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**Title:** Cell therapy with adipose tissue-derived stem/stromal cells for elastase-induced pulmonary emphysema in rats

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Body: Background: Studies demonstrating lung repair by stem cells or growth factors have been reported in animal emphysema. We focused on adipose tissue-derived stromal/stem cells (ASC) for regenerative medicine, since it has a high potential to secrete multiple angiogenic factors and differentiate various kinds of cells. Aim: To demonstrate the therapeutic impact of ASC transplantation and to elucidate mechanisms of the effects in rat emphysema models. Methods: ASC were isolated from rat subcutaneous adipose tissue. Emphysema was induced by intratracheal instillation of porcine pancreatic elastase (PPE). One week after PPE, cell transplantation was performed intravenously. One and 2 weeks after transplantation, we assessed pulmonary function and histopathological changes and measurement of chemokine levels in lung tissue. Results: ASC transplantation restored pulmonary function to near normal levels and enlargement of the alveolar airspaces was also inhibited. Immunohistochemical analysis revealed some transplanted ASC were localized at damaged alveolar spaces. Vascular endothelial growth factor (VEGF) was significantly reduced by PPE. After ASC transplantation, VEGF level was not reduced. Hepatocyte growth factor (HGF) and cytokine-induced neutrophil chemoattractant-1 (CINC-1) levels were significantly higher than PPE. Conclusion: Transplantation of ASC for emphysema rats improved pulmonary function and inhibit enlargement of the airspaces. Secretion of HGF, VEGF, and CINC-1 by surviving ASC after transplantation may have contributed to lung repair. Cell theropy with ASC may be new therapeutic strategy to improve pulmonary function and inhibit alveolar destruction.