**Genome-wide DNA methylation patterns in CD4+ T reveal significant contribution of DNA methylation to rheumatoid arthritis**

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**Abstract**

Rheumatoid arthritis (RA) is an autoimmune disease that causes chronic inflammation of the joints.  Evidence showed RA was involved with genetic and epigenetic aberrant. Recent evidence found more and more importance of the epigenetic contribution, especially the DNA methylation, to the pathogenesis of rheumatoid arthritis. To understand the extent and nature of dysregulated DNA methylation in rheumatoid arthritis T cells, we performed a genome-wide DNA methylation study in CD4+ T cells in 12 rheumatoid arthritis patients compared to 12 matched normal healthy controls. [Methods and Result] Cytosine methylation status was quantified with Illumina methylation 450K microarray (HM450K, 485512 CpG sites). We identified 810 hypomethylated and 392 hypermethylated CG sites in RA CD4+ T cells compared to normal controls, representing 383 and 785 genes hypermethylated and hypomethylated in RA patients (P<3.4\*10-7). Cluster analysis based on significantly differential methylated loci showed distinct separation between RA and normal controls. Gene ontology analysis showed alternative splicing (P=1.2\*10-7, FDR) and phosphoprotein (1.7\*10-2, FDR) were significantly aberrant in RA patients, indicating the abnormal of transcript alternative splicing and protein modification mediated by DNA methylation might play important role in the pathogenesis of rheumatoid arthritis. What’s more, the result showed human leukocyte antigen (HLA) region was frequently hypomethylated in RA patients, including HLA-DRB6, HLA-DQA1 and HLA-E, however, HLA-DQB1 showed different methylation profiles with significant hypermethylation in CpG island region and hypomethylation in CpG shelf region. Outsite of the MHC region, the most hypermethylated genes in RA included HDAC4, NXN, TBCD and TMEM61 while the most significant hypomethylated genes included ITIH3, TCN2, PRDM16, SLC1A5 and GALNT9. [Conclusion] Genome-wide DNA methylation patterns revealed significant DNA methylation change in CD4+ T cells from patients with rheumatoid arthritis.

**Keywords:**

[DNA Methylation](http://www.tandfonline.com/action/doSearch?Keyword=DNA%20Methylation)，rheumatoid arthritis，CD4+ T cells， Genome-wide，Illumina methylation 450k microarray