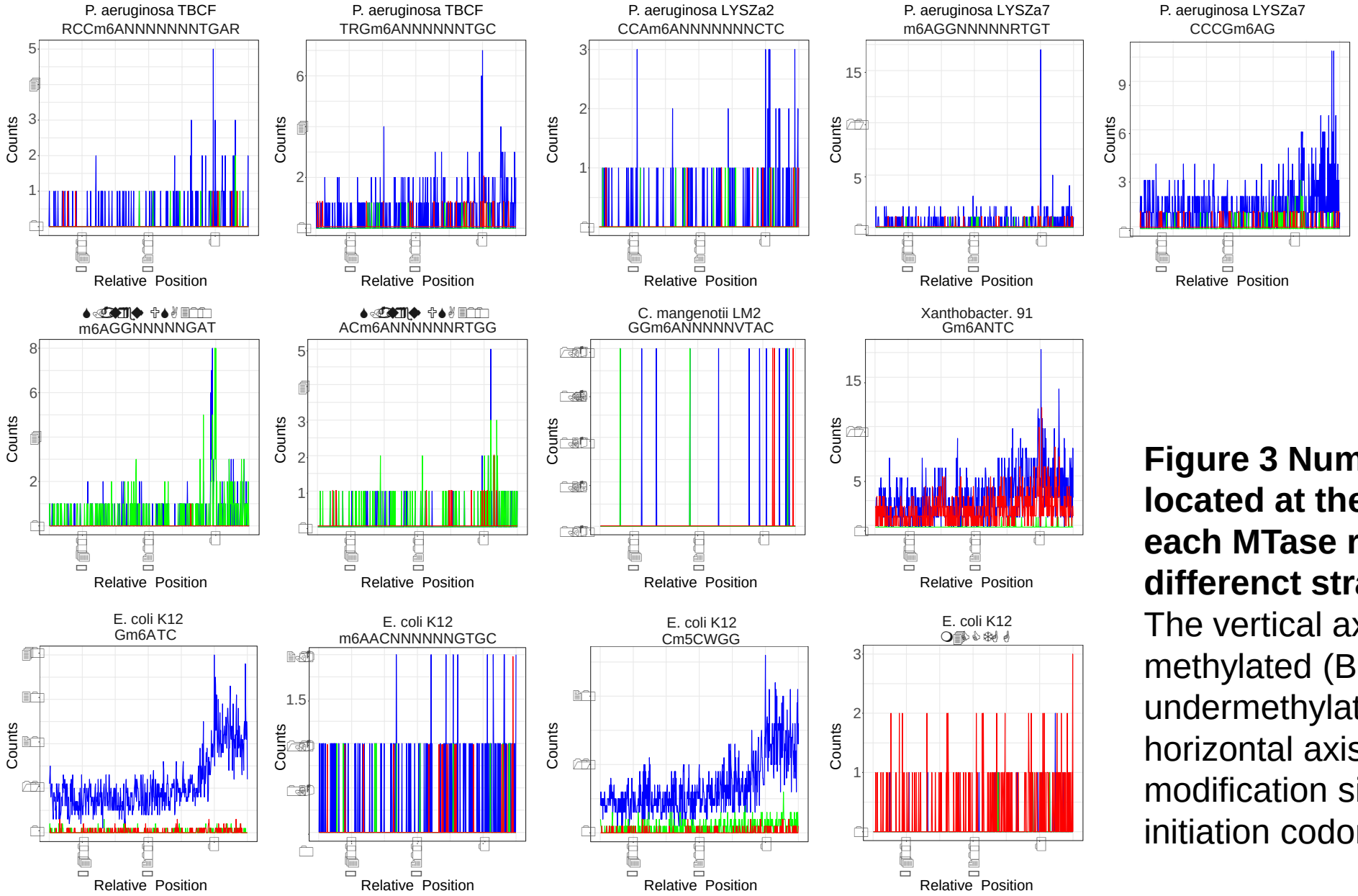


Figure 3 Number of methylated sites located at the Regulation Region for each MTase recognition motif in differenct strains.

The vertical axis shows the count of methylated (Blue), unmethylated (Red), or undermethylated (Green) sites. The horizontal axis indicates the position of modification sites located around the ATG initiation codon.

