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Title: Secreted mediators from induced pluripotent stem cells (iPSc) attenuate fibrosis in bleomycin injured rat lung

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Body: Background Idiopathic pulmonary fibrosis (IPF) is a progressive interstitial lung disease resulting from deregulated alveolar epithelial repair, after micro injuries. There are no promising treatments available hence; novel methods to regenerate the injured lungs are urgently required. We studied the role of secreted mediators from induced pluripotent stem cells (iPSc) in bleomycin injured rat lungs. Methods iPSc cells were generated from human foreskin fibroblasts by transfection of the transcription factors SOX2,OCT4, KLF4, and c-MYC; after characterization by immunohistochemistry and RT PCR, the colonies were expanded and the conditioned media (CM) was collected (iPScCM). iPScCM was subjected to proteomics to analyze the contents. Adult male rats (F344) were instilled intratracheally (i/t) with bleomycin at day 0; 7 days later were treated with iPScCM or control media (CM) (i/t) and sacrificed 7 days after iPScCM or CM treatment. Results Proteomic analysis revealed presence of various interesting cytokines and growth factors in the iPScCM, which are involved in regeneration process; the total collagen content after iPScCM treatment was reduced compared to CM group (753±56.12 ug/mg vs 4182±521.8 ug/mg of wet tissue) as measured by hydroxyproline assay. Furthermore, TGFβ1 mRNA levels were also reduced after iPScCM treatment (0.9±0.266 vs 2.4±0.9) (2-ΔΔCP). Conclusion Secreted mediators present in the iPScCM attenuate fibrosis in the bleomycin injured rat lungs and may offer a novel therapeutic option for pulmonary fibrosis.