P007 Do age-related diseases develop in cells which are pre-primed by the presence of aberrant patterns of DNA methylation? 
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Alteration in DNA methylation can effect gene transcription and in particular hypermethylation of promoter associated CpG islands leads to gene inactivation. We have studied how methylation at a group of genes alters over the life-course and how these relate to methylation changes observed in major age-related diseases (cancer, specifically ALL, and atherosclerosis). Peripheral blood leukocyte (PBL) DNA was collected from healthy volunteers from different ages and from ALL and atherosclerosis patients. Methylation levels were assessed using pyrosequencing.

The study produced a number of findings: 1) Genes exhibiting variable methylation in PBL samples from healthy volunteers and atherosclerosis patients match those that are highly methylated in leukaemia, suggesting a common underlying mechanism. 2) While methylation levels increase during ageing, a substantial proportion of methylation is already present at birth and may thus alter disease susceptibility throughout life. 3) Increased methylation levels were observed in lymphoid compared to myeloid cells, in healthy individuals, mirroring the patterns seen in leukaemia. 4) Increased methylation levels in ALL remission samples may be related to poor clinical outcome.

The studies to date are compatible with a hypothesis in which altered methylation of disease-related genes pre-exists in a subset of haematopoietic cells and that these cells may be at a significantly increased risk of progression to age-related diseases. This suggests monitoring DNA methylation may be valuable for early diagnosis of these diseases and for monitoring disease progression.