AB0020 DIFFERENTIALLY EXPRESSED GENES IN SJÖGREEN’S SYNDROME MICROARRAY

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Background: Sjögren’s syndrome (SS) is a chronic autoimmune disease characterised by a decrease in the secretion of tears and saliva, and is considered to be a common, rheumatic immune disease second only to rheumatoid arthritis. Patients with SS may have different prognoses or different reactions to the same treatment plan. Therefore, a more accurate and more practical predictor is needed to provide a basis for the individualised treatment of SS. Bioinformatics is a new approach. It applies bioinformatics methodology, tools, software and database to molecular mechanisms, new biomarkers and individualised treatment measures.

Objectives: In this study, gene expression data as the basis, combined with bioinformatics tools and literature mining methods, firstly analyses the expression differences between normal people and patients with parotid gland parotid Sjögren syndrome gene, a key pathway and further study the effect of SS involved in the occurrence and development of the application of protein interaction network screening key genes, pathogenesis help to clarify SS, and for the future of this disease and provide a new direction.

Methods: The expression profiles of mRNA in parotid gland of patients with Sjögren syndrome and normal parotid gland were obtained from the GEO database. A total of 24 patients with Sjögren’s syndrome, 6 patients with dry mouth and dry eye symptoms and 25 patients without dry mouth and dry eye were enrolled in the study. 65 samples were collected. The GEO2R tool screened the parotid differently expressed genes in the patients with SS compared with the healthy people, and the DAVID tool enriched the function and pathway of the gene. The STRING database constructs a network that differentially expresses the interaction of gene protein products and screening core genes.

Results: 24 upregulated genes and 147 down regulated genes were screened. KEGG enriched 5 pathways including cell adhesion, immune innnate network, IgA secretion, viral myocarditis pathway, rheumatoid arthritis pathway and leukocyte transendothelial migration. String protein interaction database was used to subcellular localization of differentially expressed gene protein products in parotid gland, and differentially expressed proteins were identified. The interaction network was constructed by Cytoscape software. The protein interaction network was constructed based on the 171 differentially expressed genes of SS, and the isolated and non interacting protein nodes were screened out. 108 upregulated gene encoded proteins were found to interact with each other, forming a complex network containing 390 interactions. The Degree>20 of the node was selected as the standard selection centre node, and 5 Hub genes are obtained. It was found that PTPRC, CD68, STAT1, FYN and LCP2 are key genes and may play an important role in the pathogenesis of Sjögren syndrome.

Conclusions: Above all, we used bioinformatics to find genes and critical pathways related to SS, which is expected to provide new molecular markers for the diagnosis and treatment of SS. It provides a new way of thinking for the treatment and prognosis of Sjögren syndrome.

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AB0021 A GENOME-WIDE SNP LINKAGE ANALYSIS SUGGESTS A NOVEL SUSCEPTIBILITY GENE FOR ANKYLOSING SPONDYLITIS

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Background: Ankylosing Spondylitis (AS) is a chronic, progressive and inflammatory disease, which is considered to be hereditary. However, the responsible molecular genetic determinants remain unidentified.

Objectives: To detect susceptibility gene(s) for AS by using an affected-only linkage analysis and high density single nucleotide polymorphism (SNP) in genome-wide manner.

Methods: All AS patients in three families of Cantonese were recruited. Their clinical material were collected by questionnaires. Genomic DNA derived from individual peripheral blood leukocytes was genotyped using Illumina HuamHap 610-Gold SNP Chip. Genotype data were generated using the Illumina BeadStudio 3.2 software. An affected-only linkage analysis was carried out using non-parametric and parametric linkage analysis. The customised allele frequencies were based on the 980 Cantonese healthy controls. SNP genetic map positions were interpolated as their physical positions in megabase.

Results: 1. Clinical data: The mean age was 42.3±14.9 years (ranging from 16–62 years), mean age of onset was 23.8±7.4 years (ranging from 10–30 years), mean duration of affectation was 17.0±13.0 years (ranging from 0.2–50.0 years), and the sex ratio of male to female was 2.5:1. There was no Iritis and dactylitis, hip involvement (4, 19.05%), peripheral arthritis (4, 19.05%), inflammatory back pain (21, 100%), and HLA-B27 positive (20, 95.24%). 2. Results of non-parameter linkage analysis: The highest LOD value was found in chromosome 16, which reached 2.362. Although chromosome 6 was considered to be relative to the pathogenesis of AS, its LOD value was 1.499 and the range of the peak was located in 6 p21, where 96 SNPs (such as rs9390977) were included. 3. Results of parameter linkage analysis: The LOD value of chromosome 16 was 4.6807 and higher than that of other chromosomes which were less than 3 by the same analysis. A susceptibility locus was found in 16q12, spanning 88.5 Kb with LOD value above 3 (ranging: 51030764–51915940). 4. Susceptibility genes: According to the result of parameter linkage analysis in chromosome 16, seven genes (TOX high mobility group box family member 3 (TOX3), LOC643714, LOC146253, LOC100132440, LOC390730, LOC100128523 and chromodomain helicase DNA binding protein 9 (CHD9)) could be detected in the position where the LOD value exceeded 3. Interestingly, six SNPs could be found in CHD9 gene. Likewise, they were also found in another association analysis, which included 490 AS patients and 977 healthy controls. P value for SNP rs10153130 was 0.005879 (adj p<0.00833).

Conclusions: Genome-wide SNP linkage analysis in three AS families supports that a susceptibility locus for AS was found in 16q12, spanning 88.5 Kb with LOD value above 3 (ranging: 51030764–51915940).

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AB0022 FAMILY-BASED WHOLE-EXOME SEQUENCING REVEALS THE GENETIC BASIS OF RELAPSING POLYCHONDRITIS

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Background: Relapsing polychondritis (RP) is a rare systemic disease, characterised by recurrent episodes of inflammation of cartilaginous tissues and other proteoglycan rich structures involving the cartilage of the ears, nose, larynx, tracheobronchial tree and cardiovascular system.1, 2 The susceptibility to RP has been reported to be significantly related to genetic factors.3 4 However, family occurrence has yet to be reported and the responsible molecular genetic determinants haven't been clearly elucidated.

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