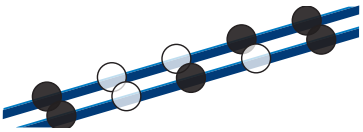
DNA METHYLATION

In vivo enzyme action



A recent study has revealed that the three mammalian DNA methyltransferases have context-dependent contributions to methylation establishment and maintenance *in vivo*.

Arand *et al.* analysed DNA from mouse embryonic stem cells (ESCs) and differentiated cells using a hairpin bisulphite-sequencing strategy. Briefly, this approach involved hairpin DNA linkers designed to capture restriction-enzyme-generated fragments of DNA from four classes of repeat sequence and four single-copy genes in the mouse genome. Bisulphite treatment was then used to convert unmethylated cytosines to uracils; importantly, the linkers contained runs of cytosines to provide accurate assessment of the efficiency of bisulphite conversion. Deep sequencing then enabled the authors to determine the DNA methylation patterns on both strands of DNA at high resolution.

They also carried out this analysis on cells that lacked each of the DNA methyltransferases (DNMTs) — DNMT1, DNMT3A and DNMT3B — alone or in combination. The authors then analysed this data using hidden Markov models to determine the relative contributions of each enzyme to methylation establishment and maintenance in the different genomic regions and cell types studied.

Their findings confirm that, contrary to some previous views based on *in vitro* data, the enzymes do not have exclusive roles in *de novo* methylation or maintenance. Furthermore, some classes of repeats require different combinations of DNMTs. Recently, there has been great interest in non-CpG methylation, and this study shows that in ESCs, CpA methylation occurs at major satellite repeats and at one of the studied single genes, and that it is mediated by DNMT3A and DNMT3B, along with DNMT3L.

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ORIGINAL RESEARCH PAPER Arand, J. *et al.* *In vivo* control of CpG and non-CpG DNA methylation by DNA methyltransferases. *PLoS Genet.* **8**, e1002750 (2012)