murine colonization testing for immune modulatory properties of individual strains.

References:

Disclosure of Interests:
None declared.

Background: Systemic lupus erythematosus (SLE) is a multifactorial disease. Gut microbiota is an important environmental factor for SLE. The perturbation of gut microbiota is often observed at onset or during the disease course. The fragment of HCMV phosphoprotein 65 (HCMVpp65, 422-439) containing B cell epitopes has been reported to elicit humoral immunity and accelerate the autoimmune response in murine lupus. However, little is there to know about the interplay between viral trigger for SLE and the change of gut microbiota during lupus progression.

Objectives: By using a murine lupus model with NZB/W F1, we investigated the differential alteration in gut microbiota associated with the progression of lupus disease in HCMVpp65 422-439 immunized mice and control mice.

Methods: Ten-week-old NZB/W F1 mice were given or not given an intraperitoneal injection of 100-μg HCMVpp65 422-439 Peptide biweekly for four times. Fecal samples, urine and blood of mice were collected once every two weeks followed by 16S rRNA genes sequencing and ELISA tests. The pathological investigation of renal tissue from sacrificed mice was conducted at 24 weeks of mice age. Statistical analysis for dynamics and alteration of the gut microbiota as well as functional prediction of bacterial communities related to the progression of lupus-like activity was performed.

Results: HCMVpp65 422-439 immunization results in the onset of lupus-like activities in NZB/W F1 mice with a higher titer of anti-dsDNA antibody, creatinine and proteinuria, and severe glomerular damage (Figure 1). Also, higher diversity and increased family abundance of several bacterial species were observed in HCMVpp65 422-439 Immunized mice (Table 1 and Figure 2a). The predicted metagenomic taxonomic profile in NZB/W F1 mice showed statistically significant enrichment of flagellar assembly, bacterial motility, and chemotaxis (Figure 2b). Spearman’s correlation analysis revealed that a significant association between the increased relative family abundance for Succinivibrionaceae, Marniiaceae, Desulfovibrionaceae, and Rikenellaceae and HCMVpp65 422-439 induced lupus-like activity in NZB/W F1 mice (Figure 2c).

Conclusion: Our results demonstrated that HCMVpp65 422-439 immunization induced the change in gut microbiota composition and suggested the association of gut microbiota alteration with lupus-like activity in NZB/W F1 mice.

References:
THU0242
REGULATORY ROLE OF TRANSCRIPTION FACTOR BLIMP-1 IN SJÖGREN'S SYNDROME

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Background: The pathogenesis of primary sjögren's syndrome (pSS) is multifactorial. Self-antigen-driven responses perform a vital function in the development of autoimmune diseases [1]. B cells, only 20-25% of total infiltrating cells in labial glands, are the cellular basis for spontaneous antibody production [2]. Genome-wide association studies (GWAS) have identified Blimp-1 as a susceptibility gene for autoimmune diseases and played an important role in the pathogenesis of autoimmune diseases [3].

Objectives: To investigate the expression and effect of B lymphocyte induced maturation protein 1 (Blimp-1) in pSS and the correlation of Blimp-1 with B cell subsets and clinical features.

Methods: The PRDM1 mRNA expression in B lymphocyte and labial gland were examined by RT-PCR. The levels of B cell subsets were examined by flow cytometry. Hematoxylin-eosin (HE) staining and immunohistochemistry (IHC) were used to examine the invasion degree of lymph cell and Blimp-1 distribution, respectively. The correlation of PRDM1 mRNA with B cell subsets and clinical indicators were also analyzed.

Results: The levels of PRDM1 mRNA expression of B cells were significantly higher in SS than in healthy controls (HC) and which were also significantly higher in the high immunoglobulin (Ig) group than that in normal Ig group (P<0.02, Fig. 1a-b). The number of CD19+B cells and CD138+ plasma cells (PC) have increased while the CD27+ cells decreased in SS (P<0.05). The percentage of PC and PC/B is positively correlated with PRDM1 mRNA (r=0.380, P=0.002; r=0.317, P=0.009, Fig. 1c-d). Blimp-1 expression level showed a positive correlation with invasion degree of lymph cell in histology (Fig. 2a-c), Ig levels and ESSDAI score and an inverse correlation with the glucocorticoids usage (Fig. 3c).

Conclusion: Blimp-1 displayed high expression in SS, which could affect pSS disease activity. SS activity is suppressed by glucocorticoid which might be through inhibition of Blimp-1.

References:

Table 1. Clinical characteristics of pSS and HC.

<table>
<thead>
<tr>
<th></th>
<th>HC (n=17)</th>
<th>pSS (n=50)</th>
</tr>
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<tbody>
<tr>
<td>Sex (Male/Female)</td>
<td>0/17</td>
<td>0/50</td>
</tr>
<tr>
<td>Age(exx)</td>
<td>45.2±18.55</td>
<td>48.6±11.05</td>
</tr>
<tr>
<td>Xerostomia(positive/negative)</td>
<td>0/17</td>
<td>43/7</td>
</tr>
<tr>
<td>Keratoconjunctivitis sicca</td>
<td>0/17</td>
<td>35/15</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>0/17</td>
<td>32/18</td>
</tr>
<tr>
<td>Fatigue</td>
<td>0/17</td>
<td>18/32</td>
</tr>
<tr>
<td>ESSDAI(exx)</td>
<td>-</td>
<td>2.78±1.61 (0–7)</td>
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<tr>
<td>ESSPRI(exx)</td>
<td>-</td>
<td>3.3±1.39 (1–6)</td>
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<tr>
<td>ANA(positive/negative)</td>
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<tr>
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<tr>
<td>SSB</td>
<td>-</td>
<td>18/32</td>
</tr>
</tbody>
</table>

pSS: primary sjögren’s syndrome; HC: Healthy controls; ESSDAI: The European League Against Rheumatism Sjögren’s Syndrome Disease Activity Index; ESSPRI: EULAR Sjögren’s Syndrome Patient Reported Index. ** P<0.01, *** P<0.001.

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