Functional enrichment of motifs

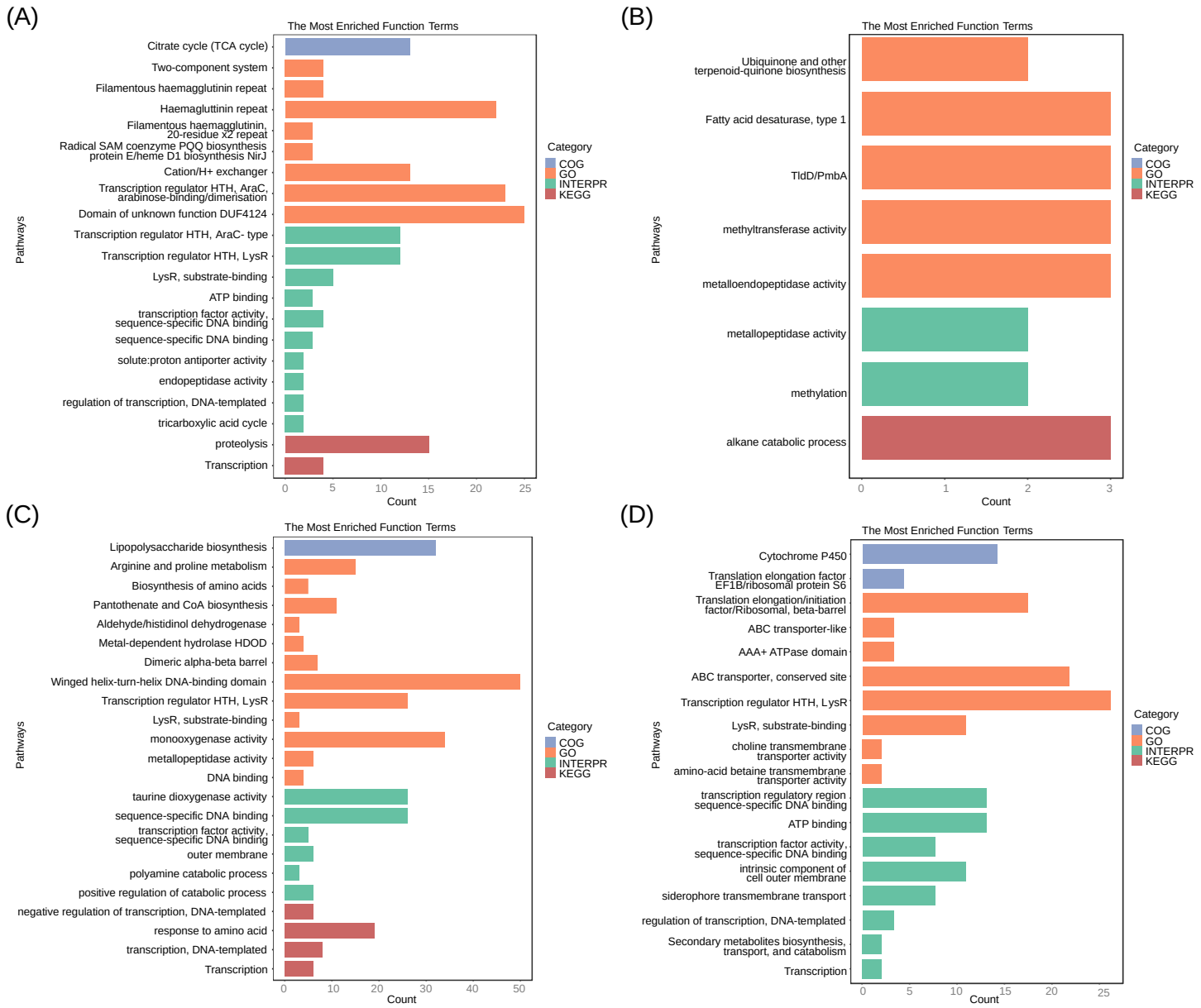


Figure 4 Function enrichment results of methylated genes in *Pseudomonas.aeruginosa* strains.

Scanning the gene regulation regions with methylated motifs to identify transcription regulation effector binding sites

