Arsenic trioxide inhibits the functions of lung fibroblasts derived from patients with idiopathic pulmonary fibrosis

Introduction
Arsenic trioxide (ATO) is a safe and effective drug used in cancer therapy. This metalloid is described to modulate myofibroblastic properties of non-IPF fibroblasts (skin, lung, skeletal...) and also to decrease pulmonary fibrosis induced by bleomycin in mice.

Hypothesis: ATO may modulate IPF fibroblastic function related to pulmonary fibrosis.

Aims: Study the effects of ATO on proliferation, migration and differentiation of IPF and control Human Lung Fibroblasts.

Methods
1) ATO did not affect the cell viability
2) ATO prevented the cell migration induced by PDGF-BB
3) ATO inhibited the proliferation induced by PDGF-BB
4) ATO perturbed cell cycle
5) ATO reduced the differentiation induced by TGF-β1
6) ATO induced NRF2 and antioxidant proteins expression
7) Nrf2 did not mediated ATO-dependent inhibition of HLF differentiation induced by TGF-β1

Results
• ATO prevented PDGF-BB induced migration and inhibited proliferation of IPF and control HLFs.
• ATO also prevented the up-regulation of α-SMA, Collagen-1 protein levels and the phosphorylation of SMAD2/3 in TGF-β1-stimulated IPF and control HLFs.
• ATO effects were associated with stabilization of the transcription factor Nrf2 and induction of the antioxidant proteins NQO1 and HO-1.

Our results demonstrate that, in vitro, arsenic trioxide concentrations, in the range of plasmatic levels measured in patients treated with standard dosing, counteracts the detrimental functions of IPF HLFs and may thus be taken into consideration as a new therapeutic option for IPF treatment.

Conclusions
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