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 differences 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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AB0020 DIFFERENTIALLY EXPRESSED GENES IN SJGREN'S SYNDROME MICROARRAY

L. Wei¹, Z. Wenjia², W. Yuanhao¹, J. Yue¹, Z. Lei¹, L. Bin¹, X. Bin¹, Z. Bo¹, D. Ran¹, C. Yue¹, W. Xiaoshuang¹. ¹First Teaching Hospital of Tianjin University of Traditional Chinese Medicine; ²Tianjin University of Traditional Chinese Medicine, Tianjin, China

Background: Sjogren'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 immuno 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 Sjogren 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 Sjogren syndrome and normal parotid gland were obtained from the GEO database. A total of 24 patients with Sjogren'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 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 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 is selected as the standard selection centre node, and 5 Hub genes are obtained. It is found that PTPRC, CD86, STAT1, FYN and LCP2 are key genes and may play an important role in the pathogenesis of Sjogren 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 Sjogren syndrome.

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

Z. Lin, L. Gui, Y. Zhang, Q. Lv, J. Qi, L. Fang, X. Zhang, J. Gu. *Department of Rheumatology, Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China*

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 HiSeq 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 megabyte.

Results: 1. *Clinical data:* The mean age was 42.3±14.9 years (ranging from 18–62 years), mean 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 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 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 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 400 AS patients and 977 healthy controls. P value for SNP rs10153130 was 0.005879 (adjust $p \leq 0.05/6 = 0.00833$).

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 POLYCHONDRIITIS

Z. Lin¹, L. Gui¹, J. Qi¹, X. Guo², Q. Lv¹, Y. Zhang¹, L. Fang¹, X. Zhang¹, J. Gu¹.

¹Department of Rheumatology; ²Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, China

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 hasn't been clearly elucidated.

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, RecQ like helicase 4 (RECQL4) 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: p.A1488T.

Conclusions: This study confirms that coinheritance of multigene mutated 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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Adaptive immunity (T cells and B cells) in rheumatic diseases

AB0023

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

J. Aldridge¹, J. Pandya¹, L. Meurs¹, A. Kerstin¹, I. Nordström¹, E. Theander², A.-C. Lundell¹, A. Rudin¹. ¹Medicine, Rheumatology Inflammation Research, Sahlgrenska Academy, Göteborg; ²Rheumatology, Lund University, Lund, Sweden

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 recently demonstrated that the balance of helper T cell subsets in blood of uERA patients is skewed towards Th2 cells relative to healthy controls.¹ RA has been shown to be a sexually dimorphic condition with current data suggesting that prevalence, disease course and treatment outcome varies between men and women.

Objectives: It is not known if sex-based disparities in immunological factors contribute to the disease process in rheumatoid arthritis (RA). Hence, we examined whether circulating T cell subset proportions and their association with disease activity differed in male and female patients with untreated early rheumatoid arthritis.

Methods: Proportions of T cell subsets were analysed in peripheral blood from 70 uERA DMARD and prednisolone naïve patients with untreated early Rheumatoid arthritis (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, uERA 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 Th1Th17 subset proportions and disease activity in males only. Proportions of Th1 and Th17 cells showed no relation to disease activity in either males 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 uERA patients, and that Th2 helper T cells may have a stronger role in the regulation of disease activity in male patients.

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AB0024

IGA-EXPRESSING BM PC ARE RESPONSIBLE FOR ENHANCED PHOSPHORYLATION OF BCR-ASSOCIATED KINASES AFTER BCR STIMULATION INDEPENDENTLY OF THEIR CD19 EXPRESSION

A. Wiedemann, A.C. Lino, T. Dörner. *Rheumatology and Clinical Immunology, Department of Medicine, Charité Universitätsmedizin Berlin and German Rheumatism Research Center Berlin (DRFZ), Berlin, Germany*

Background: Plasma cells (PC) are considered key drivers of antibody mediated autoimmune diseases. Long-lived PC survive for years in their niches, preferentially in the bone marrow (BM) but also in inflamed tissues.^{1,2} A subset of PC lacking expression of CD19 has been identified.³ Better understanding of factors and pathways involved in survival and maintenance of long-lived PC is needed to find strategies to target PC in autoimmunity since targeting B cells or proliferating cells does not affect already existing PC.⁴ B cell receptor (BCR) signalling is a critical mediator of B cell survival and it was shown before that IgA⁺ and IgM⁺ PC in the BM express a functional BCR suggesting a potential role for the BCR signalling pathway.⁵

Objectives: Expression of BCR associated molecules in BM PC and the response of CD19⁺ and CD19⁻ BM PC to BCR stimulation by anti-IgM/IgA/IgG was assessed to test whether these PC subsets are capable of responding to BCR mediated signals. We further investigated if the PC isotype has an impact on BCR signalling.

Methods: BM samples from patients undergoing routine total hip arthroplasty without systemic immune manifestations were stained for baseline expression of spleen tyrosine kinase (Syk) and Bruton's tyrosine kinase (Btk) as well as for the phosphosites pSyk (Y³⁵²) and pBtk (Y²²³). BM mononuclear cells have been isolated, stimulated with anti-IgM/IgA/IgG and the increase of fluorescence intensity of pSyk (Y³⁵²) and pBtk (Y²²³) was measured by intracellular flow-cytometric analyses. In some experiments, cells have been stimulated with anti-IgA alone and stained for the isotype additionally to the pPTK staining.

Results: Whole BM stainings revealed that both CD19⁺ and CD19⁻ PC express the PTKs Syk and Btk at baseline. Both PC subsets showed the ability to respond to BCR stimulation with enhanced phosphorylation of the PTKs with a clear trend to reduced responsiveness among CD19⁻ PC. Ig staining revealed that IgA expression was identified on both membrane and intracellularly, whereas IgG was