

Soluble CD90 as biomarker of pulmonary complications in Systemic Sclerosis

A new serological two-staged biomarker of pulmonaryarterial hypertension and pulmonary fibrosis

Technology

Systemic sclerosis (SSc) is a multi-systemic fibrotic disease which major complications are pulmonary arterial hypertension (PAH) and pulmonary fibrosis (PF). Until now there is no serological biomarker for an early detection of these both complications which are mainly causative for the high mortality of this and also other disease. Since activation of endothelial cells (PAH) and fibroblasts (PF, PAH) are pathological hallmarks of the devastating pulmonary complications, soluble CD90 (sCD90), a marker of activated endothelial cells and activated fibroblasts, serves as a marker for the most important complications of SSc – PAH and PF.

Innovation

- Easily applicable serological measurement method for the early detection of PF and PAH in SSc
- Two serum concentration cut offs of sCD90 (lower cut off for PF, higher cut off for PAH) are predictive of the major complications in SSc
- Avoiding close-meshed invasive measurements and X-radiation, caused by right-heart catheterization and computertomography of the chest
- Easily applicable follow-up tool for outpatient clinics and private practice, close-meshed right-heart-echocardiography and bodyplethysmography with measurement of diffusing capacity gets obsolete
- In contrast to markers of right heart pressure (NT-pro BNP) not influenced by left heart disease

Application

- Serological test kit for the serum concentration of soluble CD90
- Early detection of the two most important pulmonary complications in SSc

Developmental Status

ELISA system for the detection of sCD90 is already evaluated (proof of concept is present).

Responsible Scientist

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A new serological two-staged biomarker of pulmonary-arterial hypertension and pulmonary fibrosis

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Background: The mortality of Systemic Sclerosis (SSc) is high and mostly due to pulmonary fibrosis (PF) and pulmonary arterial hypertension (PAH) (1). Endothelial cell (EC) activation (PAH) and activation of fibroblasts (PAH and PF) are pathogenic hallmarks of the devastating complications in SSc (2). CD90 is expressed on activated ECs and fibroblasts (3) and can be shed from the cell surface, which is associated with lung fibrogenesis (4).

Hypothesis: We hypothesized that CD90 is overexpressed on ECs and fibroblasts of patients with SSc and PAH/PF and partially shed from the cell surface further causing elevated serum concentrations of soluble (s) CD90 in the sera of patients with PAH or PF (see **Figure 1**).

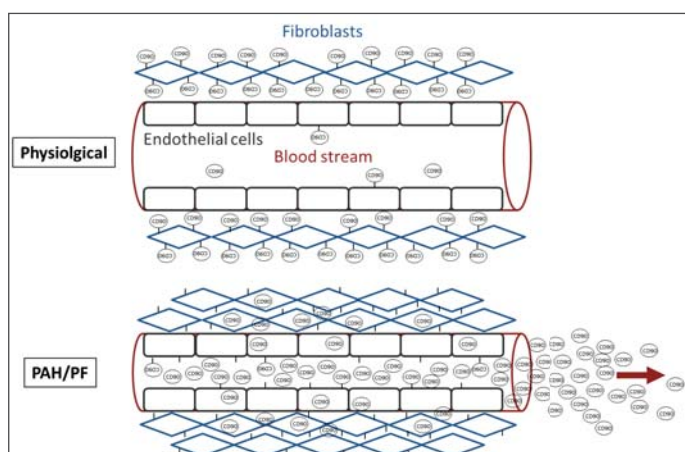


Figure 1. Vasculature under physiological condition and PAH/PF

Methods: sCD90 serum concentrations were measured in 76 patients with SSc, 29 patients with idiopathic retroperitoneal fibrosis (IRF, validation cohort), and 31 healthy volunteers by ELISA. For feasibility PAH was defined as a sPAP \geq 40mmHg in echocardiography, in this first preliminary study.

Results: sCD90 serum levels were highly elevated in patients with SSc compared to IRF (p=0.01) and healthy volunteers (p=0.0001). SSc patients with PF (p=0.006) or PAH (p<0.0001) had considerable higher concentrations than SSc patients without pulmonary complications (see **Figure 2 and 3**). sCD90 levels showed correlations with diffusing capacity (r=-0.348, p=0.005) and echocardiographic sPAP (r=0.469, p<0.001). The optimal cut off for PF was \geq 439 ng/ml (auc 0.686, 95%CI 0.565-0.806, p=0.006) and for PAH \geq 626 ng/ml (auc 0.773, 95%CI 0.648-0.898, p<0.001).

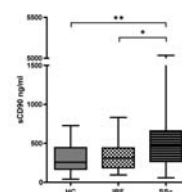


Figure 2. sCD90 serum concentrations were highly elevated in SSc. (SSc=Systemic Sclerosis, IRF=idiopathic retroperitoneal fibrosis, HC=healthy controls).

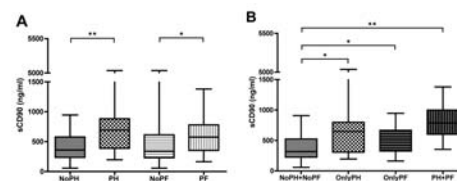


Figure 3. sCD90 serum concentrations in patients with SSc and pulmonary complications (PAH=pulmonary arterial hypertension, PF=pulmonary fibrosis)

Conclusions: sCD90 serum levels are increased in patients with SSc and indicate the occurrence of the two most important complications of this disease – PAH and PF.

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