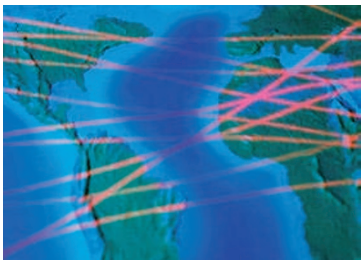
HUMAN EPIGENOMICS

Putting epigenetic variation on the map

Human epigenome projects are hoped to generate new insights into how epigenetics contributes to disease and to provide new biomarkers and therapeutic targets. An understanding of normal epigenetic variation among and within individuals is an essential starting point for such efforts. A recent study provides the most extensive insights so far into variability in DNA methylation among tissues caused by ageing and environmental exposure.

Christensen and colleagues generated array-based profiles of DNA methylation for 217 non-diseased human tissues, in which they studied 1,413 CpG loci that are associated with 773 genes. They found extensive tissue-specific differences in DNA methylation patterns, and methylation profiles at the most informative CpG sites allowed the tissue types to be distinguished. These results confirm and extend those from previous smaller-scale studies that have shown DNA methylation differences among tissues.



Earlier studies also suggested that common environmental exposures contribute to inter-individual variability in DNA methylation patterns. To investigate this connection further, Christensen and colleagues examined DNA methylation variability among individuals in relation to exposure to asbestos, alcohol and tobacco smoke. They looked at individual CpG sites in particular tissue types and found associations between DNA methylation variation and each of these exposures at specific loci.

Ageing-related variability in DNA methylation status was seen for more than 300 CpG sites across all tissues. Interestingly, although previous studies have suggested that there is a general age-associated increase in CpG methylation, the new study showed that some sites undergo a loss of CpG methylation during ageing and that some tissues actually show an overall decrease in this mark. Furthermore, the authors showed that whether a gain or a loss occurs depends on the context of the CpG site: loci in CpG islands tend to gain DNA methylation with age, whereas loci outside CpG islands tend to lose it.

By beginning to catalogue 'normal' intra- and inter-individual differences in DNA methylation, this study will guide the construction of reference epigenomes and the identification of those epigenetic differences that are most informative in relation to disease. Findings such as the context dependency of gain or loss of DNA methylation at CpG loci also provide new clues about the mechanistic basis of epigenetic variability.

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ORIGINAL RESEARCH PAPER Christensen, B. C. *et al.* Aging and environmental exposures alter tissue-specific DNA methylation dependent upon CpG island context. *PLoS Genet.* **5**, e1000602 (2009)