median method (OR=0.827; 95%CI= 0.760- 0.898; p = 4.476e-06), MR-Egger also showed a similar effect (OR=1.068; 95%CI= 0.482-0.926 P = 2.184e-02). Cochran's Q test (Q=322.683; p< 9.057e-51) found potential heterogeneity. MR-egger regression (P=0.164, intercept=0.043) was used to test the nonexistence of horizontal multi-directivity. Similarly, we examined the level of pleiotropy again with MR-PRESSO's global test, and the results showed no evidence of horizontal pleiotropy. In addition, no SNP was found to be a significant factor affecting the association in the residual analysis.

Conclusion: Our results provide causal evidence for the effect of multiple sclerosis on psoriasis risk. This Mendelian randomization study showed a causal relationship between multiple sclerosis and the risk of psoriasis. Multiple sclerosis may help reduce the burden of psoriasis.

REFERENCES:


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Disclosure of Interests: None Declared.
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Figure 1. Clonorchis sinensis-Excretory/Secretory protein (Cs-ESP) ameliorates clinical symptoms in SKG mice

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AB0100

TO STUDY THE T CELL AND CYTOKINE PROFILE IN ANKYLOSING SPONDYLITIS WITH EFFECTS OF TACROLIMUS AND TADALAFIL ON THE CYTOKINES IN-VITRO

Keywords: Adaptive immunity, Spondyloarthritis

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Background: Most studies have shown mixed results of Interleukin (IL)17 and IL-23 levels in patients with Ankylosing Spondylitis (AS) compared to controls; with animal studies showing a good correlation between activation of IL-23-IL

Keywords: Spondyloarthritis, Animal models

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Background: Ankylosing spondylitis (AS) is a sort of inflammatory arthritis that affects axial skeleton, peripheral joints, and certain extra-articular organs, including the eyes, skin, and gut. Recently, many attempts have been made to use parasite administration (e.g., ingestion of eggs of the nematode Trichuris suis) as a new modality for treating inflammatory disorders. Our group published that Clonorchis sinensis protein attenuated inflammation in AS.

Objectives: Thus, this study aimed to assess the therapeutic potential of Clonorchis sinensis-Excretory/Secretory protein (Cs-ESP) for AS.

Methods: Cytotoxicity of Cs-ESP at different doses was assessed by MTS and flow cytometry before performing experiments. Peripheral blood mononuclear cells (PBMCs) and synovial fluid mononuclear cells (SFMCs) were obtained from AS patients. Inflammatory cytokine-producing cells were analyzed using flow cytometry. The levels of INF-γ, IL-17A, TNF-a, and IL-6 were measured by enzyme-linked immunosorbent assay (ELISA). SKG mice were treated with Cs-ESP or vehicles. Inflammation was evaluated using immunohistochemistry.

Results: Treatment with Cs-ESP resulted in no reduced cell viability of PBMCs or SFMCs. In experiments culturing PBMCs and SFMCs, the frequencies of IFN-γ and IL-17A producing cells were significantly reduced after Cs-ESP treatment. In the SKG mouse model, Cs-ESP treatment significantly suppressed arthritis and enthesitis.

Conclusion: We provide the evidence demonstrating that Cs-ESP can ameliorate clinical signs and cytokine derangements in AS.
27 pathway and radiologic progression. Targeting this pathway in humans has yielded benefits with reduced inflammation and radiologic progression in AS. Controlling inflammation and fibrosis is the key to prevent osteoporosis. Tacrolimus and tadalafil have shown to inhibit the Th17 pathway and profibrotic pathways respectively.

**Objectives:** To study the T cell (Th17, PD1, CD25+ CD4 T cells) and cytokine profile (IL-17, IL-23, TGF-β) in AS with influence of disease duration and activity on the above profile. To also study the effect of tacrolimus and tadalafil in ex-vivo peripheral blood monocyte (PBMC) cultures to study their anti-inflammatory and anti-fibrotic potential.

