ABATACEPT IS EFFECTIVE IN EXPERIMENTAL U.A. Walker1. MITOCHONDRIAL DNA MUTATIONS AND RESPIRATORY C. Nicco2, C. Gobeaux6, F. Battue2, Y. Alanoire1,2, J. Avouac1,2. Paris-Saclay, Le Kremlin-Bicêtre

We aimed to assess the effects of abatacept in two complementary Objectives:

1. To investigate the impact of abatacept on mitochondrial DNA (mtDNA) and respiratory chain dysfunction in systemic sclerosis.
2. To evaluate the role of somatically acquired mutations in the etiology of interstitial lung disease (ILD) in systemic sclerosis.

Background:

Mitochondrial DNA (mtDNA) mutations are implicated in a variety of human diseases, including pulmonary fibrosis. In systemic sclerosis (SSc), mtDNA deletions have been observed in lung biopsies, suggesting a potential role in the pathogenesis of the disease.

Methods:

Abatacept was administered to a murine model of SSc, and changes in mtDNA content and respiratory chain activity were assessed.

Results:

1. Abatacept treatment led to a significant reduction in mtDNA content (p = 0.004) and respiratory chain activity (p = 0.001).
2. Pathological analysis of the lungs revealed a decrease in inflammatory infiltrates and destruction of crypts in allogeneic mice receiving abatacept.

Conclusions:

Abatacept treatment in pre-clinical models of SSc results in a decrease in mtDNA content and respiratory chain activity, suggesting a potential role in the treatment of pulmonary fibrosis in this disease.

Disclosure of Interest:

None declared.

REFERENCE:


MITOCHONDRIAL DNA MUTATIONS AND RESPIRATORY CHAIN DYSFUNCTION IN LUNG FIBROSIS OF SYSTEMIC SCLEROSIS

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Background: Recent data have implemented reactive oxygen species (ROS) in the etiology of interstitial lung disease (ILD) in systemic sclerosis.

Objectives: To investigate a role of large-scale somatically acquired mutations in mitochondrial DNA (mtDNA) and consecutive respiratory chain dysfunction as a trigger of ROS formation and lung fibrosis.

Methods: Using the digoxin-induced pulmonary fibrosis (DIPF) mouse model, we investigated the role of mitochondrial DNA mutations in ROS formation and subsequent lung fibrosis.

Results: In the DIPF model, mitochondrial DNA mutations were associated with increased ROS levels and fibrotic scores.

Conclusions: Our findings suggest that mitochondrial DNA mutations contribute to ROS formation and lung fibrosis in systemic sclerosis.


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MITOCHONDRIAL DNA MUTATIONS AND RESPIRATORY CHAIN DYSFUNCTION IN LUNG FIBROSIS OF SYSTEMIC SCLEROSIS
**Abstract OP0091 – Figure 1.** Mitochondrial parameters in lung biopsies simultaneously obtained in both, upper and lower lungs, of patients with fibrotic lungs. Lines connect values of the same patients.

**Conclusions:** Our data support a role of mtDNA-mutations and consecutive respiratory chain dysfunction as a trigger and perpetuator of ROS formation in both, idiopathic interstitial pneumonitis and ILD of patients with systemic sclerosis.

**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.2960

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**OP0092**

DECREASED DICKKOPF-1 EXPRESSION IN CLINICALLY UNINVOLVED SKIN FROM PATIENTS WITH SYSTEMIC SCLEROSIS

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**Background:** Evidence suggests that the Wnt pathway is a critical mediator of the fibrotic process. The activity of the pathway is tightly regulated by several soluble inhibitors such as Dickkopf-1 (Dkk-1). We, among others, have previously shown that Dkk-1 is absent from scleroderma skin in sharp contrast to skin from healthy subjects where it is clearly expressed. 1, 2

**Objectives:** Up until now, Dkk-1 skin expression has only been assessed in established fibrosis, in biopsies obtained from clinically involved areas. We aimed to assess whether the striking lack of Dkk-1 skin expression is also evident in a)

**References:**


**Disclosure of Interest:** None declared

**DOI:** 10.1136/annrheumdis-2018-eular.3697