C-reactive protein (CRP) and muscle-associated enzymes creatine phosphokinase (CK) and lactate dehydrogenase (LD) were measured by routine laboratory methods.

**Results** In patients with FM, serum levels of S100A4 protein were significantly higher than those observed in healthy controls or DM patients (148.6 ± 531.5 versus 80.75 ± 285.1, p < 0.01 and 43.55 ± 53.03, p < 0.05, respectively). No significant differences in S100A4 levels were found between CAM patients (119.9 ± 414.0) and healthy controls or other myositis patients. In the whole group of IIM patients, serum S100A4 levels correlated with MYOACT score (r = 0.39; p < 0.001) and its components: Constitutional Disease Activity (DA) (r = 0.34; p < 0.001) and Pulmonary DA (r = 0.44; p < 0.001). Serum S100A4 correlated also with Muscular DA (r = 0.25; p < 0.05), CK (r = 0.33; p < 0.01) and LD (r = 0.40; p < 0.01). S100A4 levels correlated with Cutaneous DA (r = 0.46; p < 0.01) in DM patients and with Extramuscular Global Assessment only in FM patients (r = 0.55; p < 0.001). No significant correlations of S100A4 serum levels in patients with CAM were found. In the 11 longitudinal IIM samples there was no significant decrease of S100A4 serum levels observed. Multiple regression of the whole IIM patients group showed significant association of S100A4 serum levels with Pulmonary DA (β = 0.369; p < 0.01), LD (β = 0.545; p < 0.01) and severity of dysphagia (β = −0.250; p < 0.05). In FM patients, S100A4 levels were associated with Extramuscular Global Assessment (β = 0.552; p < 0.01) and in DM patients with MYOACT (β = 0.557; p < 0.01) and CRP (β = 0.391; p < 0.05).

**Conclusions** This is the first study showing that circulating levels of S100A4 are associated with several features of IIM disease activity, particularly with extramuscular components. We did not find any association of S100A4 levels and cancer associated myositis. Further studies analysing bioactive form of S100A4 and the role of S100A4 in cancer associated myositis are needed.
GDF15, A MARKER OF LUNG INVOLVEMENT IN SYSTEMIC SCLEROSIS, IS INVOLVED IN ALTERED CYTOKINE SECRETION BY FIBROBLASTS, BUT DOES NOT IMPAIR FIBROSIS DEVELOPMENT

Objective

Systemic sclerosis is a progressive connective tissue disorder involving autoimmune processes. It is generally known that members of the TGF-β superfamily are involved in the regulation of connective tissue metabolism in systemic sclerosis (Scs), but also in regulating the immune system. Growth differentiation factor 15 is a distant member of this TGF-β family. We aim to evaluate the role of GDF15 in Scs-pathogenesis.

Methods

A longitudinal prospective cohort of SSc patients was screened for GDF15 serum levels by ELISA and associations with disease activity and tissue damage were analysed. Moreover, in vitro stimulation experiments were performed in lung fibroblasts. The role of GDF15 in fibrosis development in vivo was evaluated by performing the bleomycin lung fibrosis model in GDF15 deficient mice.

Results

Serum samples from a cohort of 122 patients were screened for GDF15 levels. An increase in GDF15 levels was observed in patients classified as limited SSc, limited cutaneous SSc and diffuse SSc. Moreover, GDF15 serum levels highly correlated with disease activity and clinical symptoms of lung fibrosis. This was also mimicked in the bleomycin mouse model of SSc. Here, bleomycin exposed animals displayed elevated expression levels of GDF15 in lung tissue. Isolated lung fibroblast of GDF15 deficient mice showed reduced induction of IL6 and CCL2 upon bleomycin stimulation compared to wild-type littermates. Both, IL6 and CCL2, are involved in recruitment and activation of the immune system. Surprisingly, no differences in end-stage fibrosis development were observed between wild-type and GDF15 deficient animals after bleomycin injection.

Conclusions

An intriguing profile of GDF15 serum levels was found in SSc patients. GDF15 expression is induced during fibrosis development. We hypothesise that the altered GDF15 expression by lung fibroblast may contribute to distorted interaction between the immune system and the stromal connective tissue. From our data it is clear that this protein may participate in fibrosis initiation, but is not indispensable in the course of fibrosis development in vivo.