Molecular Profiling of Radiographic Axial Spondyloarthropathies Patients Reveals an Association Between Inactive and Adaptive Cell Populations and Therapeutic Response to Adalimumab


Methods: Differential expression analysis were used to identify the most enriched pathways and mass spectrometry), pre and post (14 weeks) TNFi treatment using adalimumab.

Results: We identified 13 thousands non-overlapping survivin ChIP-peaks (>3000 peaks were present in all four conditions). Survivin ChIP-peaks were enriched near the genes and promoters (p<e-30 and p<e-8), which implied that survivin role in transcription could be mediated by known transcription factors. Thus, we analyzed survivin peaks vs binding regions of 1135 transcription regulators (TR) available in ReMap. Potential partner proteins of survivin were selected based on the enrichment of the overlapping peaks in the whole genome and in CD4-activatory regulatory areas. Both, strict overlaps and location within 10 and 100kb survivin peak vicinity were analyzed. This approach allowed us to select >150 TRs enriched in all tests. The enriched TRs were in immunity and RA-relevant pathways including cytokine response and production, JAK-STAT signaling, etc. Among the TRs co-localized with survivin were CHD8, MAX, EP300, BRD2, CTFC and RAD21, all responsible for chromatin architecture. Several TRs were massively enriched in the vicinity of DEGs after survivin depletion including CTFC, MYC and G1 Search for TR binding motifs in survivin peaks supported over-representation of binding sites for IRFs (p<e-5) and several proteins of the bZIP-family (p<e-5).

Conclusion: Analysis of the survivin bound DNA in CD4 cells demonstrated the nonrandom distribution with specific enrichment within the regulatory elements of the genes and co-localization with partner proteins to regulate their transcription.

Disclosure of Interests: None declared

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Molecular Profiling of Radiographic Axial Spondyloarthropathies Patients Reveals an Association Between Inactive and Adaptive Cell Populations and Therapeutic Response to Adalimumab

Complex Landscape of Birc5/Survivin Genome Binding in Human Cd4+ T Cells

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Methods: We recently showed to be essential for T cell differentiation and microRNA processing. The known anti-apoptotic and proliferating facilitating functions of survivin does not explain the nuclear localization of survivin in interphase.

Objectives: Our aim is to uncover nuclear functions of BIRCS/survivin in CD4 cell of RA patients and healthy.

Methods: CD4 T cells were isolated from the peripheral blood using positive selection on magnetic beads (EasySep) and activated for 48h with ConA+LPS. Chromatin immunoprecipitation (ChIP) with polyclonal anti-survivin antibodies was done in four independent samples of healthy donors (n=5), healthy smokers (n=3), rheumatoid arthritis (n=3) and breast cancer (n=2). Pooled libraries were constructed for each group and ChIPseq was carried out (Illumina). For comparative RNAseq analysis, activated CD4 T cells were incubated with or without survivin inhibitor (YM155) for 24h. State-of-the-art bioinformatics pipelines were applied for NGS data and the survivin-binding peaks were used for comparison with genes, chromatin state annotation and functional gene and regulatory regions-based functional analysis. Co-localization of peaks in the whole genome and in vicinity of the differentially expressed genes (DEG) was done using ReMap integrated ChIPseq datasets for all human cells and tissues.

Results: 10.1136/annrheumdis-2021-eular.3948

Conclusion: We aimed to uncover nuclear functions of BIRCS/survivin in CD4 cell of RA patients and healthy.

Disclosure of Interests: None declared

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Complex Landscape of Birc5/Survivin Genome Binding in Human Cd4+ T Cells

Complex Landscape of Birc5/Survivin Genome Binding in Human Cd4+ T Cells

Background: Survivin, coded by BIRC5 gene, is a multitasking protein essential for cell renewal and homeostasis. In autoimmune conditions such as rheumatoid and psoriasis arthritis, survivin was associated with inflammation severity and joint damage. Importantly, inhibition of survivin alleviated experimental arthritis in mice.

Objectives: To find tools that might help clinicians to decide what is the best available therapeutic option for each patient.

Methods: The goal of this study is to use comprehensive molecular profiling to characterize clinical response to therapy in a real-world setting. Specifically, to find tools that might help clinicians to decide what is the best available therapeutic option for each patient.