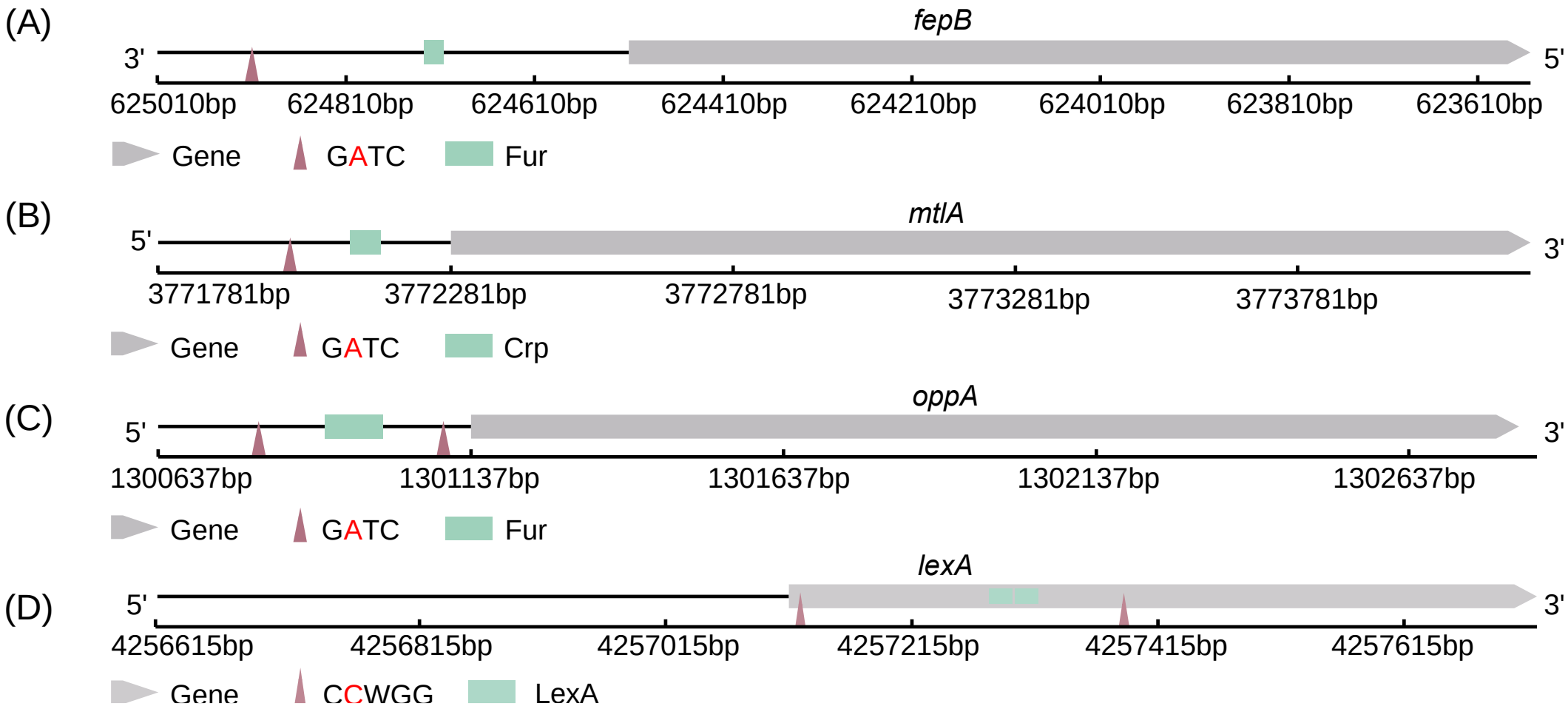


Figure 5 DNA methylation and TFBS location diagrams based on Bacmethy analysis in *E. coli* K12.

