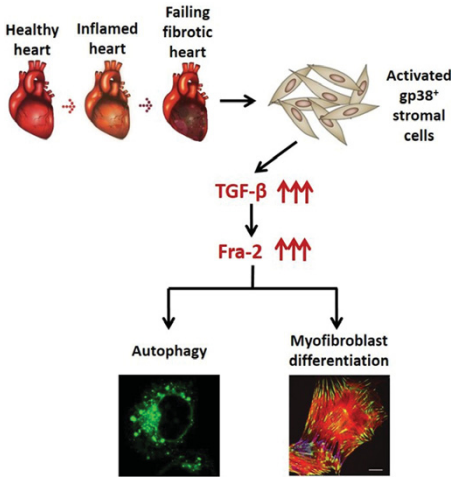
gp38+ cells: mRNA and protein levels of the profibrotic genes αSMA and collagen I were significantly downregulated (n=5; p=0.007). Moreover, Fra2 downregulation impaired the secretion of collagens (n=4; $p<0.05$) and the formation of αSMA fibers (n=3) in addition to a significant downregulation of mRNA and protein expression of LC3B, Beclin and Atg5 (n=3)



Conclusions: The TGF-β/Fra2 axis fosters an enhanced autophagy flow, leading in turn to the stromal-to-myofibroblast transition. Therefore, targeting this process might be a therapeutic strategy to abrogate fatal cardiac remodeling in SSc

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OP0085 LONGITUDINAL ANALYSIS OF THE GASTROINTESTINAL MICROBIOTA IN SYSTEMIC SCLEROSIS

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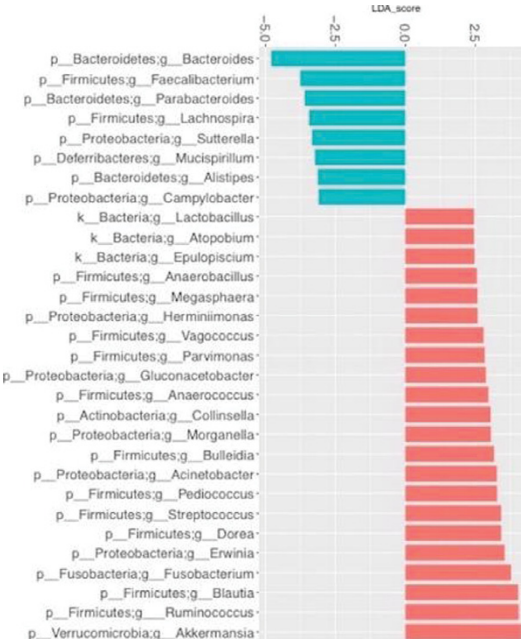
Background: Gastrointestinal tract (GIT) dysfunction affects the majority of patients with systemic sclerosis (SSc). While the etiology of SSc-related lower GIT dysfunction remains elusive, we have recently demonstrated that the SSc disease state is associated with a distinct colonic microbial consortium and that specific genera are associated with SSc-GIT symptoms in a cross-sectional analysis using colonic lavage specimens.[1]
Objectives: To evaluate changes in GIT microbial composition over time in relation to GIT symptoms in SSc patients.
Methods: Adults SSc patients not on chronic antibiotic therapy were eligible to participate. Stool specimens were collected at 0, 3, 6, 9, and 12 months. Healthy controls were matched to SSc patients in a 1:1 ratio at baseline. SSc patients completed the GIT 2.0 questionnaire to assess GIT symptom severity at each collection time. The microbiota from these samples were determined by Illumina HiSeq 2500 16S sequencing. Linear Discriminant Analysis Effect Size was used to identify the genera that showed differential expression in SSc versus controls. Mixed models evaluated changes in GIT symptoms and microbial composition over time.
Results: Among 17 patients with SSc (88% Female; Median age 52.1 years), the mean (SD) baseline total GIT 2.0 score was 0.7 (0.6). The majority of participants (71%) provided at least 4 stool samples over the course of the 12-month study. Principal coordinate analysis illustrated significant microbial community differences in SSc versus healthy controls (p=0.001). Consistent with the results of our prior study using colonic lavage specimens,[1] SSc patients had decreased commensal genera, such as *Faecalibacterium* and *Bacteroides* and increased pathobiont genera, such as *Fusobacterium* and *Erwinia* compared with healthy controls (Figure 1). GIT 2.0 scores did not change significantly over the course of the 12-month study for each subject. However, patients with longer disease durations had increased GIT symptoms over time for the total score (P=0.0038), and the following domains: fecal soilage (P=0.0217), social functioning (P=0.0116), emotional well-being (P=0.0474), and constipation (P=0.0039). There was no difference in the course of GIT symptoms over time between patients with limited versus diffuse cutaneous disease. Both the absolute and relative abundances of specific genera did not change over time within individual subjects. After controlling for age, gender, ethnicity, disease duration and SSc subtype (i.e. limited vs. diffuse), low abundance of *Bacteroides* was associated with increased GIT symptoms over time.
Figure 1. Genus level taxa associated with UCLA-SSc patients versus healthy subjects. Negative and positive effect sizes denote genera decreased (blue) or increased (red) in SSc patients, respectively.



Conclusions: This study is the first to characterize lower GIT microbiota in SSc patients at multiple time points. The findings provide further evidence that lower GIT dysbiosis is a feature of the SSc disease state and that specific genera may contribute to GIT symptoms and serve as potential targets for therapeutic intervention.

References:
[1] Volkmann et al. Arthritis Rheumatol 2016;68:1483.

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OP0086 LONG NONCODING RNA H19X AS A NEW THERAPEUTIC TARGET FOR FIBROSIS

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Background: Long noncoding RNAs (lncRNAs) are an emerging class of transcripts involved in the regulation of gene expression. We have recently identified a novel lncRNA, H19X, to be upregulated in systemic sclerosis (SSc). We also demonstrated that H19X is a key mediator of TGFβ-driven myofibroblast development and extracellular matrix synthesis.
Objectives: To assess whether (1) H19X upregulation in SSc fibroblast is anti-apoptotic and pro-proliferative thereby favoring fibrosis (2) H19X is a regulator of fibrotic diseases in general.
Methods: To study the function of H19X in apoptosis and proliferation of of dermal fibroblasts we silenced H19X using locked nucleic acid oligonucleotides (LNA GapmeRs followed by microarray analysis, qPCR, BrdU cell proliferation assay, Caspase 3/7 apoptosis assay and scratch assay. Cells were treated with 10 ng/ml TGFβ. Lung tissues were obtained from patients with SSc and idiopathic pulmonary fibrosis (IPF) undergoing transplantation, and from healthy controls (HC). Resected gut tissue from fibrotic and non-fibrotic areas was obtained from Crohn's disease patients. Non-cancer-affected gut tissue from resections because of adenocarcinoma was used as control. Expression of H19X was analyzed by quantitative (q)PCR.
Results: H19X knockdown followed by microarray analysis (n=5) showed that FAS signaling pathway, cyclins and cell cycle regulation, regulation of cell cycle progression by Plk3, and free radical induced apoptosis were among the