DNA methylation in *Escherichia coli*

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The DNA of *E. coli* K-12 contains 6-methyladenine (6-meA) and 5-methylcytosine (5-meC). Approximately two percent of all adenines are methylated and one percent of all cytosines (1,2,3). These methylated bases are formed by DNA methylases which transfer the methyl group from S-adenosyl-L-methionine to adenine or cytosine in specific base sequences in newly synthesized daughter strand DNA (3,4). Three distinct DNA methylases have been detected in *E. coli* K-12 (Table 1). For information regarding the hsd adenine methylase the reader is referred to a recent review (5).

One approach to determine the biological role of methylated bases in DNA, is to isolate and characterize mutant strains which lack modified bases. The examination of such strains may uncover the functions of methylated bases. To this end, mutant strains were isolated from *E. coli* K-12 (6,7) which are deficient in 6-meA (*dam* mutants) or 5-meC (*dcm* mutants).

The *dcm* mutations map in a single gene (8) and are recessive. The *dcm* gene product is not required for viability since a mutant deleted for this gene shows no gross abnormality (9) and the growth rate of *dcm*+ and *dcm*− strains is the same.

### Table 1

DNA methylases of *E. coli* K-12 (3,4,5)

<table>
<thead>
<tr>
<th>Gene</th>
<th>Recognition Sequence</th>
<th>Methylase</th>
</tr>
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<tbody>
<tr>
<td><em>hsd</em></td>
<td>-AAT(N6)GTGC-</td>
<td>Adenine</td>
</tr>
<tr>
<td><em>dcm</em></td>
<td>-CC(A/T)GG-</td>
<td>Cytosine</td>
</tr>
<tr>
<td><em>dam</em></td>
<td>-GATC-</td>
<td>Adenine</td>
</tr>
</tbody>
</table>

E. Usdin et al., *Biochemistry of S-Adenosylmethionine and Related Compounds* © The contributors 1982
DNA sequence analysis has shown that 5-meC is involved in generating single base changes spontaneously (10). This appears to occur through spontaneous deamination of 5-meC to yield thymine. The G/T mismatch upon DNA replication would result in a G-C to A-T base pair change. Deamination of cytosine is not mutagenic, since a specific repair system excises uracil, the deamination product.

Evidence for a role for 5-meC residues in genetic recombination has been obtained (11). One piece of evidence is that dcm mutations suppress the hyper-rec phenotype of arl-bacteria. The nature of the interaction between arl and dcm genes and/or products is not clear at present but are under intense investigation (11).

Another role for 5-meC residues might be to alter protein-DNA interactions. That is, a protein may bind differentially to a specific region of DNA depending on the state of DNA methylation. Evidence for this has recently been obtained. The lexA repressor binds less well to DNA if the binding site does not contain its single 5-meC residue (12).

All dam mutations, except one, map in a single complementation group and are recessive to the wild type allele (9). In contrast to dcm mutants, dam strains show a variety of phenotypic traits (3). These include increased spontaneous mutability; increased sensitivity to certain alkylating agents, base analogs and ultra-violet (UV) light; a hyper-rec phenotype; increased induction of lysogenic bacteriophages; inviability of dam recA-, dam recB-, dam recC- and dam lexA- double mutants and suppression of some dam phenotypic traits by mutL-, mutS-, sin- and uvrD- (13,19). These phenotypes are not present in dam+ revertants of dam mutants (13). The pleiotropy of phenotypes suggests that 6-meA and/or the dam methylase have several biological roles in cellular metabolism.

A model which accounts for some of the phenotypes of dam- strains has been proposed (15). It supposes that 6-meA residues determine strand specificity for repair of mismatched bases. That is, the unmethylated strand of a duplex DNA containing a mismatch is subject to excision, whereas the other methylated strand is not. This model can account for the mutability phenotype; the sensitivity to base analogs and the indirect suppression of dam- by mut- mutations. The mutH, L and S genes have been shown to be involved in mismatch repair (16).