POS0415

BLOOD-DERIVED DNA METHYLATION EPI-SIGNATURES ASSOCIATED WITH ANKYLOSING SPONDYLITIS

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Background: Most (~90%) of the ankylosing spondylitis (AS) susceptibility loci are undefined and located in non-coding regions. Epigenetic changes may alter the expression of genes involved in AS and explain part of the missing heritability.¹

Objectives: To identify novel DNA methylation sites significant for AS and comprehensively understand the underlying pathological mechanism.

Methods: Genome-wide DNA methylation of blood samples from 30 AS patients and 15 health controls was measured on the Infinium® MethylationEPIC Bead-Chip microarray. Methylome data were analyzed with ChAMP package in R.

Results: The epigenome-wide association analysis identified 4,794 differentially methylated positions (DMPs) (FDR <0.05 and delta β >0.05), including 3,294 (68.7%) hypermethylated and 1,500 (31.3%) hypomethylated positions in AS patients (Figure 1A). The identified DMPs allowed clear distinction of most AS cases from controls in the PCA (Figure 1B) and unsupervised hierarchical clustering (Figure 1C). KEGG pathway analysis of AS associated DMPs enriched in T cell receptor signaling pathway, Th1 and Th2 cell differentiation. Besides, a total of 1,048 differentially variable positions (DVPs) were identified, the majority of which (974, 92.9%) were hypervariable in AS, while only 74 DVPs were hypovariable. The increased DNA methylation variability in disease were in line with the previous observation in other diseases, indicating the intrinsic heterogeneity in AS patients, which might be influenced by diverse factors, such as disease activity and treatment.

Figure 1.

Conclusion: Peripheral blood mononuclear cells from AS patients display aberrant DNA methylome and increased DNA methylation variability. The results enhanced our understanding of the important role of DNA methylation in pathology of AS and offered the possibility of identifying new targets for intervention.

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SLE, Sjögren's and APS - aetiology, pathogenesis and animal models

POS0416

NOVEL LONG NON-CODING RNA EXPRESSION PROFILE OF PERIPHERAL BLOOD MONONUCLEAR CELL REVEALED POTENTIAL BIOMARKERS AND REGULATORY MECHANISM IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a complex and heterogeneous autoimmune disease, usually involving multiple systems of the whole body (1). A variety of factors can affect SLE, such as genetic, environmental, immunoregulatory, hormonal and epigenetic (2). Long non-coding RNA is a type of RNA greater than 200 nucleotides that does not encode proteins. With the development of research, lncRNA gradually becomes the key regulator of gene expression in the immune system (3). Studies have shown that several lncRNAs, such as NEAT1 and GAS5 are dysregulated in SLE and are involved in the pathogenesis of SLE (4,5). These results suggest that lncRNA can be used as a potential biomarker for disease diagnosis and treatment. However, our current understanding of SLE related lncRNAs is still limited.

Objectives: The purpose of this study was to find new lncRNAs in peripheral blood mononuclear cells of SLE patients by transcriptome sequencing and explore their potential as biomarkers and their correlation with clinical features.

Methods: Transcriptome sequencing was used to screen differentially expressed lncRNAs (DELs) and mRNAs (DEMs). DAVID and WebGestalt were used to perform enrichment analysis. Cytoscape was used to construct protein-protein network, co-expression network and competitive endogenous RNA network to reveal the regulatory mechanism of lncRNAs in transcriptome level. The expression of these selected lncRNAs in SLE patients and healthy controls were verified by qPCR.

Results: A total of 1737 DELs and 4078 DEMs were identified between 5 SLE patients and 5 healthy controls. Most of upregulated genes were enriched in defense and immune response, while downregulated genes were mainly enriched in SLE related pathways. Topology network analysis reveal the regulatory mechanism of lncRNAs in transcriptome level including directly acting on mRNA or indirectly affecting gene expression after acting on miRNA. Ten lncRNAs and eight genes was verified by qPCR in bigger samples including 77 SLE patients and 25 healthy controls. lncRNA NONHSAT101022.2 was significantly downregulated in SLE patients ($p=0.007$) and the expression of NONHSAT101022.2 showed a significant negative correlation with SLE disease activity index (SLEDAI, $r=-0.3592$, $p=0.0013$).

Conclusion: In this work, we identified a large number of mRNAs and novel lncRNAs by transcriptome sequence. The function and regulatory mechanism of these lncRNAs were analyzed by bioinformatics methods. lncRNA NONHSAT101022.2 is significantly downregulated in SLE patients and significantly related to the activity and severity of disease. Additionally, we put forward that NONHSAT101022.2 may enhance the signal transduction of β_2 -AR by cis-regulating its target gene, LMBRD2, which induces NK cells to produce high levels of IFN- γ , thereby exacerbating SLE.

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POS0417

EXOGENOUS CXCL5 RESTORES ENDOGENOUS BLOOD-TISSUE CHEMOKINE GRADIENT TO IMPROVE SURVIVAL IN MURINE LUPUS

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