Background: The preliminary animal and human studies, including ours, showed that mesenchymal stem cell (MSC) transplantation could reestablish salivary function and reduce lymphocytic infiltration in salivary glands in Sjögren’s syndrome (SS). However, the mechanisms of the encouraging results of MSCs on the SS remain to be elucidated. Myeloid-derived suppressor cells (MDSCs) represent an important class of immunoregulatory cells. MDSCs have multiple phenotypes which inhibit T cell responses by multiple mechanisms, and the environment dictates the development of suppressive properties and activation. Previous studies have demonstrated that MDSCs played important roles in systemic lupus erythematosus and rheumatic arthritis. However, the involvement of MDSCs in the immunopathology of SS is largely unknown.

Objectives: This study aims to investigate effects of MDSCs in SS progression and the potential association of MDSCs with the therapeutic effects of MSCs in the patients with SS and mice with SS-like symptoms.

Methods: The frequencies of MDSCs in the blood and bone marrow were detected by flow cytometry analysis in SS mice (NOD mice) and patients with SS. The NOD mice were adoptively transferred with MDSCs or treated with anti-Gr1 antibody to eliminate MDSCs. The salivary flow rate was measured and inflammatory infiltration in salivary glands was assessed. MSCs were infused into NOD mice to investigate the effects of MSCs on SS-like syndrome and changes of MDSCs. The percentages of MDSCs in SS patients before and after MSC transplantation were determined.

Results: The percentage of MDSCs increased significantly with the development of SS-like syndrome in NOD mice. The SS-like syndrome exacerbated after transfer of MDSCs, whereas deletion of MDSCs alleviated SS-like syndrome in NOD mice. MSC transplantation enhanced salivary flow rates and decreased lymphocyte infiltration in salivary glands in NOD mice. The percentages of MDSCs were down-regulated after MSC transplantation. MSC reduced IL-12 production in dendritic cells in vitro and in vivo. The IL-12 promoted generation of MDSCs in vitro. The numbers of MDSCs were positively correlated with disease activities of SS patients. The percentages of MDSCs were reduced after MSC transplantation in patients with SS.

Conclusion: 1. MDSC expansion positively correlated with inflammation during the progression of SS. 2. MSC transplantation had beneficial effects in SS mice. 3. IL-12 production by dendritic cells was reduced by MSCs. 4. The MDSCs expansion was induced by inflammatory IL-12 and reversed by MSC transplantation in SS. Thus, we have revealed a previously unrecognized function of MSC-mediated reduction of MDSCs in suppressing SS-like syndrome through inhibition of IL-12 production by DCs, which provided novel therapeutic strategies to treat patients with SS.

Acknowledgement: This work was supported by the National Natural Science Foundation of China (NSFC) (grant no. 81571583 and 81770061 to Genhong Yao, Jingjing Qi, Zhuoyu Zhang, Saisai Huang, Lingyun Sun. The Affiliated Drum Tower Hospital of Nanjing University Medical School, Department of Rheumatology and Immunology, Nanjing, China)

Results: Among differentially expressed renal microRNAs in LN, miR-127-3p was reduced in renal tissues of patients with LN. The miR-127-3p suppressed the fluoresce gene expression of ISRE induced by ISRE and the phosphorylation of STAT1 and STAT2. By microarray analysis, we found that most ISG was inhibited by miR127-3p in IFN-stimulated Hela cells. The functional deletion of miR-127-3p enhanced the IFN response in human primary mesangial cells, which was manifested by enhanced ISRE mediated reporter gene expression, enhanced STAT2 phosphorylation and increased ISG expression. In addition, we found that JAK1, the upstream tyrosine kinase of STAT1 and STAT2, was a new target molecule for miR-127-3p.

Conclusion: Our study shows that miR-127-3p can inhibit IFN signal transduction by targeting JAK1. The decreased expression of miR-127-3p in the kidney is associated with an overactive IFN response in the renal tissue of patients with LN. Subsequent mouse model studies indicate the therapeutic potential of miR-127-3p in treating lupus associated organ damage.

REFERENCES:

Disclosure of Interests: None declared

AB01988

BENEFIT OF CRITHIDIA TESTS IN DIAGNOSING CONNECTIVE TISSUE DISEASES

Abdul Basser Awal1, Shireen Shaffu2, Arthur Price3, Panagoula Gkargkoula2.
1University Hospitals of Leicester, Rheumatology, Leicester, United Kingdom; 2University Hospitals of Leicester HPB Unit, Leicester, United Kingdom; 3University Hospitals of Leicester HPB Unit, Immunology, Leicester, United Kingdom

Background: The diagnosis of systemic lupus erythematosus(SLE) relies on autoantibody testing, including double stranded DNA (dsDNA), the testing of which has evolved over time from the FARR assay through to ELISA/ELU. dsDNA assays can pick up non-specific single stranded DNA as false positives and can give occasional false negative results. To evaluate the implications of this we analysed our hospital's use of crithidia testing as a confirmatory assay of dsDNA results.

Objectives: Investigate the relation between dsDNA Abs measured by Crithidia test and ELIA. Define the clinical role for Crithidia testing.

Methods: All crithidia tests for an 8 months from January 2017 to August 2017 were reviewed and results of ANA, ENA, dsDNA and complement collected. Data were collected regarding referral to rheumatology and where possible rheumatology clinic letters were reviewed regarding final diagnosis.

