C-5-12

Methylome diversification through changes in the sequence specificity of DNA methyltransferases

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Helicobacter pylori, a human gastric pathogen, has a large number of DNA methyltransferase genes with each strain carrying a unique repertoire. Previous genome comparison works suggested that these methyltransferases often change DNA sequence specificity through movement of amino-acid sequences in the target recognition domains between genes and within a gene (Domain Movement). By Single-Molecule Real-Time sequencing technology, we detected methylated DNA sites throughout several closely related genomes. Number of methylated sites varied between strains and had correlation with number of methyltransferase genes in each strain. We successfully deduced DNA sequence motifs for methylation and assigned each of them to a specific amino-acid sequence group of target recognition domains in the specificity determinant genes. Overall, the methylome turned out to be quite variable among the closely-related strains, although there are hypermethylated loci conserved in all the strains. Hypomethylated sites were also found on genomic island regions. As expected from their effects on gene expression, knockout of a specificity gene led to changes in the transcriptome. These results provide evidence for proposed mechanisms of sequence-specificity change in the DNA methyltransferases and lend support to the concept of epigenetics-driven adaptive evolution.