Conclusion: The newly described antibodies against GPCR, GF and GFR are highly correlated. Associations with morbidity and mortality-determining organ involvement indicate their possible functional relevance and novel pathophysiological mechanisms. As new biomarkers, some of the ab have prognostic value for SSc; for other manifestations, their value should be evaluated in further studies.

REFERENCES:

Disclosure of Interests: Kristina Sterner: None declared, Césaire J.K. Foucodo: None declared, Ine König: None declared, Axel Künster: None declared, Hauke Busch: None declared, Harald Heidecke Shareholder of: owner of CellTrend, Anja Schumann: None declared, Antje Müller: None declared, Gabriela Riemekasten: None declared, Susanne Schinke Grant/research support from: UCb sponsors EUULAR registration fees DOI: 10.1136/annrheumdis-2021-eular.1504


Background: AX-202 is a monoclonal antibody that inhibits the bioactivity of S100A4. S100A4 is an alarm signal that is released from cells in response to stress or injury and functions as an amplifying mechanism of inflammation and fibrosis in the diseased tissue microenvironment. Previous in vitro studies have found that S100A4 induces fibroblast activation, sensitizes fibroblasts to the effects of TGFβ, drives epithelial-mesenchymal transition, and stimulates monocyte cytokine release (1-3). Moreover, S100A4-/- mice are protected from fibrosis in several animal models (1). In patients with systemic sclerosis (SSc), S100A4 is elevated both in lesional tissue and systemically and correlates with skin involvement, disease activity, and pulmonary function.

Objectives: The aim of this study was to assess the antibiotic effects of murine AX-202 in two pre-clinical models of SSs reflecting both inflammation-mediated and inflammation non-mediated fibrosis and confirm the in vivo activity of humanized AX-202.

Methods: We first evaluated the effects of murine AX-202 in the bleomycin-induced skin fibrosis model and the tight-skin 1 (Tsk-1) model. In the bleomycin (BLM) model, fibrosis was induced by 3 weeks of BLM s.c. injections followed by 3 weeks of AX-202 treatment in parallel with continued BLM s.c. injections. The control groups included NaCl s.c. injections for 6 weeks, BLM s.c. injections for 6 weeks, or BLM s.c. injections for 3 weeks, followed by NaCl s.c. injections for 3 weeks. Three dosing regimens of AX-202 were tested: 3.75, 7.5, or 12.5 mg/kg i.p. every 3rd day. In the Tsk-1 model, treatment with 7.5 mg/kg i.p. every 5 to 7 weeks was started at the age of 6 to 8 weeks, and the control groups included positive, negative, and control groups. AX-202 treatment was administered from week 5 until week 10. The control groups included pa...
the “Slow Progressor” (3303 ± 6665 pg/ml vs 13300 ± 10308 pg/ml; p=0.052) without reaching a significant value, due probably to the low number of cases.

Conclusion: Our study confirms that the presence of specific autoantibodies and capillaroscopic abnormalities correlate to an increased risk of developing SSc in patients with UCTD [6]. Beside we found significantly higher levels of CXCL4 in our 27 VEDOSS patients respect to controls, in agreement with other authors showing the association of this chemokine with early stages and specific organ involvement [4][5][7]. The finding of CXCL4 lower levels in “fast progressor” cases is consistent with our recent report of anti-CXCL4 antibodies in patients with early SSc, determining lower levels of this antigen [7]. We need deeper investigations to better evaluate the role of CXCL4 in the different stages of SSc.

REFERENCES:

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**OP0247**

**IN MYOSITIS MUSCLE FIBRE PLAYS A DIRECT AND CRITICAL ROLE IN THERAPEUTIC RESPONSE TO GLUCOCORTICOIDS**


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Background: Myositis are rare autoimmune diseases, affecting more women than men, characterized by chronic inflammation of skeletal muscle causing muscle weakness, decreased quality of life and increased mortality.

Glucocorticoids (GC) are potent anti-inflammatory drugs, and are the first line treatment of myositis. They improve muscle strength of myositis patients (therapeutic effect), yet muscle recovery is generally only partial. Moreover, GC have an iatrogenic effect on skeletal muscle fibre leading to steroid myopathy. Thus myositis care has to be improved. Despite the autoimmune terrain of myositis, our team has recently shown that muscle fibres themselves develop immuno-metabolic modifications that participate to muscle weakness and perpetuation of the disease\textsuperscript{1}. GC effects are mediated by the glucocorticoid receptor (GR), which is expressed in various cell types including immune cells and myofibres, but the cells mediating therapeutic responses remain to be determined.

Objectives: Unravel the mechanisms underlying the therapeutic effect of GC in myositis, particularly elucidate the role of skeletal muscle fibres.

Methods: Experimental myositis was induced in eight to ten-week-old C57BL/6J female mice by a single intradermal injection of part of skeletal muscle fast-type myositis, particularly elucidate the role of skeletal muscle fibres.

Results: Muscle strength was decreased in both GR L2/L2 and GR(i)skm-/- myositis mice from D 14 to D 20. GR L2/L2 myositis mice recovered muscle strength after PND treatment; no significant difference compared to D 0 was detected. In contrast, PND did not improve muscle strength in GR(i)skm-/- myositis mice (Figure 1).

Conclusion: GR in skeletal muscle fibre is crucial to mediate the therapeutic response to GC in a murine model of myositis. Autoagy is one of the candidate pathways controlled by myofibre GR underlying this effect.

REFERENCES:

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**OP0248**

**DEVELOPMENT OF A 3D SKIN MICROTISSUE MODEL FOR FIBROTIC DISEASES**

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Background: Traditional preclinical approaches, such as two-dimensional cell culture and animal models, are often inadequate to mimic the pathophysiological features of complex diseases such as systemic sclerosis (SSc). Human specific targets, such as the recently described pro-fibrotic long non coding RNA (lncRNA) H19X\textsuperscript{1}, are becoming increasingly relevant in preclinical research, creating the need of new strategies and tools in translational medicine. The employment of novel three-dimensional (3D) culture systems, where multiple cell types are included, is filling an important gap left by the traditional preclinical methods.

Objectives: To develop an easy to produce 3D fibrotic skin microtissues model for translational proof of concept studies.

Methods: Two thousand five hundred dermal fibroblasts isolated from skin of SSc patients were seeded in ultra-low attachment 96-well plates. Fibroblasts were let to aggregate into spheres for 48h. Two thousand five hundred primary normal human keratinocytes were added to the culture and let to layer onto the fibroblast spheres for 72h. H19X silencing experiments were used as proof of concept studies. H19X silencing with antisense oligonucleotides or transfections with a scrambled control were performed in fibroblasts prior to the sphere formation for 24h.

Results: Capacity of H19X silencing in fibroblasts to impact on fibrotic phenotype was assessed by quantifying the expression of specific fibrotic markers in the supernatants with ELISA.

Conclusion: H19X silencing in fibroblasts to impact on fibrotic phenotype was assessed by quantifying the expression of specific fibrotic markers in the supernatants with ELISA.