and SMARCA/BRG1 genes may suggest an epigenetic imbalance of chromatin remodelling factors involved in inflammation pathways with a potential role in PsA/pсорiatis immunopathogenesis.

Disclosure of Interests: None declared

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POS0362 INVESTIGATING THE ANKYLOSING SPONDYLITIS-ASSOCIATED REGULATORY SNPS AT THE RUNX3 LOCUS WITH A FUNCTIONAL GENOMICS APPROACH

M. Vecellio1, P. B. Wordsworth1, C. J. Cohen1. University of Oxford, NDOHMS, Oxford, United Kingdom

Background: Of the >100 genetic associations with ankylosing spondylitis (AS), RUNX3 transcription factor (TF) involved in diverse immunological processes, is mainly (10%–15%) associated.1 The biggest challenge is to understand the mechanism behind this association. We demonstrated the association between AS and the single nucleotide polymorphism (SNP) rs4648889 located in a 2kb regulatory locus upstream of the RUNX3 promoter can be explained by allele-specific effects on TF recruitment that alter gene expression, specifically in CD8+ T-cells.2

Methods: In vitro functional studies were performed to characterize the effects of SNP on TF binding. Chromosome conformation capture (3C) provided critical functional evidence for looping among AS-associated SNPs and the RUNX3 promoter.

Results: (1) In silico data revealed a c-MYC ChIP-seq peak in GM12878 lymphoblastoid cells overlapping rs4600247; (2) Mobility shift assays (EMSA) and WB-EMSA showed reduced DNA/protein binding in the presence of the AS-risk allele in CD14+ monocytes. C-MYC binding-site is disrupted and binding abolished in the presence of the AS-risk allele; (3) 3C experiments indicate low interaction frequency between SNP rs4600247 and RUNX3 promoter.

Conclusion: The enhancer upstream the RUNX3 gene has a plausible functional role in AS, probably by regulating gene transcription and DNA looping. These observations are critically important in defining disregulated pathways and potential therapeutic drug targets.

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Adaptive immunity (T cells and B cells) in rheumatic diseases

POS0363 IDENTIFICATION OF MOLECULAR PHENOTYPES AND IMMUNE CELL INFILTRATION IN PSORIATIC ARTHRITIS PATIENTS’ SKIN TISSUES BY INTEGRATED BIOINFORMATICS ANALYSIS

T. Cheng2,3, S. X. Zhang2,3, J. Qiao2,3, P. Zhao2,3, S. Song2,3, T. L. Li3, M. Vecellio1, P. F. He3, X. Liu3. 1The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China; 2Shanxi Li Xiaofeng Medical Groups, Department of Rheumatology, Taiyuan, China; 3Ministry of Education, Key laboratory of Cellular Physiology at Shanxi Medical University, Taiyuan, China; 4Shanxi Provincial People’s Hospital, Department of Rheumatology, Taiyuan, China; 5Shanxi Medical University, Medical Data Sciences, Taiyuan, China

Background: Psoriatic arthritis (PsA) is an inflammatory musculoskeletal disease associated with cutaneous psoriasis1. Heterogeneity of clinical manifestation often makes differential diagnosis difficult2. Thus, the underlying molecular pathogenesis of PsA need to be further studied to diagnose early and ensure optimal management of arthritis and key comorbidities.

Objectives: This research was conducted to identify molecular phenotypes and immune infiltration in the skin tissues of psoriatic arthritis patients according to bioinformatics analysis.

Methods: The mRNA expression profiles of GSE13356 (116 samples), GSE14905 (56 samples) and GSE30999 (162 samples) were obtained from the publicly GEO databases. Non-negative matrix factorization (NMF), functional enrichment and cisBERT algorithm were applied to illustrate the conditions of PsA patients’ skin tissues for classification after screening the differentially expressed genes (DEGs) between lesion biopsy and non-lesion biopsy.

Results: Two subsets (Sub1 and Sub2) were identified and validated by NMF typing of 612 detected DEGs (Figure 1a). A total of 54 signature genes (18 in Sub1 and 36 in Sub2) were obtained (Figure 1b). GO and KEGG enrichment analysis showed the signature genes in Sub1 were mainly involved in proliferation and differentiation of immune cells, whereas genes in Sub2 were related to humoral immune response mediated by antimicrobial peptide (Figure 1c,d). Further, immune cell infiltration results revealed Sub2 had higher levels of resting NK cells (P<0.001), macrophages M1(P<0.001), resting mast cells (P<0.001) and regulatory T cells (P<0.001) but lower concentrations of activated CD4+ memory T cells (P<0.001), activated NK cells (P<0.05), activated dendritic cells(P<0.001), eosinophils (P<0.05) and neutrophils (P<0.01) (Figure 1e).

Conclusion: The pathogenesis of psoriatic arthritis is related to both cellular immunity and humoral immunity. It is indispensable to adjust the treatment strategies according to patient’s immune status.

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Figure (a) NMF consensus clustering of 334 PsA patients based on 612 DEGs. (b) Heat map of differentially expressed genes; Each small square represents a gene; the color indicates the expression of the gene. Each column indicates the expression level of genes in a sample; the right side is the gene name. (c,d) Visualization GO enrichment analysis and KEGG pathway enrichment. (e) Violin plot show the fraction of 22 immune cell subpopulations in two subtypes based on CIBERSORT algorithm.

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