Results: LmNKLN1, dominantly located in nucleus, was up-regulated in lupus patients compared to healthy donors, and could be induced by IFNα and TLR ligands in HPMC. Silencing LmNKLN1 significantly reduced the expression of a group of interferon-inducible genes, including IFIT3, OAS1, CXCL10, etc. We used loss-of-function and gain-of-function strategy through CRISPR system to confirm that LmNKLN1 positively regulated type I interferon pathway. Furthermore, it was identified the involvement of LmNKLN1 in interferon signalling path-way was through regulating the expression of STAT1, IRF9 and phosphorylation of IRF9 and STAT1 although its mechanism is also needed to investigate.

Conclusions: Upregulated LmNKLN1 expression contributed to abnormal activation of interferon pathway of SLE.

Disclosure of Interest: None declared


AB0181

ENHANCED THERAPEUTIC EFFICACY OF APOPTOTIC VITAMIN D AND VITAMIN D RECEPTOR IN PATIENTS WITH SCLERODERMA SUBTYPES
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Background: Mesenchymal stem cells (MSCs) exhibit promising therapeutic potential in systemic lupus erythematosus (SLE). Increased apoptotic cells (ACs) were observed in SLE, and our previous study showed: MSC transplantation reduced AC levels in patients with SLE. Yet the effects of ACs on MSCs are not clear.

Objectives: This study aims to investigate the effects of ACs on MSCs and efficacy of AC treated MSCs (AC-MSCs) in SLE.

Methods: Jurkat T cells were irradiated by ultraviolet ray to induce apoptosis and then co-cultured with umbilical cord derived MSCs. Then, ACs were removed and MSCs were further co-cultured with human peripheral blood mononuclear cells (PBMCs). The inhibition of MSCs on PBMC proliferation was detected by flow cytometry. MSCs and AC-MSCs were infused into lupus prone MRL/lpr mice respectively to compare their therapeutic effects.

Results: The suppression of MSCs on PBMC proliferation was significantly enhanced after co-culture with ACs. In vivo study showed that AC-MSCs significantly increased the survival rate of MRL/lpr mice and decreased urine protein as early as one week after treatment, while MSCs decreased urine protein eight weeks post infusion. Moreover, AC-MSCs remarkably reduced the number of splenic plasma cells and serum anti-dsDNA levels, whereas MSCs only showed decreased tendency.

Conclusions: ACs enhanced therapeutic effects of MSC transplantation in lupus mice, which provides new insights into MSC modification in the treatment of SLE.

Disclosure of Interest: None declared


AB0182

MOLECULAR MECHANISMS MEDIATING ANTIOXIDANT EFFECT OF EPIGALCATECHIN-3-GALLATE IN EXPERIMENTAL SCLERODERMA MODEL
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Background: Scleroderma (SSc) is an autoimmune multisystemic connective tissue disease characterised by skin and internal organ fibrosis.1 Underlying mechanism is still unclear for SSc. Besides there is no specific treatment for SSc, various treatments may alleviate symptoms and improve the quality of life. Epigallocatechin-3-gallocate (ECGC) is a phenol with antioxidant effects in many disease processes.2 In this disease, oxidative stress may play a role for pathogenesis.3,4 Recent studies showed a relationship between oxidative/anti-oxidative markers and SSc.5

Objectives: The aim of this study was to investigate the antioxidant effects of epigallocatechin-3-gallocate in the scleroderma process in experimental mouse model with bleomycin.

Methods: Thirty-two healthy female Balb-c mouse species were used and randomly divided into four groups:control, bleomycin, bleomycin + EGCG, EGCG. At the end of the experiment, skin tissues were collected. Sodium dinitrosamine enzyme (SOD) and malondialdehyde (MDA) levels have been analysed for oxidative stress. High performance liquid chromatography (HPLC) was used for MDA measurements. Colorimetric kit was used for SOD analysis. Furthermore, the ratio of phosphorylated p38 total p38 protein, and phosphorylated Akt total Akt protein and NF-kappa B were measured by western blotting. Immunohistochemistry (ox-SMA), histochmistry (masson trichrome-hematoxylin and eosin) studies were also performed on FFPE skin samples.

Results: When the experimental and control groups were compared, the degree of fibrosis in the connective tissue of the dermis areas stained with masson trichrome decreased in the ECGG groups, and p38 phosphorylation was increased in the ECGG groups compared to the positive control group, and MDA was significantly decreased in the ECGG groups. According to Western blotting results, p38 MAPK and NF-xB were found to decrease significantly in the ECGG groups compared with the controls. Parallel to these findings, phosphorylated Akt protein was found to increase in the ECGG groups compared with the control groups.

Conclusions: It has been shown that ECGG can antioxidative effect in scleroderma.

References:

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