rheumatoid arthritis (RA) [2]. Therefore, neutralizing IL-17 might be a therapeutic option during the asymptomatic autoimmune prodromal phase in autoimmune diseases like RA, where TH17 cytokines orchestrate the emergence of a pro-inflammatory autoantibody response and the transition into active RA.

REFERENCES:

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AB0017 IMMUNE CHARACTERISTICS OF PERIPHERAL BLOOD IN SECONDARY SJOGREN’S SYNDROME PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Secondary Sjögren’s Syndrome (sSS) is diagnosed when symptoms of SS coexist with other systemic connective tissue disease, often secondary to rheumatoid arthritis(RA). The occurrence of SS secondary with RA will worsen the course of disease and increase the high incidence and mortality of RA. At present, the immune characteristics of peripheral blood of sSS with RA are not clear.

Objectives: To observe the difference of immune characteristics in peripheral blood between sSS secondary to RA, primary Sjögren’s syndrome(sS) and RA patients.

Methods: 20 sSS with RA patients, 20 pSS patients and 20 RA patients hospitalised in Shanxi Medical University The Second Hospital were enrolled. The percentage and absolute numbers of lymphocyte phenotypes and CD4+ T subsets in peripheral blood were examined by flow cytometry.

Results: As for the percentage and absolute number of total T, B, NK, CD4+T, CD8+T and the ratio of CD4+ T to CD8+ T cells, there was no significant difference between the sSS with RA, RA, and sSS group. There was also no statistical difference in the percentage of CD4+ T subsets (Th1, Th2, Th17 and Treg) between the three groups. But the ratio of Th17 and Treg in sSS with RA group was increased than pSS group. About comparison of absolute number of CD4+ T subsets, there was no statistical difference among the three groups except that the Th1 cells in RA group was significantly higher than sSS group.

Conclusion: Elevated Th17/Treg may be an immunological feature that differentiates sSS with RA patients from sSS patients. In addition, in general, peripheral blood of patients with RA and SS have similar immune characteristics.

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Figure 1. The comparison about the lymphocyte phenotypes and CD4+ T subsets in peripheral blood of sSS with RA(n=20), pSS(n=20) and RA patients(n=20). (*p<0.005, **p<0.001, *p<0.001)

Disclosure of Interests: None declared

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AB0018 ACCUMULATION OF FUNCTIONALLY MATURE CD1C+ DENDRITIC CELLS CONTRIBUTES TO SYNOVIAL INFLAMMATION IN INFLAMMATORY ARTHRITIS

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Background: Myeloid Dendritic Cells (DC) are potent antigen presenting cells that can be subdivided into CD141+ and CD1c+ DC. We have previously reported an unacknowledged role for CD141+ DC in the IA synovium. However, the identification and functional role of CD1c+ DC in the IA synovium has yet to be fully elucidated.

Objectives: To investigate if CD1c+ DC reside in the IA synovium and ascertain if they represent a unique population, distinct from peripheral CD1c+DC and if they contribute to synovial inflammation.

Methods: Synovial tissue (ST) biopsies and synovial fluid mononuclear cells (SFMC) were obtained via arthroscopy and healthy control (HC) ST was obtained during ACL surgery. Synovial tissue single cells suspensions were generated following enzymatic and mechanical digestion. Single cell analysis of synovial cell suspensions, along with PBMC and SFMC was performed by multicolour flow cytometry. CD1c+DC were sorted from IA synovial fluid and peripheral blood and bulk RNA sequencing was performed. CD1c+ DC functionality and maturation was assessed using OVA DQ phagocytosis assays, multiplex ELISA and DC: T cell co-cultures.

Results: Within the circulation the frequency of CD1c+DC are significantly decreased in IA peripheral blood compared to HC (p<0.01) in addition to expressing significantly higher levels of the maturation markers CD80 (p<0.01) and CD40 (p<0.01). IA peripheral blood DC also express significantly higher levels of CXCR3 (p<0.01) and CCR7 (p<0.05) compared to HC - suggestive of DC migration from the periphery to the synovium. Following RNA-seq analysis, IPA and differentially expressed gene (DEG) analysis revealed an enrichment in genes involved in DC maturation, TLR signalling and chemokine signalling in IA peripheral blood compared to HC. In support of the hypothesis that DC migrate and accumulate in the IA synovium, CD1c+ DC were identified in IA ST and were significantly enriched compared to IA peripheral blood (p<0.01). IA ST CD1c+DC express significantly higher levels of the activation marker CD80 compared to IA peripheral blood (p<0.05) or HC ST (p<0.05). Upon examination of IA synovial fluid, we report similar findings to ST, whereby CD1c+DC are enriched in synovial fluid compared to PB (p<0.001). Moreover, RNA sequencing and PCA analysis of synovial versus blood CD1c+DC revealed distinct transcriptional variation between both sites. Functionally, synovial CD1c+DC express higher levels of the maturation markers CD80, CD83, CD40, PD-L1 and BTLA (all p<0.05) and have distinct coexpression of these maturation markers which is unique to the synovium. Synovial CD1c+DC are less phagocytic compared to peripheral blood DC, have decreased production of MMP1 and MMP9 and importantly are still capable of additional activation in vitro. Finally, synovial CD1c+DC induce the proinflammatory cytokines TNFα, GMCSF, IL-17a and IFNγ from CD4+ T-cells in allogeneic DC: T cells cocultures.

Conclusion: Mature circulating CD1c+DC migrate and accumulate in the IA synovium. Synovial DC are present in the IA synovium in a mature state, have distinct tissue specific characteristics and can induce proinflammatory CD4+ T cell responses.

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AB0019 TREATMENT OF AUTOIMMUNE AND INFLAMMATORY SKIN DISEASES USING SKIN-TARGETING BIOMETHERAPEUTICS: A LOCALIZED IMMUNOMODULATION APPROACH

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Background: Development of therapeutic methods for skin disease poses a challenge, due to the presence of hair follicles in the skin that cells targeting agents would have to penetrate. We have previously described a novel therapeutic that uses a murine α4β1 integrin targeted immunoconjugate that binds to the skin microvasculature. Here, we describe efforts in human clinical trials to develop this approach.

Methods: We have published data from a phase 1 trial in healthy volunteers that showed the tolerability and safety of the human immunoconjugate. We describe preclinical data from non-human primates that validated the targeting, homing and killing of human keratinocytes (HC) using the human immunoconjugate. Importantly, we present data from a phase 2a clinical trial in patients with psoriasis, which demonstrated that patients with mild to moderate disease responded to treatment with the immunoconjugate.

Results: The phase 1 trial established the maximum tolerated dose (MTD) in human subjects. The phase 2a trial was conducted in 32 patients with psoriasis with disease severity ranging from mild to severe. Treatment with the immunoconjugate was generally well tolerated and the disease severity was significantly reduced in treated patients.

Conclusion: The human immunoconjugate was generally well tolerated in healthy volunteers and the phase 2a trial demonstrated efficacy in patients with psoriasis. These results are promising and show this novel therapeutic approach has potential to treat a variety of skin diseases.

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