**SAT0313** ROLE OF CD248 MOLECULE AS POTENTIAL REGULATOR OF TRANS-DIFFERENTIATION TOWARD MYOFIBROBLASTS OF PERIVASCULAR STROMAL CELLS IN SYSTEMIC SCLEROSIS PATIENTS

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**Background:** The microvascular damage is a pivotal event in the pathogenesis of Systemic Sclerosis (SSc) and, after injury, both endothelial cells (ECs) and pericytes might trans-differentiate toward myofibroblast, responsible of fibrosis. Platelet-derived growth factor B (PDGF-B) and transforming growth factor (TGF)-β play a key role in this process: PDGF-B, a potent mitogen for myofibroblasts, while TGF-β stimulates myofibroblast activation, including alpha smooth muscle actin (αSMA) expression. A key regulator of PDGF-B and TGF-β signaling may be the CD248, a trans-membrane receptor required for proliferation and migration of pericytes and fibroblasts. It has been shown that, in an animal model of kidney fibrosis, the genetic deletion of CD248 modulates the response of renal pericytes to injury, by reducing the differentiation of myofibroblasts. The expression of CD248 is required for TGF-β-induced αSMA expression in pericytes and CD248 enhances the PDGF pathway, mediating the proliferation and migration of pericyte and fibroblast cells.

**Objectives:** The aim of this work was to evaluate the expression of CD248, in SSc skin biopsies and its possible role in perivascular stromal cells proliferation, responsible to myofibroblast trans-differentiation, during SSc.

**Methods:** After ethical approval, skin biopsies and bone marrow mesenchymal stem cells (MSCs) were collected from 20 diffuse SSc patients and 10 healthy control (HC). CD248 expression was investigated in the skin, and in isolated MSCs treated with TGF-β or PDGF-B, by immunofluorescence, qRT-PCR and western. Furthermore, we silenced CD248 in SSc-MSCs, to confirm the role of this molecule in TGF-β- or PDGF-signaling modulation.

**Results:** CD248 expression in SSc skin was significantly higher when compared with HC skin. In particular, an increased expression of CD248 was found in ECs, stromal fibroblast and perivascular like stromal cells, co-expressing CD90, a marker of un-differentiated MSCs. Furthermore, in both, HC- and SSc-MSCs, TGF-β treatment induced a significant reduction of CD248 mRNA expression, in parallel with a significant increase of αSMA and a decrease of proliferation (ki67), when compared with untreated-(UT-) cells. Interestingly, the ability of TGF-β to inhibit CD248 expression in HC-MSCs was significantly higher than SSc-MSCs, suggesting that local environment in SSc patients affect TGF-β ability to suppress CD248 expression in SSc-MSCs. After treatment with PDGF-B in both SSc- and HC-MSCs, CD248 expression was not affected, while significant reduction of αSMA and an increased expression of ki67 was observed compared with UT-cells. After silencing of CD248 in SSc-MSCs, both TGF-β and PDGF-B signaling were inhibited.

**Conclusions:** CD248 over-expression may play an important role in tissue fibrosis by modulating the pericytes to myofibroblast trans-differentiation, via regulation of both PDGF-B and TGF-β signaling, during SSc.


**Disclosure of Interest:** None declared

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**SAT0315** IMATINIB-LOADED TARGETED GOLD NANOPARTICLES AMELIORATE EXPERIMENTAL LUNG FIBROSIS INDUCED BY BLEOMYCIN

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**Background:** Systemic Sclerosis (SSc) is an autoimmune disorder frequently affected by an interstitial lung involvement (ILD) that significantly deteriorates long-term outcomes. In previous experiments we proved that specifically engineered gold-nanoparticles (GNP) loaded with imatinib and targeted with an anti CD44 Ab (GNP-HCim) significantly inhibited proliferation and induced apoptosis of fibroblast-like cells derived from ILD-SSc patients [1]. In vitro, GNP-HCim showed higher efficacy compared to the drug alone.

**Objectives:** To demonstrate in vivo the efficacy of GNP-HCim in ameliorating bleomycin-induced lung fibrosis.

**Methods:** Eight-week-old C57BL6 male mice (n=8/group) were assigned to either: (1) controls receiving intratracheal aerosolization of saline solution and unloaded functionalised GNP (GNP-HC); (2) mice treated with intratracheal instillation of bleomycin (50 UL) on day 0 and GNP-HC; (3) mice treated with bleomycin on day 0 plus GNP-HCim; (4) mice treated with bleomycin plus imatinib (50 mg/kg, once daily). GNP-HC or GNP-HCim were administered by intratracheal instillation on day 10–15–20–25 and 3 h before culling. All mice were sacrificed on day 28. Lung specimens were analysed by electron microscopy, immunohistochemistry and immunofluorescence (IF). Data were evaluated by 2 blind observers and analysed with GraphPrism software for statistics.

**Results:** The administration of imatinib i.p. or via GNP-HC reduced pathologic changes of the lungs as evaluated by the Lung Injury score and the Ashcroft score (p<0.05 for both). Collagen quantification by Picro Sirius Red revealed a significantly reduced staining only in the GNP-HCim group (p=0.0135 vs controls). IF revealed a significant reduction in the number of CD45+ inflammatory cells and CD11b+ macrophages.

**Conclusions:** In the experimental model of bleomycin-induced lung fibrosis imatinib delivered to lungs through inhalation of anti CD44 targeted GNP was as effective as imatinib administered by i.p. route. These data favour the use of GNP-HCim as an alternative therapeutic approach to SSc-ILD, which might be associated to a lower toxicity and side effects of systemic treatment.