

P016 Methylation of the *ESR1* CpG island in the colorectal mucosa: An 'all or nothing' process in transformed cells and healthy human colon.

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ESR-1 is frequently silenced by CpG-island methylation, both in human colorectal tumours and, in an age-dependent manner, in healthy mucosa (Issa *et al.* Nature Genetics 1994, 7, 536-40). It is not clear however whether methylation of individual cytosines occurs randomly within the epithelial genome, or preferentially within individual cells in an "all-or-nothing" manner. Methylation can be quantified in human DNA residues recovered from faecal samples (Belshaw *et al.*, CEBP 2004, 13, 1495-1501), and methylation status of *ESR1* in faecal samples is significantly correlated with that from colonic mucosa. We used bisulphite-genomic sequencing of DNA from a colorectal cancer cell line (SW48), and from human faecal DNA, to show that the *ESR1* CpG-island is methylated in an allele-specific manner. This provides support for the "all or none" mechanism for methylation of this gene. The results show how age-related methylation of the *ESR-1* CpG-island leads rapidly to silencing of the gene within the cells, and hence the crypt within which it occurs. Preliminary studies with rodent models suggest the rate of methylation of *ESR-1* may be modifiable by dietary folate.