Implementation of methylation linear discriminant analysis (MLDA) on CpG Island microarray data of ovarian cancer

W Dai*, J.M. Teodoridis, J. Graham, C. Zeller, J. Paul and R. Brown

Epigenetics Section, OCA Centre and Dept Oncology, Hammersmith Hospital Campus, Imperial College London

Differential Methylation Hybridisation (DMH) is used for analysing genomic DNA methylation. To account for the specific biological features of DNA methylation and non-symmetrical distribution of DMH data, we have developed an algorithm, named Methylation Linear Discriminant Analysis (MLDA), to identify differential methylation based on linear regression models using non-normalised DMH data (Dai *et al.*, 2008).

We designed a focused oligonucleotide microarray covering 596 CpG islands, with on average 24 oligonucleotide probes per island, that have been chosen based on previous studies implicating them as prognostic DNA methylation markers in ovarian cancer. Analysis of methylation of ovarian cell line DNA by DMH showed good reproducibility and allowed further optimisation of methodology. MLDA has been implemented on this data and found 101 and 26 CpG islands differentially methylated between cisplatin-sensitive and resistant ovarian cancer cell lines generated in vitro and in vivo, respectively. Of 14 loci identified in a previous large-scale study (Dai *et al.*, 2008), 13 loci were independently identified by MLDA in the current study. Analysis of the data showed high sensitivity of MLDA and reproducibility of DMH using these arrays. Currently we are conducting an analysis of ovarian tumour DNA to further evaluate these potential prognostic biomarkers.

References

Dai, W. *et al.* (2008). Methylation Linear Discriminant Analysis (MLDA) for identifying differentially methylated CpG islands. *BMC Bioinformatics*, **9**:337.