Methods: Gene x, the top differentially expressed gene at base-

Conclusion: Differences in disease activity and/or inactive/adaptive immune cell type composition at baseline may be a major contributor to response to adalimumab in n-rxASPALS. Alternatively, a model including clinical and gene expression variables could be considered, particularly in patients with mild disease activity.

Disclosure of Interests: None declared

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Complex Landscape of Birc5/Survivin Genome Binding in Human Cd4+ T Cells

Background: Survivin, coded by BIRC5 gene, is a multitasking protein essential for cell renewal and homeostasis. In autoimmune conditions such as rheumatoid and psoriasis arthritis, survivin was associated with inflammation severity and joint damage. Importantly, inhibition of survivin alleviated experimental arthritis in mice.

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Disclosure of Interests: None declared

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Complex Landscape of Birc5/Survivin Genome Binding in Human Cd4+ T Cells

DNA Methylation Signatures Characterize Psoriasis and Psoriatic Arthritis in Monozygotic Twins Discordant for the Disease

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Background: Psoriatic arthritis is a chronic inflammatory disorder spanning from skin disease (psoriasis) to psoriatic arthritis (PsA). The genetic background is insufficient to explain disease onset as illustrated by not very informative Genome Wide Association Studies and monozygotic (MZ) twin studies recently performed. It is strongly assumed that epigenetics may contribute to disease susceptibility modulating gene expression. DNA methylation has been found involved in several autoimmune inflammatory diseases. Here we have analyzed the DNA methylation profile of a selected cohort of MZ twins discordant for psoriasis/PsA.

Objectives: To identify the methylation associated with psoriasis and PsA in the peripheral blood of MZ twins discordant for these conditions.

Methods: Peripheral blood from 7 couples of MZ twins discordant for psoriatic disease was collected and DNA extracted for a genome-wide evaluation of the DNA methylation profile, with the Infinium MethylationEPIC BeadChip. Minfi and the packages of the Bioconductor were used to analyse the data obtained. Quality control and exclusion criteria were applied to the raw data having a final number of 762,451 probes, which accounts for 88% of the total.

Results: The approach first identified 2564 differentially methylated positions (DMPs: "p<0.05") with 19 May 2021. Downloaded from http://ard.bmj.com/Ann Rheum Dis: first published as 10.1136/annrheumdis-2021-eular.19948 on
and SMARCA/BRG1 genes may suggest an epigenetic imbalance of chromatin remodelling factors involved in inflammation pathways with a potential role in PsA/psoriasis immunopathogenesis.

**Disclosure of Interests:** None declared

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**POS0362**  
INVESTIGATING THE ANKYLOSING SPONDYLYTIS-ASSOCIATED REGULATOR SNPS AT THE RUNX3 LOCUS WITH A FUNCTIONAL GENOMICS APPROACH


**Background:** Of the >100 genetic associations with ankylosing spondylitis (AS), RUNX3 transcription factor (TF) involved in diverse immunological processes, is notably (10−15) associated. 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.

**RUNX3** transcription factor (TF) involved in diverse immunological processes, is notably (10−15) associated. 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.

**Methods:** The epigenetic landscape of SNP rs6600247 was defined using Roadmap database. In vitro functional studies were performed to characterize the effects of this 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 rs6600247; (2) Mobility shift assays (EMSAs) and WB-EMSAs 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 rs6600247 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 dysregulated pathways and potential therapeutic drug targets.

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**POS0363**  
IDENTIFICATION OF MOLECULAR PHENOTYPES AND IMMUNE CELL INfiltrATION IN PSORIATIC ARTHRITIS PATIENTS’ SKIN TISSUEs BY INTEGRATED BIOINFORMATICS ANALYSIS

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**Background:** Psoriatic arthritis (PsA) is an inflammatory musculoskeletal disease associated with cutaneous psoriasis. Heterogeneity of clinical manifestation often makes differential diagnosis difficult. 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 GSE30989 (162 samples) were obtained from the publicly GEO databases. Non-negative matrix factorization (NMF), functional enrichment and cibersort 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. These observations are critically important in defining dysregulated pathways and potential therapeutic drug targets.

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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.