Background: Systemic sclerosis (SSc) is a heterogeneous disease characterized by fibrosis, vasculopathy, and autoimmunity. Dysfunctions causing disease pathology are characterized by the activation and recruitment of immune cells, as well as the formation of autoantibodies and cytokines. Profibrotic cytokines, such as interleukin-(IL)-13, IL4 or IL6 play a crucial role in collagen production and fibrosis development [1]. Preliminary data reveal IL13 as a main driver for oblitative vasculopathy characterized by severe Raynaud phenomenon, acral ulcers and pulmonary arterial hypertension (PAH). Particularly acral ulcerations lead to a severe impairment in functional capacity in everyday life. In addition, pulmonary arterial hypertension is one of the main causes of the high mortality rate in SSc [2].

Objectives: To prove the impact of IL13 in the pathogenesis of systemic sclerosis and thus provide the rationale for the identification of a potential new therapeutic target, we investigated IL13 expression in CD4 and CD8 T cells in patients suffering from systemic sclerosis compared to healthy controls.

Methods: Peripheral blood mononuclear cells (PBMC) obtained from systemic sclerosis (SSc, n=31) patients and healthy controls (HC, n=13) were cultured without or in the presence of phorbol myristate acetate and ionomycin to activate T cells for cytokine production. Brefeldin A was used as an inhibitor of cytokine secretion. The intracellular IL13 and IL4 expression of CD4 and CD8 positive T cells were measured by flow cytometry and were compared between the investigated subgroups.

To identify a disease phenotype mediated by IL13, the expression levels in the SSc group were correlated to clinical, laboratory and apparative parameters assessing organ dysfunction.

Results: While there were no significant differences in IL4 expression between healthy and diseased individuals, analyses of IL13 positive CD4 and CD8 T cells showed significant differences compared to HC (CD8+IL13 p=0.048; CD4+IL13 p=0.0046) revealing the functional differences though high structural homology of the two interleukins. The increased expression of IL13 in T cells from patients with systemic sclerosis further supports the assumption of an interleukin mediated pathomechanism. Considering the IL13-mediated clinical phenotype, high levels were detected in patients showing signs for vasculopathy. correlation with sPAP (CD4+IL13 p=0.0392), NTproBNP (CD4+IL13 p=0.0461), creatinine (CD4+IL13 p=0.0227), angiotensin II receptor type I and endothelin receptor type A antibodies (CD4+IL13 p=0.0105, p=0.0042) was demonstrated. In addition, patients in the fourth quartile of CD4+IL13 expression showed a higher incidence of acral ulcers and pits than patients with low interleukin levels. Moreover, this group of patients had an increased cardiovascular comorbidity including atherosclerosis, coronary heart disease and arterial hypertension.

Conclusion: Increased IL13 levels could be detected in patients with SSc, especially in patients with the phenotype of an oblitative vasculopathy. This indicates preliminary evidence for the use of IL13 blockers as a new therapeutic approach in systemic sclerosis.

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Vasculitis - Large vessel vasculitis

PATTERNS OF LARGE-VEssel LESIONS AND POOR TREATMENT OUTCOMES IN PATIENTS WITH LARGE-VEssel GIANT CELL ARTERITIS

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