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Antisense RNA and DNA methylation in cancer

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DNA methylation is an important epigenetic mark involved in gene regulation. In general, methylation of DNA leads to its repression. In cancers, normal gene expression often becomes disrupted. One way this occurs is by changes in the patterns of DNA methylation. This phenomenon is characterised by an overall loss of genomic DNA methylation. In addition there is *de novo* methylation of CpG islands at tumour suppressor genes and loss of their expression. Such epigenetic changes are coincident with cancer progression, however the underlying molecular mechanisms responsible for these aberrancies are poorly understood.

Antisense RNAs have been implicated in gene silencing and DNA Methylation. These RNAs are believed to play a role in methylation during normal gene regulatory processes such as imprinting and X-inactivation. Furthermore, antisense RNA has been shown to cause methylation at the CpG island of the α -globin gene, *HBA2*, in a patient with α -thalassaemia (Tufarelli *et al.*, 2003).

Since antisense RNAs are associated with DNA methylation and gene repression, the potential links between antisense RNA and hypermethylation of tumour suppressor genes in cancer will be investigated. Cell culture and primary cell models will be examined to establish if antisense transcription is present at tumour suppressor genes in cancer and if this correlates with loss of expression and changes in DNA methylation.