subsets were defined by flow cytometry. Healthy donors and patients with rheumatoid arthritis served as controls.

**Results:** We observed that ATA- and ACA-positive SSC patients harbour circulating B cells that secrete either ATA-IgG or ACA-IgG upon stimulation, depending on their serotype. In addition, we noted spontaneous secretion of ATA-IgG and, more remarkably, extensive secretion of ATA-IgA in ATA-positive patients. This degree of spontaneous, antigen-specific IgA secretion was specific for the ATA response in ATA-positive patients, while spontaneous ACA-IgA secretion was undetectable in the ACA-positive patient group. FACs experiments showed that spontaneously ATA-IgA secreting B cells were primarily present in the plasmablast compartment.

**Conclusion:** Our findings demonstrate that ATA-positive SSC patients harbour an activated ATA-IgG and ATA-IgA B cell response, as indicated by the spontaneous secretion of both ATA isotypes by circulating plasmablasts. Remarkably, the ACA B cell response was far less active and lacked the active IgA component which suggests a difference in the triggers driving these autoreactive B cell responses in patients. Moreover, the remarkable ATA-IgA secretion points towards a potential mucosal origin of the ATA response.

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We investigated the fibrotic effect of IL-6 stimulation on dermal fibroblasts. Antibodies from patients with systemic sclerosis (SSc) target dermal fibroblasts in the skin. IL-6 is a pro-inflammatory cytokine, which is increased in SSc patients. We investigated the fibrotic response of dermal fibroblasts to IL-6 + sIL-6R stimulation. IL-6 modulated the fibronectin level and modulated the collagen type III formation in a somewhat dose-dependent manner. In combination with TGFβ, IL-6 decreased collagen type I and IV formation and fibronectin. However, in this study inhibition of IL-6R by TCZ did not change the fibrotic response of the dermal fibroblasts. This study indicated that IL-6 did not induce collagen formation in dermal fibroblasts, except type III collagen formation with high IL-6 concentration.

**Figure:**

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We investigated the fibrotic effect of IL-6 + sIL-6R in a dermal fibroblast model and assessed fibrosis by neo-epitope biomarkers of extracellular matrix proteins.

**Methods:** Primary healthy human dermal fibroblasts were grown for up to 17 days in DMEM medium with 0.4% fetal calf serum, ficoll (to produce a crowded environment) and ascorbic acid. IL-6 [1-90 nM] + sIL-6R [0.1-19 nM] alone or in combination with TGFβ [1 nM] were tested in three different donors. TGFβ [1 nM], PDGF-AB [3 nM] and non-stimulated cells (w/o) were used as controls. Tocilizumab (TCZ) with TGFβ + IL-6 + sIL-6R stimulation was tested in one donor. Collagen type I, III and VI formation (PRO-C1, PRO-C3 and PRO-C6) and fibronectin (FBN-C) were evaluated by validated ELISAs (Nordic Bioscience). Western blot analysis investigated signal cascades. Gene expression of selected ECM proteins was analyzed. Statistical analyses included One-way and 2-way ANOVA and area under the curve analysis.

**Results:** Formation of the three layers during the culture period. The fibroinectin and collagen type VI signal were consistent between the three tested donors, whereas the formation of type III collagen was only increased in one donor, but in several trials. Type I collagen formation was unchanged by IL-6 + sIL-6R stimulation. The gene expression of type I collagen was induced by IL-6 + sIL-6R. Western blot analysis validated trans-signaling by the IL-6+sIL-6R stimulation. IL-6 modulated the fibronectin level and modulated the collagen type III formation (p=0.0002).

**Conclusion:** We investigated the fibrotic response of dermal fibroblasts to IL-6 + sIL-6R stimulation. IL-6 modulated the fibronectin level and modulated the collagen type III formation level in a somewhat dose-dependent manner. In combination with TGFβ, IL-6 decreased collagen type I and IV formation and fibronectin. However, in this study inhibition of IL-6R by TCZ did not change the fibrotic response of the dermal fibroblasts. This study indicated that IL-6 did not induce collagen formation in dermal fibroblasts, except type III collagen formation with high IL-6 concentration.

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