

P050 Epigenetic variants of Type 1 diabetes Susceptibility genes
Beyan H¹, Rakyan VK¹, Hawa MI¹, Beck S²
and RDG Leslie¹

¹ICMS, Queen Mary University, UK. ²Cancer Institute, UCL, UK

Background: Type 1 diabetes mellitus (T1DM) is associated with genetic susceptibility but twin studies emphasize importance of environmental or epigenetic influences. We used monozygotic (MZ) twin pairs discordant for T1DM to analyze methylation of T1DM genes including MHC. Aim: We aim to: A) Identify T1DM-specific epigenetic variant; B) Determine whether T1DM-susceptibility genotypes are associated with specific epigenotypes. We present below the result of the gene analysed. Methods: DNA was extracted from peripheral blood mononuclear cells from 10 selected MZ twin pairs (6 male) mean age 31 years discordant for T1DM (disease duration 17 years) in which the non-diabetic twin is at low disease risk. Candidate regions were analysed for DNA methylation by bisulfite sequencing and whole-genome DNA methylation profiling; results are presented for bisulphate sequencing of HLA-DPB1. Results: Gene methylation profiles were highly conserved within twin pairs (HLA-DPB1 $p < 0.001$) but varied between individuals. HLA-DPB1 variance at 11 methylation sites was less between MZ twins than individuals ($p < 0.01$). Conclusion: Methylation profiles for MHC genes are conserved within a twin pair, indicating that epigenotype variability is influenced by genotype. Suggesting that some genomic regions, variability of epigenotypes is heritable. In summary, specific epigenotypes could account, in part, for known genotype susceptibilities to T1DM.