Introduction:
Although mesenchymal stem cells (MSCs) transplantation has been shown to promote lung respiration in acute lung injury (ALI) in vivo, its overall restorative capacity appears to be restricted mainly because of low engraftment in the injured lung. Ang II are upregulated in the injured lung. Our previous study showed that Ang II increased MSCs migration in an Angiotensin II type 2 receptor (AT2R)-dependent manner [1]. The objective of our study was to determine whether overexpression of AT2R in MSCs augments their cell migration and engraftment after systemic injection in ALI mice.

Methods:
A human AT2R expressing lentiviral vector was constructed and introduced into human bone marrow MSCs. We also down-regulated AT2R mRNA expression using a lentivirus vector carrying AT2R shRNA to transduce MSCs. The effect of AT2R regulation on migration of MSCs was examined in vitro. A mouse model of lipopolysaccharide (LPS) induce ALI was used to investigate the engraftment of AT2R-regulated MSCs and the therapeutic potential in vivo.

Results:
Overexpression of AT2R dramatically increased Ang II-enhanced human bone marrow MSC migration in vitro. Moreover, MSC-AT2R accumulated in the damaged lung tissue at significantly higher levels than control MSCs 24h and 72h after systematic MSC transplantation in ALI mice. Furthermore, MSC-AT2R-injected ALI mice exhibited a significant reduction of pulmonary vascular permeability and improved the lung histopathology and had additional anti-inflammatory effects. In contrast, there were less lung engraftment in MSC-ShAT2R-injected ALI mice compared with MSC-Shcontrol after transplantation. Thus, MSC-ShAT2R-injected group exhibited a significant increase of pulmonary vascular permeability and resulted in a deteriorative lung inflammation.

Conclusion:
Our results demonstrate that overexpression of AT2R enhance the migration and lung engraftment of MSCs in ALI mice and may provide a new therapeutic strategy for the injured lung.

References: