diagnosis of these patients are shown in Table 1. In the cluster analysis we could not identify clinical phenotypes, perhaps because of the small sample size. Only 50% of patients with myositis developed ILD. Regarding the final diagnosis, only 1 patient (5%) was diagnosed of scleromyositis. Besides detecting them in patients with SSc (39%) and idiopathic inflammatory myopathy (9%), anti-Ku Ab were detected in other SAD, the most frequent were systemic lupus erythematosus, rheumatoid arthritis (RA) and overlap syndrome of SSc + RA.

Table 1. Main clinical-analytical manifestations and final diagnosis of pacientes with anti-Ku Ab.

<table>
<thead>
<tr>
<th>CLINICAL MANIFESTATIONS</th>
<th>(patients could have more than one):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raynaud's phenomenon in 81% (14/23)</td>
<td></td>
</tr>
<tr>
<td>Inflammatory arthritis/arthritis in 52% (12)</td>
<td></td>
</tr>
<tr>
<td>Lung involvement in 30.5% (7: NSIP 2, UIP 2, other patterns 2)</td>
<td></td>
</tr>
<tr>
<td>Serositis: in 26% (6: pericarditis 4, pleuritis 1, pleuropericarditis 1)</td>
<td></td>
</tr>
<tr>
<td>Cardiac involvement: in 26% (6: PhT by echocardiogram 3, myocarditis 2, arrhythmia 1)</td>
<td></td>
</tr>
<tr>
<td>Dry syndrome: in 17% (4)</td>
<td></td>
</tr>
<tr>
<td>Myositis: in 17% (4)</td>
<td></td>
</tr>
<tr>
<td>Esophageal involvement: in 17% (4)</td>
<td></td>
</tr>
<tr>
<td>autoimmune cytopathies: leucopenia/leucopenia: in 17% (4) / thrombocytopenia: in 13% (3)</td>
<td></td>
</tr>
<tr>
<td>Telangiectasias: in 13% (3)</td>
<td></td>
</tr>
<tr>
<td>Photosensitivity: in 13% (3)</td>
<td></td>
</tr>
<tr>
<td>Other: non-androgenic alopecia: in 9% (2); sensory-motor neuropathy: in 4.5% (1); Purdy hands: in 4.5% (1); fever: in 4.5% (1); lymphadenitis: in 4.5% (1); cold sores: in 4.5% (1), and retinal hemorrhage: in 4.5% (1).</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: Anti-Ku Ab are related to a great variety of SAD, without being a specific marker of any of them, nor being associated with any specific clinical manifestation. We could not confirm the existence of clinical phenotypes associated with the presence of these antibodies.

Disclosure of Interests: L Montolio-Chiva: None declared; J. Narváez: None declared.


ACTIVITIES OF THE OXIDATIVE-RELATED ENZYMES IN SYSTEMIC SCLEROSIS

E. Mozgovaya1, I. Zborovskaya1, S. Bedina1, A. Trofimenko1, M. Manus1, E. Tikhomirova1, S. Spitina1. 1Research Institute of Clinical and Experimental Rheumatology named after A.B. Zborovsky, Volgograd, Russian Federation

Background: The oxidative-related enzymes are involved in the pathogenesis of various stages of systemic sclerosis (SSc). SSc is a chronic autoimmune disorder that is intimately associated with vascular damage and therefore with chronic perfusion/reperfusion and oxidative organ injury. Mesenchymal cell activation in SSc is now also considered to be mediated primarily through oxidative burst. Regulation of oxidative stress by specific enzymes including several purine metabolism enzymes is likely to play an important role in SSc progression.

Objectives: To characterize interrelationships among circulating xanthine oxidase (XO), xanthine dehydrogenase (XDH), superoxide dismutase (SOD) activities and SSc activity.

Methods: The study was performed according to bioethical standards. 51 patients with verified SSc and 30 healthy controls were included in the study. The diagnosis was verified according to ACR/EULAR 2013 criteria. We assessed SSc activity in compliance with the original activity scale that is commonly used in Russia [Guseva N.G., 1993] and by the 2001 European Scleroderma Study Group Activity Index. XO (EC 1.17.3.2), XDH (EC 1.17.1.4), and SOD (EC 1.15.1.1) plasma activities were measured using spectrophotometric techniques as previously described [Dubinina E.E., 1986; Karpova O.V., 2006]. Results are expressed as means±SD. The Mann-Whitney U test and Spearman’s correlation coefficient were used for statistical analysis.

In Table 1, activities of the oxidative-related enzymes are presented in SSc patients and health controls.

![Table 1](https://example.com/table1.png)

Table 1. The oxidative-related enzymes in SSc patients and health controls.

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>SSc (n=51)</th>
<th>Healthy Controls (n=30)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>XO (nmol/ml min)</td>
<td>7.10±2.19</td>
<td>3.78±0.71</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>XDH (nmol/ml min)</td>
<td>5.19±0.71</td>
<td>4.00±0.56</td>
<td>0.004</td>
</tr>
<tr>
<td>SOD (units)</td>
<td>5.40±1.03</td>
<td>4.60±0.89</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Conclusion: The oxidative-related enzymes are involved in the pathogenesis of SSc. The oxidative-related enzymes are involved in the pathogenesis of SSc. The oxidative-related enzymes are involved in the pathogenesis of SSc. The oxidative-related enzymes are involved in the pathogenesis of SSc. The oxidative-related enzymes are involved in the pathogenesis of SSc. The oxidative-related enzymes are involved in the pathogenesis of SSc. The oxidative-related enzymes are involved in the pathogenesis of SSc. The oxidative-related enzymes are involved in the pathogenesis of SSc. The oxidative-related enzymes are involved in the pathogenesis of SSc. The oxidative-related enzymes are involved in the pathogenesis of SSc.

Disclosure of Interests: None declared, J. Narváez: None declared.
Attending to CXCL8, it was associated to consumption of the C4 fraction of complement (P=0.013) and the presence of tortuositys in capillaroscopy (P=0.02) with no other significant findings.

**Conclusion:** The presence of GDF-15 is associated with diffuse SSC, lung impairment, disease activity and changes in capillaroscopy. In addition, CXCL4 was only associated with skin involvement, while CXCL8 was not related to any organic damage in our patients.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2020-eular.5218

---

**AB0166**

**IMMUNOGLOBULIN G DERIVED FROM PATIENTS WITH SYSTEMIC SCLEROSIS IMPRINTS A PRO-INFLAMMATORY AND PRO-FIBROTIC PHENOTYPE IN MONOCYTE-LIKE THP-1 CELLS**


1University of Luebeck, Department of Rheumatology and Clinical Immunology, Luebeck, Germany;
2University of Luebeck, Department of Dermatology, Allergy, and Venerology, Luebeck, Germany;
3University of Luebeck, Luebeck Institute for Experimental Dermatology, Luebeck, Germany

**Background:** Regulatory IgG autoantibodies directed against diverse G protein-coupled receptors (GPCR), i.e. antibodies with agonistic or antagonistic activity are abundant in human serum. The serum titers of autoantibodies to GPCRs, i.e. angiotensin receptor type 1 (AT1), and endothelin receptor A (ET-A) are specifically altered in autoimmune diseases such as systemic sclerosis (SSc).

**Objectives:** Disease-promoting mechanisms regulated by anti-AT1 and anti-ET-A IgG are still elusive, but induction of pro-inflammatory and pro-fibrotic chemokines (CXCL8, CCL18) has been suggested to be one of them.

**Methods:** To determine the cytokine and phospho-kinase profiles induced in monocyte-like cells by IgG derived from SSc patients (SSc-IgG) enriched with anti-AT1, and anti-ET-A antibodies in comparison to IgG derived from healthy donors (IgG-HD).

**Results:** In general, SSc-IgG induced the release of most cytokines by THP-1 cells more pronouncedly than HD-IgG. The bio-mathematical analysis suggested that stimuli, responsible for the shift of the THP-1 cell cytokine profile, are more abundant in SSc-IgG than in HD-IgG. Based upon these findings a gene set enrichment analysis for transcription factors yielded the transcription factors NF-kB, AP-1, and PRDM1 (Blimp-1) as putative major regulatory hubs for the expression of IL-8 and CCL18 when stimulated by autoantibodies from SSc patients or HD for up to 30 minutes. Thereafter, cells lysates were assayed for the kinome TGF-β1 as a potential on-off switch, whereas the inhibition was dose-dependent in TGF-β1 induced collagen type III and VI formation to the levels of w/o throughout the remainder of the study. In TGF-β1 treated fibroblasts, Nintedanib added either from day 0 or 7 reduced collagen type I and VI formation. The fibroblast levels were dose-dependently reduced by Nintedanib. The biomarker levels were at study end at the level of w/o. Nintedanib at a concentration of 1 μM and higher significantly decreased the biomarker levels. Nintedanib (≥100μM) in fibroblasts stimulated with both TGFβ and PDGF significantly reduced collagen type I, III and VI collagen and fibronectin.

