Purpose
The inhalation delivery of prostaglandin E (PGE2) in combination with siRNA(s) was proposed and tested for the efficient treatment of idiopathic pulmonary fibrosis (IPF).

Methods
Nanostructured lipid carriers (NLC) were used as a delivery system for PGE2 with and without MMP3a, CCL12, and HIF1-alfa siRNAs. In vivo experiments were carried out on SKH1 mice. Bleomycin was administered intratracheally to the mice in 1.5 U/kg dose to develop IPF mouse model. Mice were treated for 3 weeks (twice a week starting one day after bleomycin administration) with NLC-PGE2, NLC-siRNAs, or NLC-PGE2-siRNAs by inhalation. Development of IPF and treatment progress was monitored using MRI and CT scan. Lungs were excised and used for the hydroxyproline concentration measurements. RNA was isolated. A standard Mouse Fibrosis RT Profiler™ PCR Array panel (84 key proteins) from SABiosciences (Quiagen, Valencia, CA) was used. Mortality and body weight of animals were monitored.

Results
The data showed that NLC-PGE2 in combination with three siRNAs delivered locally to the lungs effectively prevented the decrease in the mouse body mass, substantially limited hydroxyproline content in the lungs, disturbances in the mRNA and protein expression, restricted lung tissue damage, and completely prevented animal mortality. These effects can be a result of the ability of PGE2 to limit fibroblast proliferation and the ability of siRNAs to suppress synthesis on the profibrotic proteins.

Conclusion
Our data provide an evidence that pulmonary fibrosis can be effectively treated by inhalation of the NLC form of PGE2 in combination with siRNAs delivered locally into the lungs. This affect could not be achieved when using NLC containing just PGE2 or siRNA(s) alone.