**Methods:** Patients with AS (ASAS classification criteria) without peripheral disease and not on biologic therapy were recruited and their demographic, clinical profile, disease activity and radiologic indices were recorded. Age and sex matched healthy controls (HC, n=21) were also recruited. Peripheral blood was drawn and sera stored; PBMCs were isolated and cultured. Serum and PBMC culture supernatant (CS) were measured for IL-17, IL-23 and TGF-β. These cytokines were measured at baseline, after stimulation with anti-CD3/CD28 antibodies, and after treatment with tacrolimus (10μM/mL), tadalafil (10μM/mL) and both the drugs combined by ELISA(R&D systems, USA). The T cell profile was characterized by flow cytometry (CD4 Th17, CD4 PD1, CD4 Th17 PD1 and CD4 CD25). Statistical analysis was done using GraphPad prism v9.

**Results:** Twenty-five patients [28(24-36)1M,7:3:1] were enrolled with 90% HLA-B27 positivity. The majority had moderate-high disease activity as per ASAS CRP and were on NSAIDs(24), complementary medications (7) and two each on methotrexate and sulfasalazine. Serum IL-17 and TGF-β were significantly elevated in AS compared to controls. All the measures cell populations were significantly elevated in AS compared to HC. When stratified by duration of disease, clinical parameters, disease activity indices, cytokine and T-cell profile was similar across the two groups. ASAS CRP showed a significant correlation with CD4Th17+ cells (r=0.7, p=0.009) and CD4 PD1/T reg (r=0.6, p=0.03). A positive association as observed with some cells but not with the cytokines on generalized linear modeling (Table 1). No significant correlation was observed between cytokines or T cell profiling with Modified Stokes Ankylosing Spondylitis Score. There was a significant decline in TGF-β levels in the culture supernatant with tacrolimus and tadalafil combined, however, no such difference was observed with IL-17 or IL-23. (Figure 1)

**Conclusion:** Serum IL-17 and TGF-β were elevated in the peripheral blood in AS. There was no difference in the cytokine and T-cell profile across early and late disease. A significant decline in TGF-β levels was seen with combined tacrolimus and tadalafil. This needs further exploration in a larger sample size with subgroup characterization as well as testing on synovial fluid and joint tissue samples.

**Table 1. Association of disease activity and T cell/cytokine profile**

<table>
<thead>
<tr>
<th>Model</th>
<th>OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1</td>
<td></td>
</tr>
<tr>
<td>CD4+Th17</td>
<td>4.1(0.6-22.2)</td>
</tr>
<tr>
<td>CD4+PD1+</td>
<td>-0.3(-0.7-0.1)</td>
</tr>
<tr>
<td>PD1+Th17</td>
<td>-0.1(-0.1-0.01)</td>
</tr>
<tr>
<td>Model 2</td>
<td></td>
</tr>
<tr>
<td>CD4+Th17CD25+</td>
<td>3.5(0.7-6.3)</td>
</tr>
<tr>
<td>CD4+PD1+CD25+</td>
<td>-0.2(-0.4-0.02)</td>
</tr>
<tr>
<td>PD1+Th17CD25+</td>
<td>-0.6(-2-3.1-1)</td>
</tr>
<tr>
<td>Model 3</td>
<td></td>
</tr>
<tr>
<td>Serum IL-17</td>
<td>-0.01(-0.05-0.03)</td>
</tr>
<tr>
<td>Serum IL-23</td>
<td>-0.01(-0.1-0.08)</td>
</tr>
<tr>
<td>Serum TGF-β</td>
<td>-0.00(-0.00-0.00)</td>
</tr>
</tbody>
</table>

**REFERENCES:**

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**AB0101 ABNORMAL KUENRYNEINE LEVEL CONTRIBUTES TO THE PATHOLOGICAL BONE FEATURES OF ANKYLOSING SPONDYLITIS**

**Keywords:** Spondyloarthritides


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**Background:** Ankylosing spondylitis (AS) exhibits paradoxical bone features typically characterized by new bone formation and systemic bone loss.