**A. S. Sieb Burmester, G. M. Karsdal, P. Juhl, A. C. Bay-Jensen.**

**Disclosure of Interests:** None declared, Melanie Wannick: None declared, Gabriela Riemekasten: Consultant of: Cell Trend GmbH, Janssen, Actelion, Boehringer Ingelheim, Speakers bureau: Actelion, Novartis, Janssen, Roche, GlaxoSmithKline, Boehringer Ingelheim, Pfizer

**DOI:** 10.1136/annrheumdis-2020-eular.5218

---

**AB0167**

**TOFACITINIB AND NINTEDANIB MODULATE COLLAGEN FORMATION IN DERMAL FIBROBLASTS**


1University of Luebeck, Department of Rheumatology and Clinical Immunology, Luebeck, Germany;
2University of Luebeck, Department of Dermatology, Allergy, and Venerology, Luebeck, Germany;
3University of Luebeck, Luebeck Institute for Experimental Dermatology, Luebeck, Germany

**Background:** Primary healthy human dermal fibroblasts were grown in DMEM media containing 0.4% fetal calf serum, Ficoll (to produce a crowded environment) and ascorbic acid for up to 17 days. The cells were stimulated with PDGF [3 nM] and/or TGFβ [1 nM] in combination with Nintedanib [1 nM-10μM] treatment initiated at day 0 or 7 or Tofacitinib [3-100 nM] treatment initiated at culture start together. Media and treatments were changed twice a week. Non-activated cells (w/o) were used as control. Type I, III and VI collagen formation (PRO-C1, PRO-C3 and PRO-C6, respectively) and fibronectin (FBN-C) were evaluated by validated ELISAs (Nordic Bioscience). Statistical analysis included 1-way and 2-way ANOVA, AUC and Mann-Whitney U-test.

**Results:** PDGF significantly increased collagen type III and VI formation and collagen type I formation minimally. PDGF did not induce collagen type I and VI formation but did not induce formation of collagen type III. TGFβ increased fibronectin levels, where PDGF did not. Nintedanib (≥100 nM) added either from day 0 or 7 reduced PDGF induced collagen type III and VI formation to the levels of w/o throughout the remainder of the study. In TGFβ treated fibroblasts, Nintedanib added either from day 0 or 7 reduced collagen type I and VI formation. The collagen type I and II formation significantly lowered the collagen type I formation and fibronectin (both p<0.005) and Tofacitinib of 25 nM decreased collagen type III formation significantly (p<0.0001).

**Conclusion:** Nintedanib dose-dependently decreased the TGFβ induced type I and III collagen formation and fibronectin. Tofacitinib (100 nM) decreased the level of collagen type I and III formation to the level of w/o, where as the level of collagen I decreased by 80 % of TGFβ. Tofacitinib as low as 12.5μM significantly lowered the collagen type I formation and fibronectin (both p<0.05) and Tofacitinib of 25 nM decreased collagen type III formation significantly (p<0.0001).

**Disclosure of Interests:** None declared, Ann-Daniela Hennig: None declared, Simone Gräf: None declared, Christian Müller: None declared, Georgios Eleftheriadis: None declared, Gabriela Riemekasten: Consultant of: Cell Trend GmbH, Janssen, Actelion, Boehringer Ingelheim, Speakers bureau: Actelion, Novartis, Janssen, Roche, GlaxoSmithKline, Boehringer Ingelheim, Pfizer

**DOI:** 10.1136/annrheumdis-2020-eular.5218

---

**Background:** The presence of GDF-15 is associated with diffuse SSC, lung impairment, disease activity and changes in capillaroscopy. In addition, CXCL4 was only associated with skin involvement, while CXCL8 was not related to any organic damage in our patients.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2020-eular.5019

---

**References:**
