controls) of IL-2 positive cells; 6 patients and 1 control of IL-4 positive cells and 7 patients and 0 control of IFN- γ positive cells. Six patients presented increased percentages of both IL-2 and IL-4 and IFN- γ (i.e. they had both Th1 and Th2 activation), 4 of IL-2 positive cells and 1 IFN- γ only (isolated Th1 activation).

After PMA stimulation 6 patients presented increased percentages of IFN- γ positive cells; 1 of IL-4 and 0 patient of IL-2 positive cells.

Conclusion Our study demonstrates that Th1 activation occurs in peripheral blood of SSc patients. The role, if any, of such activation must be investigated.

OP0040 BUCILLAMINE AND ITS METABOLITES INDUCE SYNTHESIS OF VEGF DOSE DEPENDENTLY IN SYSTEMIC SCLEROSIS FIBROBLASTS VIA THE NF-KB PATHWAY

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Background Bucillamine (BUC) is an immunomodulatory drug used in the treatment of rheumatoid arthritis with inhibitory effects on B- and T-cell functions. However, the impact of Bucillamine on metabolic pathways of fibroblasts has not been addressed.

Objectives Since an altered metabolism of fibroblasts is a hallmark of systemic sclerosis (SSc), we investigated whether BUC and its metabolites SA981 and SA679 influence the cytokine pattern of skin fibroblasts and might be of therapeutical use in SSc.

Methods Cultures of skin fibroblasts from 6 patients with SSc and 5 healthy controls were incubated with BUC, SA981 and SA679 at different concentrations for 6 to 24 h. Quantification for VEGF, IL-6 and TGF- β 1 mRNA was performed with real-time PCR (TaqMan). Supernatants were analysed for VEGF by ELISA. In addition, fibroblasts were preincubated with the NF- κ B inhibitor pyrrolidine dithiocarbamate (PDTC) and analysed for the expression of VEGF as describe above. The trypan blue dye exclusion test was used to assess the viability of the cells. The effects on the chemotactic activity of fibroblasts were examined in a modified Boyden chamber assay.

Results VEGF mRNA was increased in all fibroblast cultures after BUC treatment compared to non-treated controls, whereas no effect was observed on the levels of IL-6 and TGF- β 1. VEGF mRNA increased dose dependently with both BUC and its metabolites. The most significant induction was observed after treatment with SA981 (1 mg/ml: 7.7 ± 4.3 , 0,6 mg/ml: 5.2 ± 2.3 ; 0,15 mg/ml: 2.9 ± 1.4 , 0,05 mg/ml: 2.5 ± 1.9 fold increase, $p < 0.05$). Fibroblast cultures from patients with SSc showed a consistent higher inducibility of VEGF than cultures from healthy controls (SSc: 9.9 ± 4.3 ; healthy controls: 5.2 ± 2.8 fold increase, $p < 0.05$). These results were confirmed on the protein level with a significant rise of VEGF in SSc cultures, but not in healthy controls. The increase of VEGF was not due to unspecific toxicity, since the cell viability was $>95\%$ in treated and non-treated fibroblasts. Preincubation with the NF- κ B inhibitor PDTC reduced the production of VEGF by 60%. Interestingly, there was a significant increase in the chemotactic activity of supernatants from fibroblasts treated with BUC (133 ± 39 cells/high power field = hpf), SA679 (72 ± 19 cells/hpf)

and SA981 (43 ± 5 cells/hpf) compared to non-treated controls (26 ± 7 cells/hpf).

Conclusion Our results indicate that BUC and its metabolites, in addition to the known immunomodulatory effects, may have favourable influence on neoangiogenesis in SSc through the release of VEGF by skin fibroblasts. Since impaired angiogenesis and inflammatory infiltrates are hallmarks in the pathogenesis of SSc, BUC may be of benefit in the treatment of this disease.

OP0041 ESOPHAGEAL MANOMETRY FINDINGS IN PATIENTS WITH RAYNAUD'S PHENOMENON AND POSITIVE ANTINUCLEAR ANTIBODIES

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Background

Objectives To study the esophageal manometry in patients with Raynaud's phenomenon and positive antinuclear antibodies (ANA) in the absence of esophageal, skin or internal organs manifestations.

Methods 14 patients, 13 women and 1 man (46,8 mean age; 9–65 years) with mean evolution time of Raynaud's phenomenon of 5 years were included in this study. Nailfold capillary microscopy study, autoantibodies profile and esophageal manometry (Synetics Manometry Unid. Synetics neumocapillary Pump and Poligraph) were performed in all patients. The lower esophageal sphincter, esophageal body and upper esophageal sphincter pressures were analysed independently.

Results 44% patients had a lower esophageal sphincter hipotonia which showed a significant relationship ($p < 0.05$) with the presence of both articular disease (33.5%) and anti-centromere antibodies (44.4%). However, the nailfold scleroderma pattern (61%) did not show a significant relationship with lower esophageal sphincter hipotonia. 33.3% patients showed unspecific motor alterations in the esophageal body. There was significant relationship ($p < 0.001$) between esophageal body alterations and the nailfold scleroderma pattern. In all patients studied, the function of the upper esophageal sphincter was within the normal limits. In the control group of patients with Raynaud's phenomenon and negative ANA, the esophageal manometry was normal.

Conclusion Alterations in the esophageal manometry are frequent in patients with Raynaud's phenomenon and positive ANA and they suggest the presence of systemic disease even in the absence of skin or internal organs involvement.

OP0125 OVEREXPRESSION OF VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) AND ITS RECEPTORS IN SYSTEMIC SCLEROSIS (SSC): EVIDENCE FOR PROTECTIVE EFFECTS OF VEGF AGAINST THE DEVELOPMENT OF FINGERTIP ULCERS

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