**Objectives:** Although abnormal kynurenine (Kyn), a tryptophan metabolite, has been closely linked to the disease activity of AS, the distinct role of its pathological bone features remains unknown.

**Methods:** Kynurenic sera level was collected from healthy control (n = 22) and AS (n = 87) patients and measured by ELISA. In the AS group, we analyzed and compared the Kyn level based on mSASSS scores, MMP13, and OCN. Under osteoblast differentiation, the effect of Kyn in AS-osteoprogenitors resulted in cell proliferation, alkaline phosphatase activity, bone mineralization-related alizarin red (ARS), von kossa (VON), hydroxyapatite (HA) staining, and mRNA expression markers (ALP, RUNX2, OCN, and OPG) for bone formation. TRAP staining was used for osteoclast formation in RANKL-mediated RAW264.7 cells.

**Results:** Kyn sera level was significantly elevated in the AS group compared to the healthy control group. In addition, Kyn sera level was correlated with mSASSS score (r = 0.038, p = 0.067), MMP13 (r = 0.327, p = 0.093), and OCN (r = 0.043, p = 0.052). During osteoblast differentiation, treatment with Kyn exhibited no difference in cell proliferation and alkaline phosphate (ALP) activity for bone matrix maturation but promoted ARS, VON, and HA staining for bone mineralization. Interestingly, osteoprotegerin (OPG) and OCN expression was augmented in the presence of Kyn treatment during differentiation. In growth medium, Kyn treatment of osteoprogenitors resulted in induction of OPG mRNA, protein expression, and AhR response genes (AhRR, CYP1b1, and TiRAP). Secreted OPG proteins were observed in the supernatant of osteoprogenitors treated with Kyn. Notably, the supernatant addition to osteoclastogenesis interrupted the TRAP-positve osteoclast formation of RANKL-mediated RAW264.7 cells and reduced osteoclast differentiation markers.

**Conclusion:** Our results revealed that elevated Kyn level increased the bone mineralization of osteoblast differentiation in AS and decreased RANKL-mediated osteoclast differentiation by inducing OPG expression, suggesting a potential therapeutic target where abnormal Kyn level could be involved in pathological bone features of AS.

**REFERENCES:**

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**AB0102 POTENTIAL BIOMARKERS TO PREDICT TNF INHIBITORS OUTCOME IN PSORIATIC ARTHRITIS**

**Keywords:** bDMARD, Psoriatic arthritis, Biomarkers

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**Background:** Psoriatic Arthritis (PsA) is a chronic immune-mediated inflammatory disease characterized by axial and peripheral arthritis, dactylitis, nail changes and most of the time, is associated with psoriasis. Patients are initially treated with conventional synthetic Disease-Modifying Anti-Rheumatic Drugs (csDMARDs), but if they do not respond to these, they are treated with biologics, particularly TNF inhibitors (TNFi) which are common first-line biologics. However, about 40% of patients do not or only partially respond to TNFi. Blood biomarkers predicting response to TNFi would allow patients to be treated earlier with a more appropriate drug [1].

**Objectives:** We studied pro- and anti-inflammatory cytokines and adaptive immune cells that could be used as biomarkers for TNFi outcome. Predicting responses to TNFi will help clinicians to choose a more appropriate treatment for patients. TNFi would allow patients to be treated earlier with a more appropriate drug [1].

**Methods:** Blood from patients with PsA (n = 8) was analysed before starting TNFi and compared with blood from patients with rheumatoid arthritis (RA) (n = 8). PsA patients were characterised as ‘psoriasis positive’ and ‘psoriasis negative’. Patients were followed at 3 and 6 months after treatment (n = 6). Leuko-cytes were isolated with Lymphoprep and their phenotype was characterised by

**REFERENCES:**

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Disclosure of Interests: None Declared.

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**Figure 1. In vitro effect of drugs on culture supernatant cytokine levels at baseline, CD3 CD28 stimulation, and after addition of tacrolimus, tadalafil and its combination.**

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**Figure 2.**