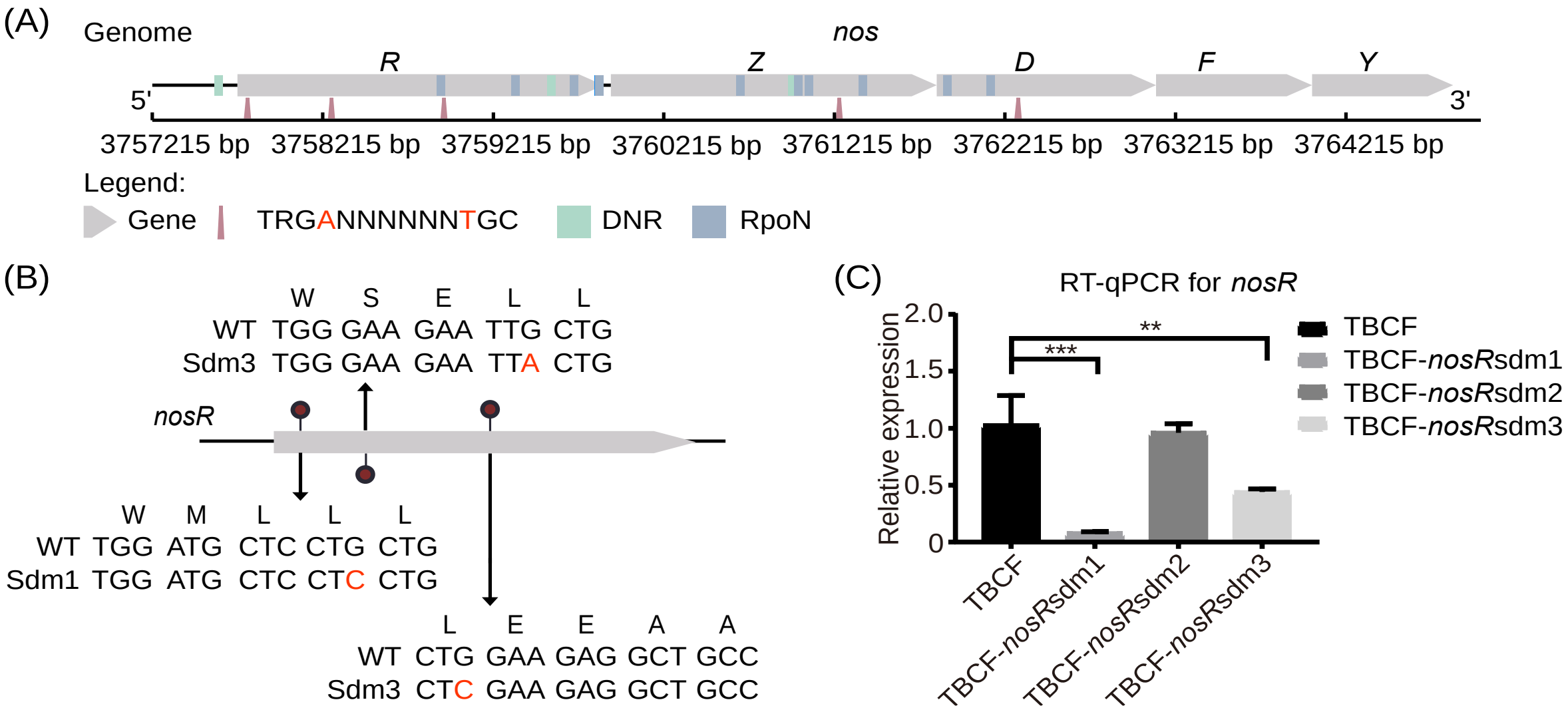


Figure 6 Experimental validation of Bacmethy analysis results for the *P. aeruginosa* TBCF strain.

Summary

- In this study, we developed Bacmethy, a novel and convenient tool for investigating bacterial DNA methylation pattern and their transcriptional regulation effects.

- The Bacmethy tool can contribute to the identification of putative novel targets of DNA methylation regulation, thereby deepening our understanding on bacterial epigenetics network and advancing our knowledge of cellular and physiological function regulation

- Bacmethy code is freely available, and Docker image is downloadable. Bacmethy has been made available as user-friendly webserver interface at https://bacmethy.med.sustech.edu.cn.

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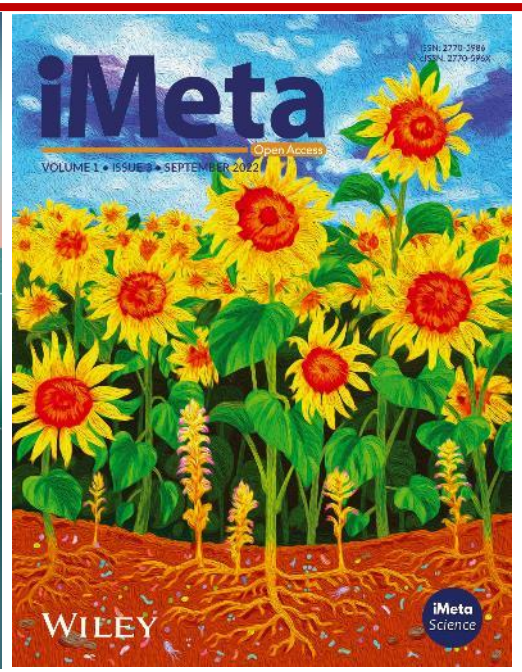

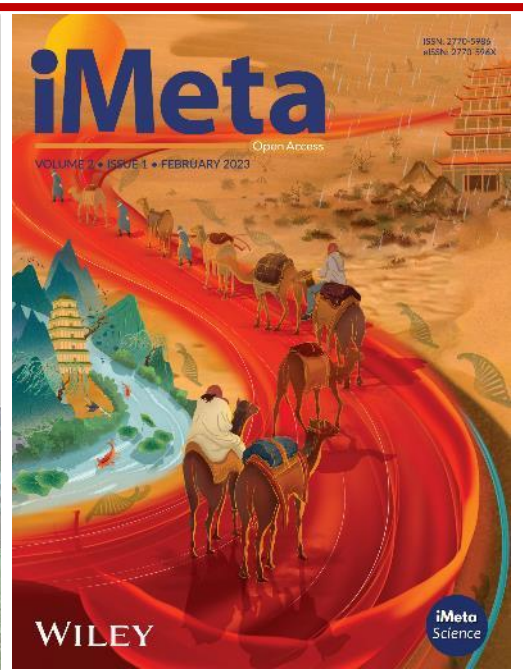

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