Results: One hundred and four crithidia tests were undertaken of which 91 were negative and 13 positive.Sixteen of the 104 patients were ANA negative, 18 ANA 1:100, 70 ANA >/=1:400, and 14 patients had a positiveENA. Positive crithidia had a dsDNA range from 2 to 333 and negative crithidia from <1 to 131 however positive crithidia were more likely to have higher dsDNA and ANA titres. Of the 65 patients seen by rheumatology 4 did not have available notes for analysis. Ten of the 13 positive crithidia test results, 2 had a negative dsDNA level, one of whom was ANA 1:400 Ro positive and diagnosed with RA, the other was diagnosed as TNF induced lupus. Of the crithidia negative patients the median dsDNA level was 20, a range of diagnoses were made including 5 patients with SLE who had a positive Ro or La, 3 patients with SLE who were ANA negative, 2 with GCA/PMR, 2 MCTD, 2 with RA and 5 with inflammatory arthropathy. Twenty patients were documented as having no evidence of connective tissue disorders (CTDs),others remain under assessment.

Conclusion: We have shown a significant number of patients using our ELIA assay are dsDNA positive and crithidia negative. In patients with crithidia positivity autoimmune disease is more likely to be diagnosed. Crithidia testing appears to influence whether or not a patient will be referred to rheumatology, with negative crithidia less likely to be referred. This highlights some of the limitations of dsDNA ELISA testing however there is a clear role for this assay as depicted above in preventing over diagnosis of CTDs and unnecessary commitment to immunosuppression.

Disclosure of Interests: None declared

Systemic sclerosis, myositis and related syndromes – etiology, pathogenesis and animal models

Nouria Bennoufesta1,2,3, Samy Slimani4, Samir Raouhbia5, Daoud Roula6, Luc Mouthon5, Rechid Malek1,5, Frerhat-Abbas Séfit1 University, internal medicine, sétif, Algeria; 2Séfit Hospital University, internal medicine, sétif, Algeria; 3Cochin Hospital, internal medicine, Paris, France; 4Mostefa-Ben Boudaïf Batna University, Rhumatology, Batna, Algeria; 5Sallah-Boubnider Constantine 3 University, internal medicine, Constantine, Algeria; 6National Referral Center for Rare Systemic and Autoimmune Diseases, Hôpital Cochin, Assistance Publique-Hôpitaux de Paris, Université Paris Descartes, Paris, France, Internal medicine, Paris, France

Objectives: To assess the construct validity of the Arab Hand Function Index (AHFI), an Arab and adapted version of the Cочкиn hand functional scale (CHFS) and an Arab version of the Health Assessment Questionnaire (HAQ) in SSc.

Methods: We evaluated 100 patients with SSc followed between 2015 and 2017. All patients were white and fulfilled the American College of Rheumatology/European League Against Rheumatism criteria and/or the Lenyo and Medsger (2) criteria for SSc. Mean±SD age at the time of evaluation was 47.6±12.28 years. The mean±SD disease duration was 6.54±6.23 years. Forty-one (41%) patients had diffuse cutaneous SSc and 59 (59%) had limited cutaneous SSc. Global hand and wrist mobility were evaluated using the hand functional index (HFI) and Kapandji index. Global disability and hand disability were assessed by an Arabic and adapted version of the HAQ and by the Arab hand functional index, an Arabic and adapted version of the CHFS, respectively. Anxiety and depression significant symptoms were assessed with the Arabic version of Hospital Anxiety and Depression Scale (HADS) anxiety and HADS depression. Construct validity was assessed by convergent and divergent validity (Spearman's rank correlation coefficient) and factor analysis.

Results: The AHFI had correct convergent validity with global disability assessed by the HAQ (0.61) and the HFI (0.55), moderate correlation with the Kapandji Index (-0.48; inverse correlation), depression (HADd) (0.45) and anxiety (HADa) (0.42) and no correlation with the disease duration (0.29) and the age (0.19) (Table 1). Factor analysis (Table 2) extracted 2 factors that accounted for 64.45% of the total variance. The HAQ has a good correlation with hand disability (AHF: 0.61, anxiety (0.57) and the HFI (0.51), a moderate correlation with depression (0.47) and Kapandji index (-0.46) and a little correlation with the age (0.28) and the disease duration (0.10) (Table 1). The factor analysis of the HAQ, extracted 1 factor that accounted for 50.64% of the total variance (Table 2).

Conclusion: In patients with SSc, the AHFI and the Arabic HAQ have good construct validity. The total score of the AHFI explained 61% of the variance of the HAQ.

Acknowledgement: All the patients who participated in this study

Disclosure of Interests: Nouria Bennoufesta: None declared, Samy Slimani: None declared, Samir Raouhbia: None declared, Daoud Roula: Speakers bureau: Yes, Luc Mouthon: None declared, Rechid Malek: None declared

Table 1. Convergent and divergent validities of the AHFI and the HAQ for patients with SSc (correlation with other variables)***

<table>
<thead>
<tr>
<th>Scales</th>
<th>Spearman's correlation Coefficient</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHFI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Convergent validity</td>
<td>HAQ</td>
<td>0.61</td>
</tr>
<tr>
<td>HiFi</td>
<td>0.55</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Kapandji</td>
<td>-0.48</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Divergent validity</td>
<td>Depression (HADd)</td>
<td>0.45</td>
</tr>
<tr>
<td>Anxiety (HADa)</td>
<td>0.42</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Disease duration</td>
<td>0.29</td>
<td>0.003</td>
</tr>
<tr>
<td>Age</td>
<td>0.19</td>
<td>0.058</td>
</tr>
</tbody>
</table>

Longer version: There is a clear role for this assay as depicted above in preventing over diagnosis of CTDs and unnecessary commitment to immunosuppression.