vs. 25.68%, p=0.049, OR=0.508, 95% CI 0.258–0.985, compared with patients with the normal ESR, respectively). After stratification according to the sex, similar results in the GT genotype frequencies were seen and even intensiﬁed only for female JIA patients (15.38% vs. 31.37%, respectively, p=0.022, OR=0.398, 95% CI 0.180–0.897). In addition, a signiﬁcant increase in the GG genotype proportion and a tendency towards a decrease in the T allele proportion were observed in girls with the elevated ESR (GG: 83.76% vs. 68.63%, p=0.038, OR=2.358, 95% CI 1.058–5.110; T: 8.55% vs. 15.69%, p=0.057, compared with girls with the normal ESR, respectively).

Conclusions: In the present study, the association of the IL2-IL21 rs6822844 locus polymorphic variants with a predisposition to the ESR elevation in female JIA patients was shown.

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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 prognosis 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 GEO database, which contained differentially 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, intestinal immune network, IgA secretion, viral myocarditis pathway, rheumatoid arthritis pathway and leucocyte 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 is 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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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 questionnaire. Genomic DNA derived from individual peripheral blood leukocytes was genotyped using Illumina HuamHap 610-Quad 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 15-92.9 years), age of onset was 23.8±7.4 years (ranging from 10-30 years), mean duration of affection 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 dactyliitis, 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 related 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 rs6930977) 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 chromodomall 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 (adjust 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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A NOVEL 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, 5 However, family occurrence has yet to be reported and the responsible molecular genetic determinants hasn’t been clearly elucidated.

Disclosure of Interest: None declared

Objectives: The purpose was to detect the susceptibility genes of RP through whole-exome sequencing (WES) in a Chinese family and deepen our understanding of the pathogenesis of RP.

Methods: A 32 year-old Chinese female proband with RP and her family in which only her mother was RP patient were recruited in the current study. The genomic DNA of 6 human subjects was extracted from the peripheral blood monocyte cells (PBMCs) and then identified gene allele mutations using WES. Candidate variants with low frequency (<0.1%) in general population and predicted deleterious on gene function were identified. Sanger sequencing was then used to validate the analysis results of WES and further validated the gene variants in 12 human subjects.

Results: 38 genes mutated were confirmed by WES among RP patients. Of them, 10 gene mutated were validated by Sanger sequencing, including Collagen Type XXII Alpha 1 Chain (COL22A1) rs200464636, folliculin (FLCN) NM_144606; c.G838A: p.E280K, glycosylphosphatidylinositol anchor attachment 1 (GPAA1) rs201424010, DNA ligase 3 (LIG3) rs761808558, RecO like helicase 4 (RECOL4) rs757703895, ring finger protein 207 (RNF207) NM_207396: c.T425C:p.I142T, coiled-coil domain containing 61 (CCDC61) rs777816675, Purkinje cell protein 2 (PCP2) rs144974437, tubulin alpha 3e (TUBA3E) rs749780020 and myosin heavy chain 15 (MYH15) NM_014981:c.G4462A:c.A1448T.

Conclusions: This study confirms that conformation of multigene mutation may contribute to the susceptibility to RP. The candidate genes mutated we discovered are potential targets for in-depth functional studies.

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AB0023

SEX-BASED DIFFERENCES IN ASSOCIATION BETWEEN CIRCULATING T CELL SUBSETS AND DISEASE ACTIVITY IN UNTREATED EARLY RHEUMATOID ARTHRITIS PATIENTS

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Background: Genetic association studies strongly support the role of CD4+ T cells in promoting RA pathology. In a cohort of untreated early RA patients, we hypothesized that sex-based differences in immunological factors contribute to the disease process in rheumatoid arthritis (RA). Hence, we examined sex-related differences in circulating T cell subsets and their association with disease activity in male and female patients with untreated early rheumatoid arthritis.

Methods: Proportions of T cell subsets were analysed in peripheral blood from 70 untreated early RA patients (50 females and 20 males) and in 31 healthy age-matched controls. Broad analysis of helper and regulatory CD4+ T cell subsets was done using flow cytometry. Disease activity in patients was assessed using DAS28, CDAI, swollen joint counts, tender joint counts, CRP and ESR.

Results: Multivariate factor analyses showed that male and female untreated early rheumatoid arthritis patients display distinct profiles of association between disease activity and circulating T cell subset proportions. In male, but not female, uRA patients Th2 cells showed a positive association with disease activity and correlated significantly with DAS28-ESR, CDAI and tender joint counts. Likewise, proportions of non-regulatory CTLA-4− T cells associated positively with disease activity in male patients only, and correlated with DAS28-ESR. In contrast, there was a negative relation between Th1 and Th7 subsets proportions and disease activity in males only. Proportion of Th1 and Th7 cells showed a relation to disease activity in either male or females. There were no significant differences in proportions of T cell subsets between the sexes in patients with untreated early rheumatoid arthritis.

Conclusions: In conclusion, our findings show sex-based differences in the association between T cell subsets and disease activity in uRA patients, and that Th2 helper T cells may have a stronger role in the regulation of disease activity in male patients.

REFERENCE: