

## BOA6

### **Aberrant CpG island methylation is both an early diagnostic and predictive marker of ovarian cancer**

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Aberrant methylation of CpG islands (CGIs) is a frequent epigenetic event observed at all stages of epithelial ovarian cancer development and is associated with transcriptional silencing of key tumour suppressor genes. Methylation of CGIs can be detected in tumour DNA released into plasma, which means it has potential clinical use both as an early diagnostic and prognostic/predictive marker of this disease. We initially analysed the methylation status of 24 CGIs in a retrospective group of 142 epithelial ovarian cancers and 16 normal adjacent tissues using methylation-specific PCR (MSP) and Combined Bisulphite Restriction Analysis (COBRA) methods. CGI methylation was a frequent event in both early (78%) and late stage (60%) disease. We identified a group of loci which were methylated in 64% of early stage tumours (CGIs linked to the OPCML, RASSF1A and HIC1 genes) and are potentially useful as early detection markers. In addition, the HIC1 CGI was frequently methylated in matched normal adjacent tissues but not in normal ovarian surface epithelium which therefore may represent a premalignant epigenetic event. In late stage tumours, methylation of CGIs associated with either BRCA1, GSTpi or MGMT genes was correlated with improved response to chemotherapy ( $p=0.013$ ). Our findings suggest that CGI methylation patterns may have the potential to impact on early diagnosis and prediction of clinical outcome in patients with ovarian cancer. We are currently validating our results in a prospective collection of 300 epithelial ovarian tumours and matched plasma samples.